HM Government

Tackling antimicrobial resistance 2019–2024

The UK's five-year national action plan

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Foreword

Antimicrobials, particularly antibiotics, have saved millions of lives since they were first discovered. Our generation, and that of our parents, has benefited enormously from these important medicines.

But no new classes of antibiotic have been discovered since the 1980s. This, together with the increased and inappropriate use of the drugs we already have, means we are heading rapidly towards a world in which our antibiotics no longer work. We need to act, and act now, to make sure that our children and future generations continue to benefit from these life-saving medicines.

We are proud of the work that the UK has done to secure antimicrobial resistance (AMR) on the global agenda, not just as a health issue, but as a 'One-Health' issue with enormous social and economic impact. We have worked hard with the World Health Organization, the World Organisation for Animal Health and the Food and Agriculture Organization to secure commitment to a global action plan in 2014 and the historic political declaration on AMR at the United Nations in 2016. We have invested to turn declarations into concrete action and to support countries to develop their capacity to tackle AMR, to improve global surveillance and to do the research and development work that we need through international collaborations.

In the UK, we have human and animal surveillance systems and levels of research coordination and collaboration that are respected by many of our global partners and we want to share our good work and innovative approaches while continuing to learn from the best.

Our vision for AMR in 2040 recognises that a global problem as significant and complex as antimicrobial resistance will not be addressed in a single five-year plan. The national action plan, published alongside the vision, aims to build on our achievements so far. It is essential that we continue to make progress and through this plan, we are pushing ourselves harder with a new set of challenging ambitions for the next five years.

Preventing infections is essential and our new plan has a strong focus on infection prevention and control. We are the first country to set an ambition to reduce the actual number of resistant infections. We aim to develop real time patient level data so that clinicians can see infection, treatment and resistance histories to optimise life-saving treatments for serious infections, including sepsis, and to help develop new interventions for AMR. We will build on our already considerable achievements in reducing antibiotic use in animals by working to improve animal health and address endemic disease issues, and we will improve our understanding of the routes of transmission of resistance including the impact of the environment and food.

We are leading the way in testing solutions that will address our global failure to incentivise the development of new antimicrobials and alternative treatments. We will test a new model that will de-link the payments made to companies from the volumes of antibiotics sold, basing the payment on a NICE led assessment of the value of the medicines and supporting good stewardship.

The plan is structured using the United Nation's Ad-hoc Interagency Framework for Action on AMR and sets out the need for action in 15 areas, together with what we are doing domestically and how we are supporting global action in each area. We will work with other countries to help build this as a blue print for their own plans.

Our 20-year vision and five-year plan have been developed collaboratively across diverse government agencies, working with governments in Scotland and Wales, the administration in Northern Ireland, our national health services and animal health and welfare agencies. Together, we have set out a fully integrated and aligned UK One-Health approach.

Through this plan we are setting out our challenge to ourselves and to other countries to continue our excellent work together to preserve and develop these essential medicines for generations to come and help us address one of the most pressing global health challenges we face this century.

Michael Gove

Secretary of State for
Environment, Food and Rural Affairs

Matt Hancock

Secretary of State for
Health and Social Care

Abbreviations

AHSN	Academic Health Science Network
AMR	Antimicrobial resistance
ATLASS	Assessment Tool for Laboratory and Antimicrobial Resistance
AWaRe	Access, Watch and Reserve
BSAVA	British Small Animal Veterinary Association
BVA	British Veterinary Association
BVD	Bovine Viral Diarrhoea
CCG	Clinical Commissioning Group
CPO	Carbapenemase producing organism
DEFRA	Department for Environment, Food and rural Affairs
DHSC	Department of Health and Social Care
EC	European Community
EU	European Union
EP	Enzoonotic Pneumonia
FAO	Food and Agriculture Organisation
FIND	Foundation for Innovative New Diagnostics
FSA	Food Standards Agency
FSS	Food Standards Scotland
GAMRIF	Global Antimicrobial Resistance Innovation Fund
Gavi	The Global Vaccine Alliance
GAP	Global Action Plan
GARDP	Global Antibiotic Research and Development Partnership
GLASS	Global Antimicrobial Resistance Surveillance System
G7	The Group of 7 (Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States.)
G20	The Group of 20
HAI	Healthcare Associated Infection
IACG	Interagency Coordination Group
IHR	International Health Regulation
IID	Intestinal Infectious Disease
IPC	Infection prevention and control
JPIAMR	Joint Programming Initiative on Antimicrobial Resistance
LMICs	Low- and middle-income countries
Mg/kg	milligram per kilogram
MHRA	Medicines and Healthcare Products Regulatory Agency
NAP	National Action Plan
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
OIE	World Organisation for Animal Health

PDP	Product Development Partnership
PDSA	People's Dispensary for Sick Animals
PHE	Public Health England
POM	Prescription Only Medicine
PSC	Patient Safety Collaborative
PRRS	Porcine Reproductive and Respiratory Syndrome
R&D	Research and Development
RCGP	Royal College of General Practitioners
SDGs	Sustainable Development Goals
SMEs	Small and Medium Enterprises
SNAP	AMR Supporting the National Action Plan for AMR in Tanzania
STEM	Science Technology Engineering and Mathematics
TARGET	Treat Antibiotics Responsible, Guidance, Education and Tools
TB	Tuberculosis
UK	United Kingdom
UKRI	United Kingdom Research and Innovation
UN	United Nations
UNICEF	United Nations Children's Fund
UTI	Urinary Tract Infection
VMD	Veterinary Medicines Directorate
WASH	Water Sanitation and Hygiene
WHO	World Health Organisation

Executive summary

Antimicrobial resistance (AMR) is a global problem that impacts all countries and all people, regardless of their wealth or status. The scale of the AMR threat, and the need to contain and control it, is widely acknowledged by country governments, international agencies, researchers and private companies alike.

This document sets out the UK's 2019–2024 national action plan to tackle AMR within and beyond our own borders. Developed in consultation with a broad range of stakeholders across different sectors, it builds on the achievements of our last strategy (2013–2018), and is aligned with global plans and frameworks for action.

The plan has ultimately been designed to ensure progress towards our 20-year vision on AMR, in which resistance is effectively contained and controlled. It focuses on three key ways of tackling AMR:

- reducing need for, and unintentional exposure to, antimicrobials;
- optimising use of antimicrobials; and
- investing in innovation, supply and access.

These are underpinned by actions across 15 'content areas', ranging from reducing infection and strengthening stewardship to improving surveillance and boosting research. The plan also sets out four measures of success to ensure progress towards our 20-year vision. These include, among others, targets to:

- halve healthcare associated Gram-negative blood stream infections;
- reduce the number of specific drug-resistant infections in people by 10% by 2025;
- reduce UK antimicrobial use in humans by 15% by 2024;
- reduce UK antibiotic use in food-producing animals by 25% between 2016 and 2020 and define new objectives by 2021 for 2025; and
- be able to report on the percentage of prescriptions supported by a diagnostic test or decision support tool by 2024.

Fulfilling our commitments over the next five years requires action across many spheres; we will implement our plan using a risk-based approach, targeting interventions where the evidence for impact is strongest.

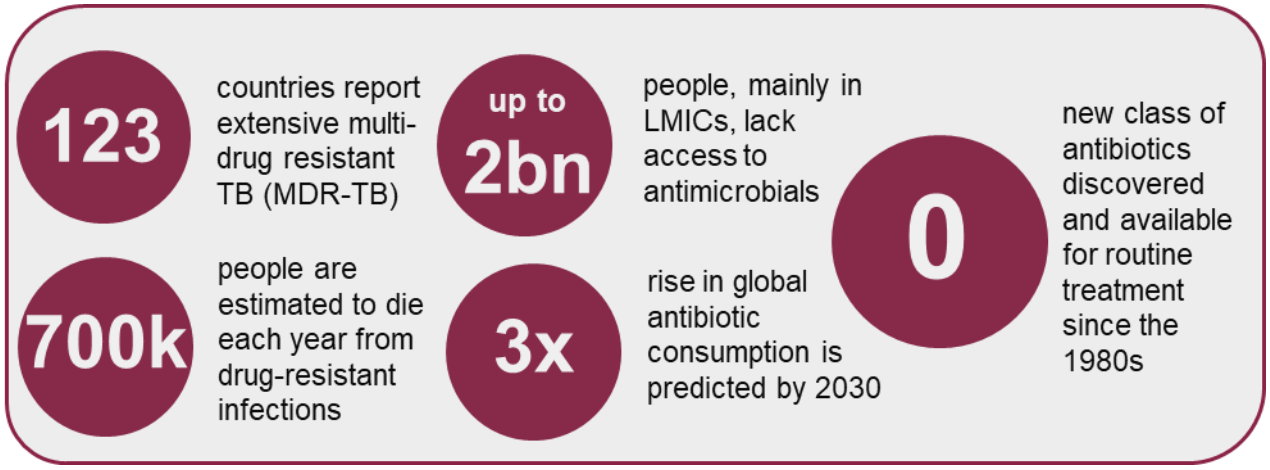
We rely on the active participation of public and private sector bodies, including investors, across the human health, animal health, the food chain and environment communities. There is too a central role for members of the public, as patients, consumers, animal owners and investors.

1. Introduction

The rise and spread of antimicrobial resistance (AMR) is creating a new generation of ‘superbugs’ that cannot be treated with existing medicines. The impacts of leaving AMR unchecked are wide-ranging and extremely costly, not only in financial terms but also in terms of global health, food sustainability and security, environmental wellbeing, and socio-economic development.

Already, AMR infections are estimated to cause 700,000 deaths each year globally. That figure is predicted to rise to 10 million, alongside a cumulative cost of $100 trillion, by 2050 if no action is taken. AMR also threatens many of the Sustainable Development Goals (SDGs). The World Bank estimates that an extra 28 million people will be could be forced into extreme poverty by 2050 unless AMR is contained.

Figure 1. The rise and spread of AMR [1]



In the United Kingdom (UK), rising AMR will cause people to suffer longer infectious illnesses as they become more difficult to treat, the number of human deaths and suffering attributable to infectious disease will increase as will the socio-economic costs associated with treating ill health in humans.

AMR is a global problem that impacts all countries and all people, regardless of their wealth or status. Resistant organisms respect no borders, neither geographical nor ecological: the organisms and their resistance genes can easily spread through movements of people, animals, food or water; and certain resistance genes can transfer from one species into another (these genes are called plasmids or transposons). This means that containing and controlling AMR requires coordinated national and international action across all stakeholders, including governments, international organisations, private businesses, investors, civil society, academia and philanthropy.

In 2015, Member States of the World Health Organization (WHO), Food and Agriculture Organization (FAO) and World Organisation for Animal Health (OIE) endorsed a Global Action Plan on Antimicrobial Resistance (GAP), which includes five strategic objectives that, taken together, offer a framework for national action plans (NAPs) to combat AMR over the following decade.

A year later, in 2016, the GAP was reaffirmed as the world's blueprint for tackling AMR during the 71st session of the UN General Assembly, where 193 Heads of State adopted resolution A/RES/71/3, which included a high-level political declaration committing countries to support and implement the GAP at national, regional and global levels.

Since then, the global Ad-hoc Interagency Coordination Group on AMR (IACG) established by the UN Secretary General because of the declaration has developed a 'Framework for Action' that puts AMR in the wider context of the Sustainable Development Goals (SDGs), helping to align political agendas and provide a common language and a dynamic structure for all sectors to work from, while respecting countries' endorsement of the GAP.

THE UK'S 2013–2018 AMR STRATEGY: A RE-CAP

The UK's 2013-2018 AMR strategy included three strategic aims, underpinned by actions in seven key areas.

Aims:

- Improve knowledge and understanding of AMR.
- Conserve and steward effectiveness of treatments.
- Stimulate development of new products.

Action areas:

1. Improve infection prevention and control practices.
2. Optimise prescribing practice.
3. Improve professional education and public engagement.
4. Develop new drugs, treatments and diagnostics.
5. Better access and use surveillance data.
6. Better identify and prioritise AMR research needs.
7. Strengthen international collaboration.

The UK was one of the first countries to establish a National Action Plan (NAP) on AMR (even before the GAP), with a strategy and action plan in place as early as 2000. In 2013, we reinforced our NAP approach with a One-Health perspective and published our first fully integrated five-year strategy for tackling AMR across human and animal health. The 2013–2018 AMR strategy committed the UK to action in seven key areas, including infection prevention and control, prescribing practice, professional education and public

engagement, development of new and innovative treatment and technologies, surveillance, research and international collaboration.

This document sets out our next five-year NAP (2019–2024) for tackling AMR. It has been developed in consultation with a broad range of stakeholders across different sectors, including the administrations in Scotland, Wales and Northern Ireland as well as experts, professional bodies, industry and academia. To support a coordinated approach, we use the IACG Framework for Action to set out our commitments across humans, animals, food and the environment.

Building on the achievements of our 2013–2018 AMR strategy, this UK NAP sets out challenging ambitions and actions for the next five years that will set us on course for achieving our long-term national and international ambitions, as outlined in our 20-year vision on AMR.

OUR 20-YEAR VISION FOR AMR

By 2040, our vision is of a world in which antimicrobial resistance is effectively contained and controlled through strong mitigation.

The United Kingdom is determined to sustain its efforts to combat resistance, taking local, national and global 'One-Health' approaches across humans, animals the environment and food, in line with global ambitions and in collaboration with other nations, partners and the international community.

In our vision, stakeholders at local, national and global levels are collectively strengthening policy and practice, ever improving understanding through research, and surveillance, developing effective regulation and advocacy to contain and control resistance. In the UK, we will contribute to the global effort through:

1. **A lower burden of infection,** treatment of resistant infection and minimised transmission in communities, the National Health Service (NHS), farms, the environment and all other settings.

2. **Optimal use of antimicrobials** and good stewardship across all sectors, including access to safe and effective medicines that have been manufactured responsibly for all who need them, achieving usage levels, by sector, as good as the best countries in the world where comparable data is available.

3. **New diagnostics, therapies, vaccines and interventions** in use, and a full antimicrobial resistance research and development pipeline for antimicrobials, alternatives, diagnostics, vaccines and infection prevention across all sectors.

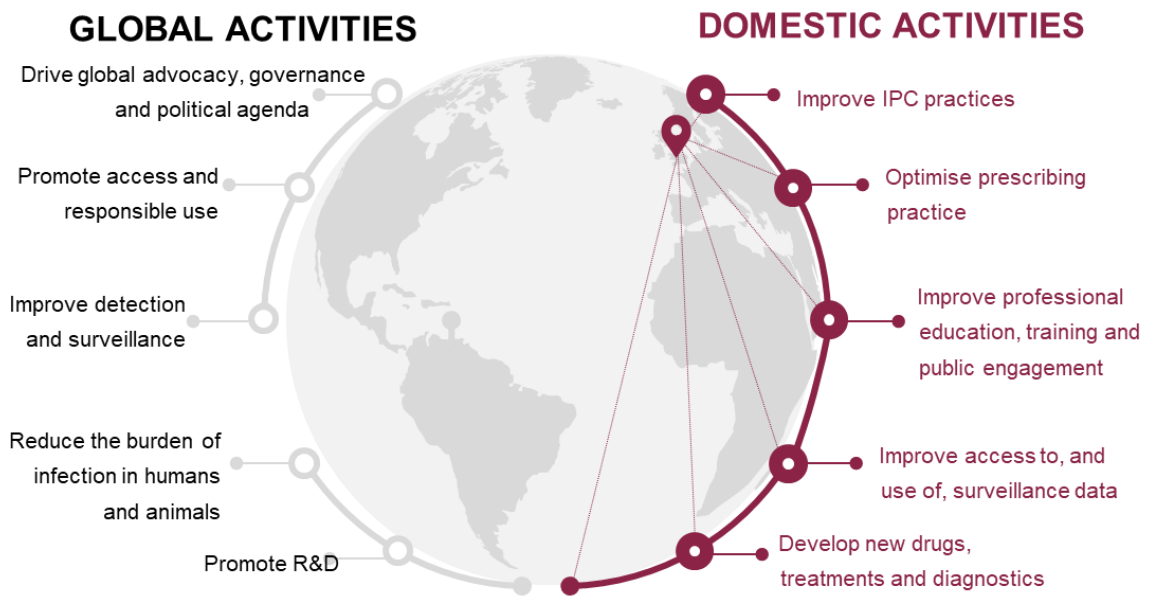
1.1. Existing efforts

The UK recognises the need to pursue actions at home and abroad to tackle the global threat that is AMR, as highlighted in both our 2013–2018 AMR strategy and the overarching UK Biological Security Strategy. On both fronts, we undertake a range of activities and partnerships, as outlined below (see Figure 2).

1.1.1 At a global level

UK action at a global level to tackle AMR is driven by an underlying commitment to international collaboration, as made in our 2013–2018 AMR strategy (through the seventh key area for action). It is underpinned by our belief that effective regulatory, delivery and quality assured systems for humans, animals and the food chain are crucial to preventing and responding to AMR. Strengthening these systems in the UK and overseas will be a key part of what we do over the next five years.

Figure 2. UK efforts to tackle AMR include global and domestic activities, identifying drivers of AMR emergence and spread



Driving global advocacy and political agenda

Ensuring tangible global progress against the UN's high-level political declaration and the GAP forms a key pillar of the UK's international work on AMR. We actively support the IACG in reviewing progress to date and developing recommendations for the future, and will continue to advocate for bold and ambitious next steps to sustain global momentum.

At the same time, we continue to push the AMR agenda forward through our involvement in major international groups and partnerships, including the G7, G20, the Tripartite and

UN and inter/multi-lateral organisations, the Alliance of Champions in Geneva and Group of Friends in New York, to combat AMR and the Global Health Security Agenda. In the animal health sector, strong UK engagement ensured that a milestone was achieved at the 2017 G7 Chief Veterinary Officers' (CVO) forum where CVOs adopted a position paper setting out a common position on AMR definitions.

To strengthen global collaboration, the UK will:

- help ensure that AMR remains a global priority by continuing to lead international policy dialogue at the highest political levels through the G7, G20 and other international and regional fora, and as a major supporter of the UN and wider multilateral system;

- urge sustained, joined-up international action to address AMR including holding the Tripartite Plus (WHO, the FAO OIE and UN Environment (UNEP) and the wider UN family to account for their individual and collective efforts to address it, and by increasing links to the delivery of the Sustainable Development Goals.

- back the development of internationally agreed solutions to promote robust stewardship and access plans for new and existing antimicrobials and to protect antimicrobials as global public goods.

Promoting access and responsible use

Antimicrobials are crucial medicines in modern healthcare, yet up to two billion people still lack access to them. Our goal is to optimise antimicrobial use to ensure that more people, especially in low income countries, have access to appropriate medicines when they need them, including for TB. The UK funds projects overseas to help optimise the use of antimicrobials through, for example, initiatives to develop NAPs and roll out key protocols and tools needed to survey AMR and use (see box "The Fleming Fund").

We work closely with governments in low- and middle-income countries (LMICs) to strengthen their health systems, including by improving the quality of care, water and sanitation infrastructure in health facilities and approaches to medicines (see, for example, box 'Supporting Nepal' overleaf).

As well as supporting individual countries to promote appropriate use in both human and animal health, we work with international organisations such as WHO, Gavi, OIE and the Global Fund to Fight AIDS, Tuberculosis and Malaria to build reliable supply chains that can support effective prevention strategies and ensure quality-assured antimicrobials are available where and when they are most needed.

CASE STUDY THE FLEMING FUND

The Fleming Fund is a £265m UK Aid programme established to help low and middle income countries tackle AMR focusing particularly on surveillance:

- The fund finances activities to collect and share data (on antimicrobial quality, use and resistance, alongside the associated burden of disease) with relevant decision makers globally.
- Working through the WHO, FAO and OIE, the fund has supported more than 30 countries to develop a NAP and to roll out protocols and tools needed to survey antimicrobial use and resistance in humans, animals and the environment.
- Through its 'Country and Regional Grants Programme', the fund helps 24 countries across Sub-Saharan Africa, South and South-East Asia to build sustainable One-Health surveillance systems.
- To sustain progress, the fund builds the capacity of AMR leaders through a range of fellowships that offer mentorship, secondments, training and networking opportunities for individuals in both scientific and policy fields.

Improving detection and surveillance

Through initiatives like the Fleming Fund, the UK supports LMICs to collect and share globally high-quality surveillance data on AMR as well as antimicrobial use and quality for human and animal health (see box 'The Fleming Fund').

We also work to ensure our own AMR surveillance data are consistent and coherent with other countries' data by participating in WHO's Global Antimicrobial Resistance Surveillance System (GLASS), the European Surveillance of Antimicrobial Consumption Network and the European Antimicrobial Resistance Surveillance Network (EARS-Net) in the human sector and in the OIE scheme, the European Surveillance of Veterinary Antimicrobial Consumption and European Food Safety Authority projects in the animal sector.

Reducing the burden of infection in humans and animals

Globally, the UK helps to reduce the burden of infection by supporting programmes to strengthen health systems in LMICs. This includes working with countries to implement WHO's International Health Regulations (IHR) 2005, particularly to build core capacities on IPC.

Immunisation is one of the most effective public health interventions to prevent infection in humans, animals and fish. The UK supports the delivery and uptake of vaccines both at home and overseas through UK Aid programmes. UK Aid is also a global leader in preventing malnutrition (another major driver of infectious disease and antimicrobial use), providing support for safe infant feeding and key micronutrient supplements to vulnerable populations across the world.

CASE STUDY SUPPORTING NEPAL

In Nepal, the UK supports work to reduce the risk of AMR through technical assistance to the Ministry of Health and Population.

This includes support to update Standard Treatment Guidelines/Protocols and roll them out; and to define a basic package of health care services – those provided free of charge at the point of use – drawing on local and international evidence; as well as work to help define, implement and monitor minimum service standards at primary and secondary level.

Finally, we support Nepal's efforts to strengthen the procurement of medicines and supply chain management through, for example, work to develop a technical specification bank as part of the quality assurance process for the procurement of health commodities. This will help ensure that patients in Nepal have access to safe, effective and affordable treatments.

The UK also supports international programmes spanning animal and human health, and works with a broad range of international bodies to promote a One-Health approach to AMR. The key focuses of our international engagement work are supporting the UN Tripartite (WHO, OIE, FAO) and encouraging a stronger One-Health focus in its work on AMR. We also work with other UN agencies, the G7, G20, the World Economic Forum and OIE, to reduce levels of resistant pathogens in both humans and animals and advocacy for environmental stewardship.

To support countries to prevent, diagnose and treat infection, the UK will:

- use UK Aid to support countries' efforts, promoting prevention by continuing to fund delivery of vaccinations through international initiatives such as Gavi, the vaccine alliance.

- invest in effective regulatory and delivery systems for human and animal health, the food chain, in AMR surveillance, and in linked work on nutrition and water, sanitation and hygiene (WASH) in LMICs – all of which help to prevent resistant infections spreading.

- promote equitable access to quality antimicrobials and responsible use through system strengthening approaches in LMICs and our support to the Global Fund and other initiatives that provide diagnosis and treatment, as well as prevention, for the diseases of poverty, including drug-resistant tuberculosis (TB) to help meet the first, globally-agreed AMR target: to successfully treat 1.5 million people with the disease worldwide between 2018 and 2022.

Incentivising R&D

The UK funds research initiatives to improve global knowledge and understanding of AMR. For example, through the £50 million UK Global AMR Innovation Fund (GAMRIF), we are supporting:

- the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator, a non-profit international partnership supporting research on the most dangerous drug-resistant bacteria;

- in-country research to tackle AMR in agriculture and the impact on the environment (for example, in Argentina);

- the work of the Foundation for Innovative New Diagnostics (FIND) to enhance the impact of diagnostic tools, in particular the connectivity of point-of-care diagnostics for AMR surveillance; and

- the development of a new antibiotic for drug-resistant gonorrhoea through the Global Antibiotic Research and Development Partnership (GARDP).

We also promote EU and international AMR research collaborations through other initiatives including UK Research and Innovation (UKRI) AMR initiative which has committed £41million from 2014-2018, to support projects in partnership with members of the Joint Programming Initiative on AMR (JPIAMR) and through partnerships with low- and middle-income countries (see box "SNAP-AMR") and the recently launched Global AMR R&D Collaboration Hub, which is coordinated by Germany.

CASE STUDY SNAP-AMR

The Supporting the National Action Plan for AMR in Tanzania (SNAP-AMR) project is one example of how UKRI and the Department of Health and Social Care (DHSC) use research and capacity building efforts to understand and address AMR in LMICs.

The project team, led by the University of Glasgow, is made up of researchers and policy experts in both the UK and Tanzania. Working together, the team expects to provide novel insights into the socio-economic, cultural and biological drivers of AMR in Tanzania. These will then be used to identify and prioritise workable approaches to behaviour change in hospitals and communities to alleviate the country's burden of AMR-related illness and help deliver its NAP.

Developing new treatments

As a leading investor in Product Development Partnerships (PDPs), the UK harnesses the strengths of academia and the pharmaceutical industry to support the development and roll out of new antimicrobial therapies and diagnostics for priority diseases, such as TB.

To support research and innovation, working with the research community and the private sector the UK will:

- use our funding for research and innovation to include support for research groups, including public-private partnerships, to promote the development of new, priority vaccines, therapeutics and diagnostics, including for diseases of poverty such as TB and spanning both human and animal health. It will also encompass investment in applied health research and behavioural science to help us understand which approaches to tackling AMR work, where and when.

- work with the private sector to build on our support for research innovation and the development of affordable tools to tackle AMR across the whole One-Health agenda, to improve approaches to antimicrobial development, marketing and environmental risk management as well as promoting better corporate social responsibility where investors and consumers can bring their own influence to bear.

By supporting initiatives like the AMR Benchmark, UK Aid helps engage industry and stimulate better performance against various AMR indicators (see Figure 16 below). And

through projects like the Medicines Discovery Catapult, funded by Innovate UK, the UK helps small and medium-sized enterprises (SMEs) drive the development of diagnostics, devices and therapeutics to ensure patients get the right treatment at the right time.

1.1.2 In the UK

In parallel to our global efforts to tackle AMR, we undertake a range of activities within the UK, as set out in the first six key areas for action in our 2013 - 2018 strategy (and outlined below). Underlying all our efforts is recognition that an effective response to AMR is a cross-sectoral one that draws on robust and responsive systems across health, agriculture, the food chain and the environment. In human health, specific actions to implement the 2013-2018 strategy varied across the four countries (England, Scotland, Wales and Northern Ireland). Our new action plan has been developed with multiple partners and with all four countries working together.

Improving infection prevention and control (IPC) practices in animals and humans

Diverse tools and tactics have been used over the past five years throughout the UK to improve IPC practices in humans. These include:

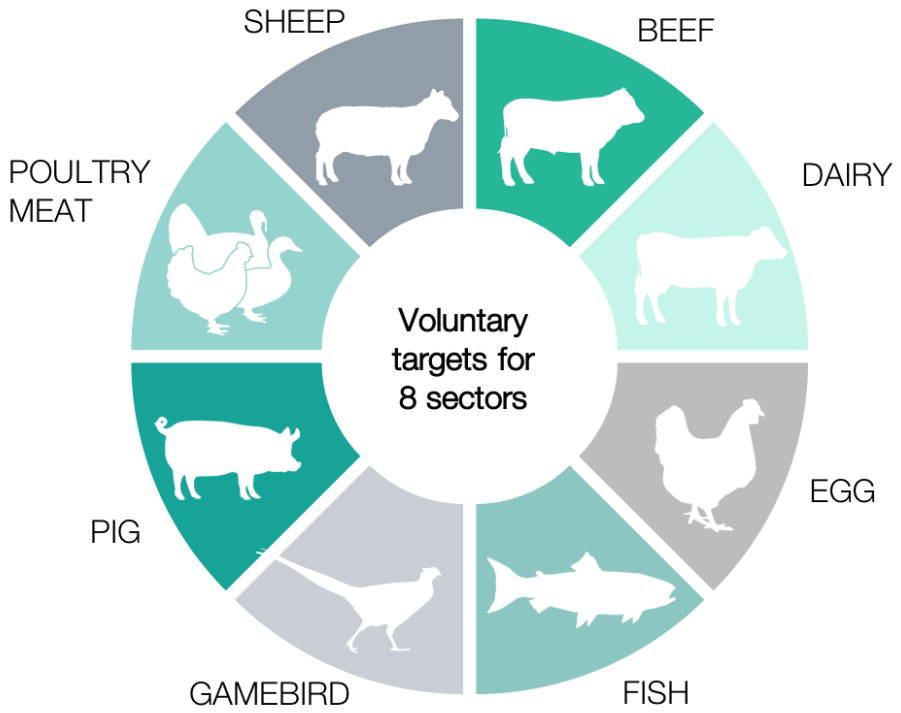
- regulations such as the Health and Social Care Act on the prevention and control of infections and related guidance in England;
- training of health and social care workers in practices such as hand hygiene and aseptic technique;
- use of surveillance systems to recognise infections and target action to prevent spread;
- audit practices to ensure policies and procedures are effective;
- vaccination of healthcare workers to protect patients from spread in healthcare settings;
- decontamination of medical devices; and
- environmental cleaning.

Monitoring of compliance with all the above is delivered through regulators.

There has also been significant progress in improving IPC in animals. In October 2017, voluntary targets for reducing antibiotic use in animals were agreed for eight key livestock

sectors (see Figure 3 below). The targets are tailored to the specific circumstances and features of each sector; but all are based on the principle that “prevention is better than cure”.

Figure 3. The eight livestock sectors with voluntary targets (Source: Targets Task Force Report 2017)



Delivering on these targets, combined with better disease control and improved data on antibiotic use (which can be used to inform interventions) is expected to catalyse sustainable and meaningful change not only in antibiotic use but also animal health and welfare.

(For more information on the targets, see the Task Force report 2017).

Optimising prescribing practice

Various initiatives have helped embed stewardship programmes in both human and animal settings. One of the most successful is the development and dissemination of the TARGET antibiotic toolkit, which provides diverse resources to support health professionals and educate patients in appropriate use of antibiotics in humans (see box ‘TARGET toolkit’), contributing to the reductions in use illustrated in figure 4.

In Scotland, the Scottish Reduction in Antimicrobial Prescribing (ScRAP) toolkit similarly provides educational resources to improve antibiotic prescribing. The Start Smart Then Focus toolkit provides resources for secondary care in England.

CASE STUDY **TARGET antibiotic toolkit**

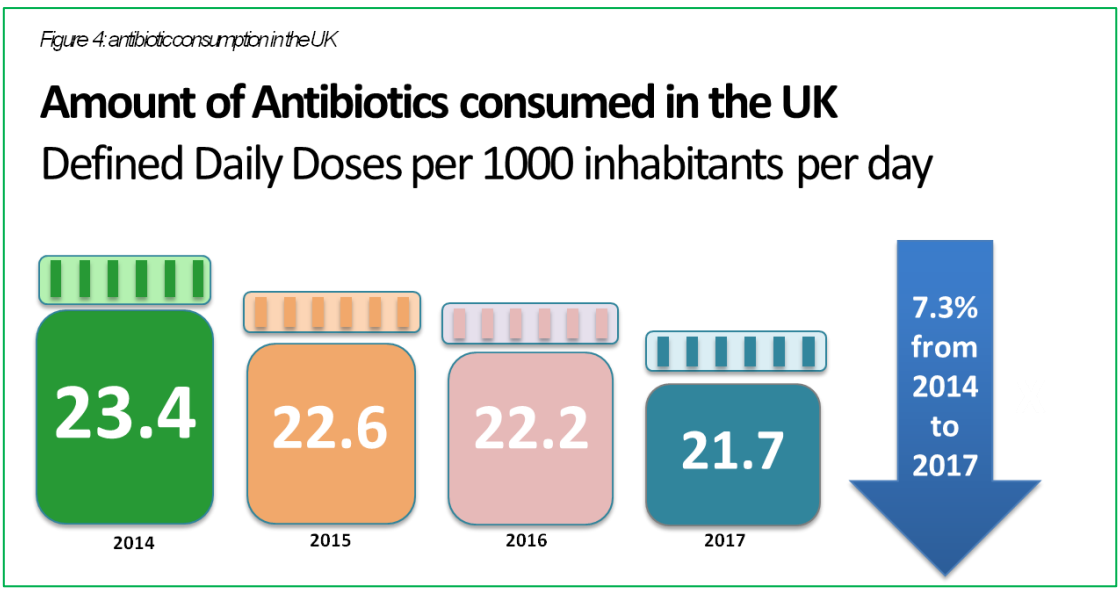
The Treat Antibiotics Responsibly Guidance, Education and Tools (TARGET) toolkit is designed to support antimicrobial stewardship in primary care. Made up of diverse resources, it includes: leaflets for patients, posters and videos for waiting rooms, audit templates, diagnostic guidance, self-assessment checklists, training resources, antibiotic prescribing data platforms and resources for commissioners. Used effectively, the toolkit helps influence both prescribers and patients towards appropriate antimicrobial use.

The TARGET toolkit is free to use and is the most accessed resource on the Royal College of General Practitioners (RCGP) website, attracting more than 69,000 visits between July 2017 and June 2018.

Nearly all (99%) England's Clinical Commissioning Groups that plan and commission local health care services promote the TARGET toolkit to their GP practices.

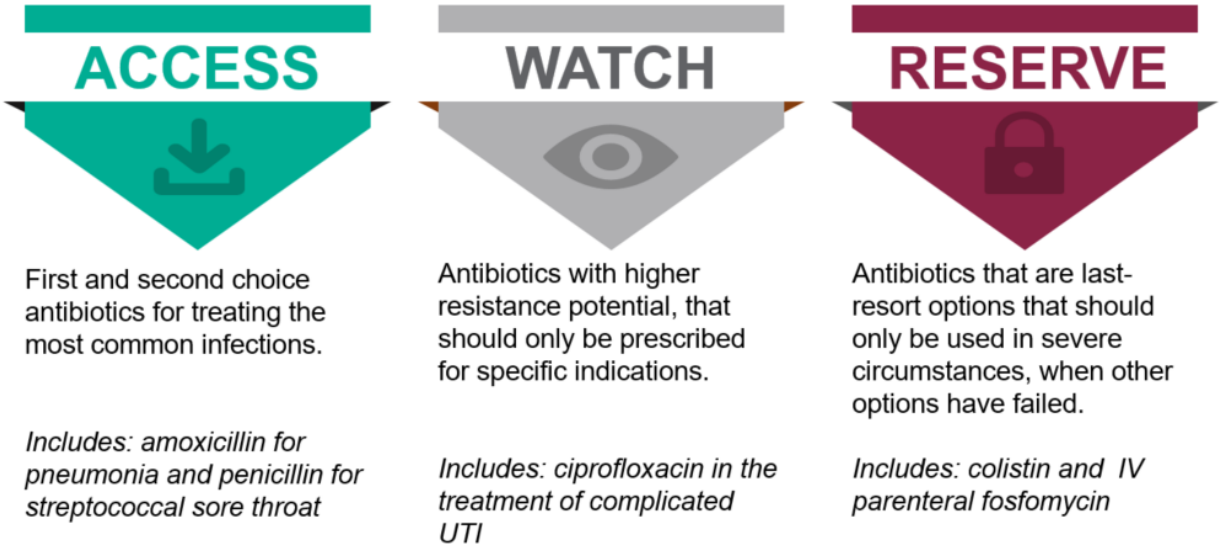
The PrescQIPP Antimicrobial Stewardship Hub is another initiative to support better prescribing in primary care in England. A joint initiative between NHS England and NHS Improvement, the PrescQIPP Hub offers online access to ready to use antibiotic prescribing data sets for all Clinical Commissioning Groups and GP practices in England, shares successful practice, and links to other AMR-related resources, including those published by TARGET, Health Education England and the Antibiotic Guardian campaign. Data in the PrescQIPP Hub is offered in multiple formats to allow comparisons across time, and organisations.

Figure 4: antibiotic consumption in the UK



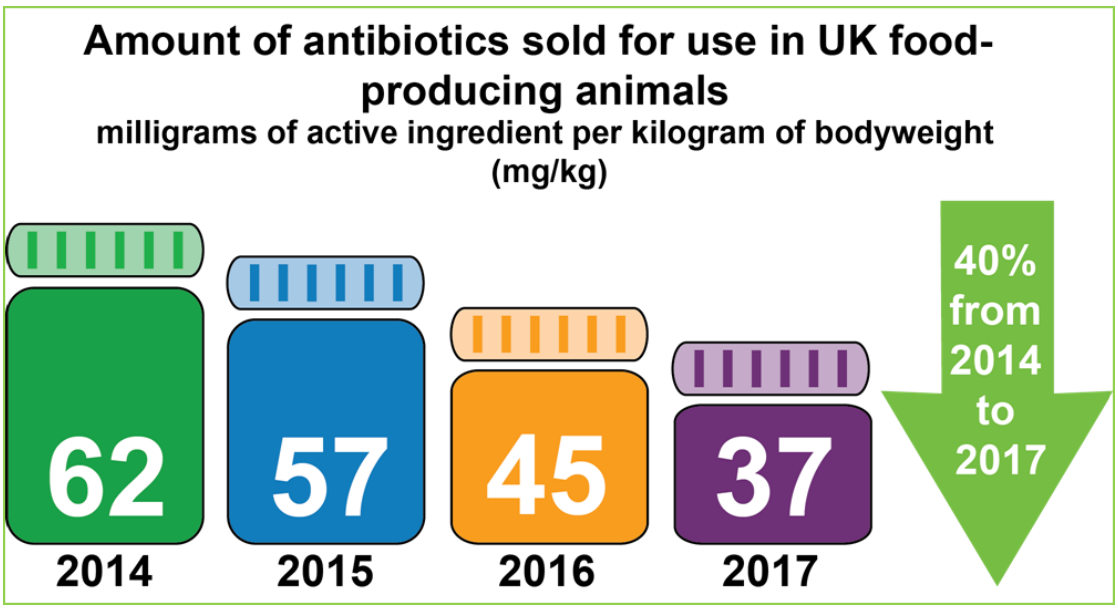
Most recently, the UK has adapted the WHO's new categorisation of antibiotics (the 'AWaRe' index from the 20th Essential Medicines List) for use in England, Scotland and Wales. The AWaRe index categorises antibiotics into three groups; Access, Watch and Reserve, and provides recommendations on when each category should be used, with the aim of enhancing treatment outcomes, reducing the development of resistance, and preserving the effectiveness of "last resort" antibiotics that are needed when all others fail (see Figure 5). In England, the index has been used to re-categorise two antibiotics that form the focus of our national stewardship policy: piperacillin-tazobactam and carbapenems (from access to watch and reserve). The UK was the first country to use the AWaRe index in national policy and so translate this international guidance into an effective stewardship intervention.

Figure 5. The AWaRe index categories



In the animal health sector there are many initiatives and tools supporting responsible use and contributing to the reductions in use shown in figure 6. Examples include the British Veterinary Association's (BVA) "7-point plan" poster to support responsible prescribing by veterinary surgeons and the British Small Animal Veterinary Association (BSAVA) PROTECT guidelines to responsible use of veterinary medicines,.

Figure 6. Sales of antibiotics in UK food producing animals



Improving professional education, training and public engagement

Resources like the TARGET antibiotic toolkit serve as useful training resources for health professionals. They also help engage patients and their families to support changes in behaviour that can prevent infection and reduce the use of antimicrobials. Implementing the UK antimicrobial prescribing and stewardship competences provides a further opportunity to strengthen capability of healthcare professionals. These competences have been recently adapted to include national antimicrobial stewardship competencies for UK undergraduate healthcare professional education.

The UK also works with veterinarians and industry representative groups to support training and public engagement to reduce infection in our animals and to promote their health and welfare.

The Animal Medicines Best Practice training course was launched in 2018; developed by the National Office of Animal Health in collaboration with stakeholders and providing farmers and their vets, tools to support the responsible use of antibiotics on farms.

We launched the "trust your vet" campaign in collaboration with the veterinary industry in 2018 to reach out to pet owners.

We recognise the need to raise public awareness of the importance of good hygiene (in people, animals and food) to help prevent infection and keep antibiotics working. All four countries use diverse engagement activities to do that, and participate annually in World Antibiotic Awareness week. In 2014, Public Health England (PHE) launched the One-Health Antibiotic Guardian campaign, which encourages people to make pledges about

how they can contribute to tackling AMR; its resources have been adapted for use in Scotland, Wales and Northern Ireland. And, in October 2017, PHE launched a national awareness campaign, Keep Antibiotics Working, aimed at improving the public's understanding of AMR and reducing their expectation for antibiotics.

Developing new drugs, treatments and diagnostics

The UK recognises the continued need to enhance support for research and development of new products and technologies for addressing AMR in humans and animals, especially in areas of market failure.

We continue to work with industry bodies to see how the UK can lead the world in developing new ways of purchasing antimicrobials that will encourage industry to continue to invest.

Improving access to and use of surveillance data

Across the UK, the NHS collects a wealth of data. In England, both hospital and community antimicrobial use data are now open access and available through the PHE Fingertips platform, which allows users to browse a wide range of health and wellbeing indicators at different geographical levels, benchmark them against regional or national averages and export data for further use. In the devolved administrations, similar data are available through counterpart platforms.

In 2015, the UK published its first UK One-Health report, which provides human and animal antibiotic use, sales and resistance data for key zoonotic pathogens, with recommendations on how to improve a One-Health approach to data production and analysis.

Identifying and prioritising AMR research needs

To coordinate and prioritise the UK's national and international research response and provide a link with policy, the Medical Research Council (MRC) established the UK AMR Funders Forum in 2014. The Forum brings together 21 research funders, including the UK Research and Innovation Councils, government departments, devolved administrations and charities.

The Forum identified four key research themes to target investments.

- Better understanding resistant bacteria;
- Accelerate therapeutic and diagnostic development;

- Understand real world interactions;
- Investigate how behaviour of the public, professionals and organisations impacts on AMR.

The Forum has reviewed the research skills and capacity needs of the field. To address the themes, UK Research and Innovation councils have supported 78 interdisciplinary projects at a total commitment of £44 million, and, in recognition of the global dimension of AMR, have committed £41 million, to support projects in partnership with members of the Joint Programme Initiative in AMR, and with emerging economies and low- and middle-income countries. In addition, as part of this Forum, the National Institute for Health Research (NIHR), has promoted research for an integrated understanding of the complex health interactions that contribute to AMR. For example, by using a range of epidemiological investigations to identify the causes of increased rates of *E. coli* bacteraemia observed in recent years to better target interventions and support local teams to reduce the number of cases.

This support has helped establish an active cross-sector AMR research community. This includes widely recognised expertise in building predictive system models and conducting trials, which can now be used to focus domestic interventions and help other countries develop their own context-specific, evidence-based strategies.

There is so much more still to do. The spread and impact of AMR in the environment and between and among people and animals remains poorly understood and needs more study so we can identify what actions are required to reduce that spread and impact.

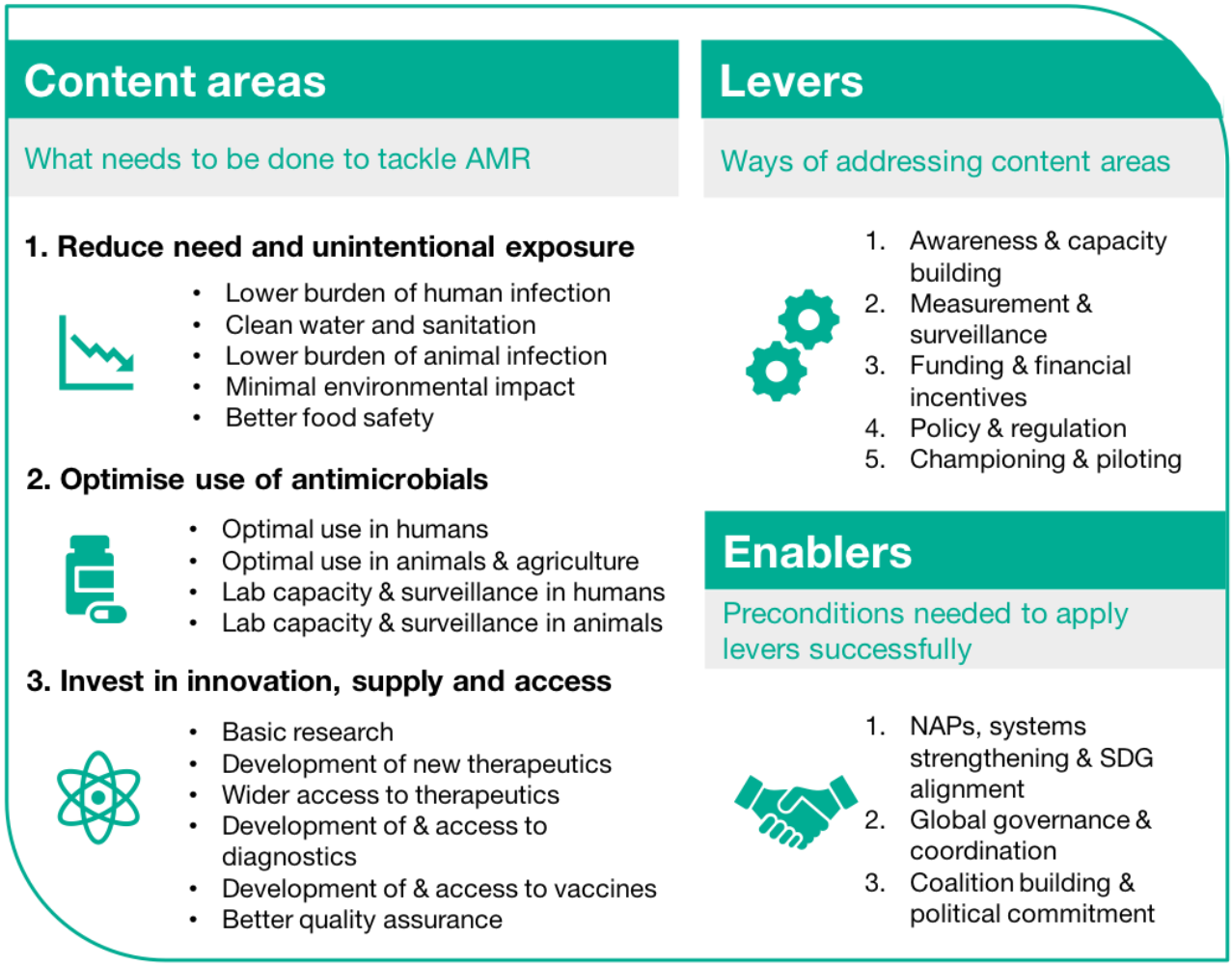
1.1.3. About our NAP

Our new five-year national action plan (NAP), outlined in sections 2-4 below, builds on our existing efforts and achievements to date to prioritise early actions and establish a secure basis for the step change required to fulfil our 20-year vision for AMR.

Co-developed across government departments, agencies and the health family, with Scotland, Wales and Northern Ireland, as well as in consultation with diverse stakeholders, the NAP uses the Ad-hoc IACG's framework for action to set out the UK's commitments for the next five years. The framework identifies three main ways of tackling AMR and 15 different 'content areas' that describe what needs to be done. The IACG framework points to five 'levers' that describe how the content areas can be addressed; and three 'enablers', describing the preconditions necessary to apply the levers successfully (figure 7). Both are embedded in the UK's NAP, through the specific activities and initiatives mentioned to support our commitments.

Fulfilling our commitments over the next five years requires action across many spheres. Spreading resources too thinly could limit our ability to achieve meaningful change; so our plan will be implemented using a risk-based approach, targeting interventions where the evidence for impact is strongest.

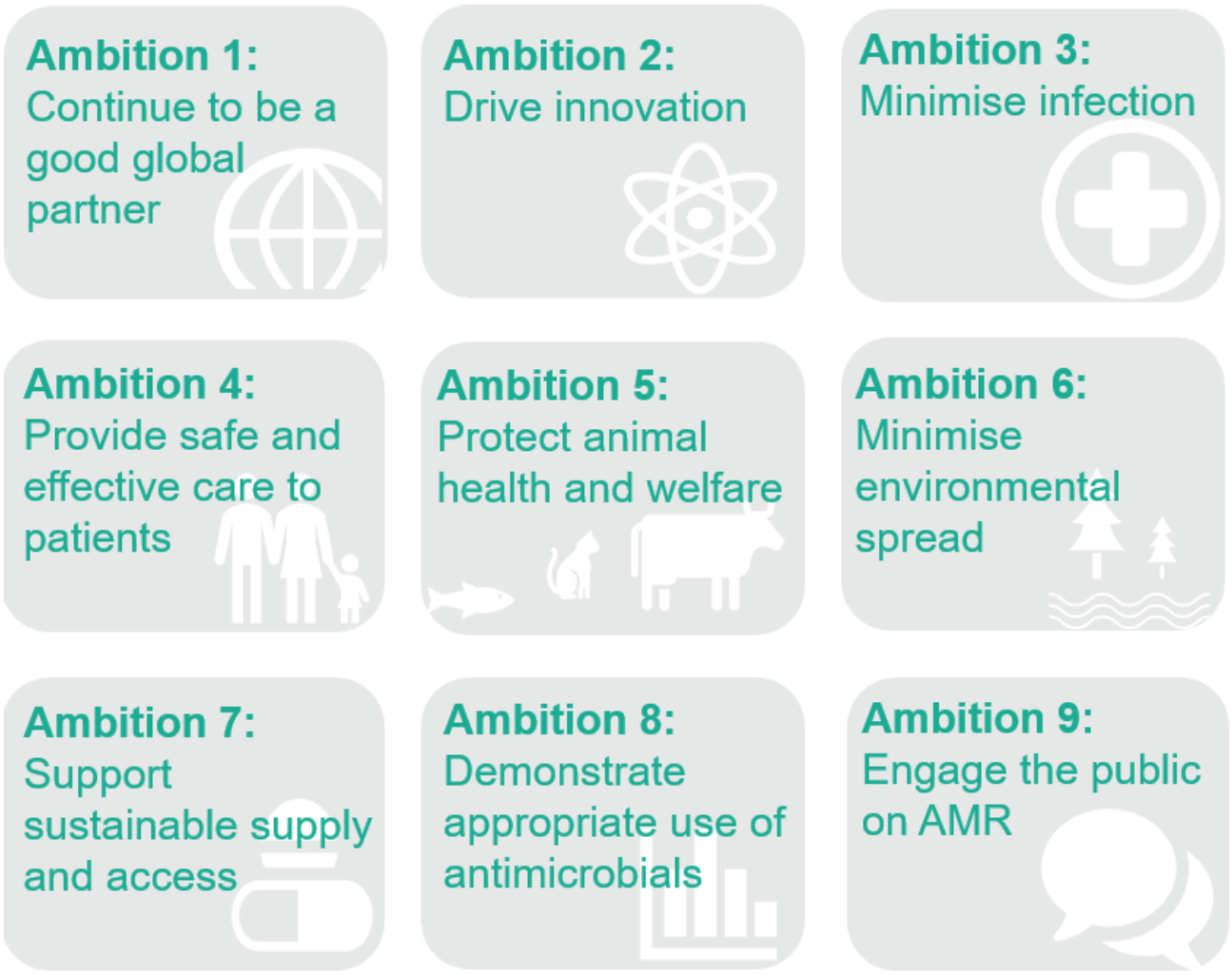
Figure 7. A framework for the UK NAP



We rely on the active participation of public and private sector bodies across the human health, animal health and environment communities. There is a role too for members of the public as patients, consumers, animal owners and investors. A summary of the expected roles and responsibilities for different stakeholders is provided in our vision for AMR in 2040.

The sections that follow take each content area in turn (what we are aiming for) and describe the issue at hand and the range of strategies that we will deploy to address it, alongside the UK's specific commitments to action. For each content area, we highlight the link to our long-term, high-level ambitions (as outlined in the UK's 20-Year Vision, and summarised in Figure 8 below).

Figure 8. The UK's nine ambitions for change, as defined in our UK 2040 AMR Vision



Given that the Ad-hoc IACG Framework for Action was developed as a global tool for use by all countries and stakeholders, it is not surprising that some content areas are more relevant for the UK than others. We have identified actions across all content areas but some remain high priority and, for these, we have set quantifiable ambitions so we can measure our success over the lifetime of this plan. This includes measures of success for infection rates, antibiotic use and use of diagnostic tools and tests (see boxes 'Measuring success' below).

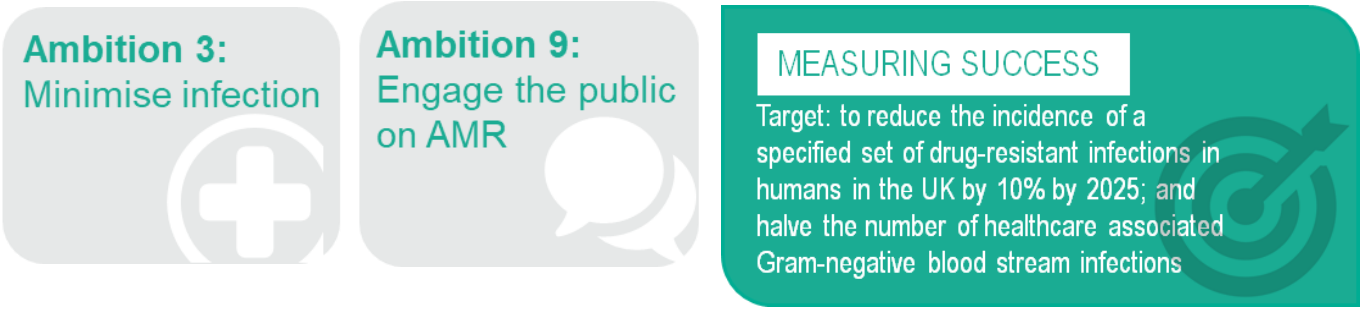
2. Reducing need for and unintentional exposure to antimicrobials

AMR is naturally occurring. Preventing and controlling infections that are likely to be treated with antimicrobials is one way of reducing the need for these medicines, and as such is fundamental in tackling AMR. The more we use and misuse anti-infectives and antimicrobials, in both human and animal medicine, the faster resistance will develop and spread. We need to take every opportunity to prevent infections and the need to use antimicrobials.

Globally, unmonitored quantities of waste disposed by pharmaceutical manufacturers, hospitals, farmers and livestock producers and consumers can enable development of resistance through its dispersal in the environment.

Reducing the unintentional exposure of people, animals and environments to anti-infectives (including cleaning products such as antibacterial sprays), antimicrobials and drug-resistant organisms (for example by reducing environmental contamination and improving food safety) is important in reducing the risk of AMR developing and spreading.

2.1. Lower burden of human infection



Lowering the burden of human infection will lead to fewer antimicrobials being used and less risk of resistance. That puts preventing and managing infections firmly at the core of any AMR strategy.

Ensuring that health and social care providers have the capacity, capability, physical environment and tools for effective infection prevention and control (IPC) is critical. So is

increasing the public's and those who work in the food chain's awareness and practice of IPC. Across these areas, research has a role in turning evidence into practice and steering behaviour change.

2.1.1 Strengthen the prevention and control of priority infections

At a global level, the WHO has developed a set of eight core components to help countries and individual healthcare facilities plan, organise and implement IPC programmes (see 'IPC core components'). The WHO stresses that all these components are required for IPC programmes to be effective, but that activities within each component should be tailored to reflect local priorities and resources.

IPC CORE COMPONENTS

The WHO identifies eight core components for effective IPC programmes in healthcare:

- ✓ Organisation of IPC programmes
- ✓ Technical guidelines
- ✓ Human resources (training, staffing, occupational health)
- ✓ Surveillance of diseases and compliance with IPC practices
- ✓ Microbiology laboratory support
- ✓ Clean and safe environment
- ✓ Monitoring and evaluation of IPC programmes
- ✓ Links with public health and other services

Find out more at www.who.int/infection-prevention/tools/core-components

The UK is a major supporter of the WHO, as well as other global health initiatives. We also contribute to international policy dialogue on strengthening IPC at the G7 and G20. Our UK Aid support to health system strengthening and related work on nutrition and water, sanitation and hygiene (WASH) also helps to strengthen IPC and reduce the need for antibiotics in partner countries overseas.

Vaccination is one of the most effective ways of preventing infections in both humans and animals. By supporting initiatives like Gavi, the vaccine alliance, we are helping improve vaccinations overseas (see section 4.5 below). In the UK, we have a comprehensive

schedule of vaccinations available for children and adults to help prevent infections spreading.

In the UK, the biggest drivers of resistance are:

- a rise in the incidence of infections, particularly Gram-negatives;
- the import of resistant infections through international travel (see 'Importing resistance'); and,
- antimicrobial use.

The number of *E. coli* blood stream infections (BSIs) diagnosed across the UK has increased from 45,885 in 2015 to 50,400 in 2017 (a change in rate from 70.5 to 76.8 per 100,000 population). In some countries, the level of resistance among Gram-negative organisms is so high it is compromising the ability to provide safe healthcare.

IMPORTING RESISTANCE

International travel is widely recognised to play a major role in the global spread of AMR.

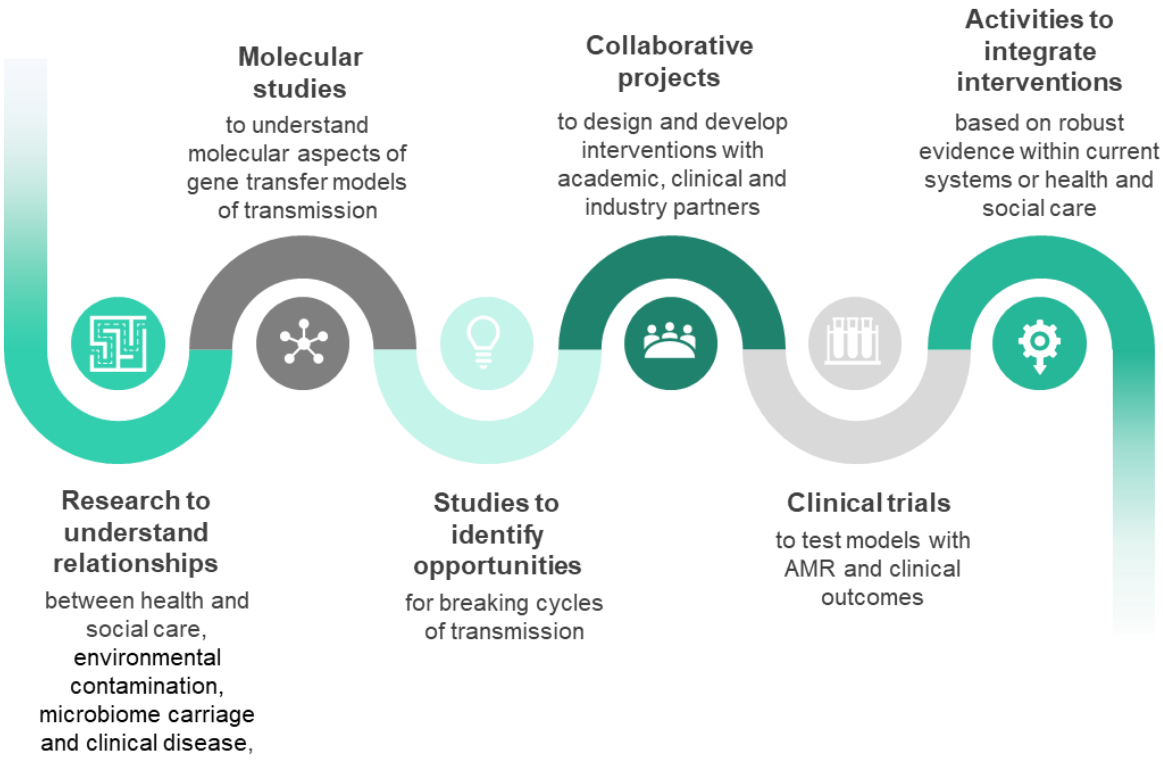
People travelling to regions with a high prevalence of resistant bacteria (such as Carbapenemase-producing Gram-negative organisms, or 'CPOs') are at greater risk of being colonised in their gut by these organisms in their microbiomes. This makes them more likely to acquire a drug-resistant infection themselves, and to spread it to others when they return home.

The rise in Carbapenemese-producing Gram-negative (CP-GN) infections is of concern as these cannot be treated with key antibiotics (carbapenems) and there are few treatment alternatives. Identifying where and how these difficult-to-treat infections occur and acting to prevent them is essential to maintain the effectiveness of our go-to antibiotics. In practice, that means:

- **Stronger surveillance.** Public Health England (and equivalents in the devolved administrations) survey infectious diseases and already have good quality data on many Gram-negative infections; Carbapenemase- producing Gram-negative infections are more difficult to monitor and will need further enhanced surveillance.
- **A systematic approach.** This includes understanding the chain of causality and the relationship between health and social care, environmental contamination and clinical disease, including a focus on hospitals as amplifiers of transmission.

- **Better understanding.** Understanding how the built environment favours the spread of AMR, and how it can be designed to limit such spread.

Figure 9. A systematic approach to prevent Gram-negative infections and reduce the burden of disease



To strengthen the prevention and control of priority infections, the UK will:

- Reduce the incidence of a specified set of drug-resistant infections by 10% by 2024.

- Add Carbapenem-resistant Gram-negative infections to the list of notifiable diseases in existing laboratory reporting systems.

- Continue work to halve healthcare associated Gram-negative BSIs, adopting a systematic approach to preventing infections (Figure 9) and delivering a 25% reduction by 2021-2022 with the full 50% by 2023-2024.

- Work through UK Aid to help reduce the global burden of drug-resistant infections, in line with agreed global targets on key diseases, including TB.

2.1.2 Improve the professional capacity and capability for IPC

Health and social care providers have a key role in preventing and controlling infection (and its contribution to the growth of AMR) through their policies and practice. Individual workers can be vectors for infection in health and care settings; and healthcare facilities are often a reservoir for infection and resistance.

In the UK, we support health and social care providers delivering IPC in many ways, including: education and training programmes, professional networks and peer review, standards (for example, the evidence-based NHS Scotland National Infection Prevention and Control Manual, which was first published in January 2012 and is mandatory for NHS Scotland best practice in all care settings), regulations and regulatory inspections, and national improvement services (see Table 1). Through health system strengthening, the UK also helps build IPC capacity overseas.

But equipping professionals for effective IPC is not easy. Healthcare in the NHS is provided through a large and disparate system, and the four countries vary in their arrangements for improving quality. The social care sector is also fragmented across many more providers. This makes it difficult to ensure consistency in policy and practice. IPC interventions confined to individual organisations cannot achieve optimum control: there is need for a broader systems approach that spans the full healthcare collective and is connected to local health protection teams to ensure whole communities are engaged. Acknowledging variation is also important: we will improve use of national measurement tools to identify opportunities for the greatest impact and to benchmark, target and inform individual organisations and practices.

Table 1. Equipping professionals: a selection of activities targeted at supporting professionals in the UK.

Type of activity	State of play	Next steps
Training and education	Professional education is overseen by Health Education England, NHS Education for Scotland, Health, Education and Improvement Wales, and a range of bodies in N. Ireland. All regularly review the most effective educational techniques that impact behaviours.	More targeted communications for health and social care, particularly to improve behaviour around hand hygiene.
Professional networks	Professional regulatory bodies and Royal Colleges across the UK give professionals IPC guidance, educational activities and peer review.	Continue to advocate improved standards of practice.

Standards	In England, each organisation writes its own standards, adhering to the Health and Social Care Act; in Scotland and N. Ireland there's a national IPC manual and standard care bundles to reduce variation in practice. Wales recently adopted the same approach, officially endorsing the Scottish manual.	England will adopt the Scottish model IPC manual and care standards.
Regulations & oversight	Different leadership and regulatory arrangements are in place in the devolved administrations. All include regulatory inspections to assess adherence.	Ensure a whole system approach through cross-organisational bodies and/or a specialist IPC workforce to support and guide others.
Improvement services	The four countries have different arrangements for quality improvement. For example, the 1000 lives HAI and AMR collaborative in Wales connects healthcare providers with experts to share learning and best practice and reduce the incidence of HAIs and AMR.	Draw on behavioural and implementation science to ensure guidelines and training are put into practice.
Built environment	Built environments can support good IPC, for example through single occupancy rooms for isolation. But these facilities are in high demand and there may be insufficient capacity.	Research how to optimise our use of the built environment, and use the findings to inform action and investment.

To improve the professional capacity and capability for IPC, the UK will:

- Ensure board-level leadership with a combined IPC and antimicrobial stewardship role for all regulated health and social care providers. The four countries will decide how best to achieve this within their own frameworks, but all will ensure a local accountable role that enables regular self-assessment, training and data-driven review.

- Assess current and future workforce needs for strong IPC and antimicrobial stewardship across health and care settings; and develop future workforce targets based on the results of this assessment.

- Facilitate and support an open and learning culture within healthcare settings on AMR by supporting the dissemination and implementation of learning strategies that are most likely to bring about behavioural change.

- Establish the IPC and care standards developed in Scotland (and already adopted in Wales) as the national standards in England, to be measured annually by the regulators.

- Commission a review of the optimal facilities and infrastructure required to reduce transmission and enhance IPC in hospitals and community care settings.

2.1.3 Promote better IPC practices among the public

Health and social care providers can only do so much to prevent infections; when it comes to acquiring and transmitting infections in the community, the public have a huge part to play. Handwashing compliance is known to be poor, in both high and low-income settings. Globally, only 19% of people consistently wash their hands at key times. In the UK, most people know they should wash their hands but whether they do or not varies significantly.

Across the UK, diverse engagement initiatives are used to increase public awareness of why and how to prevent infections, from specific events, such as IPC Week and World Hand Hygiene Day to mass media campaigns and targeted communications. Social media and other digital technologies offer innovative ways of surveying public attitudes and awareness and evaluating the success of campaigns and communications.

CASE STUDY E-BUG LEARNING

PHE operates e-bug, an evidence-based educational resource for schools and communities that makes learning about micro-organisms, and the spread, prevention and treatment of infection fun and accessible for young people and hard-to-reach groups.

Freely available in 23 languages, e-Bug features diverse educational materials, activities and games around infection prevention, including food hygiene, oral hygiene and farm visits. Its 'train the trainer' workshops give educators the knowledge, confidence and skills they need to teach about IPC and AMR.

Future plans include redeveloping the website, scaling up educator training (across the UK and Europe) and developing new resources around food hygiene and the human microbiome.

Schools and other learning environments are key fora for promoting better practice among the public: schoolchildren amplify messages across communities; and university students can support antimicrobial stewardship through peer education of younger students and volunteering (for example, through STEM ambassador schemes).

To promote better IPC practices among the public, the UK will:

- Develop more targeted interventions to improve behaviour around hand hygiene.
- Work with educators and local authorities to ensure that all school leavers understand how to wash hands, prevent infections and use antimicrobials appropriately, and that those messages are shared in all communities.
- Survey public attitudes to and awareness of AMR and self-reported behaviours through new technologies, including social media; and use these to assess the impact of national public health campaigns and local awareness-raising activities.

2.1.4 Turn research into practice for effective IPC

The UK has invested heavily in AMR-related research, but we are not always quick to get the outcomes of that research into front line practice. When it comes to infection prevention, there is a clear need to ensure that potential interventions to stimulate behaviour change identified through research are piloted and evaluated, and then implemented quickly and effectively and widely.

THE BUILT ENVIRONMENT

The Chief Medical Officer's 2011 report on infections and AMR (published in 2013) stated that the design, construction and maintenance of healthcare facilities have a substantial bearing on the risk of developing an HAI.

Evidence shows that drug-resistant Gram-negative infections pose a huge threat to global health; and that research and clinical efforts should be directed at reducing their burden as a matter of priority.

There is growing recognition that hospitals can act as major nodes of transmission of these infections. This makes understanding exactly how the built environment spreads infection (and AMR), and how it can be designed to limit such spread, critical.

Research networks, such as the Academic Health Science Network (AHSN) in England, already have a role in translating research into practice for infection prevention, although more can be done through local and national improvement networks and initiatives like the NHS Patient Safety Collaboratives (PSC) in England.

In some cases, further research is required to better understand how to drive IPC most effectively.

This includes making more use of behavioural science, particularly to test interventions that can nudge behaviours towards better infection prevention and control.

Similarly, more research on how to optimise our use of the built environment to prevent infections and transmission in both hospitals and communities is needed to generate evidence to develop a plan for action and investment that can deliver better IPC.

To turn research into practice for effective IPC, the UK will:

- Support research to better understand the routes and burden of transmission of drug-resistant infections and potential interventions to inform control measures and behaviour change initiatives.

- Strengthen research commissioning to ensure interventions are piloted and evaluated to help translate evidence-based research into practice more quickly.

- Assess the average time taken for national guidelines to go from publication to implementation; and develop a plan using national and local improvement networks and the NHS PSC to drive improvements.

- Include AMR as a priority area in the contracts and licenses NHS England has with AHSNs as they are renewed over the five years of this plan.

2.2. Greater global access to clean water and sanitation

Ambition 1: Continue to be a good global partner

Ambition 3: Minimise infection

Universal access to clean water and safe sanitation is an SDG (SDG 6). But it is also critical in reducing the spread of infectious diseases and AMR in people, animals and the environment. The presence of bacteria and antimicrobials in sewage is a major concern because of the potential release into surface waters, groundwater, onto land and into the air. Similarly, contaminated drinking water presents a worrying risk for both infection and resistance, although more work is needed to understand the regional and global spread of AMR from this source.

In the UK, robust regulation and monitoring means citizens can be assured the water they receive is safe to drink; and that their sewage waste is properly managed and treated. The only exceptions to this are the households (particularly in rural areas) that rely on private water supplies and local storage waste solutions (such as septic tanks). In these cases, regular monitoring is required to ensure proper management and to identify and mediate risks as and when they arise.

UK Aid for WASH

- UK Aid supports community WASH programmes in **more than 20 countries**
- This will help more than **60 million people** gain access to basic WASH facilities by 2020.
- UK Aid also runs two centrally-run programmes that work across **13 countries** to deliver sustained access to WASH.
- In 2015, UK Aid provided **£183 million** of water/WASH-related bilateral and multilateral financial assistance.

Unfortunately, there are still many countries in the world where access to clean water and sanitation is not a given. The baseline report for the SDGs published by the WHO/UNICEF Joint Monitoring Programme shows that nearly a third (29%) of people do not have access to a safely managed drinking water supply and nearly two-thirds (61%) do not have safely managed sanitation. This lack of access to WASH facilities is a major driver of infection, as well as having much broader impacts on people's health and wellbeing.

Better global access to clean water and safe sanitation would significantly reduce the incidence of infections and in so doing, the need for antimicrobial use and the rise and spread of AMR.

To support greater access to clean water and sanitation, the UK will:

- Integrate consideration of AMR thinking into the UK's case for investing in WASH programmes in low- and middle-income countries.

- Support world class science to improve understanding of how to change behaviours for improved hygiene.

- Promote research in countries affected by contaminated drinking water to identify its role in the global spread of AMR.

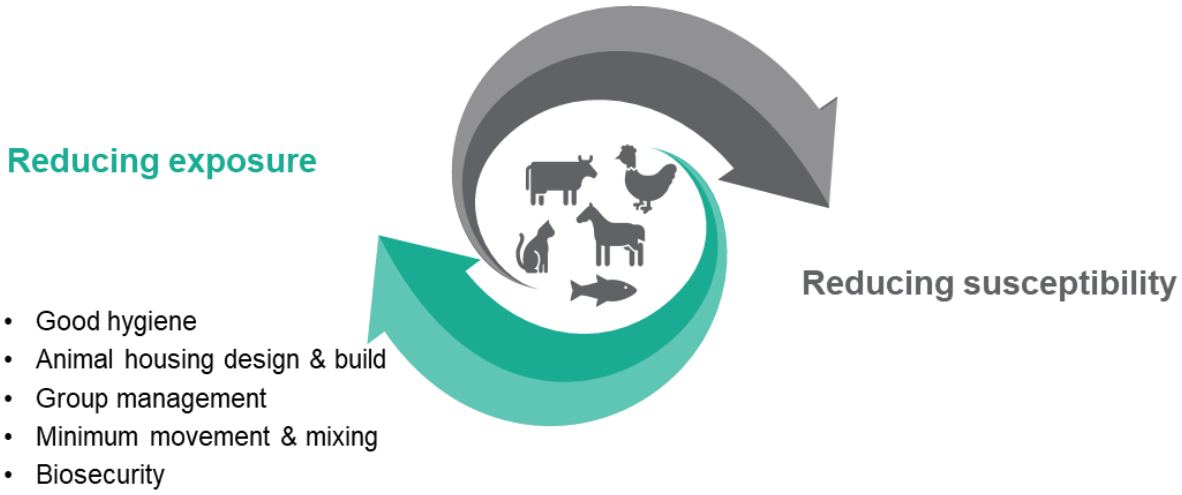
2.3. Lower burden of animal infection

Just as lowering the burden of human infection decreases the use of antimicrobials (and the risk of AMR), so too does lowering the burden of animal infection. The UK has committed to work with the livestock sector to significantly reduce endemic disease using industry-government collaborative mechanisms in place and through its 25-Year Environment Plan in England and the Wales Animal Health and Welfare Framework, the Scottish Animal Health and Antimicrobial Resistance Group's programme on control of infection in animals and through a new Animal Health and Welfare Strategic Framework in Northern Ireland. We intend to build on excellent schemes already in place in the UK such as the BVD eradication schemes in Wales, Northern Ireland and Scotland, and the project funded by the Rural Development Programme in England providing testing and advice for farmers. Industry, the veterinary profession and Government working together on schemes to tackle BVD and other similar chronic endemic diseases will be an important part of reducing the burden of infection.

Our approach focuses on reducing animals' exposure and susceptibility to pathogens that could result in the need for treatment with antimicrobials. We cannot hope to reduce these to zero, but we can try to minimise them (see Figure 8). Effective infection control is critical, not only by animal owners but also by their veterinarians, people who organise animal movements or gatherings, and anyone else that regularly comes into contact with one or more animals. Good animal husbandry practices are also important. So too is increasing the range and uptake of animal vaccines.

Across all these strategies there is a need for further research and awareness-raising to deliver a better understanding among animal owners, policymakers and the public alike, of how AMR may spread between and among people, animals and through the environment, and what works to control it.

Figure 10. Ways of reducing animals' exposure and susceptibility to pathogens that may need treatment with antimicrobials



2.3.1 Support animal husbandry practices that prevent endemic diseases

There is an opportunity to move to high health production systems that result in healthier, more productive animals, better financial performance for keepers of farmed animals and reduced need for antibiotics.

Optimising biosecurity and animal husbandry practices, for example, by obtaining information on the health status of bought in animals, is important in managing common disease. In the UK, we have worked with our livestock industry and animal keepers to raise awareness of the importance of preventing disease. In partnership, we have developed standards on animal welfare and responsible use of medicines, and work collaboratively to ensure those standards are met.

A range of husbandry practices are already known across the UK and there is an opportunity to encourage their uptake (for example, see 'Colostrum protection' case study). The challenge is changing the culture of livestock keeper towards disease prevention. We want to encourage industry, retailers and researchers to keep consistently applying known interventions and, as more evidence becomes available, to work with them to refine existing guidance and develop livestock sector-specific advice. We also need to understand how we can promote uptake of effective practices by animal owners.

Understanding the cost-effectiveness of any new intervention is also important. The need to adopt practices that reduce antibiotic use may be clear to society; but the investment required by farmers is yet to be formally evaluated in the UK. While there are undoubtedly productivity benefits in tackling livestock disease, insidious diseases are difficult to quantify and so the cost-benefit of intervention is unclear. Faced with uncertain markets and narrow

profit margins, many farmers lack the incentive to invest in disease control measures without more evidence of productivity benefits.

CASE STUDY COLOSTRUM PROTECTION

If enough quality colostrum is fed to calves, piglets or lambs quickly after birth, it helps establish the animal's acquired immune system and reduces the need for antibiotics later in life.

In Powys, a new way of freezing surplus quality colostrum from calving cows and then thawing it for just-in-time use on calves has delivered dramatic results. It has improved consistency in colostrum quality (in terms of immunoglobulin concentration) and has reduced calf mortality. It is also believed to have been key in reducing antibiotic use across the whole farm business by a third in 12 months.

At a global level, as nationally, the UK supports research to improve the health and nutrition of different livestock, which reduces the risk of infection and the use of antibiotics. For example, ongoing work funded by the UK through the Consultative Group on International Agricultural Research includes investigations into how nutrition, housing and overall husbandry improves herd productivity. The UK is also involved in the International Research Consortium on Animal Health (STAR IDAZ) .

To promote animal husbandry that prevents endemic diseases, the UK will:

- Develop plans with the veterinary profession and livestock industry to improve animal health and address endemic disease issues through disease control schemes, veterinary advice and health planning, and tools for promoting knowledge transfer (such as guidance, training and communication).

- Work with the veterinary profession to encourage best practices for infection control in companion animals (pets) and horses and address infection risks specific to companion animals.

- Evaluate the impact of changes in animal husbandry practices and antibiotic use on farm economics and use the findings to promote best practice.

- Encourage regular monitored animal health planning as a key strategy for infection prevention and control in farmed animal enterprises. Review the effectiveness of animal health planning interventions to learn and disseminate best practice at regional and national level

2.3.2 Promote vaccination to prevent endemic disease

Vaccination is a widely recognised way of preventing infection in animals (see 'Salmon success' case study), when supported by good hygiene, biosecurity and management practices.

There may not be a vaccine for every disease in every animal, but there are readily available vaccines to control a broad range of infectious diseases in animals. There is scope to improve their uptake; and to explore alternatives to antibiotics in animals and aquaculture.

The first step must be understanding why farmers choose not to vaccinate their animals (including fish). This includes identifying the extent to which veterinarians promote vaccination and investigating the barriers where vaccine use is low.

CASE STUDY SALMON SUCCESS

In the 1980s, thousands of Scottish farmed salmon got infected with furunculosis, a bacterial fish disease. At the time, there was no effective vaccine and farmers were advised to use antibiotics to control the disease.

Acknowledging that such widescale use of antibiotics was not sustainable, (or responsible in the long term) the Scottish Salmon Producers Organisation worked with academia and the UK government to develop an effective vaccine that was commercially viable and practically feasible.

It took several years, but a workable and effective vaccine was produced and today, nearly all Scottish salmon are vaccinated and the use of antibiotics to treat furunculosis has been virtually eliminated.

To promote vaccination to prevent endemic disease, the UK will:

- Identify the barriers to veterinarians promoting vaccines, and to farmers using them; and use these to inform future actions, while recognising the need for a sector-specific approach.
- Encourage greater uptake of available vaccines.
- Explore potential alternatives to antibiotics including novel therapies, nutrition and genetics.

2.3.4 Better understand how AMR spreads between and among humans, animals and the environment

In the UK, we work with industry to collect, analyse and share surveillance data that can monitor resistance through the food chain. Such data are vital in understanding endemic disease and informing the design of suitable interventions: knowing when and where diseases are present in the food chain can help us understand how they got there and how they can be controlled. But there are gaps in our knowledge, especially on how AMR moves between and among animals, humans and the environment.

The need to increase knowledge on how infection and resistance spread through the food chain does not only apply to policymakers or professionals. It is just as relevant to the public.

There are many activities, in the UK and elsewhere, to increase public awareness of the need for good animal health and hygiene, and how to achieve it (see e-bug case study). Mapping these initiatives could maximise the collective impact by identifying where there are gaps and by coordinating efforts.

Improving global human and animal health security is good for everyone. We will continue to mitigate the impact of infectious or emerging diseases and the spread of resistant bacteria in animals by promoting adoption of infection prevention and control in low- and middle-income countries.

CASE STUDY **E-BUG LESSON PLAN**

In 2009, a large outbreak of *E. coli* among young school children that originated at Godstone farm in Surrey prompted the e-Bug team to develop a free, interactive lesson plan for teachers on microbes and farm hygiene.

Developed and evaluated in collaboration with Farming and Countryside Education (FACE) and farmers who host educational visits for schools, the e-Bug lesson plan has been shown to significantly improve understanding among 9 to 11 year olds in England.

To better understand how AMR spreads within and between animals, humans and the environment, and how to control it, the UK will:

- Identify and address evidence and knowledge gaps on transmission pathways of AMR between animals and the environment within a systems approach.

- Improve our understanding of available disease data by working with the industry and the veterinary profession. Consider how to expand this and share at farm, regional, national and species level. Use in tandem with the development of a new Livestock Information Service to develop more targeted interventions to improve animal health and reduce antibiotic use.

- Explore options to map awareness-raising activities and support collaboration, including running collaborative campaigns to promote good animal health and measure change over time.

2.4. Minimise spread of AMR through the environment

AMR exists in natural environments around the world. But a broad range of human, animal and agricultural activities increase its prevalence, posing a potential health risk to people, animals, food sustainability and ecosystems.

Researchers suspect that heavy metals and other biocides in the environment may also promote AMR through a process known as co-selection, although this remains an evolving area of research that requires further study. Either way, it is clear is that reducing antimicrobial contamination is an important consideration in tackling the spread of AMR.

There is, however, still a lot that we do not know about AMR in the environment, including the relative importance of different sources, how it spreads (transmission pathways), what the implications are for people, animals, food and ecosystems (risks and impacts); and what the options are to reduce risks (effective interventions).

The calls for more action on antimicrobials in the environment can be heard on many fronts: in 2016, Lord O'Neill's AMR review said this topic had not received enough focus in the UK; the EU's AMR action plan, 2017,advocates strategic action on pharmaceuticals in the environment; and in 2017, the UN Environment Assembly reached consensus on the need for environmental surveillance to further understanding on antimicrobial contamination.

2.4.1 Deepen understanding about AMR in the environment

Without more research into AMR in the environment we cannot design effective interventions to minimise risk and protect public health, food production and natural ecosystems. It is critical that our policy and regulatory regimes are guided by robust evidence and scientific advice.

AMR IN THE WATER

The scale and complexity of AMR contamination of aquatic environments is widely recognised, and a subject of much study. In the past five years, almost 1000 research papers were published on AMR and the water environment. There is no question that antibiotics can be found in both final effluents and in rivers downstream of sewage treatment plants.

As the volume of academic study expands, scientists have begun to reveal the role of the environment as a pathway for humans to pollute the environment and both acquire and develop AMR.

In 2015, researchers found the first link between environmental exposure of people in British coastal waters and colonisation by resistant bacteria[2]. Surfers in the sea exposed to resistant organisms from sewage treatment works were found to carry resistant bacteria of the same genotype as those in the plants.

That is why developing an improved evidence base on AMR in the environment will be a UK priority over the next five years. This includes:

- stepping up our activity to identify and assess the sources, pathways, and exposure risks to people, animals and ecosystems;
- evaluating our regulatory regime to see how well existing regulations (for example, sludge and slurry management, see figure 11) work to control environmental contamination by antimicrobials and public health risks, and amending them where appropriate; and
- engaging with the growing community of international organisations, national action plan committees, and leading pharmaceutical companies debating AMR in the environment.

These efforts to deepen understanding must go hand in hand with action to implement surveillance systems to monitor antimicrobial presence in the environment, as advocated by the IACG "plan for action"; and initiatives to increase public awareness too.

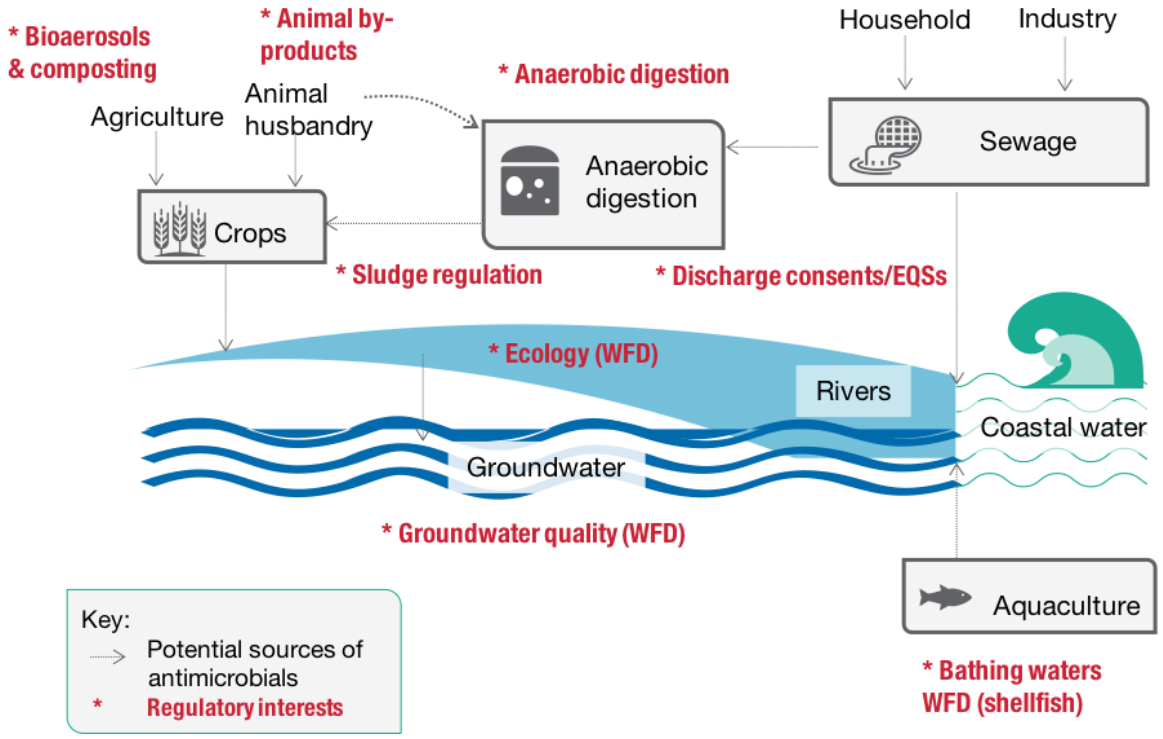
To deepen understanding about AMR in the environment, the UK will:

- Support research to reduce evidence gaps and improve understanding of the hazards and risks from AMR in the environment.

- Explore the establishment of a river catchment based research programme with clear standards for sample collection, analysis and review, with the aim of delivering AMR monitoring data that can be used to evaluate existing management interventions and inform any new policy initiatives.

- Increase public awareness of the hazard and risk of AMR in the environment.

Figure 11. Regulatory interests that impact on human sources of antimicrobials in the environment (Source: adapted from Dr Andrew Singer).



2.4.2 Minimise antimicrobial contamination

Antimicrobial contamination is found wherever antimicrobials are used. The UK is committed to maintaining EU environmental quality standards (EQSs) for priority substances under the Environmental Quality Standards Directive as amended by the Priority Substances Directive. The current Water Framework Directive's chemicals watch list includes three macrolides, a class of antibiotic. Monitoring of these across EU river basins will inform decisions by the European Commission on their prioritisation and possible inclusion in future revisions of the directives together with appropriate EQSs.

There are many sources of this and other antimicrobial contamination (including household disposal of unused antibiotics). But the emission and disposal during the manufacture of

active pharmaceutical ingredients (APIs) is of particular concern, with the UN Declaration calling on industry to employ environmentally responsible practices and the Davos declaration supporting measures to reduce environment contamination from antibiotics.

Getting international agreement on the right approach is not easy. One suggestion is to establish a voluntary certification scheme; this would require strong global collaboration to define a process, establish guidance and monitoring as well as provide capital funding to get started.

The UK supports the Access to Medicines Foundation AMR Benchmark which includes an assessment of company performance in environmental management. The AMR Benchmark highlights environmental risk management by antibiotic producers.

AMR Benchmark: environment

The AMR Benchmark ranks the efforts of the world's largest pharmaceutical companies on AMR to improve accountability, strengthen competition and drive better performance. From the latest report, published in 2018:

18 Manufacturing and production companies were analysed

15 of those companies have an environmental risk management strategy in place

8 have set discharge limits for antibiotics

0 disclose actual discharge levels

1 discloses names of third-party manufacturers

To minimise antimicrobial contamination, the UK will:

- Look to maintain in domestic legislation, the standards set by the Environmental Quality Standards Directive as amended by the Priority Substances Directive for harmful substances in the aquatic environment which might otherwise contribute to the spread of AMR; and to amend our lists of priority substances and contaminants of emerging concern (including antimicrobials) and their corresponding standards in future to take account of technical and scientific developments.

- Work with other countries to ensure responsible antimicrobial procurement from manufacturers with transparent world class environmental stewardship in their supply chains.

- Collaborate with industry to promote the development of a global environmental stewardship certification system that can distinguish responsible manufacturers of antimicrobials.

- Continue to support the AMR Benchmark to 2020 to stimulate improved accountability.

2.5. Better food safety

Food and feed can be contaminated with resistant bacteria on the farm and from various sources such as slaughter and processing. Once in food, some of these bacteria can spread AMR far and wide through trade, causing infections throughout the food chain.

Foodborne diarrhoeal diseases in themselves already pose a major health threat; the WHO estimate these diseases kill 230,000 people globally each year. Those caused by drug-resistant bacteria, such as Salmonella, pose a particular risk to human health because of possible treatment failure; bacteria like *E. coli* and *Enterococcus* spp., can carry resistance genes that can be transferred to other human pathogens, fuelling the spread of resistance even further.

Better food safety and production can help limit the contamination of foodstuffs and spread of resistance. Achieving it requires strong risk-management and a solid understanding of how AMR travels through the food chain.

2.5.1 Strengthen the evidence base for AMR and food safety

To better understand AMR in the food chain we need more evidence. This includes more research on the diversity and burden of AMR genes in foods and the gut microbiome to help quantify the AMR intake through food in the UK diet and inform risk assessments for foodborne AMR.

Strengthening the evidence base is also about having a comprehensive surveillance system of the food chain that can provide robust data to monitor the emergence, spread and decline of AMR in real time and to exchange and compare genetic data across the world.

It will take time to build such a system. And it will be expensive: a collective effort is required, involving many different stakeholders surveying numerous points in the manufacturing and retail chain, in and out of the UK. New technologies and approaches,

such as genomic surveillance, offer exciting opportunities to spot emerging AMR threats more quickly.

Research studies are needed to improve our understanding of AMR in the food chain. The UK Advisory Committee on the Microbiological Safety of Food , for example, has called for more information on the impact of processing on the presence of AMR bacteria, especially mild processing technologies, to help the Food Standards Agency (FSA) and Food Standards Scotland (FSS) better assess the safety of processed meats.

RESISTOME RESEARCH

Population-based infectious intestinal disease (IID) studies determine the burden of IID in the UK using various indicators. There have been two IID studies in the UK to date (1993–6 and 2008–9). Both focused on foodborne pathogens, rather than the specific presence of resistant bacteria in the population.

By combining archived data from the IID studies with an assessment of current resistomes (the ensemble of genes encoding AMR in a given microbiome), we have the unique opportunity of making population-based estimates of carriage of resistant microbes in the intestine over time, and how this might be impacted by changes in dietary intake.

We also need long-term surveillance data to assess the impact of reducing antimicrobial use in food producing animals, and to understand how environmental sources of AMR impact the food chain (for example, through fruit and vegetables).

To strengthen the evidence base for AMR and food safety, the UK will:

- Support a collective surveillance effort for the food chain by working with industry and exploring data-sharing options and the wider use of new technologies and approaches such as genomics.

- Explore research collaborations and partnership working to improve the scientific evidence base, including contributing to the Codex AMR taskforce.

- Do a third IID study to gather population-based data on the gut resistome.

2.5.2 Promote good practice across the food chain

In the long term, our vision is of a generational improvement in UK food hygiene leading to reduced exposure to AMR through the food chain. Getting there requires good food hygiene practices to be used by all participants in the food chain, from producers to manufacturers and suppliers to food handlers and consumers (see Figure 12).

At a global level, standards for such practices are set by the Codex Alimentarius Commission. In 2017, the commission agreed to extend and expand its code of practice for food chain actors on minimising and containing AMR and to develop new guidelines on integrated surveillance for AMR in the food chain by 2020. 2017 was also the year that Codex established an ad-hoc Intergovernmental Task Force on AMR, which aims to develop science-based guidance on managing foodborne AMR.

Figure 12. Participants in the food chain

Good hygiene is a cross-cutting theme running through the health, animal, food and environmental sectors. In the UK, the FSA and FSS lead efforts to improve food hygiene among consumers, which are largely driven by a need to avoid food poisoning. AMR presents a new challenge because it requires going beyond pathogens like Salmonella to include *E. coli*, which can lead to drug-resistant infections but not necessarily food poisoning.

There remain good opportunities to build on existing work to promote good hygiene in the kitchen, including the ‘4Cs’ messaging, cleaning (including handwashing), cooking, chilling and avoiding cross-contamination, that is used in the food sector.

To promote good practice across the food chain, the UK will:

- Assess and track the perceptions and understanding of food handlers and consumers about AMR bacteria in food and what can be done to protect people through food hygiene at home.

- Advocate for all relevant stakeholders to adopt the new code of practice for food chain actors, once developed by the Codex Alimentarius Commission.

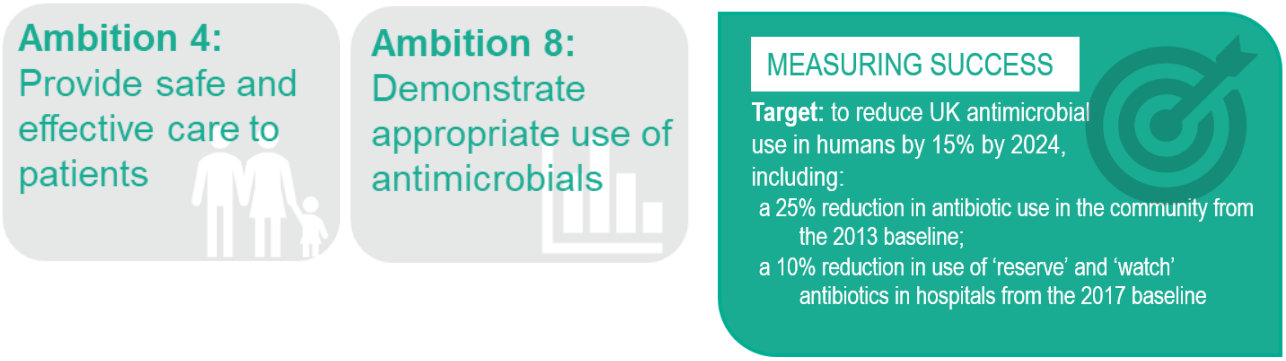
3. Optimising use of antimicrobials

Even if many infections are successfully prevented, unavoidable infections that need treatment with antimicrobials will continue to occur. Many situations will still require the use of effective antimicrobials, for example in medical procedures such as organ transplants, and in cancer chemotherapy, diabetes management and major surgery. That means optimising the use of antimicrobials to ensure people and animals take the right drug at the right time, in the right quantity, form and over the right period, is especially important.

By taking the wrong kind of antimicrobial drug, not taking them as directed, or using inappropriate concentrations of antimicrobials (either unintentionally through poor quality medicines, or in some countries, to promote growth in animals), we are helping organisms that cause infections to develop resistance the world over.

Optimising use requires strong stewardship programmes to be embedded across human and animal health and agriculture, informed by robust data and evidence collected through effective surveillance systems.

3.1. Optimal use of antimicrobials in humans



Sub-optimal use of antimicrobials in human medicine is one of the main drivers of AMR, in the UK and internationally. It occurs when patients take the wrong type or quantity of antimicrobial through misdiagnosis, over-prescription or lack of awareness as well as when low concentrations of antimicrobials are used. This is because people do not take their treatment as directed or, in countries where regulation is poor, buying only a day's supply at a time in markets and using poor quality medicines.

The UK prescribes fewer antibiotics than the average of comparator countries tracked by the OECD. But we still prescribe around twice as many antibiotics as parts of Scandinavia and the Netherlands. Modelling studies suggest that at least 20% of the antibiotics prescribed in UK primary care are inappropriate. Worryingly, the real figure may be much higher because many prescriptions lack a diagnostic code. There is also variation in antibiotic prescribing between healthcare organisations in both the community and hospital settings. There is no evidence to explain this variation and reducing variation between organisations should be a priority focus for enhanced actions.

3.1.2 Strengthen stewardship programmes

While access to antimicrobials continues to be limited in many LMICs, stewardship programmes play an important role in ensuring that antimicrobials are only used when appropriate. They include many of the actions described in Section 2 above on IPC, as well as other factors such as leadership commitment, accountability, education, training and communications, and robust auditing and feedback. Regulatory frameworks also have a big role in supporting stewardship programmes.

In the UK, we have stewardship programmes in place for both primary and secondary care settings, comprising a range of activities and resources to ensure antimicrobials are used appropriately and improve prescribing behaviours.

DIAGNOSTIC STEWARDSHIP

Stewardship programmes are needed for both therapeutics and diagnostics.

Good diagnostic stewardship promotes appropriate, timely testing (including specimen collection, pathogen identification and antibiotic susceptibility, and audited reporting of results) to guide care. It discourages tests that are unnecessary or that can yield misleading results; and it uses microbiological data to inform local treatment guidelines and AMR control strategies.

These include, for example, the identification and categorisation of essential antibiotics using the WHO's 'AWaRe' index (see Figure 4).

The NHS' increasing deployment of clinical pharmacists working in primary care, including within care homes and GP practices, offers new opportunities for enhancing antimicrobial stewardship through knowledge exchange and learning.

These pharmacists also represent a key link to primary care pharmacists, who have a critical role in reviewing prescriptions for antimicrobials and challenging those that may be inappropriate. The rise in electronic prescribing in secondary care additionally presents opportunities to support stewardship, as a source of data for healthcare providers to track prescribing rates and guidance compliance, and potentially link prescribing activity to outcomes through linked datasets.

Increasing public awareness of AMR to reduce expectations of being prescribed antibiotics is a big component of many stewardship programmes, including those in the UK. We run various public health campaigns to promote behaviour change, and support diverse educational resources, such as those published through TARGET, Health Education England, and the Antibiotic Guardian campaign.

Our stewardship activities are not just focussed on reducing prescribing but also ensuring timely treatment where rapid treatment with antibiotics is essential to save lives and reduce the long-term consequences of serious infection, for example from sepsis. Since publication of the 2015 cross-system Sepsis Action Plan, we have increased the number of patients being screened and treated for sepsis and, importantly, through the combined sepsis and AMR Commissioning for Quality and Innovation (CQUIN), increased the number of inpatients who have a clinical antibiotic review between 24-72 hours, reducing the use of broad-spectrum antibiotics.

Greater interoperability of patient data, and provision of information in real-time, will go further in supporting antibiotic stewardship.

To strengthen stewardship programmes, the UK will:

- Develop a patient-level prescribing and resistance data source (including health and infection outcome and impact data) with timely access at point of care to support clinical decision making along with access to NICE guidance.

- Enhance the role of pharmacists in primary care to review the dose and duration of antimicrobial prescriptions (especially long-term or repeat ones) and work with prescribers to review those that are inappropriate through evidence-based, system-wide interventions.

- Raise public awareness to encourage self-care and reduce expectations of antibiotics.

3.1.3 Improve data management

Being able to access and evaluate robust data, including the coding and recording of diagnoses, prescriptions and outcomes in both primary and secondary care, helps us understand prescribing behaviours and identify where and how practice might be changed and improves the effectiveness of clinical decision support tools which rely upon accurate coding.

In England, we are accelerating the uptake of electronic prescribing in secondary care. This makes it easier to access information about prescribing decisions, although a lack of data at the patient level on diagnostic code and indication means it is still hard to evaluate the extent to which diagnostic tools and guidelines are being used to support those decisions. In Scotland, electronic prescribing is being implemented in acute hospitals on a rolling programme and unique patient identifiers across primary and secondary care have been used to support national surveillance and evaluate changes in antimicrobial use.

In both countries, clinical and prescribing data remain underexploited. Linking and analysing datasets should lead to new insights on the dynamics of resistant infections, as well as allowing better monitoring of antimicrobial use.

To improve data management, the UK will:

- Require all infection consultations to record an appropriate diagnostic code, and be subject to audit.

- Ensure that all NHS hospitals have electronic prescribing systems within the electronic health record by 2025, and that these systems support and drive good antimicrobial stewardship by coding, auditing and providing feedback for surveillance.

- Use electronic prescribing data to give healthcare providers feedback on guidance compliance and prescribing rates.

- Use sentinel general practice surveillance linked to hospital data to monitor the impact of fewer prescriptions for antimicrobials.

- Increase training to ensure death certification correctly records AMR.

3.1.4 Promote evidence-based guidance and interventions

Antibiotics have been available for decades, but gaps remain in our knowledge on their use, particularly when it comes to knowing the best dose, duration and route of

administration to use for certain infections. For example, it was only relatively recently that the guidance for treating uncomplicated urinary tract infections (UTIs) recently changed from seven to three days. There is clearly a balance to be struck between adequately treating the infection and not treating for longer than necessary; in many cases, that balance will vary according to individual circumstances and requires further research.

There is some evidence to suggest that increasing the diversity of prescribed antibiotics may reduce resistance. This suggests we need to continue to increase the diversity of antibiotic prescribing. At the same time, we must carry out further studies to quantify the effectiveness of such strategies.

CASE STUDY **NHS England QP (Quality Premium) and CQUIN (Commissioning for Quality and Innovation)**

Quality Premium in primary care from 2015
Year 1: 96% CCGs met or exceeded the target of a 1% reduction in prescribing from a 2013/14 baseline delivering an 8.3% reduction nationally, or the equivalent of 2.7 million antibiotic items.

Year 2: 88% CGGs met or exceeded a 'stretch' reduction target of 4% from baseline.

After 2 years, prescribing of **'broad spectrum**' antibiotics had **reduced by 23%;** a reduction of 904,881 items.

Total payments made to CCGs: £15.9m; total prescription and dispensing costs avoided estimated at £19.3m.

CQUIN in secondary care from 2016/17
Year 1: 0.6% reduction in hospitals' total consumption of antibiotics, **7.8% reduction in "antibiotics of last resort"** carbapenems and piperacillin/tazobactam; **88%** of antibiotic prescriptions **reviewed within 72 hours** of first being administered.

Year 2: complications with supply chains led to a year-on-year increase of 4.7% in total antibiotic consumption. Carbapenem and piperacillin/tazobactam consumption continued to fall.

The CQUIN has identified outliers and has made it easier to set improvement targets for secondary care providers.

Knowing how best to influence practitioner and patient behaviour is another area where we could use more evidence. We know some interventions work well, for example incentive schemes such as Scotland's quality indicators and NHS England QP (Quality Premium) and CQUIN, both of which offer CCGs and acute care providers incentives to reduce antibiotic prescribing.

But to improve our evidence base we must also foster innovative approaches, for example those that use behavioural and social sciences to explore the drivers of sub-optimal practice, or those arise through local and regional quality improvement initiatives (for example, see box ‘To dip or not to dip’, and Figure 13).

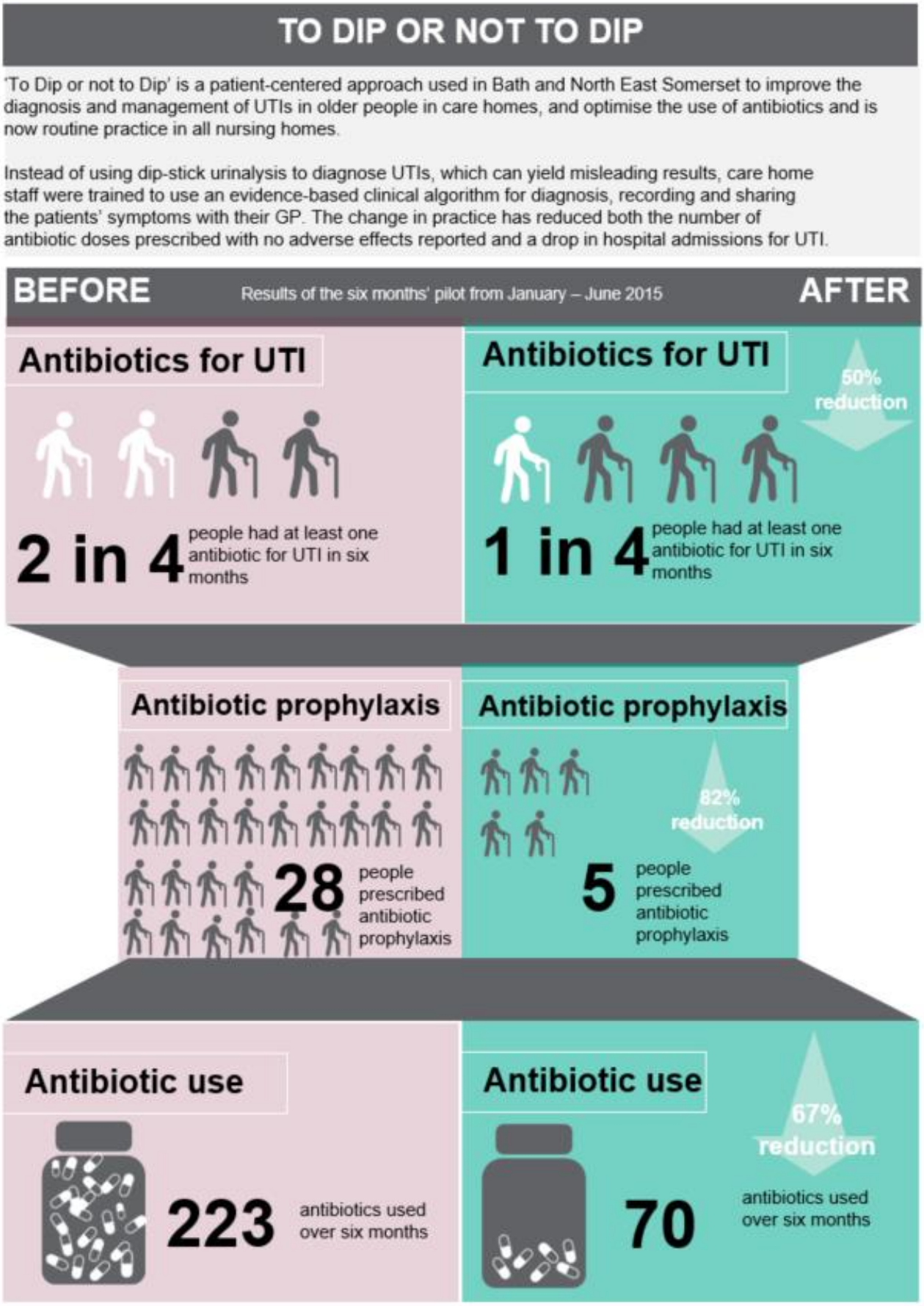
To promote evidence-based guidance and interventions, the UK will:

- Support multidisciplinary research to identify which AMR interventions work to reduce antimicrobial use at different levels and in different contexts.

- Test and implement national and local behaviour change interventions to nudge improved antibiotic prescribing and consumption using behavioural science.

- Work with global partners to commission and implement evidence-based guidance (including health technology assessments) to optimise infection management for all common infections and syndromes.

Figure 13. Results of the six months pilot for the improvement programme 'To dip or not to dip' (January to June 2015)



3.2. Optimal use of antimicrobials in animals and agriculture

Ambition 5: Protect animal health and welfare

Ambition 8: Demonstrate appropriate use of antimicrobials

MEASURING SUCCESS

Target: to reduce UK antibiotic use in food-producing animals by 25% between 2016 and 2020 through implementation of industry targets; and define new objectives for individual animal sectors by 2021.

As in humans, the sub-optimal use of antimicrobials in agriculture and veterinary practice contributes to the rise and spread of AMR all over the world.

In the UK, although good data on overall antibiotic use is now available for many livestock sectors, it can be improved in others. There is also a need for more information on various related factors such as reasons for treatment, demographic, disease and treatment history.

That means that alongside strong antimicrobial stewardship, there is a clear need for more robust data on how antimicrobials are used to improve our understanding of the links between animal health and welfare, productivity, drug usage and resistance and to provide the evidence we need to design effective interventions and controls.

3.2.1 Strengthen stewardship for responsible use

From setting targets to sharing best practice to raising awareness, there are many ways of encouraging the responsible use of antibiotics in agriculture and animals. At a global level, we help explore and evaluate options by working with international partners, promoting stewardship initiatives for new and existing antibiotics and helping countries improve their regulation of antibiotics.

CASE STUDY STERILE SURGERY

In 2010-11, the vet charity People's Dispensary for Sick Animals (PDSA) significantly reduced its use of antibiotics peri-operatively after introducing a routine sterile surgery protocol stating that antibiotics should only be used in certain circumstances.

There was no increase in post-operative complications.

In the UK, we similarly use a range of tactics. This includes supporting innovative approaches and proven interventions (see ‘Sterile surgery protocol', 'Targeted medication', and 'Communications for change'). Most recently, the Veterinary Medicines Directorate of Defra has worked with the livestock industry and the veterinary profession to set voluntary targets for reducing antibiotic use in eight food-producing animal sectors (see ‘Improving infection prevention and control practices’ in Section 1 above).

CASE STUDY TARGETED MEDICATION

In 2015, a targeted medication technique was used in Wiltshire to successfully eliminate the common respiratory disease Enzoonotic Pneumonia (EP) from six large outdoor pig herds totalling 5,000 sows.

Each sow was prescribed 31g of active antibiotic which was administered under veterinary prescription in the feed over a six-week period. Strict rules on biosecurity, minimum age at start of treatment, and pig movements were observed throughout.

By the end of the intervention, EP had completely vanished from all six herds, which remain test-negative more than two years later. In effect, the treatment got rid of the disease reservoir and in so doing, the need to treat the 125,000 piglets produced by the sows each year. That, in turn, has reduced average antibiotic use from 120mg/kg to less than 30mg/kg.

Our commitment to responsible use means that we have reduced our sales of antibiotics for livestock by 40% over the past five years to 37mg/kg: we fall well below the 2016 European average of 125 mg/kg. Building on this achievement, we will reduce UK antibiotic use in food producing animals a further 25% between 2016 and 2020 through the livestock sectors implementation of actions to achieve the targets they have set; the livestock sector targets will be under continued review. To make more progress we now need to assess prescribing practices and work with industry to develop evidence-based tools that can better guide these practices (including finding quicker and more reliable diagnostics tools). We also need to explore business models that can make better use of veterinary expertise in optimising antibiotic use.

CASE STUDY COMMUNICATIONS FOR CHANGE

In south-west England, a prolonged communications campaign by a farm veterinary practice has effectively improved antibiotic use on dairy farms.

The campaign, which was launched by large animal veterinary surgeons at Friars Moor Livestock Health in 2015, was designed to limit the veterinary use of the highest-priority 'critically important antibiotics' and to increase uptake of selective dry cow therapy.

The surgeons worked with researchers to share best practice, identify alternative treatment protocols and develop technical and case study information for dairy farmers. Using farm disease incidence and medicines sales data, the team were able to engage dairy farmers one-to-one. Enthusiasm for change was spurred by reduced treatment costs.

By 2017, the practice pharmacy no longer stocked third or fourth generation cephalosporins or fluoroquinolones, with no report of treatment being impeded as a result. Today, farmers continue to discuss the issue with their vets, and antibiotic use has become a central pillar in all farmer meetings and training. The practice is now planning to drive antibiotic use down even further by promoting alternatives to antibiotics such as vaccination and improved calf management.

To strengthen stewardship for responsible use, the UK will:

- Work with industry to develop appropriate training, guidance and other communications for antimicrobial users and prescribers to encourage the uptake of recommended practices and evaluate their impact.

- Explore, in collaboration with industry, options to develop rapid and reliable diagnostic tools to inform veterinarians' prescribing decisions; and promote the uptake of these tools.

3.2.2 Improve data and control

Robust data and control mechanisms are critical in shaping evidence-based policy and practice. Yet globally there are few comparable data available for antibiotic use in animals. In Europe, the only antibiotic use data available for inter-country comparisons are 'sales of veterinary antibiotics', which do not distinguish between different animal species. Domestically, there is a need to improve the availability and quality of data (both on

species-specific antibiotic use as well as related factors such as reasons for treatment and outcomes).

In the UK, we continue to develop and coordinate data collection systems to monitor antibiotic use in different animals, with systems now in place covering a high percentage of the sector for the pig, meat, poultry, laying hen, gamebird, salmon and trout industries, and in development for others (dairy, cattle and sheep). We also collect data on veterinary sales of antibiotics, which, can be used to validate antibiotic use data. These systems should allow both veterinarians and farmers to benchmark their use and review their approach to antibiotic use, such as the one set up for the pig industry. These systems may make it possible to identify risk factors for higher use and practices that contribute to lower use.

MONITORING PETS AND HORSES

Responsible prescribing and use of antibiotics in pets and horses is especially important because of the close relationship they have with their owners.

More evidence and improved monitoring are needed to understand how using different antibiotics (including highest priority critically important ones) in pets and horses impacts the selection of resistant bacteria of concern to public and animal health.

With the advent of more data and better understanding, it is important to review and update control mechanisms to make sure these are rooted in the latest evidence. The UK currently follows EU controls for veterinary antibiotics sales and distribution, which are set out in the veterinary medicines and medicated feed legislation. The legislation has been revised and the new proposals are to be adopted in early 2019.

CASE STUDY ELECTRONIC MEDICINE BOOK FOR PIGS

In the pig sector, the electronic medicine book (eMB-pigs) was developed by the Agriculture and Horticulture Development Board with support from the Veterinary Medicines Directorate and launched in April 2016. eMB-pigs allows farmers to add their antibiotic usage data on a quarterly basis. This has become a requirement under the key farm assurance schemes Red Tractor and Quality Meat Scotland. eMB-pigs now allows farms to benchmark their antibiotic use with similar farms across the UK, which helps stimulate the vet-farmer conversation and encourage higher users to review their approach to antibiotic use. The latest 2017 data from eMB represents 87% pig production and shows that the sector has reduced use by 53% over the last two years."

To improve data and control, the UK will:

- Improve the data available on levels of antimicrobials used in main livestock sectors and work with industry to review, refine and implement sector-specific targets.

- Explore and work with existing systems that are monitoring the use of antibiotics and AMR in companion animals and horses to refine our understanding of the situation in these sectors; and report on collective use of antibiotics in household companion animals.

- Aligning with EU legislation, we will implement the provisions of the new EU Veterinary Medicines legislation on the use of antibiotics, subject to the official public consultation process and through collaboration with stakeholders to agree how it can be applied in practice.

- Work with global partners to build regulatory capacity in LMICs' animal health sectors (by supporting control options for manufacturing, authorising, distributing, marketing, inspecting and surveying use of veterinary medicines).

3.3. Stronger laboratory capacity and surveillance of AMR in humans

To better understand and respond to AMR patterns and drivers, we need to collect clinical and economic information on AMR related disease burdens and antimicrobial use at a national level and share it to build a global picture. Some countries are better equipped for the task than others.

Across the UK, the NHS collects a wealth of data and has many reporting guidelines in place to support surveillance. But important gaps remain, including a lack of robust diagnostic datasets in the community and limited surveillance of surgical site infections. Surveillance guidelines are not consistently applied and data can similarly be collected inconsistently across individual laboratories and IT systems.

3.3.1 Harmonise data collection and use

For AMR data to be truly useful it needs to be both comparable and coherent, across time, space and sector.

At a global level, the UK supports many surveillance initiatives to help harmonise the way data is collected and shared, including:

- Grants to individual countries to support health system strengthening, including surveillance.
- Participation in the Global Antimicrobial Resistance Surveillance System (GLASS) that promotes standardised approaches to global AMR data collection, analysis and sharing.
- Aligning AMR agendas with existing mechanisms through the International Health Regulations (2005).
- Promoting the development of an international reference centre collaborative for One-Health AMR surveillance.

We also work to build capacity for strong surveillance in LMICs (see ‘Supporting global alignment’ and ‘Grant for Ghana’).

CASE STUDY GRANT FOR GHANA

Through a Fleming Fund country grant, the UK is helping Ghana implement its NAP on AMR within the wider context of UK support for Ghana health system strengthening. In particular, the fund is supporting Ghana to collect, analyse and share data on AMR and antimicrobial use in humans and animals.

Key activities supported by the grant include:

- Development and use of the FAO Assessment Tool for Laboratories and Antimicrobial resistance Surveillance Systems (ATLASS).
- ATLASS tool to facilitate the assessment of capability in veterinary laboratories; giving a baseline level to support plans for capacity building.
- Participating in the WHO Tricycle Protocol for surveying drug-resistant *E. coli* in humans, animals and environments.
- Setting up of governance structures to strengthen the Ghana Food and Drugs Authority as it accesses data on antimicrobial use.
- Providing technical information and recommendations for the Ghana AMR Platform, a national information resource.

Fleming Fund funding has also been used to help the government review its regulatory frameworks for antibiotic use and management.

In the UK, standard reporting guidelines specify which organisms to report and how, although these are not always applied consistently. To ensure data is comparable across the whole NHS and continue to align across countries, laboratories should only use the latest EU agreed antibiotic sensitivity breakpoints to determine resistance. Similarly, new surveillance approaches such as genomics should be coordinated and optimised.

When it comes to diagnostic data, the inconsistencies across laboratories are even greater: the lack of standardised IT systems and coding means test results are recorded differently in different laboratories.

The NHS has set a 2020 deadline for all computer data systems involved in patient care to use the standard SnoMed Clinical Terms coding system. Most microbiology laboratories, however, have yet to adopt the standard.

To support cross-sector analysis, the UK publishes a One-Health surveillance report every two years that includes data on antibiotic resistance and use for animals and humans.

To harmonise data collection and use, the UK will:

- Implement universal data coding (using SnoMed) and interoperability of data systems across health and social care.
- Further develop standard, evidence-based laboratory testing practice and reporting guidelines, mandating their use where appropriate.
- Work with global partners to promote the establishment of a One-Health reference centre collaborative to better harmonise data on common or emerging threats.

3.3.2 Enhance existing data and guidelines

There is little doubt that there are opportunities to build on, or make more use of, our existing datasets to improve our understanding of resistance and to better target interventions.

CASE STUDY ENHANCED SURVEILLANCE

In Scotland, enhanced surveillance programmes for *Staphylococcus aureus* and *E. coli* bacteraemia are mandatory, implemented by trained data collectors, using nationally agreed definitions. These programmes have been critical in:

- identifying patient population risk factors in the community and different healthcare settings;
- informing a focused approach to reducing infections in local and national improvement plans; and
- providing data for epidemiological patient-related Whole Genome Sequencing research in collaboration with two Scottish Universities.

This includes using existing data to:

- **Optimise surveillance**, using electronic patient records and data links to optimise systematic surveillance for high-risk infection sites, such as abdominal surgery, to identify resistance hot spots and emerging patterns.

- **Demonstrate impact**, for example linking diagnostic/ indication codes to electronic prescribing and medicines administration systems and other clinical datasets to demonstrate the impact of diagnostics on prescribing and clinical outcomes.

- **Share learning and best practice**, including sharing AMR guidelines, educational resources and data through a single information portal that can be easily accessed by healthcare professionals and the public alike to learn about AMR, detect emergent problems, assess trends and monitor local and national progress.

To enhance existing data and guidelines, the UK will:

- Promote adherence to existing guidelines through accrediting and professional bodies, and commissioning processes, within a strengthened regulatory framework.

- Maximise use of existing datasets to understand resistance hotspots by developing new surveillance methods and infrastructure to detect the emerging drug resistance.

- Use patient e-records and data links to optimise surveillance of community and healthcare-associated infections (including surgical site infection).

- Develop a single UK portal as a source of data and information on AMR.

3.4. Stronger laboratory capacity and surveillance of AMR in animals

Reliable surveillance schemes that collect data on antimicrobial use and resistance in animals and agriculture are needed to guide treatment and prescribing, detect the emergence of AMR threats, identify animal populations at risk, evaluate trends, inform policy development and assess the impact of interventions.

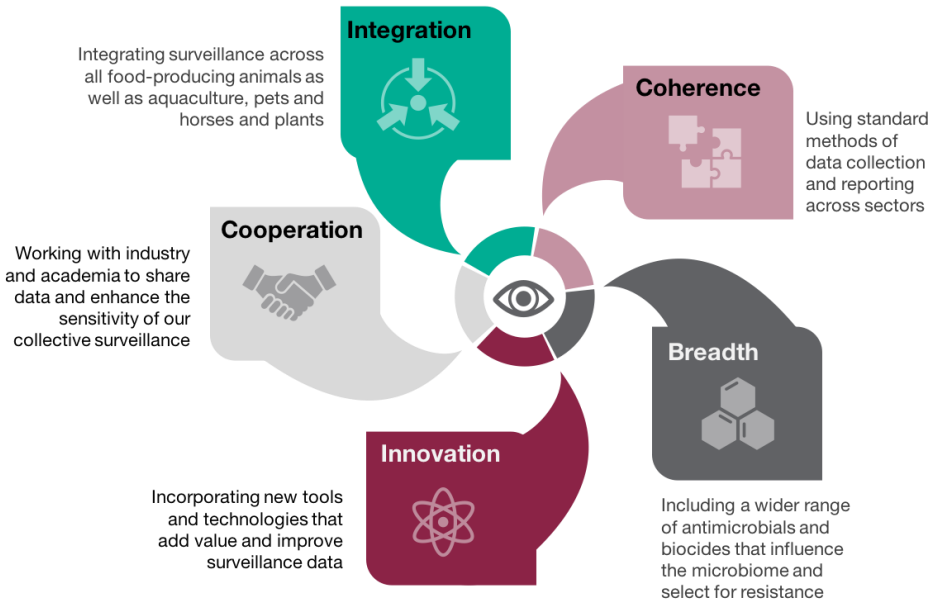
At a global level, many countries do not have systems in place to monitor AMR in zoonotic pathogens or pathogens of animal health concern and detailed data on antibiotic use are lacking.

In the UK, we have various schemes for monitoring antibiotic use and resistance in different animal sectors. In the future, these surveillance schemes should, in addition to food-producing animals, cover aquaculture, pets and horses and, in the longer term, plants. It should include:

- monitoring infectious disease in domestic animals;
- monitoring AMR levels and patterns in zoonotic and animal pathogens of greatest concern;
- monitoring trends in antibiotics used in animal and plant health, including sales and imports/ exports; and
- monitoring samples from food-producing animals for residues of veterinary medicines and prohibited substances.

These schemes need to be integrated, standardised and harmonised across human, agriculture and environment sectors to support high-level and cross-sectoral analyses. Harmonisation will make data more easily used, compared and shared at national and international levels and will support the development of stronger laboratory capacity and surveillance (see Figure 14).

Figure 14. Five dimensions to strengthening surveillance.



We will explore how to coordinate and harmonise surveillance schemes across the different sectors (human, animal, food and environment), taking a One-Health approach to provide a more complete picture of antimicrobial use and AMR that will enable analysis of trends over time and across sectors.

To strengthen laboratory capacity and surveillance of AMR in animals, the UK will:

- Explore how to coordinate and integrate surveillance schemes to provide a more complete picture of antibiotic resistance, use and residues that can facilitate analysis of trends over time and across animal sectors.

- Work with the private sector, industry and academia to develop ways to share data to enhance the sensitivity of our surveillance systems for antibiotic resistance and use.

- Explore options for including new monitoring tools, such as whole genome sequencing and other molecular-based methods, to improve and add value to our surveillance data.

- Explore ways of using UK surveillance data to better understand AMR transmission pathways between animals, environment and humans.

- Work with global partners to promote the establishment of surveillance systems overseas, and establish an international AMR One-Health UK reference centre to work within an international collaborative to better harmonise and integrate data on common or emerging threats across human, animal, food and environment sectors.

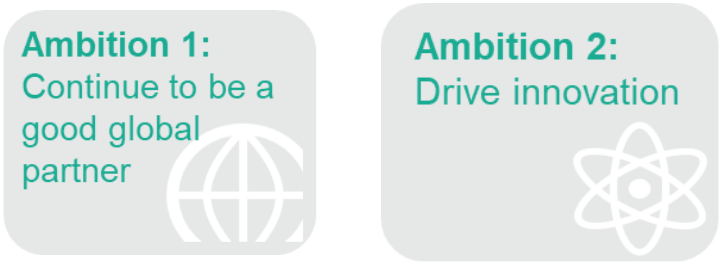
- Further develop harmonised One-Health AMR surveillance including laboratory methodologies and reporting approaches.

4. Investing in innovation, supply and access to tackle AMR

Reducing the need for antimicrobials and optimising their use will slow down the rise and spread of resistance. But evolution will inevitably lead to more resistance. That is why any effort to tackle AMR must include a focus on improving the development of, and access to, good quality old and new antimicrobials, vaccines diagnostics and infection prevention and control products, as well as promoting alternatives to antibiotics.

Investing in research is critical: not only for new product development but also to support predictive modelling, interdisciplinary analyses and intervention research that can help inform effective AMR interventions and strategies.

4.1. Sustainable investment in basic research



Despite high levels of coordination, collaboration and investment in basic research for AMR, gaps remain.

We still do not know much about AMR in the environment; innovation in IPC is low, as is research to improve protein yield in food production; and drug pipelines remain weak. There is also a pressing need for interdisciplinary research to better prioritise and understand which AMR interventions work for which populations, where and when.

4.1.1 Provide strategic leadership in AMR research

The UK already has a pivotal role in leading AMR research, both basic research and intervention research.

Since 2014 the UK Government has invested more than £360 million in research and development on AMR, coordinated through the AMR Funders' Forum. This includes £117 million interdisciplinary AMR research and infrastructure. It also includes the £50 million GAMRIF fund, which runs until 2021, and funds various projects to support innovation in product development, £55 million of capital funding, and the £85 million UKRI initiative, which has built a portfolio of national and international interdisciplinary research projects.

Funding has been committed through the NIHR, in clinical and applied health research to evaluate public health measures, health care interventions and health services addressing the use of antimicrobial drugs. The UK also emphasises the need for this kind of intervention research in global AMR fora.

In all areas, it is important that we continue to align our efforts with globally agreed research strategies to avoid unneeded duplication of effort and ensure the world's collective priorities are effectively covered.

Internationally, the UK supports product development research for drugs, vaccines, diagnostics and insecticides for the diseases of poverty through ten public-private product development partnerships (PDPs). PDPs are designed to stimulate research and development where market incentives are insufficient. They prioritise public health need over profit and work in partnership with a wide range of different organisations, covering the public, private and philanthropic sectors.

To provide strategic leadership in AMR research, the UK will:

- Support coordinated AMR related research on priority areas, including TB.
- Continue to influence global research strategies on AMR-related topics through JPIAMR and the Global AMR R&D Hub, ensuring the alignment of UK-funded research, and emphasising the need for research to be useful for front-line teams.
- Keep supporting successful product development partnerships; and evaluate the effectiveness of current investments to inform future investment decisions.

4.1.2 Strengthen insight and capacity for doing high-quality research

The discovery and development of new health products and technologies requires time and expertise. We need to continue our efforts to provide the right incentives, and promote industry investment, to further strengthen the UK's capacity for the task. This matters also for global efforts to combat infections with epidemic potential, captured by the WHO Priority Pathogens List .

At the same time, we need to boost our scientific skills in related fields and disciplines and improve our ability to identify, prioritise and embed effective and sustainable interventions that produce change at scale. Being able to build predictive models of the UK AMR system and its core components will be essential, as this will enable us to direct our efforts to best effect.

We have made some progress, developing a qualitative AMR systems map in 2014 to visualise the factors influencing AMR development and how these interact. Now we need to quantify the map, make it country-specific and dynamic, and make it predictive. This will require the combined efforts of experts across many different disciplines, including sector specialists, modellers, geographers, designers, social and economic scientists, generating and synthesising evidence from across the human, animal, food and environment sectors

To strengthen our insight and capacity for doing high-quality research, the UK will:

- Continue to develop the scientific capacity needed to support and deliver ongoing high-quality research in infectious disease, prevention and microbiology-related disciplines.

- Develop multidisciplinary networks to better undertake predictive analysis and inform interventions across all sectors.

4.2. Development of new therapeutics

Antimicrobial pipelines are slow. It has been more than 30 years since the last new class of antibiotics was discovered and came into routine treatment. Across the 30 companies analysed in the 2018 AMR Benchmark, there are 276 antimicrobial R&D projects in place, but only 28 of these are for antibiotics in late stages of clinical development (Figure 15 overleaf').

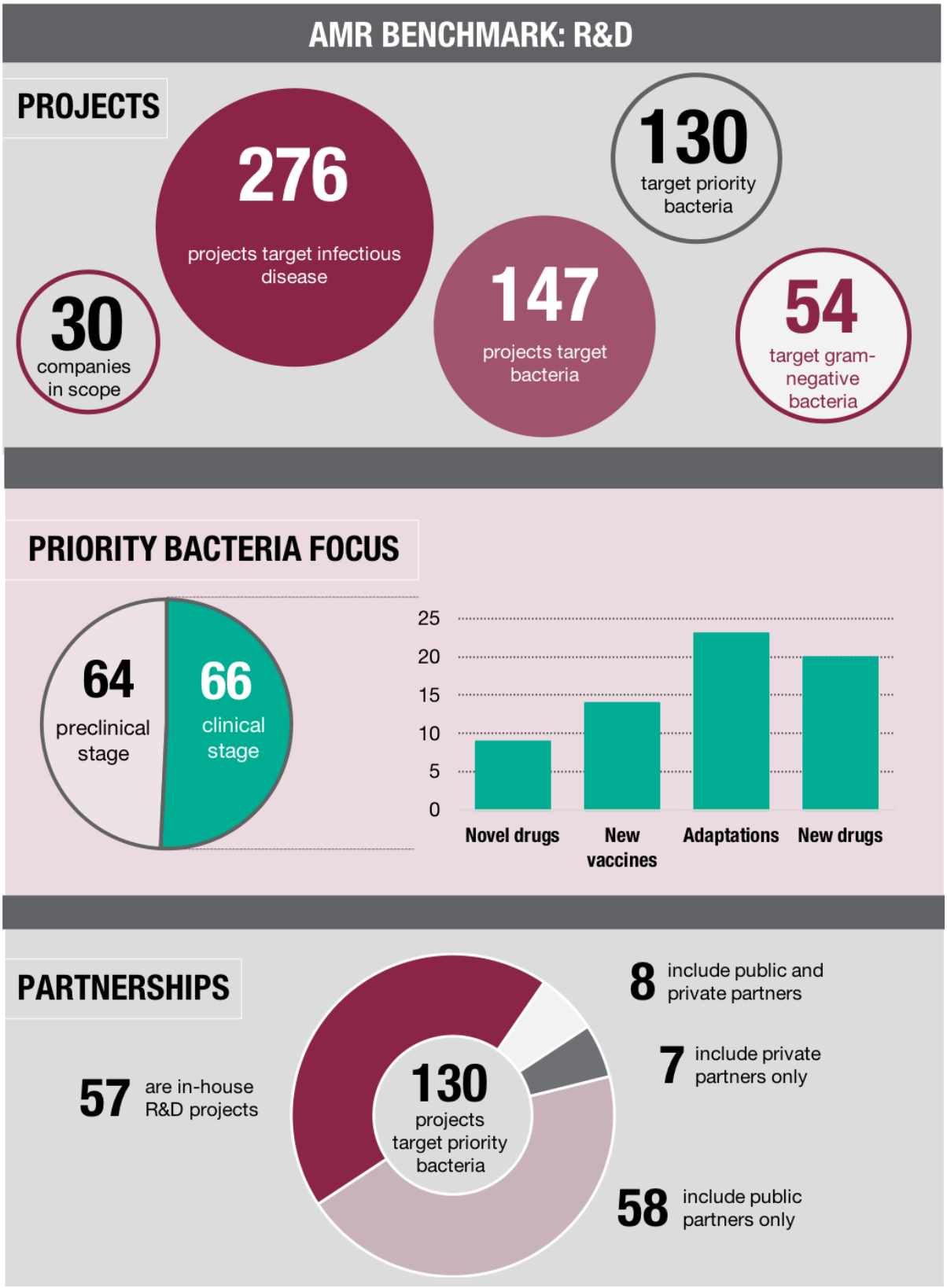
An analysis of the global antibacterial pipeline in support of the GAP was published in Lancet Infectious Disease in October 2018. The study looked for new drugs active against pathogens included in the WHO priority pathogen list. It concluded that there was limited innovation and new antibacterial drugs without pre-existing cross-resistance are under-represented and urgently needed, especially for geographical regions with high resistance rates among Gram-negative bacteria.

The scientific challenges of developing new therapeutics are significant. And the financial costs are high. And yet we urgently need alternatives to replace those that are no longer effective. Many common diseases, including TB, sexually transmitted diseases, UTIs, pneumonia, blood-stream infections and food poisoning, can already resist a wide range of antimicrobial drugs. Some strains of TB and gonorrhoea can resist even 'last line' antibiotics, which makes them effectively untreatable.

Establishing a more robust pipeline requires:

- diverse starting points supported by investigations of bacterial virulence factors, disease mechanisms, and novel therapeutic targets;
- a better understanding of the host response and the microbiome; and
- studies of alternative strategies including novel chemistry, the use of antibodies, innate immunity stimulation, countering resistance mechanisms, and the mining of natural products.

Figure 15. A selection of findings from the 2018 AMR Benchmark report.



More importantly perhaps, ensuring the development of new therapeutics means finding a way to bridge the large gap that exists between the commercial returns to developing a new treatment (which are low relative to most drugs) and their value to society (which is high).

The UK cannot solve such market failures alone, but we can catalyse efforts to address the problems at an international level and work to change the incentives to improve the rewards for investment within our domestic market. This includes, for example, supporting a broader range of companies to engage in R&D or benchmarking performance of big companies to stimulate positive competition (see Figure 15 above). It also includes exploring new approaches, such as de-linking the price paid for antimicrobials from the volumes sold (see Section 4.3 below), or adopting a 'pay or play' approach (see 'Pay or play').

PAY OR PLAY

The UK-funded 2016 Review on AMR, led by Lord O'Neill, the report argued that there is a strong case for companies to invest in AMR research to sustain their revenue from areas that rely on maintaining a supply of effective antibiotics, such as oncology or surgery.

It proposes that governments should consider imposing an antibiotic investment charge on the pharmaceutical sector on a 'pay or play' basis, whereby companies can choose to either pay the charge or invest it in AMR research and development.

To support the development of new therapeutics, the UK will:

- Work with international partners to agree a coordinated global system for incentivising new therapeutics.
- Establish collaboratives that link UK researchers and industry to make best use of data, information and skills.
- Support successful and emerging Product Development Partnerships for priority therapeutics.
- Invest in research in academia and businesses, including SMEs, through UKRI and other funding agencies.
- Continue to support the AMR Benchmark to stimulate improved accountability and positive competition in industry.

4.3. Wider access to therapeutics for those who need them

Globally, around two billion people lack access to safe, effective, high-quality and affordable essential medicines, including half the people living in sub-Saharan Africa. Improving access to quality therapeutics (including older, off patent drugs) for those who need them is important, not only to save lives, but also to tackle AMR. A lack of access to the right treatment option drives people to use the next best option available, leading to the misuse or sub-optimal use of drugs that fuel resistance.

Securing wider access to antimicrobials requires international action to improve global supply chains and strengthen health systems, as well as action at a national level to ensure our own procurement and supply mechanisms conserve antimicrobials and do not incentivise unnecessary use of new and existing drugs.

4.3.1 Support global initiatives to increase access

The UK remains committed to supporting wider access to antimicrobials, vaccines and alternative therapies for all who need them. We already advocate for interventions to support new therapeutics to include access and stewardship provisions. Now we also want to explore the re-development and use of older antibiotics as a route to improve access (see ‘Old drugs for human health’).

OLD DRUGS FOR HUMAN HEALTH

Many antibiotics developed during the 1950s–70s are not widely used anymore. In part because newer, more effective drugs are available and because old drugs were not as closely assessed and regulated as their modern counterparts.

Systematically re-developing some of these old antibiotics is likely to be a faster route to bringing effective treatments into use than new product development. It could even help treat bacteria that are resistant to today’s therapies.

Through UK Aid, we support global multilateral funds, such as Unitaid and the Medicines Patent Pool, that work to improve access to treatments for HIV/AIDs, TB, malaria and Hepatitis C in LMICs.

UK Aid also supports a range of partners in LMICs to strengthen health systems, support access and promote stewardship including use of national drug formularies and treatment protocols.

To support global initiatives increasing access and stewardship, the UK will:

- Include access provisions in the design of market incentives and relevant AMR-specific capacity building projects.

- Support global health initiatives to accelerate access to new health technologies, especially in LMICs.

- Work with international organisations to develop a global approach to supply and access for new and existing essential antimicrobials, advocating the development of global supply chain mapping.

- Will work with WHO, GARDP and other partners to determine economic models of optimal pricing for generic antibiotics.

- Develop and test new models for national purchasing arrangements that de-link the price paid for antimicrobials from the volumes sold, using a NICE led healthcare technology assessment to support robust stewardship.

4.3.2 Strengthen national procurement and supply

Lord O'Neill's 2016 Review on AMR argued that countries should support international action through better national purchasing arrangements that balance innovation with good stewardship. The UK is keen to demonstrate that this can be done.

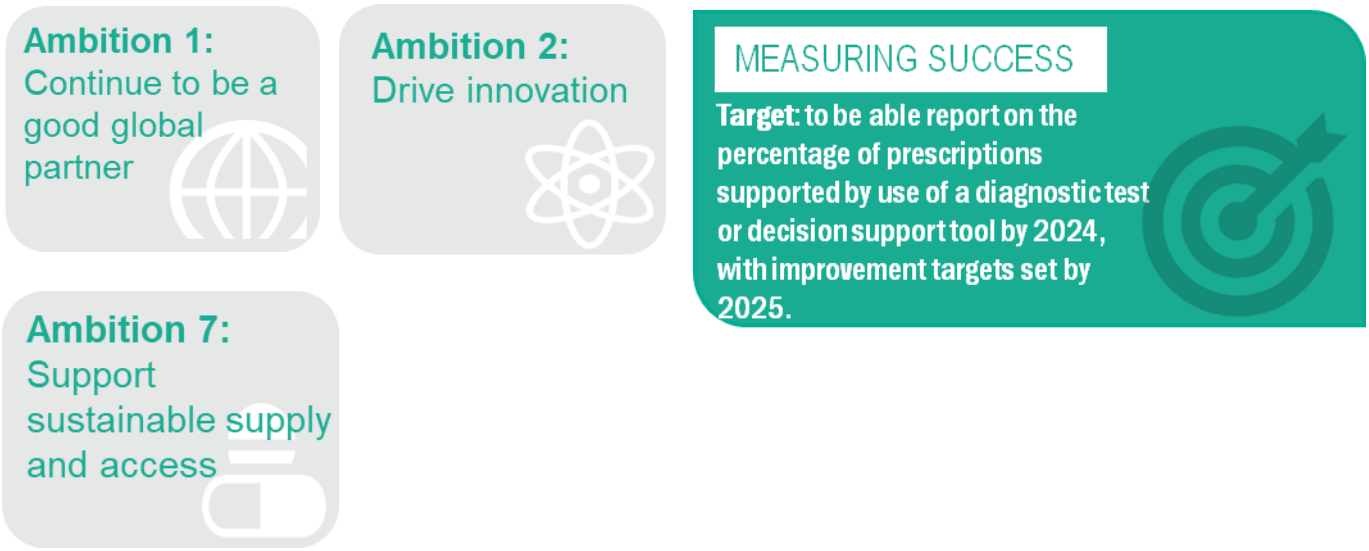
We also want to ensure our procurement and supply mechanisms strike the right balance between maintaining adequate supply with financial cost to the NHS. Avoiding shortages of critical first-line antibiotics is important to support good clinical management and make sure that health workers can prescribe the right drug, not just the one at hand. Shortages can also be very expensive: the piperacillin/tazobactam shortage in 2017 cost the NHS more than £30 million in temporary price increases.

Robust forecasting and strong supplier relations can help minimise the risk of shortages.

To strengthen national procurement and supply, the UK will:

- Assess whether our antimicrobial procurement and supply mechanisms provide the best balance between ongoing supply and financial cost to the NHS.

4.4. Development of, and access to, diagnostics



Rapid and accurate tests at the point of care help healthcare professionals identify the problem at hand and give their patients the right drug to treat it, which improves patient safety and health outcomes, as well as reducing AMR pressures. But in practice, most prescribing, supply and administration of antibiotics is carried out in the absence of any information about the nature of the infection.

In part, that's because there is no quick, reliable and affordable diagnostic test available, especially in LMICs. In part, it is also because health and agricultural systems often do not make the best use of those diagnostic tests that are available.

4.4.1 Incentivise R&D for new diagnostics

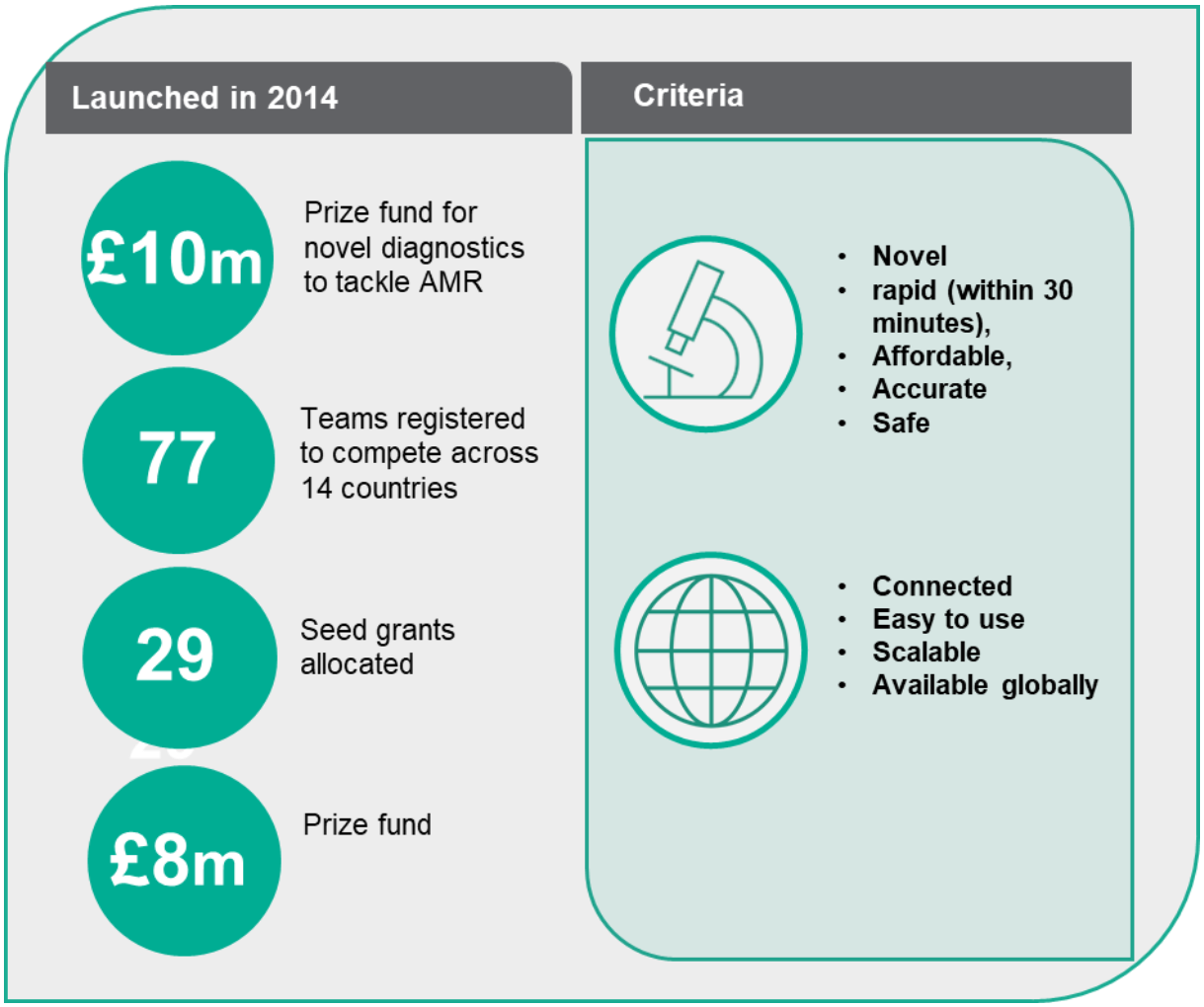
The need for new diagnostics is clear. There are gaps in the diagnostics portfolio. Research needs include identifying new biomarkers, as we still lack effective means to distinguish between bacterial and viral infections, and between commensal and pathogenic bacteria, and faster tests. For most bacterial infections, the tests that are available take approximately 48 hours to yield results, meaning that they are more often treated empirically, sometimes wrongly or unnecessarily.

Designing incentives for new diagnostic development faces similar challenges to incentivising new therapeutics. For example, existing diagnostic methods such as plate culture are generally cheap so companies are reluctant to invest in developing new ones.

These market failures need to be addressed and coupled with other activities to ensure we cover the full range of research required to deliver the type of rapid point of care testing

that can make a real difference to clinical practice. The longitude prize was launched in 2014 to incentivise the development of novel approaches (figure 16).

Figure 16. The Nesta and Innovate UK funded Longitude prize



The Office for Life Sciences, the NHS and industry are taking steps to tackle some of these challenges through implementation of the Life Sciences Industrial Strategy and the response to the Accelerated Access Review. The Life Sciences Sector Deal supports programmes under the 'From data to early diagnosis and precision medicine' challenge. The Accelerated Access Collaborative will support uptake of the most transformative innovations, including new diagnostics. The Academic Health and Science Networks have a role in improving local adoption and uptake of innovative medical technologies through the Pathway Transformation Fund. These build on existing schemes to encourage quicker patient access such as the Innovation Technology Tariff and the Innovation Scorecard which track the uptake of cost-effective new medicines approved by NICE.

To incentivise R&D for new diagnostics, the UK will:

- Address R&D gaps, including in the identification of biomarkers.
- Work with international partners to develop global plans for incentivising new diagnostics and for stimulating the behaviour change needed to realise the benefits for human and animal patients.
- Support the establishment of the Accelerated Access Collaborative and Pathway and ensure antimicrobials and diagnostics can be supported by its work.
- Work with NHS partners and industry to tackle the barriers to new innovations being adopted in the NHS, building on the Life Sciences Industrial Strategy and the response to the Accelerated Access Review.
- Prepare a 2 to 5 year urgent diagnostics priority list and use Target Product Profiles to push research and development.
- Introduce incentives to develop and evaluate rapid diagnostics.
- Support existing and emerging PDPs for new diagnostics, including through the Foundation for Innovative New Diagnostics (FIND).

4.4.2 Support rapid uptake of diagnostics

Research alone is not enough to ensure the rapid uptake and impact of new diagnostics. Researchers, industry and policymakers also need to work together to address pull factors including health economics, regulation and buyer behaviour.

DIAGNOSTICS DATA SUPPORT

Once point-of-care diagnostics are in use on the frontlines, their data can be used to improve our understanding of AMR in different health settings, tracking patterns of AMR in real time and identifying emergent 'hot spots' quickly.

Through the Fleming Fund and the Global AMR Innovation Fund, UK Aid is supporting vital work on diagnostic connectivity, helping 24 LMICs improve their capacity to capture point-of-care diagnostics data in national surveillance systems, including from geographically isolated communities.

In the UK, we do not make the best use of available diagnostic tests. For example, our regulatory requirements for diagnostics make it difficult to assess the value of any new diagnostic test to the overall AMR agenda: if a new promising diagnostic came out tomorrow, the NHS is not equipped to get it into front-line use quickly.

Uncertainty about requirements for research evidence, lack of engagement to understand frontline needs, and 'silo budgeting' all serve to delay the uptake of new diagnostic technologies. Clearer guidelines and new methods for demonstrating the value of AMR diagnostics (including case studies, pilot studies and cost-effectiveness models) could help change the behaviour of health commissioners and practitioners and increase the uptake of diagnostics.

At a global level, the UK also helps LMICs make better use of the data from point-of-care diagnostics to survey AMR and identify threats as and when they arise (see 'Diagnostics data support').

To support rapid uptake of diagnostics, the UK will:

- Make antimicrobials and diagnostics a priority area for the Accelerated Access Pathway.

- Use modelling and test-pilot data to develop alternative funding models for faster diagnostics that support targeted treatment. This includes commissioning work to develop a method for assessing the value of new technologies that considers not only cost-effectiveness but the value proposition at a system level.

- Maximise use of NICE guidance, including the Medical Technology Innovation briefs, to assess new diagnostic tests and offer prescribers advice on their use.

- Streamline the regulation process to help get new diagnostics through as quickly as possible, including developing evidence-based guidance for using tests.

4.5 Development of, and access to, vaccines

Vaccines, for humans and animals alike, play a key role in tackling AMR; by promoting herd immunity and reducing the prevalence of infection, they reduce the need for antimicrobials.

In the UK and across the world, vaccination has already saved the lives of millions of people and has successfully tackled many infectious diseases in animals. It had a key role in enabling the elimination of both smallpox (in 1980) and the devastating viral livestock disease Rinderpest (in 2011). Improving global vaccination coverage through routine immunisation, and increasing the uptake of new and underused vaccines, would help save millions more lives.

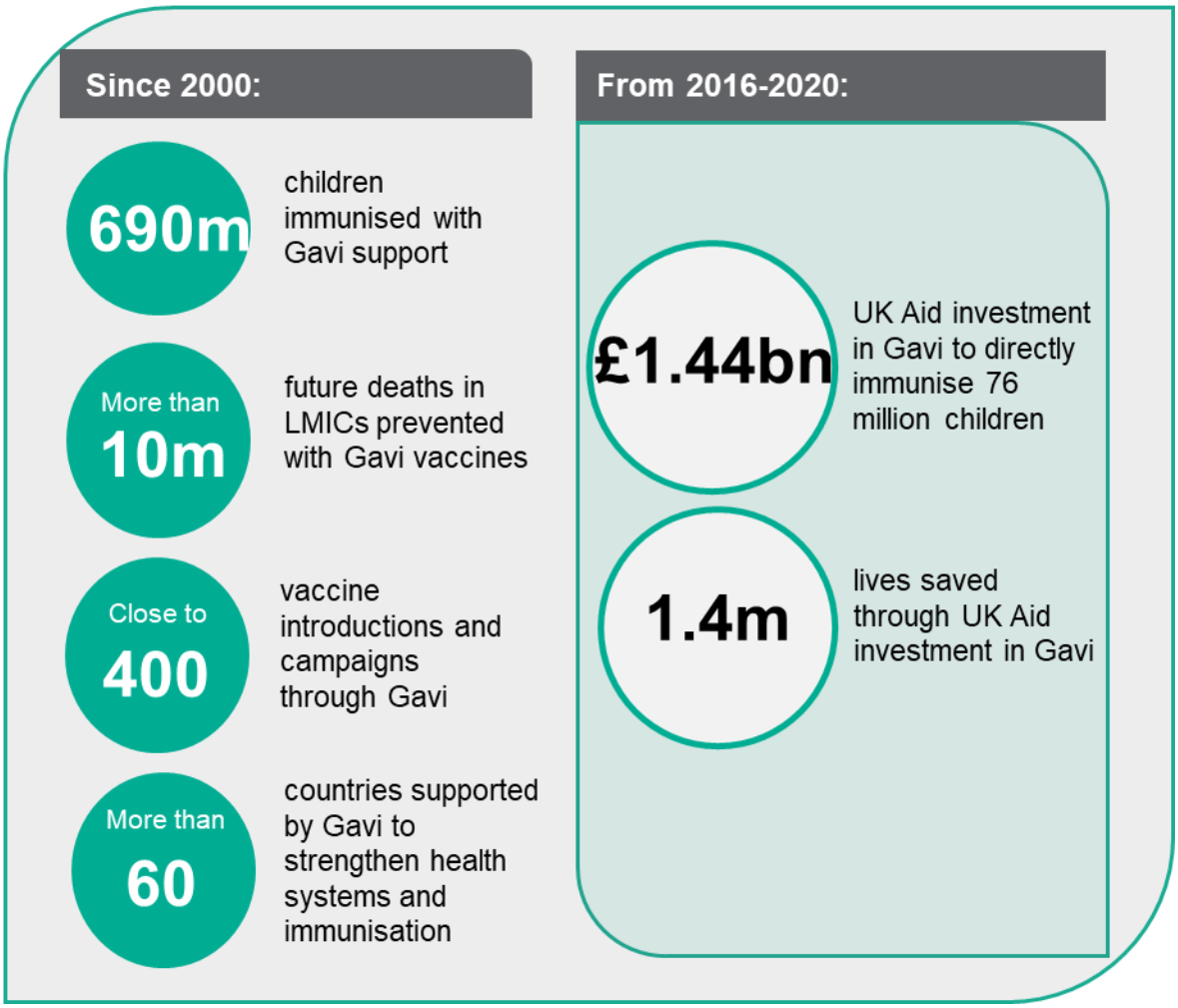
As well as ensuring comprehensive deployment of existing vaccines, there is a need to expand the range available, and evaluate alternative approaches.

4.5.1 Stimulate broader access to vaccines for humans and animals

In 2016, the AMR Review led by Lord O'Neill assessed the role of vaccines and alternative approaches in AMR, concluding that available vaccines should be more widely used, both in humans and animals; and that this may require financial support. At global level, the UK supports initiatives such as Gavi, the Vaccine Alliance and the Global Vaccine Action Plan to improve equitable access to vaccines for people, and GALVmed for animals, especially in LMICs (Figure 17).

For example, UK Aid is the largest donor to Gavi, investing £1.44 billion in the alliance from 2016 to 2020. UK Aid also supports initiatives to ensure that all LMICs have introduced one or more new or underused vaccines by 2020.

Figure 17. Improving vaccine access through UK Aid support to Gavi



In the UK, a comprehensive vaccine schedule is in place to protect children and adults from serious infections, but not everyone chooses to follow it.

Even among frontline NHS healthcare staff, the take up of influenza and chickenpox vaccinations, for example, is variable.

Uptake of vaccines could be better in the UK animal health sectors too. Farmers and vets should be encouraged to increase levels of vaccination to improve herd of flock immunity on their farms. For example, some figures from 2016 suggest only 17% of cattle that could be vaccinated against Bovine Respiratory Disease (BRD) were given a vaccine despite half of herds being affected. Proper storing and administration of vaccines is also important to keep them effective.

To stimulate broader access to vaccines for humans and animals, the UK will:

- Continue to support global initiatives, including Gavi and the Global Vaccine Action Plan, to expand access to vaccines and increase immunisation coverage, especially in LMICs.

- Support the animal medicines industry in their initiative to improve image and uptake of vaccines through proactive campaigns and encourage private investment in vaccine development.

4.5.2 Stimulate more R&D into vaccines and alternatives

As well as ensuring broad use of existing vaccines, there is also a need to develop new ones and explore alternatives for people and animals, including for example, autologous vaccines, bacteriophages and products to improve gut health. That requires a strong capacity and capability for R&D, including expertise and funding.

In human health, many infections (such as pneumonia) can be prevented with vaccines; but there are still significant gaps in the available vaccine portfolio. In some cases, such as TB, the effectiveness of available vaccines needs improving. New vaccines are also needed to prevent infections with a high risk of resistance, such as gonorrhoea and infections caused by *E. coli*, and *Klebsiella* spp; based on existing efforts, these are still likely to be 5-10 years away.

The development of vaccines to prevent some of the more common resistant HAIs would be particularly beneficial in improving patient safety and preserving the effectiveness of existing antimicrobials through reduced use. But the development costs for these vaccines are very high.

In animal health, vaccines are similarly available to prevent many infections (such as Salmonella in poultry or Porcine Reproductive and Respiratory Syndrome (PRRS) in pigs), yet there are gaps where new or improved vaccines and alternative technologies could improve animal health and help tackle AMR. Identifying the priorities and options for new product development is the first step to filling those gaps. That includes identifying factors that may influence uptake and use (for example, method of administration or vaccine design). In LMICs, putting in place logistical arrangements to allow safe storage and deployment of existing vaccines and assistance with developing effective regulatory framework may be a priority over technical innovation.

To stimulate more R&D into vaccines and alternatives, the UK will:

- Evaluate existing R&D capacity for developing, improving, adapting vaccines or other alternatives to antibiotics for humans.

- Support existing and emerging PDPs for human and animal vaccines, including for meningitis and diarrhoeal diseases.

- Use UK Aid to promote the global use of accelerated access approaches to vaccines for priority pathogens in humans and animals.

- Work with the pharmaceutical industry, the OIE and veterinary profession to identify market gaps and options for new product development in animal sectors.

- Explore options to set up a co-ordinated research programme to develop novel and improved vaccines, strategies and diagnostics for livestock, fish, companion animals and horses, based on identified market gaps.

4.6. Better quality assurance of AMR health products

Antimicrobial quality matters: falsified drugs that contain no active ingredient are ineffective and leave infections free to spread; substandard drugs that contain active ingredients but are not strong enough to treat the infection can encourage the rise and spread of resistance. The WHO estimates that one in ten medications in LMICs breach acceptable quality standards and may serve to drive AMR.

A lack of appropriate regulations and enforcement in the sale of antimicrobials is a major contributor to the use of falsified and substandard drugs. For example, a growing number of online pharmacies exploit gaps in global regulatory mechanisms to sell antibiotics around the world, often without prescription or clinical guidance (see ‘Exploiting loopholes for online sales’). In many LMICs, antimicrobials can be bought without a prescription.

Poor manufacturing standards, limited enforcement and surveillance and improper supply chain management, also increase the prevalence of poor quality antimicrobials in the marketplace.

Delivering better quality assurance of AMR health products requires us to find robust ways of taking substandard and falsified drugs out of circulation.

Identifying where and when poor quality antimicrobials are being used is the first step towards taking them out of circulation. That makes strengthening surveillance a priority. The UK supports the WHO’s Global Surveillance and Monitoring System for building regulatory capacity to identify and report substandard and falsified products. We also support individual LMICs to strengthen their capacity for quality assurance and, through the Fleming Fund, to establish systems that allow healthcare workers to monitor drug quality and its impact on treatment effectiveness.

Another route to improving antimicrobial quality is to tackle illegal sales through tighter legislation and control. The UK undertakes a broad range of regional and global activity to promote strong international standards and regulations and drive appropriate enforcement on antimicrobials. This includes active participation in the Pharmaceutical Inspection Co-operation Scheme (human and animal), International Coalition of Medicines Regulatory Authorities, and Heads of Medicines Agencies.

EXPLOITING LOOPHOLES FOR ILLEGAL SALES

In the UK, illegal sales of antimicrobials include:

- getting antibiotics without a prescription;
- buying products that are legal in other countries but illegal in the UK (including, buying from overseas websites);
- selling genuine or falsified products for the UK market illegally, even if the buyer has a prescription.

Online platforms pose a particular challenge to illegal sales in the UK. The UK is one of only six EU countries to allow the online sale of human prescription-only medicines (POMs). This raises jurisdictional issues when someone in a country where POMs cannot be sold online buys them from a UK-registered pharmacy.

The ability for registered European doctors to issue prescriptions that can be dispensed anywhere in the EEA poses further problems. Many online companies registered in Europe now employ EEA doctors to 'consult' patients online and, where a POM is needed, to send an electronic prescription to a UK pharmacy, which dispenses it and posts it back to the patient. This regulatory 'loophole' is the cause of frequent complaints to the UK.

Through the UK Medicines and Healthcare Products Regulatory Agency (MHRA) and the Veterinary Medicines Directorate (VMD), we also work with Interpol and the Working Group of Enforcement Officers to shape and enforce global regulations that limit online and over-the-counter sales.

To improve quality assurance of AMR health products, the UK will:

- Commission research into the extent of on-line purchasing and of illegal sales of antimicrobial agents in the UK.
- Use our regulators (MHRA and VMD) close working relationships with major websites to tackle the illegal sales of human and veterinary antimicrobials online.
- Explore options for including veterinary medicines in the EU's Falsified Medicines Directive.
- Continue to support international monitoring of therapeutic quality through the Global Surveillance and Monitoring System and, with partners, advocate for animal medicines to be included.

- Work with global industry to promote ways of formulating and packaging products that reduce the risk of falsification.

Glossary of terms

Term	Definition
Agriculture	The cultivation of land and breeding of animals and plants to provide food, fibre, medicinal plants and other products.
Antimicrobial	A drug that selectively destroys or inhibits the growth of microorganisms. Sometimes referred to as an 'antimicrobial agent'. Examples include antibiotics (also known as antibacterials) antiviral and antifungal agents. In the context of this document references to antimicrobials includes anti-infectives where that would be relevant in the context of the text.
Antibiotic resistant bacteria	Bacteria with the ability to resist the effects of an antibiotic to which they were once sensitive.
Antibiotic resistant genes	Occurs due to changes, or mutations, in the DNA of the bacteria, or the acquisition of antibiotic resistance genes from other bacterial species through horizontal gene transfer.
Anti-infective	Is a general term used to describe any medicine that can inhibit the spread of an infectious organism; in the context of this document, it includes cleaning products such as antibacterial sprays.
Animals	Unless specified otherwise, the term animal is used in this publication to refer to food-producing animals and aquaculture as well as companion animals and horses.
Antimicrobial resistance (AMR)	Occurs when the microorganisms that cause disease (including bacteria, viruses, fungi and parasites) cease to be affected by the drugs we use to kill them and treat the disease.
Antimicrobial stewardship (AMS)	A key component of a multifaceted approach to improve the safety and quality of patient care whilst preventing the emergence of AMR. Good antimicrobial stewardship involves selecting an appropriate drug and optimising its dose and duration to cure an infection while minimising toxicity and conditions for selection of resistant microbes. Good AMS includes a review of the continuing need for antibiotics following clinical diagnosis and documented actions to stop, continue or change antimicrobial treatment.
Autologous vaccines	A therapeutic agent produced by isolating cells from an individual and processing these cells into a vaccine formulation for treatment of that individual.
Bacteriophage	A group of viruses that infect specific bacteria, usually causing their disintegration or dissolution.
Bacteraemia	The presence of bacteria in the bloodstream.
Broad-spectrum antibiotics	These are drugs effective against a wide range of bacteria. For example, meropenem is a broad-spectrum antibacterial. Their use needs to be

	limited to resistant infections because they tend to increase the risk of resistance in other bacteria.
Carbapenems	Broad-spectrum antibiotics, often used as the last line of treatment for hard to treat human infections caused by Gram-negative bacteria.
Carbapenemese Producing Gram-negative Organisms	A group of bacteria that is resistant to carbapenems class of antibiotics.
Cephalosporins	A class of beta-lactam antibiotic exhibiting broad-spectrum activity to bacteria.
Third -generation cephalosporins	Cephalosporins with activity against a wide range of Gram-positive and Gram-negative bacteria.
Commensal	Living on or within another organism, and deriving benefit without harming or benefiting the host individual.
Commissioning for Quality and Innovation (CQUIN)	An NHS initiative intended to deliver clinical quality improvements and drive transformational change in the acute sector or hospitals. Achieving improvement against a defined set of criteria enables an NHS Trust to qualify for a payment.
Critically Important Antimicrobials (CIAs)	Antibiotics identified by the World Health Organisation as critically important for human health and their use needs to be restricted, especially in the veterinary sector. In the UK, we use the European Medical Agency definition of the CIAs. There are three classes of Highest Priority CIAs to which the animal industry applies restrictions.
Disease burden	This includes the number of infections in the population and includes economic costs like treatment costs for hospital admissions and the cost to health in terms of mortality and morbidity.
Escherichia coli (*E. coli*)	A type of bacteria common in human and animal intestines, and forms part of the normal gut flora (the bacteria that exist in the bowel).
Extended-spectrum beta-lactamase (ESBL)	Enzymes that can be synthesised and expressed by bacteria, resulting in resistance to many penicillin and cephalosporin antibiotics and often to other types of antibiotic. In humans, the most frequently identified bacteria that produce ESBLs are Escherichia coli (*E. coli*) and Klebsiella species. The ESBLs that *E. coli* most often produce are called CTX-M enzymes. *E. coli* with ESBLs may cause urinary tract infections (UTIs) that can sometimes progress to more serious infections like blood poisoning, which can be life threatening. Resistance makes these infections more difficult to treat.
Falsified medications	Medications that deliberately or fraudulently misrepresent their identity, composition or source and are likely to be ineffective.
G7	The Group of Seven (G7) is a group consisting of Canada, France Germany, Italy, Japan the United Kingdom, and the United States. These

	countries, with the seven largest advanced economies in the world, represent more than 62% of the global net wealth ($280 trillion).
G20	The G20 (or Group of Twenty) is an international forum for the governments and central bank governors from Argentina, Australia, Brazil, Canada, China, the European Union, France, Germany, India, Indonesia, Italy, Japan, Mexico, Russia, Saud Arabia, South Africa, South Korea, Turkey, the United Kingdom, and the United States. Founded in 1999, the G20 aims to discuss policy pertaining to the promotion of international financial stability.
Gram-negative bacteria	Those bacteria that do not retain crystal violet dye in the Gram-staining procedure. They can cause many types of infection and include *E. coli* and *Pseudomonas aeruginosa*.
Gram-positive bacteria	Those bacteria that are stained dark blue or violet in the Gram-staining procedure. They include *Staphylococcus aureus* and *Clostridium difficile*.
Healthcare associated infections (HAI)	Infections associated with the provision of healthcare in either a hospital or community setting.
Healthcare associated Gram-negative blood stream infection	A laboratory-confirmed positive blood culture for a Gram-negative pathogen in patients who had received healthcare in either the community or hospital in the previous 28 days.
Hepatitis C	A virus that can infect the liver**.**
Human immunodeficiency virus (HIV)	A virus that damages the cells in your immune system and weakens your ability to fight everyday infections and disease.
Acquired immune deficiency syndrome (AIDS)	The name used to describe a number of potentially life-threatening infections and illnesses that happen when your immune system has been severely damaged by the HIV virus.
Inappropriate prescribing	For the purpose of delivering the ambition of halving inappropriate prescribing in the UK, inappropriate prescribing is defined as: Prescribing an antibiotic for a patient in the absence of (documented) evidence of bacterial infection. Prescribing a critical broad-spectrum antibiotic (piperacillin-tazobactam or carbapenems in secondary care; co-amoxiclav, cephalosporins and quinolones in primary care) to patients in the absence of a (documented) rationale. Continuing an antibiotic prescription beyond the course length recommended in local or national guidelines, in the absence of a (documented) rationale.

Intestinal infectious diseases	Viral, bacterial or parasitic infections that cause gastroenteritis, an inflammation of the gastrointestinal tract involving both the stomach and the small intestine.
Klebsiella spp	Gram-negative bacteria that can cause infections including bloodstream infections; wound or surgical site infections; and meningitis.
Low- and Middle-Income Countries (LMICs)	As included at any time in the OECD Development Assistance Committee (DAC list) – a list of all countries and territories eligible to receive official development assistance (ODA). These consist of all low- and middle-income countries based on gross national income (GNI) per capita as published by the World Bank, except for G8 members, EU members, and countries with a firm date for entry into the EU. The list also includes all the Least Developed Countries (LDCs) as defined by the United Nations.
Malaria	A life-threatening disease caused by parasites that are transmitted to people through the bites of infected female *Anopheles* mosquitoes.
Macrolides	A class of antibiotic effective in the treatment of a range of infections, including respiratory, skin, soft tissue and sexually-transmitted infections. Erythromycin, azithromycin and clarithromycin are examples of macrolide antibiotics.
Meticillin-resistant *Staphylococcus aureus*	A strain of *Staphylococcus aureus* that is resistant to beta lactam antibiotics which include penicillins (e.g. methicillin and oxacillin) and almost all cephalosporin antibiotics.
Microbiome	The microbiome comprises all the genetic material within a microbiota (the entire collection of microorganisms in a specific niche, such as the human gut).
Milligram per kilogram of use in animals	A measure of the use of antibiotics in animals. For example, a 50 mg/kg figure for food producing animals would mean that on average, and over the course of a year, 50 mg of antibiotic active ingredient was used for every kg of bodyweight at time of treatment
Multi-drug resistant	Resistant to multiple classes of antimicrobial.
Sensitivity breakpoints	A chosen concentration (mg/L) of an antibiotic which defines whether a species of bacteria is susceptible or resistant to the antibiotic. If the Minimum Inhibitory Concentration (MIC) is less than or equal to the susceptibility breakpoint the bacteria is considered susceptible to the antibiotic. If the MIC is greater than this value the bacteria is considered intermediate or resistant to the antibiotic.
SNOMed CT	A structured clinical vocabulary for use in an electronic health record.
Infectious disease surveillance	The systematic collection of data from the population at risk, the identification of infections using consistent definitions, the analysis of these data and the dissemination of the results to those who collected the data, those responsible for care of the patients and those responsible for prevention and control measures.

"One-Health" approach	Collaborative multi-disciplinary work at local, national, and global levels to attain optimal health for people, animals and the environment.
Pathogen Pathogenic	An infectious agent (bug or germ), a microorganism such as a virus, bacterium, or fungus that causes disease in its host.
Patient Safety Collaborative	The largest safety initiative in the history of the NHS, supporting and encouraging a culture of safety, continuous learning and improvement, across the health and care system. It is a joint initiative, funded and nationally coordinated by NHS Improvement, with the 15 regional PSCs organised and delivered locally by Academic Health Science Networks (AHSNs).
Piperacillin-Tazobactam	A drug combination that has activity against many Gram-positive and Gram-negative bacteria including *Pseudomonas aeruginosa*. Piperacillin is a synthetic penicillin; tazobactam enhances the effectiveness of piperacillin.
Population Correction Unit	A theoretical unit of measurement developed by the European Medicines Agency (EMA) in 2009 and adopted across Europe. It takes account of a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics.
Prevalence	A snapshot at a point in time of the total number of cases of interest e.g. cases of healthcare-associated infection, in a given population.
Primary care	Services provided by GP practices, dental practices, community pharmacies and high street optometrists.
Quality Premium	An NHS scheme intended to reward clinical commissioning groups (CCGs) for improvements in the quality of the services that they commission and for associated improvements in health outcomes and reducing inequalities.
Quinolones	A family of antibiotics, including broad-spectrum agents like ciprofloxacin.
Responsible prescribing	The use of antimicrobials in the optimal way, for the right pathogen, at the right dose, for the right duration, for the treatment or prevention of infectious disease.
Resistome	The antibiotic resistome is the collection of all the antibiotic resistance genes, including those usually associated with pathogenic bacteria isolated in the clinic, non-pathogenic antibiotic producing bacteria and all other resistance genes.
Staphyloccocus aureus	*Staphyloccocus aureus* (*S.aureus*) is a Gram-positive bacterium which is not always pathogenic (and can commonly be found existing as a commensal) but is a common cause of infection and bacteraemia. Meticillin-resistant *Staphylococcus aureus* (MRSA) is the antibiotic-resistant strain of *S. aureus*.
Secondary care	Covers acute healthcare, either elective care (planned specialist medical care or surgery, usually following referral) or emergency care.

Sepsis	Is a serious complication of an infection. Without quick treatment, sepsis can lead to multiple organ failure and death.
Substandard medications	Medications produced by legitimate companies, but are damaged or degraded through poor manufacturing, storage or distribution.
Susceptibility testing	Testing to detect possible drug resistance in common pathogens and to assure susceptibility to drugs of choice for treatment of infections.
Sustainable Development Goals	Otherwise known as the Global Goals, are a universal call to action to end poverty, protect the planet and ensure that all people enjoy peace and prosperity. The 17 Goals build on the successes of the Millenium Development Goals while including new areas such as climate change, economic inequality, innovation, sustainable consumption, peace and justice, among other priorities.
Therapeutics	The branch of medicine concerned with the treatment of disease. In this context specifically, the treatments against microbial infection.

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[1] Figure 1:

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[2] Text Box: AMR in the Water

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