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DH UK 5 Year Antimicrobial Resistance (AMR) Strategy 2013-2018

Annual progress report, 2015

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September 2016

Title: DH UK 5 Year Antimicrobial Resistance (AMR) Strategy 2013-2018 - annual progress report, 2015.
Author: Public and International Health Directorate/ Health Protection and Emergency Response Division/ HPP/ 10200
Document Purpose: Policy / Transparency
Publication date: 16 September 2016
Target audience: Patients and the public, clinical professionals, NHS and Social Care managers, primary and secondary care prescribers, other professionals, healthcare workers, veterinary healthcare workers, agricultural sector workers.
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Published to gov.uk, in PDF format only.
www.gov.uk/dh

DH UK 5 Year Antimicrobial Resistance (AMR) Strategy 2013-2018

Annual progress report, 2015

Prepared by: The UK AMR Strategy High Level Steering Group

Contents

Foreword

In the foreword to the first annual progress report, published in December 2014, we said that we hoped that the international alliances we had built, working closely with governments and partners across human and animal health, would help to ensure a sustained global commitment to take action on antimicrobial resistance.

We are pleased to be able to say in this second annual report, setting out activity undertaken in 2015, that we now have a World Health Organisation (WHO) Global Action Plan (GAP) and a commitment for all WHO member countries to develop their own national action plans within the next two years. Our hope for this year is that working with partners we achieve a strong declaration or resolution at the United National General Assembly when it meets in September. If we achieve this, AMR will be securely on the agenda at all political levels around the world.

The global facing Review on AMR led by Lord O'Neill published its final report on 19 May 2016; it has already stimulated action, including a declaration during Davos by over 85 pharmaceutical and diagnostics companies in 18 countries setting out their commitment to a sustainable new drug and diagnostic test pipeline. We look forward to working with partners in other countries to take forward the final recommendations of the Review. The Government's initial response to the report is published alongside this progress report.

On the domestic front, once again there has been an enormous amount of activity going on across all sectors and by a wide range of organisations. This is true of the animal as well as the human health side: the meat poultry sector for example was the first to be able to show reduction in use of antibiotics. This is a significant step towards a better monitoring system in the animal sector. However, overall, in humans and animals the data are yet to clearly demonstrate that our actions are making a difference. This is why, this year we are focusing on local action, supporting teams at local levels to analyse their data and drive improvement.

Finally, we are pleased to note that AMR has been included on the Government National Strategic Risk Register as a tier one threat and hope that this will ensure that organisations prioritise AMR and support local teams to take the action they need to make a difference.

Professor Dame Sally C. Davies
Chief Medical Officer
Chief Scientific Adviser
Department of Health

Professor Nigel Gibbens, CBE
Chief Veterinary Officer, UK
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Executive summary

The UK Five Year Antimicrobial Resistance (AMR) Strategy 2013-2018, published in September 2013, represented an ambitious programme to slow the development and spread of AMR taking a “One-Health” approach spanning people, animals, agriculture and the wider environment. This second annual progress report describes what was achieved in the second year of implementation, including a number of significant achievements on the international stage.

In 2015 our focus was on ensuring that the regulatory and operational infrastructure is in place to drive progress at the national level. At the same time, recognising that AMR is a global problem requiring global solutions, we have continued to demonstrate leadership at an international level. We worked with international partners to successfully negotiate resolutions on AMR through the machinery of the World Health Organisation (WHO), the Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE). We also promoted the work of the independent Review on AMR led by Lord O’Neill and launched by the Prime Minister in July 2014.

We made considerable progress at a national level putting the building blocks for success in place including better data, guidance and a strengthened framework for antimicrobial stewardship. However, we were acutely aware that we had yet to see unequivocal evidence that we are making a difference, although, at the end of 2015, early signs suggested that initiatives begun earlier in the year were having good results. The challenge now is to shift focus from the development of national tools and guidance to local delivery. We have begun to empower and support local leaders to drive change and hold them to account for delivery, not least through increased transparency of the detailed data local teams need to understand their own performance; these local data are transparent, simple to understand and accessible by both professionals and members of the public. To support local action, we will continue to work to change behaviours around the demand for, and prescribing of, antibiotics by increasing the understanding of AMR among the public, and by supporting professionals to reduce prescribing for both humans and animals.

Internationally we will build on what has been achieved in 2015 by reinforcing the importance of AMR as a global economic and social threat, to secure wider international political support for tackling AMR. In particular, we are working with international partners to achieve a successful high level declaration or resolution on AMR at the United Nations General Assembly in 2016.

Our strategy rests on the three pillars of prevent, protect and promote: preventing infection, protecting the antibiotics that we have and promoting the development of new drugs and alternative treatments. This report is structured around those pillars. The pillars are underpinned by better surveillance, better identification of research needs and collaboration, improved understanding and awareness of AMR and greater international collaboration. A summary of key work and achievements in 2015 is included in Annex A.

While we have a UK Strategy, Scotland, Wales and Northern Ireland have their own strategies and delivery plans reflecting local issues and systems; these strategies are in line with the UK Strategy. The four UK nations also report separately on progress and surveillance. Much of the activity described in this report has an England focus but we use headline data from all four UK nations and highlight significant initiatives underway in the Devolved Administrations in order to present the overall UK position. Population data is included in Annex B to provide the context for each country’s contribution to the UK data.

Executive summary

The current position (end 2015)

In June 2014, the High Level Steering Group, comprising a range of government departments and agencies tasked with driving delivery of the UK five year strategy, published the outcome measures it would use to gauge the success of the strategy in slowing the growth of antimicrobial resistance.

To assess whether the strategy is having an impact on the growth of resistance, we are monitoring the trends in resistance in a number of selected infections and the proportion resistant to specific antibiotics.

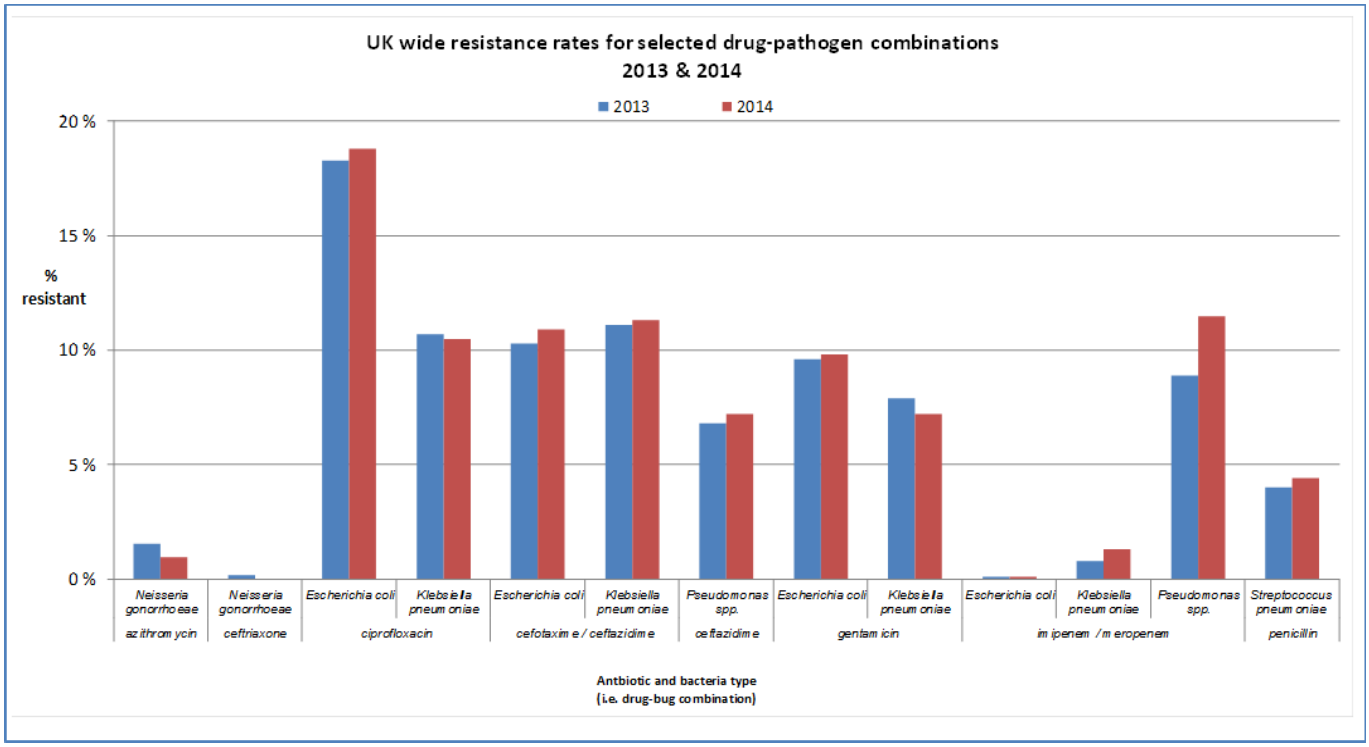
In our last annual report, we published baseline data for a list of key micro-organisms and antibiotic (or drug-bug) combinations. A list of drug-bug combinations for 2014, with revisions for 2015, is included in Annex C. Bacteraemias (bloodstream infections) represent the most severe forms of infection and are the focus of many surveillance systems. An increase in blood stream infections and their increasing resistance to antimicrobial therapy is indicative of trends in all infections.

Trends in resistance – human health

Figure 1 and table 1 show the level of resistance in five micro-organisms, of which four cause bloodstream infections, to different types of antibiotics across the UK. The **proportions** of isolates of each species of bug that are resistant to each antibiotic were generally stable between 2013 and 2014. However, the increased incidence of some infections (e.g. bloodstream infections caused by E. coli or K. pneumoniae) means that for these infections the **actual numbers** of resistant infections is increasing (table 2). This highlights the importance of initiatives focussing on infection prevention and control. Annex D provides the detailed data for figure 1.

The data shown in figure 1 are for the UK as a whole. The proportion of bacteria resistant to the indicated antibiotics in 2014 in England, Northern Ireland, Scotland and Wales are given in table 1. For each country, the results of antimicrobial susceptibility testing reported by hospital laboratories were collected. Data for England were extracted from the PHE Second Generation Surveillance System, data for Northern Ireland were retrieved from CoSurv, data for Wales were extracted from the regional Data Store system, and data for Scotland were extracted from the ECOSS (Electronic Communication of Surveillance in Scotland) system. For Neisseria gonorrhoeae data were extracted from the Gonococcal Resistance to Antimicrobials Surveillance Program (GRASP) for England and Wales, and the Gonococcal Antibiotic Surveillance in Scotland (GASS).

Figure 1: UK wide resistance rates for selected drug-pathogen combinations



Note: Figures shown here for Neisseria gonorrhoea are for the UK excluding Northern Ireland.
Source of data and for gonorrhoea resistance: England & Wales GRASP 2014 annual report[1]
Data for Scotland[2]:
Source of data: Guy R , Geoghegan L, Heginbothom M, et al. Non-susceptibility of Escherichia coli, Klebsiella spp., Pseudomonas spp., Streptococcus pneumoniae and Staphylococcus aureus in the UK: temporal trends in England, Northern Ireland, Scotland and Wales J Antimicrob Chemother, 2016 doi:10.1093/jac/dkw018

With the exception of Pseudomonas spp., where resistance to carbapenems showed a statistically significant increase, the **proportions** (%) of isolates of each species resistant to each antibiotic were generally stable between 2013 and 2014

For Neisseria gonorrhoea there is a degree of resistance to ceftriaxone and azithromycin, although for ceftriaxone these remain isolated cases: there have been none in Scotland and are at very low levels in England and Wales. However there is persistent resistance in both England and Wales and in Scotland to azithromycin, at still low but concerning levels.

1 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/476582/GRASP_2014_report_final_111115.pdf

2 http://www.hps.scot.nhs.uk/utility/fullimage.aspx?imageurl=./images/weekly_report/2015/1524/gass_table3.gif

Table 1: resistance rates (%) for selected drug-bug combinations in England, Northern Ireland, Scotland and Wales in 2014.

Specific antibiotic	Antibiotic class	Bacteria	England	Northern Ireland	Scotland	Wales	UK
azithromycin	Macrolide	*Neisseria gonorrhoeae**	1.0	n/av	1.3	*	1.0
ceftriaxone	Cephalosporin	*Neisseria gonorrhoeae**	0.0	n/av	0.0	*	0.0
ciprofloxacin	Fluoroquinolones	*E. coli*	18.7	16.3	18.2	22.3	18.8
ciprofloxacin	Fluoroquinolones	*Klebsiella pneumoniae*	10.9	11.0	10.9	5.0	10.5
cefotaxime / ceftazidime	Cephalosporin	*E. coli*	11.1	6.4	9.1	14.1	10.9
cefotaxime / ceftazidime	Cephalosporin	*Klebsiella pneumoniae*	12.1	10.0	8.7	10.0	11.3
ceftazidime	Cephalosporin	*Pseudomonas* spp.	7.4	5.5	5.4	6.3	7.2
gentamicin	Aminoglycosides	*E. coli*	9.6	7.2	10.7	11.1	9.8
gentamicin	Aminoglycosides	*Klebsiella pneumoniae*	7.5	8.1	6.8	4.9	7.2
imipenem / meropenem	Carbapenem	*E. coli*	0.1	0.0	0.0	0.0	0.1
imipenem / meropenem	Carbapenem	*Klebsiella pneumoniae*	1.5	2.7	0.0	0.3	1.3
imipenem / meropenem	Carbapenem	*Pseudomonas* spp.	11.5	12.1	11.8	12.0	11.5
penicillin	Beta-lactam	*Streptococcus pneumoniae*	4.2	6.5	5.8	4.1	4.4

*** Data for Wales included in England estimate. The UK value does not include Northern Ireland's data.**

To assess the inherent variability, and show the coverage across the four nations for the estimates of resistance, the numbers of isolates tested are shown in table 2. Smaller numbers result in less reliable estimates. It should be noted that the numbers are based on voluntary reporting.

Table 2: number of isolates tested in 2014.

Specific antibiotic	Antibiotic class	Bacteria	England	Northern Ireland	Scotland	Wales	UK
azithromycin	Macrolide	*Neisseria gonorrhoeae**	1,568	n/av	929	*	2,497
ceftriaxone	Cephalosporin	*Neisseria gonorrhoeae**	1,568	n/av	929	*	2,497
ciprofloxacin	Fluoroquinolones	*E. coli*	22,579	1,103	4,350	2,352	30,384
ciprofloxacin	Fluoroquinolones	*Klebsiella pneumoniae*	3,972	146	717	323	5,158
cefotaxime / ceftazidime	Cephalosporin	*E. coli*	19,523	850	4,279	2,233	26,885
cefotaxime / ceftazidime	Cephalosporin	*Klebsiella pneumoniae*	3,460	109	705	301	4,575
ceftazidime	Cephalosporin	*Pseudomonas* spp.	2,571	91	167	191	3,020
gentamicin	Aminoglycosides	*E. coli*	24,528	1,361	4,605	2,360	32,854
gentamicin	Aminoglycosides	*Klebsiella pneumoniae*	4,290	172	770	325	5,557
imipenem / meropenem	Carbapenem	*E. coli*	20,964	1,077	4,271	2,264	28,576
imipenem / meropenem	Carbapenem	*Klebsiella pneumoniae*	3,759	150	704	304	4,917
imipenem / meropenem	Carbapenem	*Pseudomonas* spp.	2,677	91	238	191	3,197
penicillin	Beta-lactam	*Streptococcus pneumoniae*	2,621	77	345	267	3,310

*** Data for Wales included in England estimate. The UK value does not include Northern Ireland's data.**
Source: Written communication, PHE Sources for Neisseria gonorrhoea isolates as above.

Trends in resistance – animal health

The range of resistance to selected antibiotics of key organisms from animals in EU/EEA countries in 2013 is shown in table 3 together with the ranking of the UK within the countries reporting. The UK had the lowest or joint lowest level of resistance for six of the 16 drug-bug combinations, and was in the lower half of the rankings (lowest level of resistance) for all drug-bug combinations but one.

The UK started a new statutory EU harmonised monitoring programme for the first time in 2014; the results of this monitoring are presented in the veterinary antibiotic sales and antibiotic resistance (VARSS[3]) report together with results from the clinical isolates surveillance which has been conducted for many years. EU harmonised monitoring samples come from healthy animals; clinical surveillance samples come from animals being investigated for disease by their veterinarians. Results from the harmonised monitoring programme are presented in figure 2 and annex D. Due to the complexity of the data (various species and two different surveillance systems); the full dataset is not presented in this report but is available in the VARSS reports.

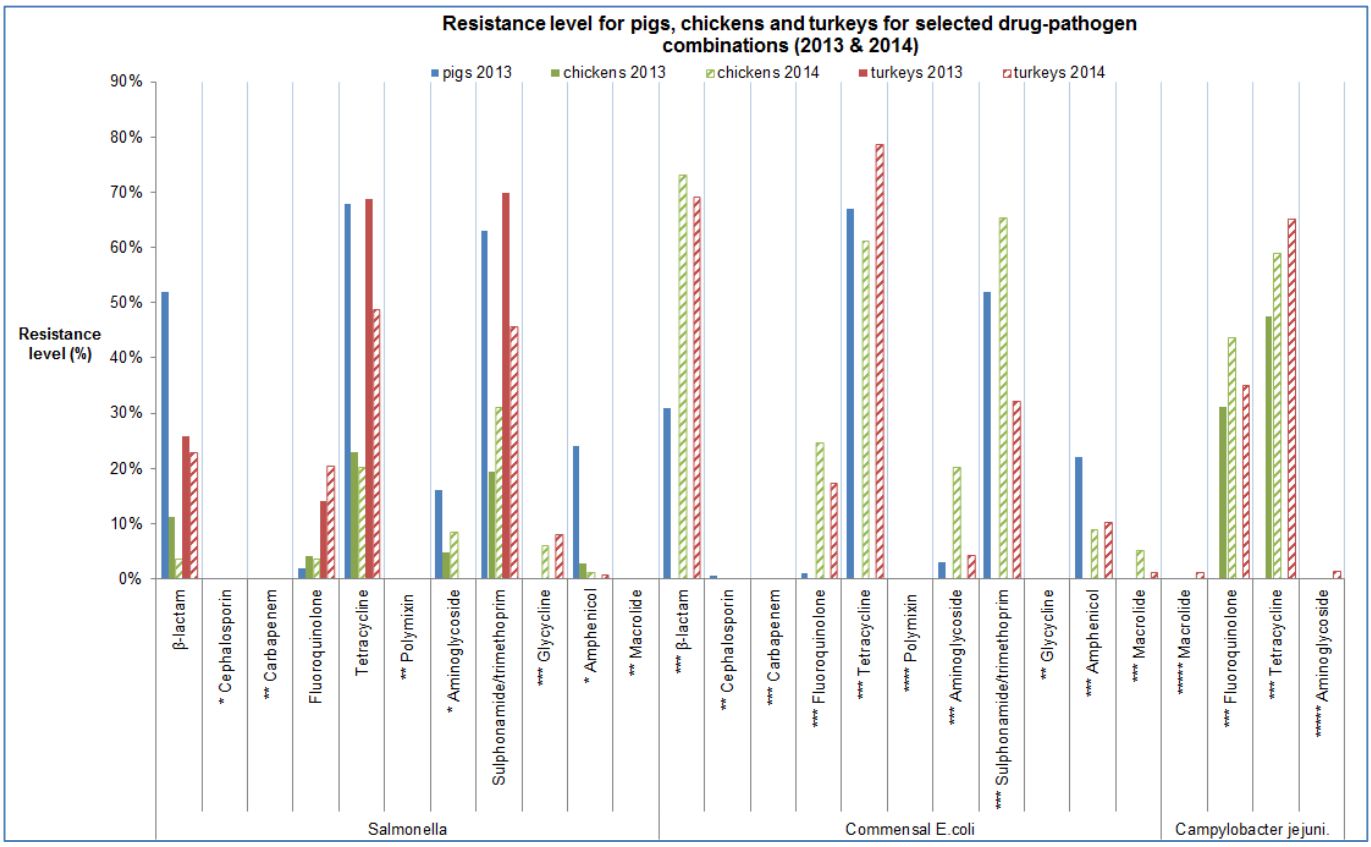
Table 3: Comparison of proportion of resistant isolates to key antibiotics for selected bacteria in animals, UK compared to EU/EAA countries, 2013/2014.

Bacteria	Animal Species	Antibiotic Tested	Number of countries that submitted data	% of resistant isolates from the UK	UK rank, where 1 is the lowest % resistant	Range of % resistance of isolates in EU countries
E. coli	Pigs*	Cefotaxime	11	0.6	3	0 (DK) – 4.6 (PL)
		Ciprofloxacin	11	1.3	2	0 (NL) – 32.9 (ES)
Salmonella spp.	Turkeys	Cefotaxime	9	0	1	0 (All MS)
		Ciprofloxacin	9	20.4	2	7.7 (DE) - 92.9 (ES)
	Chickens	Cefotaxime	23	0	1	0 (AT, BG, HR, DK, FR, DE, EL, HU, IE, NL, PL, SK, ES, IS, UK) – 27.3 (IT)
		Ciprofloxacin	23	3.6	3	0 (DK, IE, IS) - 94.1 (BG)
	Pigs*	Cefotaxime	11	0	1	0 (UK, RO, NL, IE, EE, DK, HR) – 4.5 (IT)
		Ciprofloxacin	11	2.0	2	0 (DK, EE) – 45.5 (RO)
C. jejuni	Chickens	Ciprofloxacin	26	43.6	7	3.6 (IS) - 100 (LV)
		Erythromycin	26	0	1	0 (AT, HR, FI, FR, EL, HG, NL, SI, ES, SE, UK, IS) – 39.1 (BG)
	Turkeys	Ciprofloxacin	10	34.6	1	34.6 (UK) – 95.4 (HG)
		Erythromycin	10	0.7	2	0 (AT, HG, RO) – 10.8 (ES)
C. coli	Chickens*	Ciprofloxacin	9	42.4	1	42.4 (UK) – 94.1 ES)
		Erythromycin	9	3.0	4	0 (CZ, DE, HG) – 42.6 (ES)
	Pigs*	Ciprofloxacin	7	13.5	2	6.1 (NL) – 93.5 (ES)
		Erythromycin	7	27.0	5	2.3 (FI) – 58.3 (ES)

*** Data for species followed by an asterisk are based on 2013 data from the EFSA AMR SR[4]. Non-asterisked are from 2014 data[5].**
Country codes: AT: Austria; BG: Bulgaria; HR: Croatia; CZ: Czech Republic; DE: Germany; DK: Denmark; EE: Estonia; EL: Greece; ES: Spain; FI: Finland; FR: France; HU: Hungary; IE: Ireland; IS: Iceland; IT: Italy; LV: Latvia; NL: Netherlands; PL: Poland; RO: Romania; SE: Sweden; SI: Slovenia; SK: Slovakia; UK: United Kingdom.

[3] https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2014
[4] EFSA and ECDC, 2015. EU summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013. EFSA journal, 13(2):4036, 178pp.
[5] EFSA and ECDC, 2015. EU summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013. EFSA journal, 13(2):4036, 178pp.

Figure 2: Resistance level for pigs, chickens and turkeys for selected drug-pathogen combinations in 2013 and 2014



Source, EFSA report 2015 & 2016; based on the EU harmonised monitoring programme

* blanks = None of the samples tested were resistant (0%).

** blanks = None of the samples tested in 2014 were resistant (0%); No samples tested in 2013.

*** blanks = No samples tested.

**** blanks = No samples tested in poultry (2013); None of the samples tested in pigs (2013) and poultry (2014 were resistant.

***** blanks = None of the samples tested in chickens were resistant (0%); No sample tested in turkeys & pigs (2013).

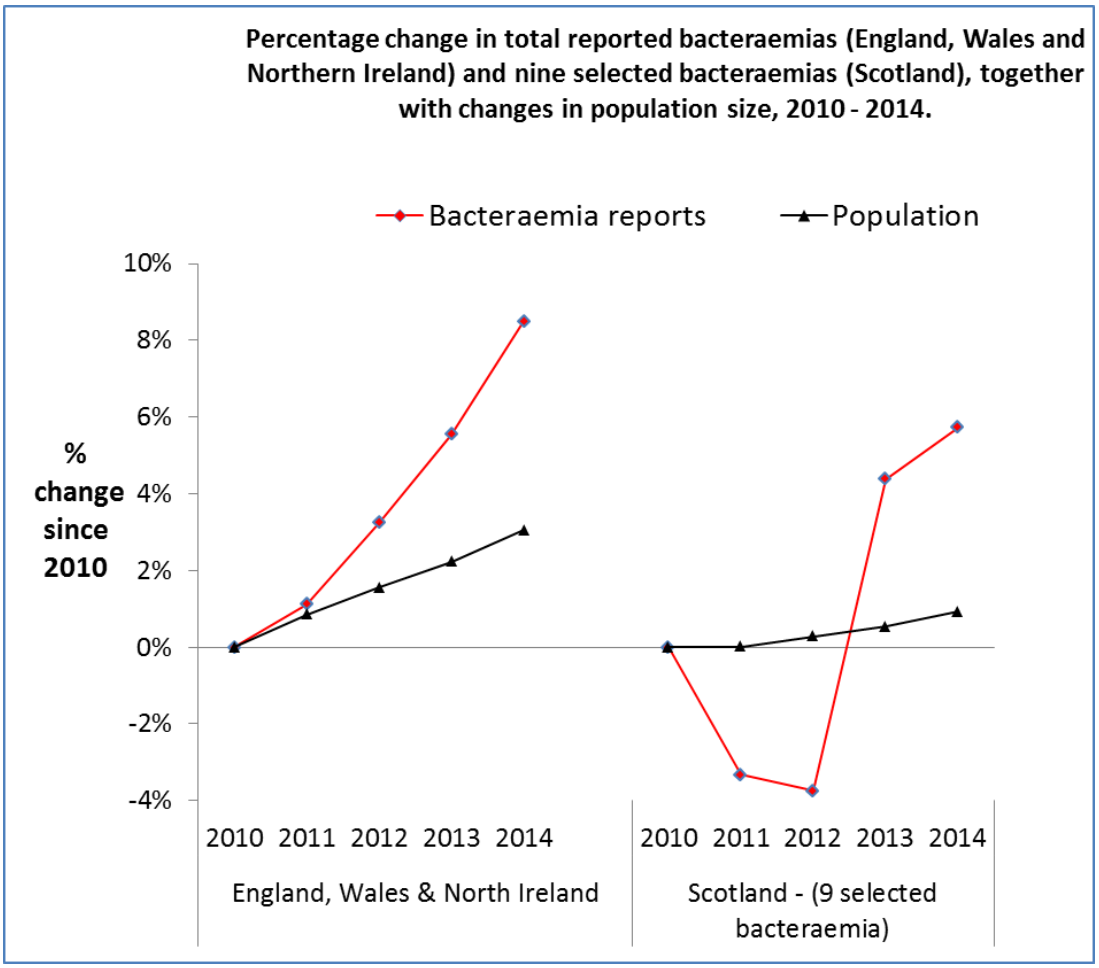
PREVENT infections

This section highlights the increase in occurrence of key infections from 2010 to 2014, what has been done to improve the prevention and control of these infections and what is planned for 2016.

Antibiotic resistance occurs when the bugs that cause infections are able to resist the antibiotics used to treat them. There is good evidence that the more antibiotics are used, the greater the likelihood that infections will become resistant. Every infection prevented is a treatment avoided. The first step in tackling AMR is therefore to **PREVENT** infections requiring antibiotics from occurring in the first place.

An increase occurred in reported blood stream infections in England, Wales and Northern Ireland from 2010 to 2014 (figure 3). In Scotland, data are only available for nine selected bacteraemias: these also suggest an increase in occurrence since 2010. The increases observed cannot be explained by increases in population size. It is not possible, however, to rule out improved reporting of infections as an explanation for the increase of blood stream infections. The causes of the rise in bacteraemia incidence are complex and may include closer observation and monitoring of people at risk, the increase in frail older people and multi-morbidity and the increased use of instrumentation in clinical practice.

Figure 3: % change in numbers of bacteraemia reports in England, Wales and Northern Ireland, and % change in a combination of 9 reported bacteraemia for Scotland.



Sources: Health Protection Report Weekly report Volume 9 Number 21 19 June 2015[6]
Health Protection Scotland, Antimicrobial Use and Resistance in Humans in 2014[7]

Effective infection prevention and control (IPC) can prevent the spread of all infections, including those that are resistant to antibiotics, as demonstrated by the reduction in incidence of MRSA. Through effective hospital IPC, the proportion of S. aureus blood stream infections (BSIs) that are resistant to meticillin (MRSA) in England has fallen from 15% in 2010 to 8% in 2014.Through effective community IPC, including vaccination programmes, there was a 23% reduction in Streptococcus pneumoniae bloodstream infections in England from 2010 to 2014[8].

Regulation

To reduce the incidence of infections further, we have tightened regulation in England. In 2015 we revised the Health and Social Care Act 2008 Code of Practice on the prevention and control of infections and related guidance. The revised Code strengthens the IPC and antimicrobial stewardship framework for healthcare providers clarifying accountability and leadership within primary and secondary care. The NHS Standard Contract published in March 2015 included amendments to require compliance with the Code of Practice. This enables regulators such as the Care Quality Commission (CQC) to look at compliance with the Code within its inspection programme.

Guidance and tools

At the same time, a range of guidance and tool kits have been produced to support healthcare staff to manage particular infections. In 2015, guidance and standards have been published and updated including:

- a Carbapenemese-producing Enterobacteriaceae (CPE) toolkit for the non-acute and community sector was published in June 2015, as incidence of CPE resistant to antibiotics of last resort has become an increasing problem both nationally and internationally,
- the National Institute for Health and Care Excellence (NICE) quality standard for management of “urinary tract infection in adults” was published in June 2015.

In Scotland, the Healthcare Associated Infection (HAI) Standards (2015) were published in February[9] 2015. They specify the minimum level of HAI performance for NHS boards and apply to all healthcare organisations and practitioners in Scotland, including independent healthcare providers. Importantly, they specify what patients and the public can expect of healthcare services in Scotland and require NHS boards to demonstrate that they have met, or are working towards meeting, these standards as part of their Healthcare Environment Inspections. Scotland continues to develop and update the HAI compendium, which provides a single source for all guidance on the prevention and control of HAI.

6 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/436558/hpr2115_plmcrbls.pdf

7 http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Publications/2015-10-06/2015-10-06-SAPG-2014-Report.pdf

8 8 Figure 2.7 Data Reference Table; Annual S. aureus bacteraemia reports of tested and non-susceptible episodes to methicillin by NHS region in England; 2010 to 2014 of the 2015 ESPAUR Report. Data reference tables Chapter 2. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/476941/ESPAUR-Report_Web-Appendix-1_Chapter2-Antimicrobial_Resistance.xlsx

9 http://www.healthcareimprovementscotland.org/our_work/inspecting_and_regulating_care/hei_policies_and_procedures/hai_standards_2015.aspx

In Wales, a public consultation on the draft AMR Delivery Plan was launched in December 2015 and ran until 29 February 2016. It invites comments on the actions proposed in Wales to support the key priority areas in the UK Five Year Antimicrobial Resistance Strategy 2013-18.

In Northern Ireland, the Strategic Antimicrobial Resistance and Healthcare Associated Infection (SAMRHAI) Group first met in March 2015. The group is responsible for maintaining a strategic overview of AMR, HAI and implementation of the Strategy for Tackling Antimicrobial Resistance (STAR), 2012-2017[10] ensuring that actions are aligned with the UK 5 year AMR strategy.

Local resources to support healthcare staff are available on the Public Health Agency's website[11] and additional resources to support GP practices are available via their primary care intranet. The Northern Ireland Management of Infection Guidelines for Primary and Community Care settings were refreshed in 2015 and are now accessible in digital format including through smartphone/tablet app.

PHE's CPE toolkit for the non-acute and community sector was also endorsed by the DHSSPSNI and issued to health and social care staff for use in Northern Ireland.

Local AMR indicator set.

In the UK AMR Strategy implementation plan, published in 2014, we made the commitment to develop an integrated IPC, AMR and antimicrobial stewardship indicator set based on existing data for England. These indicators would be publically available to be scrutinised by a range of health and care providers and the public. Transparency of data and performance would then encourage services locally to improve standards in care and patient outcomes.

We have developed a single data source where a set of key data and links to information are accessible to clinicians, commissioners, public health teams and the public to support local action to address AMR. The data portal became available for use in the NHS in England from April 2016 with more data streams coming on line through the year.

This development will enable teams to identify issues in their areas and to implement interventions tailored to those local issues. Local plans should incorporate the strengthening of local IPC activities. The new data source provides a much better and more accessible picture of the occurrence of infections and will enable local teams to agree ambitious, locally-owned and locally-sensitive quality improvement plans. In Northern Ireland it is proposed that by March 2017, all HSC Trusts and the Public Health Agency should have in place the data collection and reporting arrangements necessary for the introduction of the Northern Ireland Integrated Indicator for Healthcare-Associated Infections and Antimicrobial Resistance and Stewardship.

Example of local action:

A NHS England-led Clostridium difficile infection (CDI) collaborative in the West of England is working with CCGs and the PHE field epidemiology service to implement enhanced surveillance of community acquired CDI across Bath, Gloucester, Swindon and Wiltshire. Data from 168 cases of community acquired CDI have been collated and are informing commissioner led strategies to prevent and reduce the number of future cases.

Contact Elizabeth.beech@nhs.net for further information

10 https://www.dhsspsni.gov.uk/sites/default/files/publications/dhssps/star-doc.pdf

11 http://www.publichealth.hscni.net/antibiotic-awareness

In animal health, we are encouraging and supporting animal keepers to adopt biosecurity and husbandry practices that minimise disease occurrence and improve disease control. Through compliance with the Red Tractor assurance scheme standards on biosecurity, animal health and welfare (including segregation pens for sick animals) and responsible use of medicines, more than 85% of the poultry meat industry, 95% of dairy farms and 92% of pork production are working to implement biosecurity and husbandry practices that minimise disease occurrence and transmission. All Red Tractor farms are assessed regularly to ensure compliance with the standards. However, there are still a small percentage of farms that have not signed up to work to Red Tractor standards, that are not regularly assessed and where improvements may be required to meet the Red Tractor standards[12].

Through our engagement with a range of organisations, a number of sector specific initiatives have been launched during the year addressing hygiene and infection control procedures for veterinary practice. These include self-audit tools, campaigns, guidance and sector specific professional operating standards[13][14][15].

Forward look

We are supporting local action in England to address infection rates by providing local data through the local AMR indicator set which will also provide links to information on evidence based interventions to support implementation locally; and by building a network of AMR leaders who will promote the need to tackle AMR and drive local action. As the building blocks have been laid, we will now focus on supporting local teams to make best use of the guidance and tools in place to drive down rates of infection.

12 http://www.redtractor.org.uk/contentfiles/RedTractor-573.pdf

13 http://www.thebellamossfoundation.com/practice-hygiene-self-a

14 http://assurance.redtractor.org.uk/rtassurance/schemes/Standards%20home/Standards2014.eb

15 http://www.rcvs.org.uk/document-library/practice-standards-scheme-manual/

PROTECT the antibiotics that we have

The second pillar in slowing the growth in resistance is stewardship: protecting the antibiotics we have by making sure that they are prescribed and taken appropriately; that the right drugs are taken at the right dose and at the right time. There are few new antibiotics in the development pipeline that can replace those to which infections have become resistant. Many of the antibiotics currently used are prescribed unnecessarily. Some of this prescribing occurs when clinicians are unable to distinguish between a viral or bacterial infection, but many are prescribed for conditions where we know that antibiotics are unlikely to have an effect. We need to **PROTECT** the antibiotics that we have by using them appropriately.

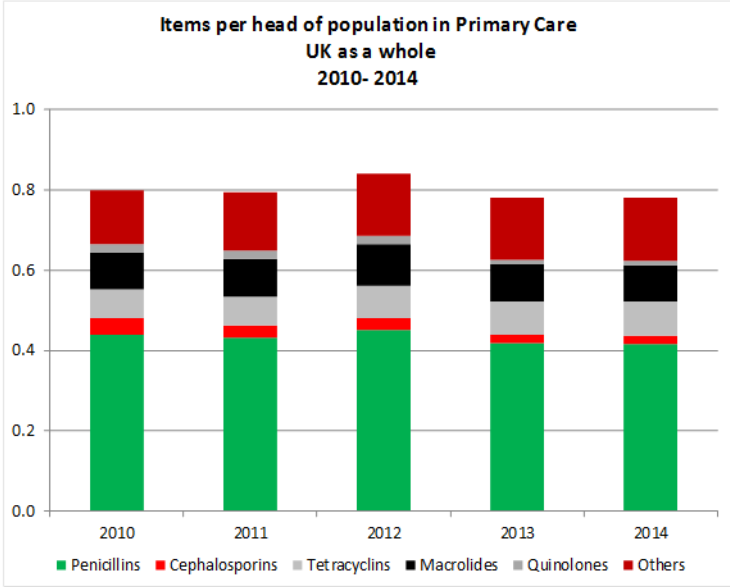
How are we doing?

“Rates of prescribing” are a readily available measure that provides some indication on progress with stewardship. Reductions in prescribing are likely to indicate, at least in part, reductions in inappropriate prescribing.

The standard measure of prescribing is Defined Daily Dose (DDD) per 1000 population. We have published prescribing data for **England** in 2014 in the second English Surveillance Programme for Antimicrobial Usage and Resistance (ESPAUR) annual report in November 2015. The 2014 data shows prescribing of antibiotics continuing to increase with **total consumption increasing by 2.4%** between 2013 and 2014. Total antibiotic prescribing continues to increase in all NHS areas, though with a slower rate of increase from 2013 to 2014 than in previous years.

Despite the overall increase, the number of prescriptions per head of population has decreased slightly (figure 4). This is likely to be explained by increases in population size, and increases in the standard dosages used in prescriptions of some frequently used antibiotics. Total defined daily doses, as opposed to the number of prescriptions, is thought to give the best indication of impact on resistance. Clinical guidance changes with time and there are indications where guidance changed in 2015 with some recommending a higher dose and others a reduced dose. All of these changes will impact on the total DDDs; by monitoring both DDDs per 1000 population and the number of prescriptions per head, we will have a better picture of what is happening and will be better able to assess the impact of our interventions.

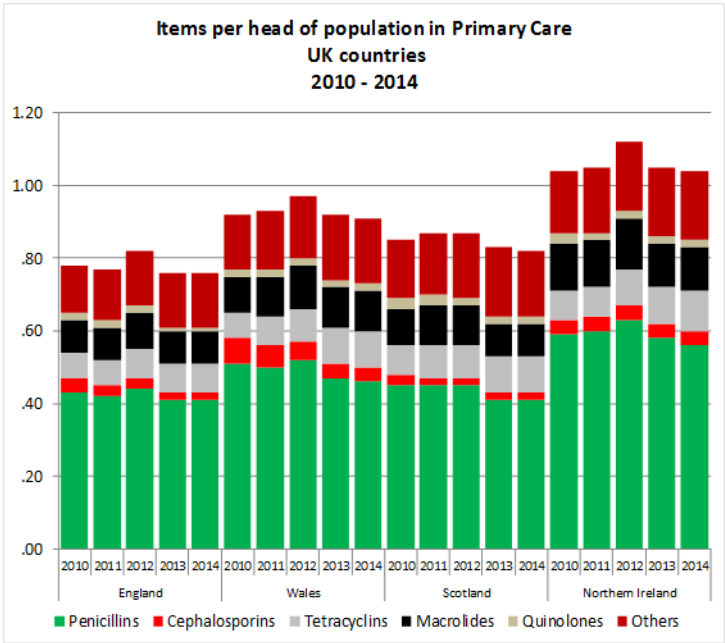
Figure 4: items per head of population in primary care



UK items per head of population in Primary Care

By antibiotic class

	2010	2011	2012	2013	2014
Penicillins	.44	.43	.45	.42	.42
Cephalosporins	.04	.03	.03	.02	.02
Tetracyclins	.07	.07	.08	.08	.08
Macrolides	.09	.09	.10	.09	.09
Quinolones	.02	.02	.02	.01	.01
Others	.13	.14	.15	.16	.16
Total	.80	.79	.84	.78	.78



UK items per head of population in Primary Care By country

	2010	2011	2012	2013	2014
England	.78	.77	.82	.76	.76
Wales	.92	.93	.97	.92	.91
Scotland	.85	.87	.87	.83	.82
Northern Ireland	1.04	1.05	1.12	1.05	1.04
UK average	.80	.79	.84	.78	.78

Source: UK Prescription Cost Analysis (PCA) data. HSCIC publish for England, ISD publish for Scotland Wales publish on Gov.Wales, and NI published by HSC Business Services Organisation. Note: all except Scotland publishing data by calendar year, Scotland publish for a financial year. This may cause a slight discrepancy in the figures when making the comparison, but all cover a 12 month period

Differences in data definitions and prescribing arrangements exist between the four countries and care is required in interpretation of data; for instance, outpatients prescribed drugs by hospital doctors in Northern Ireland[16] will have their prescription filled by their GP; in England, by contrast, such a prescription will be dispensed by the hospital (reducing the pressure on the primary care budget).

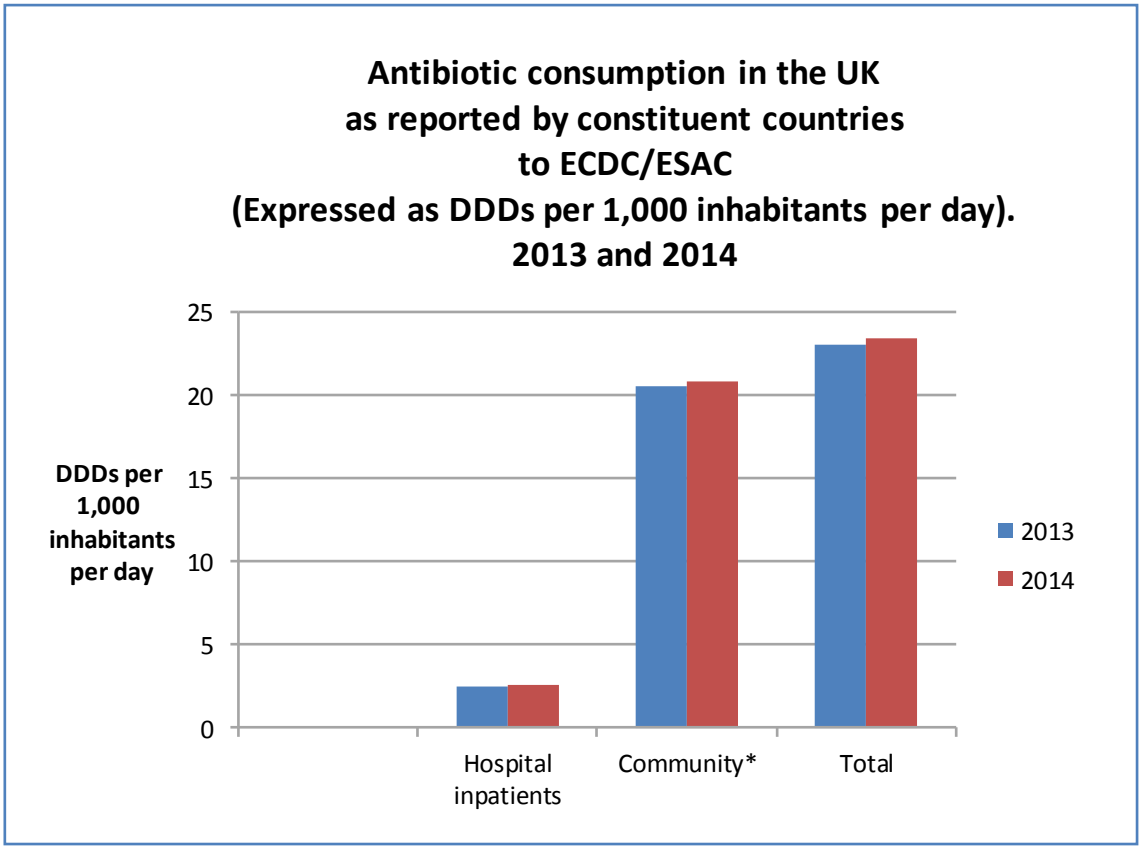
16 http://www.niauditoffice.gov.uk/primary_care_prescribing-2.pdf

Figure 5 shows UK consumption of antibiotics in hospitals and in the community. Data submitted to the European Centre for Disease Control (ECDC) shows an increase greater in hospital consumption across the UK than in the community. ECDC data are for hospital inpatients which does not equate to secondary care as measured in the UK, where secondary care includes hospital inpatients and outpatients. In Northern Ireland, the situation is different regarding outpatients. Outpatient prescriptions are usually dispensed in primary care therefore ECDC data for Northern Ireland hospital inpatients would equate to secondary care.

Figure 5: Antibiotic consumption reported to ECDC/ESAC by constituent countries of the UK.

Total antibiotic consumption expressed as DDD per 1000 inhabitants per day

UK from ECDC ESAC	2013	2014	% change
Hospital inpatients	2.45	2.59	5.7%
Community*	20.61	20.86	1.2%
Total	23.06	23.45	1.7%



note: as reported by constituent countries to ECDC/ESAC
***including hospital outpatients to ensure comparability with ECDC countries**
SOURCE: ECDC ESAC[17].
Note: In Northern Ireland - 2013, data was for 3 out of 5 Trusts (of the 2 which were unable to participate, 1 was the Belfast Trust which is the biggest Trust in NI). In 2014, all Trusts in Northern Ireland participated.

17 http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/database.aspx

The prescribed DDDs per 1000 population (and the annual percentage change) in antimicrobial prescribing over the four years, 2011 – 2014, is shown in figures 6,7 and 8 for primary care in the four UK countries.

There are clear differences between the 4 countries, with England having the lowest use and Northern Ireland the highest.

An increase in DDDs per 1000 population is seen in all four countries in each of the years from 2011. The UK as a whole showed a 5.3 % increase over the four year period.

Figure 6: primary care antibiotic prescribing

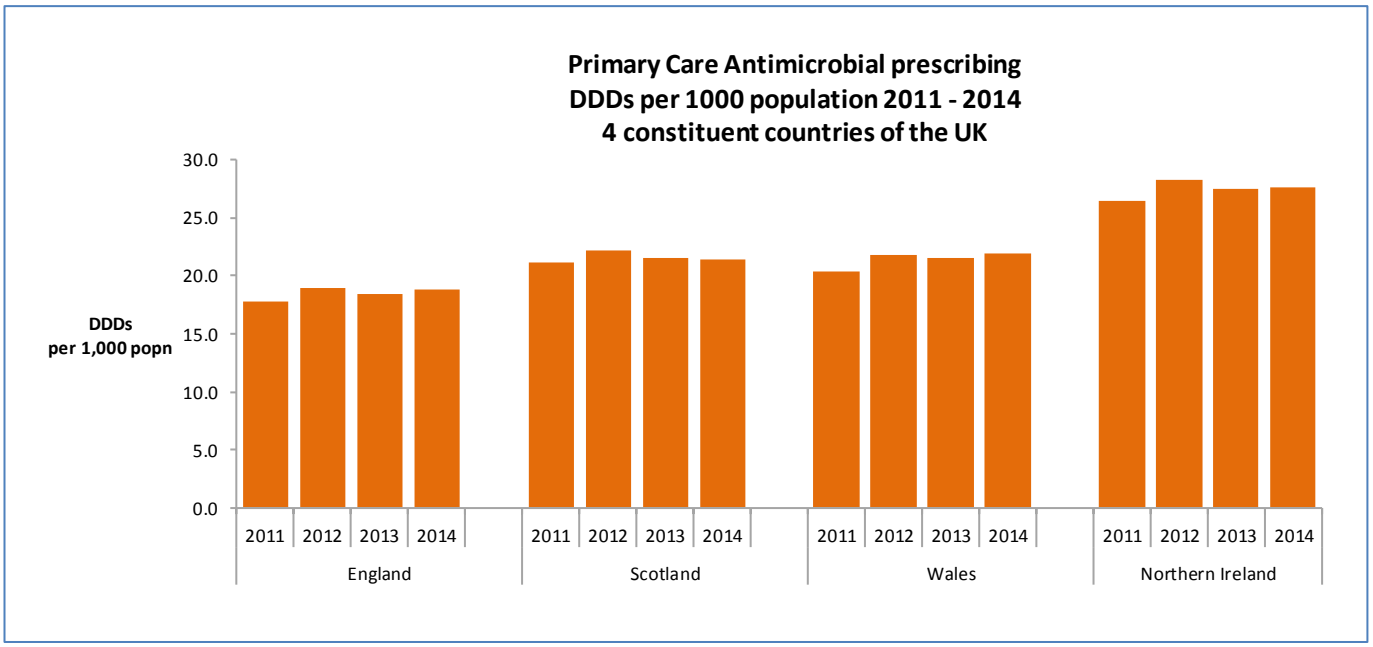


Figure 7: primary care % change in DDDs per 1000 population.

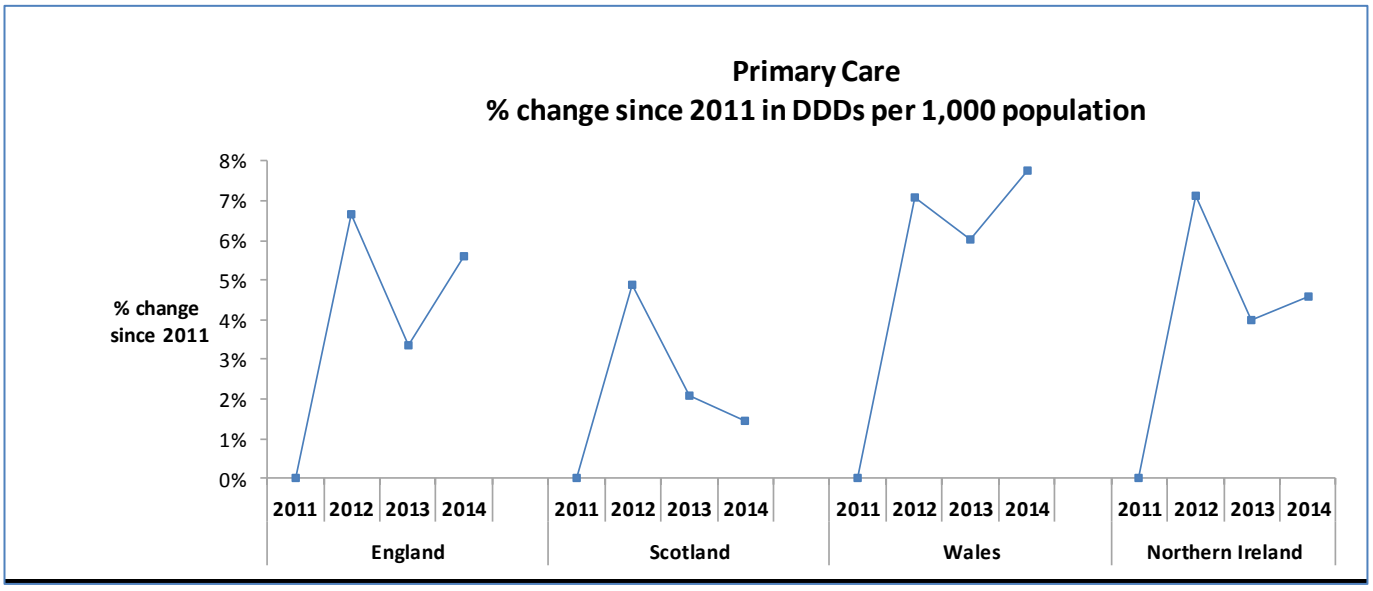
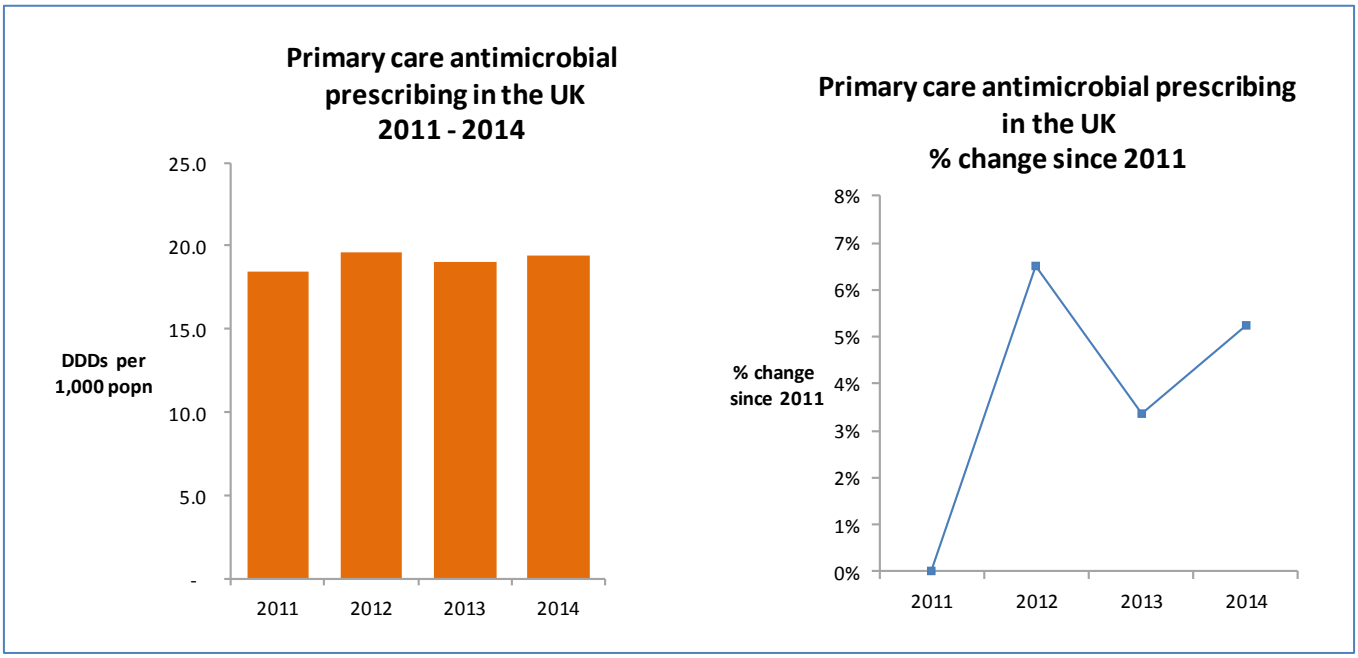


Figure 8: primary care aggregate figures for the UK.



Sources: England: ESPAUR 2015[18] . Scotland[19]. Wales: Personal communication: Antimicrobial Resistance Programme - Surveillance Unit[20]. Northern Ireland: Personal communication from DHSSPS. Populations quoted ONS MYE4: Population Estimates Summary for the UK, mid-1971 to mid-2014 published June 2015

The majority of antibiotic prescribing occurs in primary care. In secondary care, however, more broad-spectrum antibiotics, such as cephalosporins, are prescribed. Broad spectrum antibiotics are effective against a wide range of bacteria. These are more likely to drive resistance than narrow spectrum antibiotics.

What steps are we taking?

The High Level Steering Group published antibiotic prescribing quality measures for England in June 2014. In 2015, their implementation has been supported by NHS England through the Quality Premium (QP), providing a financial incentive for a reduction in prescribing of antibiotics in primary care and for validation of data in secondary care. The AMR Quality Premium, published in March 2015, required a reduction in antibiotic prescribing in primary care (1% total, 10% in broad spectrum antibiotics) and the validation of secondary care prescribing data. We have seen encouraging progress: achieving an almost eight percent reduction in antibiotics prescribed in primary care across England between April and December 2015.

In addition, we have trialled an approach whereby the CMO wrote to high prescribing GP practices to inform them where they stood in comparison to the prescribing levels of general practices generally. This trial saw prescribing of antibiotics in these practices fall by just over 3%.

NHS England is actively supporting better prescribing. It is:

18 https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation

19 http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Publications/2015-10-06/2015-10-06-SAPG-2014

20 http://www.primarycareservices.wales.nhs.uk/prescription-cost-analysis

- funding a programme aimed at placing over 350 clinical pharmacists into GP practices to give patients the additional support of an expert pharmacist in their GP surgery. Antimicrobial Stewardship is one of the priority themes on the training pathway for the pharmacists[21],
- through the Chief Pharmaceutical Officer, working toward the creation of local networks of pharmacists involved with antimicrobial stewardship across the whole health economy. The intention is to drive stewardship at a local level through these networks,
- working with PrescQIPP[22] to establish an Antimicrobial Stewardship Hub (free at the point of access) providing AMR resources, primary care prescribing data at CCG and GP practice level and a platform for sharing innovative practice,
- working with the NHS Business Services Authority (BSA) to publish a national antibiotic quality premium dashboard to support commissioner quality premium monitoring activity.

In Scotland continued progress has been made with a quality indicator for reduction of total antibacterial prescribing in primary care. This quality indicator introduced in 2013-14 is that antibiotic use, expressed in items/1000population/day, in at least 50% of GP practices in each NHS board will be at or below the current 25th percentile of Scottish practices or will have made an acceptable move toward that level. The indicator is supported by a national facilitated education programme for GP Practices. This quality indicator will run for a further year and complements a suite of quantitative and qualitative prescribing indicators available at GP practice level.

Hospital prescribing in Scotland has been subject to a prescribing indicator supporting the C. difficile HEAT[23] [24] target since 2009. Data is collected from a sample of patients each month in selected wards and results are fed back to clinical teams and reported at national level. In 2015 following successful achievement of good prescribing practice in acute receiving units and a period of testing new measures, a four element indicator focusing on documentation of prescribing initiation, review and administration was introduced in continuing care wards across all acute hospitals.

Detailed analysis of prescribing in one health board, which has electronic prescribing, is underway to gain an understanding of the reasons for increasing antibiotic use in hospitals. In parallel, a study to gather intelligence about use of carbapenems and piperacillin/tazobactam will support improvements in use of these important agents. The outputs from these initiatives will inform future national targets for hospital prescribing.

In Northern Ireland, local data are provided to GPs to enable them to monitor against a range of prescribing measures and a Medicines Optimisation Quality Framework was published in March 2016[25]. A scheme, similar to the NHS England scheme, where pharmacists are based in GP practices providing prescribing support, was launched in December 2015.

Other activity in support of improved prescribing of antibiotics includes the **NICE guidance** on Medicines Optimisation in March and on Antimicrobial Stewardship in August 2015. In Scotland, an electronic workbook for nurses and midwives was launched in 2015 to support their role in stewardship; pharmacists have a role as educational supervisors in their antimicrobial

21 https://www.cppe.ac.uk/wizard/files/developing_career/cppe%20hee%20general%20practice%20pharmacist%20learning%20pathway2.pdf

22 https://www.prescqipp.info/prescqipp-bulletin-downloads/viewcategory/5

23 http://www.gov.scot/About/Performance/purposestratobjs

24 http://www.gov.scot/About/Performance/scotPerforms/partnerstories/NHSScotlandperformance/HEATstandards

25 https://www.dhsspsni.gov.uk/sites/default/files/consultations/dhssps/medicines-optimisation-quality-framework.pdf

stewardship programme. In Wales, the impact of a series of new antimicrobial treatment guidelines is under review.

Health Education England (HEE) has been collaborating with various stakeholder organisations to explore ways of improving the signposting of prescribers to relevant AMR **resources and sources of support**. In addition to this, a basic introductory free e-learning module: 'Reducing Antimicrobial Resistance - An Introduction' was launched to coincide with World Antibiotic Awareness Week and European Antibiotics Awareness Day.

Patient awareness is an important factor in prescribing. PHE data[26] suggest that one in five people expect antibiotics when they visit their doctor and that four in ten members of the public believe that antibiotics can be used to treat viral infections. In the previous year to the survey, four in ten people with cough or symptoms of a cold and six in ten people with a sore throat had taken antibiotics. These conditions do not usually require antibiotics. GPs commonly express concerns that they feel pressured to prescribe antibiotics; we will continue to work to support GPs to manage these expectations.

In Northern Ireland public views regarding antibiotics were sought via a Department of Health, Social Services and Public Safety health survey 2014/15[27]. The results of this survey will help inform planning for a public information campaign in Northern Ireland in the future.

Launched in 2015 by the World Health Organisation (WHO), World Antibiotic Awareness Week (WAAW; 16-22 November 2015) augmented national antibiotic resistance campaigns such as the UK Antibiotic Guardian, European Antibiotic Awareness Day and analogous campaign weeks such as those in the USA, Canada and Australia with the aim of having a greater synergetic impact.

There is a clear increasing trend in **prescribing in secondary care**. Prescribing of broad spectrum antibiotics is more likely to drive resistance. We need to understand what is causing this increase and to improve infection prevention practices in secondary care to ensure that we are minimising the risk of healthcare associated infection that might be a contributory factor. In England, the new integrated indicator data sets will provide the data that will allow local teams to look at their local resistance patterns and factors that might be affecting those, and enable them to take local action to address this trend. All English NHS users can also access local, regional and national hospital and community data on AMR through the PHE Second Generation Surveillance System.

Better use of diagnostic testing is essential to improve antibiotic prescribing. Considerations of speed and cost often bias clinicians towards prescribing antibiotics "just in case". We need to take action to improve the **availability and use of diagnostic tests** that support improvement in prescribing. To date, we have commissioned a report looking at new diagnostics technologies on the horizon; this was published in July 2015. A microbiology laboratory survey was also undertaken. While the survey was limited by a low response rate with less than 35% of Trusts responding, it has identified significant variation in practice between laboratories; for example, at least 50% of responding Trusts did not use automated susceptibility testing and there was low uptake of direct molecular pathogen detection. The survey, together with the outcome of stakeholder workshops held in the summer of 2015, has informed the planned next steps.

26 https://www.gov.uk/government/news/entrenched-misconceptions-about-antibiotics-revealed-in-new-survey

27 health survey

Example of local action:

The Academic Health Science Networks (AHSNs) are promoting activity to combat AMR through a pilot scheme in the South West AHSN. This is a collaboration between the AHSN, NHS England dental leads and AMR lead and NHS Kernow CCG. The collaborative will be working with local dental practices, the dental school, and local community pharmacies to identify dental antibiotic prescribing patterns, and improve antimicrobial stewardship activities with the intention of sharing a resource tool for rapid adoption by other AHSNs. Contact Elizabeth Beech for more information.

Animal health

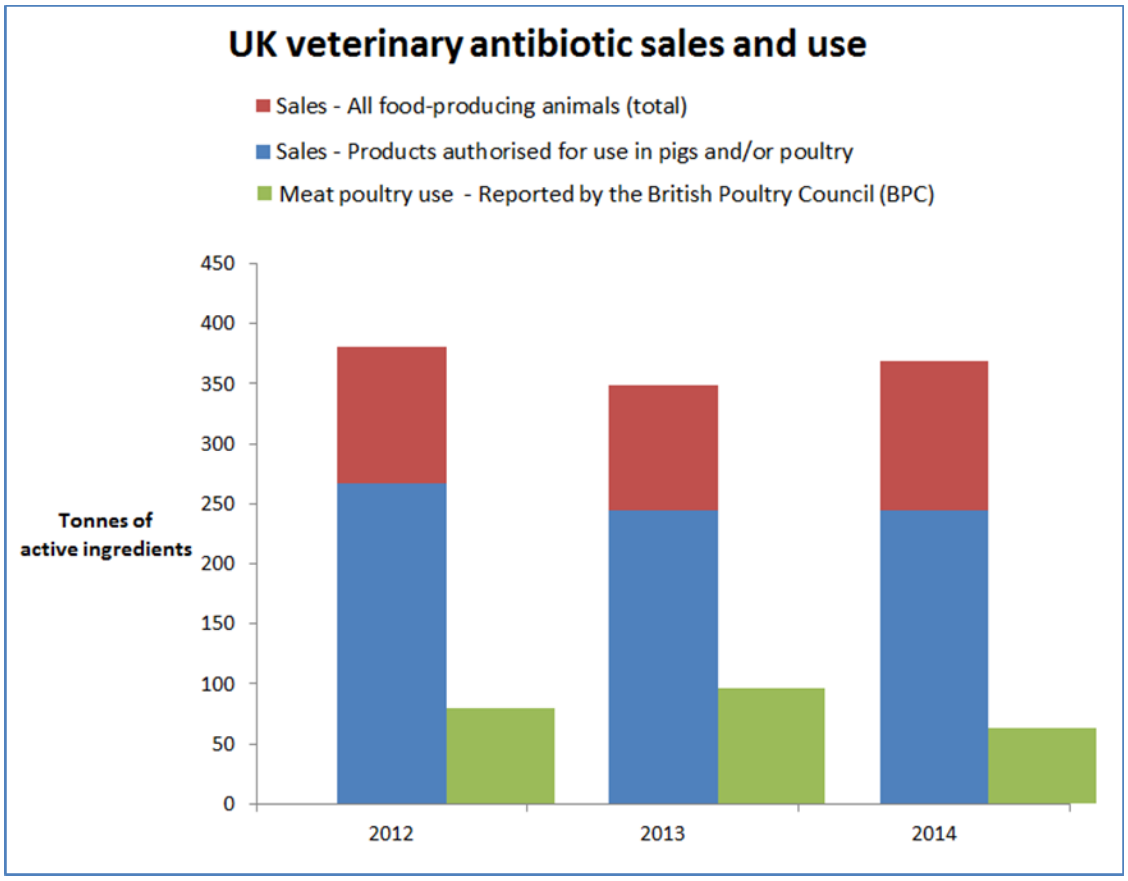
In November 2015, the Veterinary Medicines Directorate (VMD) published the third combined report of UK veterinary antibiotic sales and antibiotic resistance (VARSS), which describes 2014 data. It introduced, for the first time, consumption data from the British Poultry Council (BPC), (which represents approximately 90% of the meat poultry sector) and results from the 2014 statutory EU harmonised monitoring scheme in poultry. Key findings include:

- in 2014, a total of 369 tonnes of veterinary antibiotics were sold in the UK for use in food-producing animals, of which 244 tonnes were authorised for use in pigs and poultry. Preliminary 2015 BPC data shows a further reduction in use (28% drop) and a 53% reduction in fluoroquinolone use. Use data for pigs are not yet available but will be in the near future. Figure 9 shows total sales of antibiotics for food-producing animals, total sales for products authorised for use in pigs and poultry and usage data for the meat poultry sector between, 2012 and 2014.
- 57 milligrams (mg) of antibiotic (57 millionths of a kg) were sold in the UK for every kilogram of farm animal raised during that year. This represents little change from the 2013 figure of 56 mg/Population Correction Unit (PCU[28]) or to the previous six year mean of 55.5mg/PCU. Figure 10 shows the variation of the mg/PCU results between 2008 and 2014;
- fluoroquinolones and 3rd/4th generation cephalosporins (critically important antibiotics) accounted for only 0.3% and 0.6% of total sales respectively;
- colistin sales were less than 0.2% of UK antibiotic sales in livestock. Only four countries in Europe use less colistin in animals than the UK (three of these four countries use none).

Annex H contains an explanation of the caveats and limitations of comparing human and animal health data as described in the One-Health surveillance report.

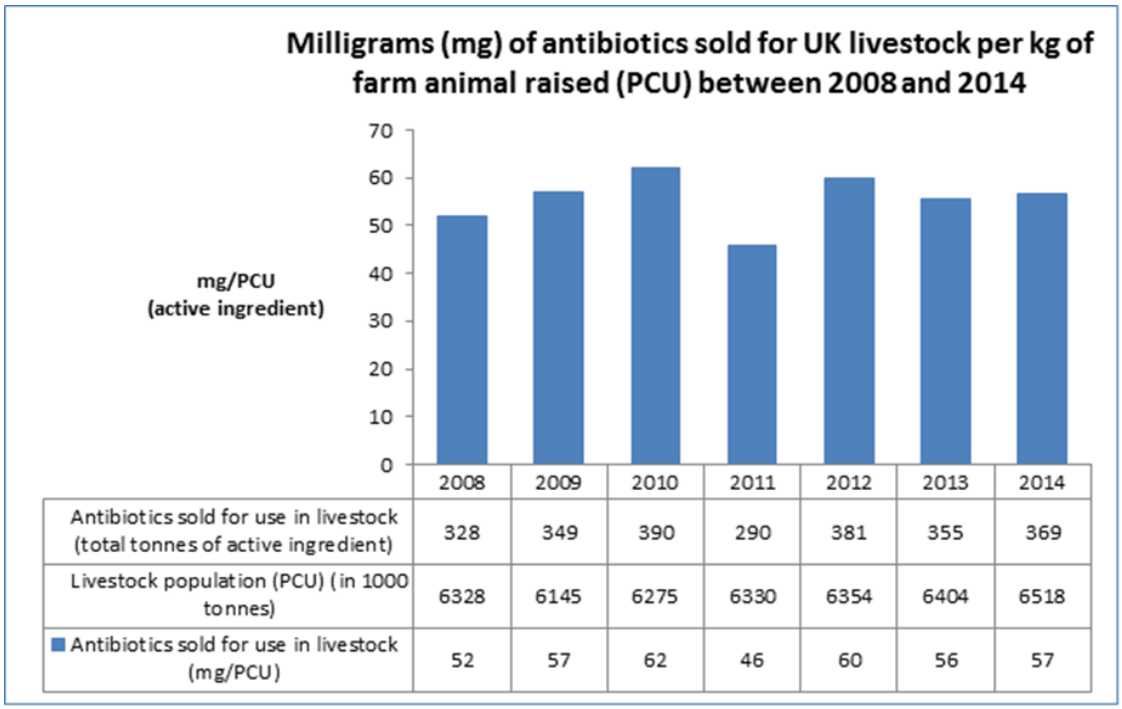
Figure 9: Sales and use of antibiotics (tonnes of active substance 2012-2014).

28 As total sales of antibiotics would be affected by changes in the size of the animal population and distribution of animal species, EU countries report on the average amount of antibiotic used in a year per kg of food producing animal raised, which is reported as mg/PCU (VARSS report, 2015).



Source: VARSS 2015

Figure 10: milligrams (mg) of antibiotics sold for UK livestock per kg of meat at time of treatment (PCU) between 2008 and 2014 (mg/PCU).

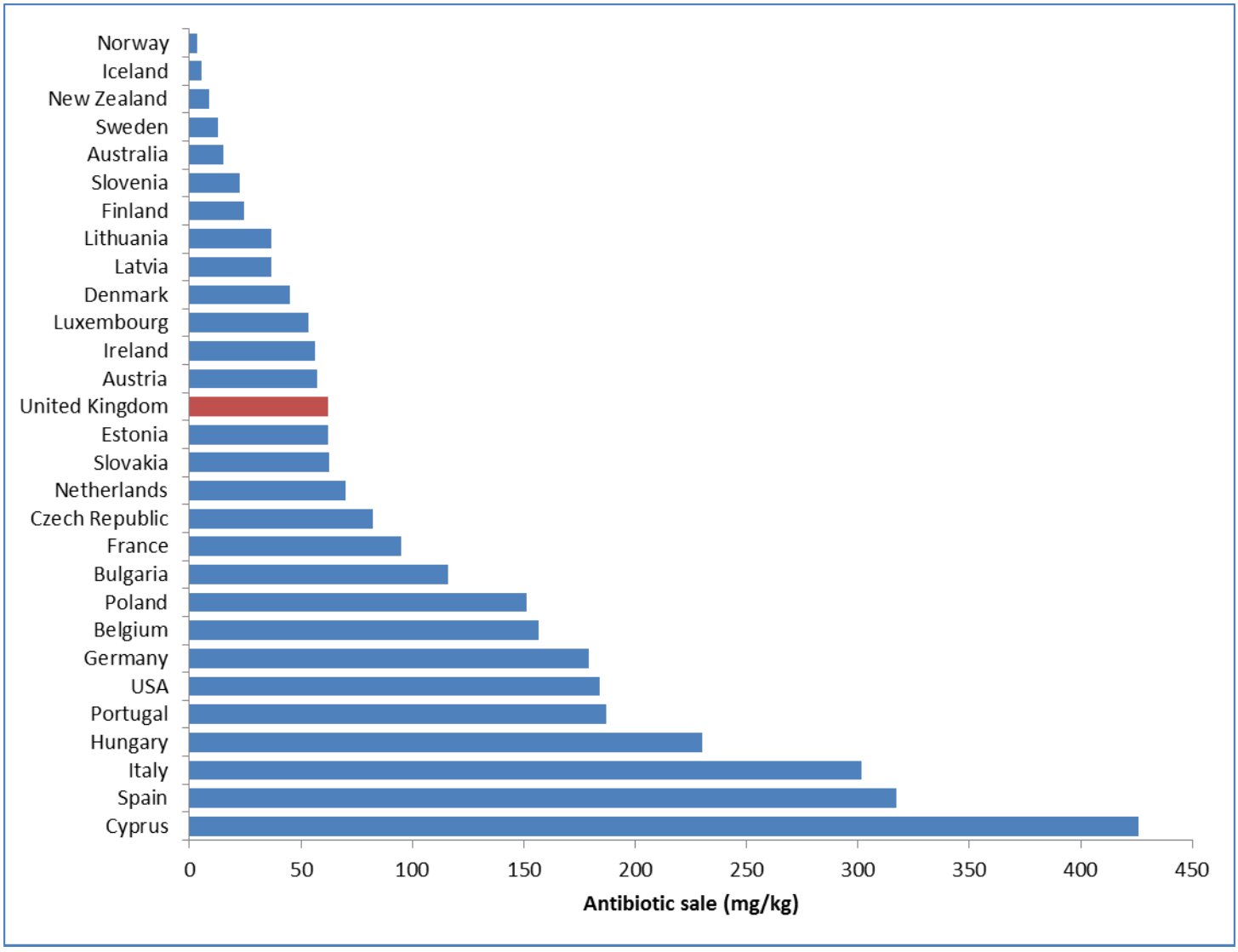


	2008	2009	2010	2011	2012	2013	2014
Antibiotics sold for use in livestock (total tonnes of active ingredient)	328	349	390	290	381	355	369
Livestock population (PCU) (in 1000 tonnes)	6328	6145	6275	6330	6354	6404	6518
Antibiotics sold for use in livestock (mg/PCU)	52	57	62	46	60	56	57

Source: VARSS 2015

In comparison with other EU/EEA countries, in 2013, the UK was the12th lowest user of antibiotics per kg of livestock out of 26 countries which provided data (ESVAC Report, 2015). For comparison purposes, results from New Zealand, Australia and USA were added to figure 11 (AMR review[29], 2015). Overall, the UK has a reasonably low use of antibiotics when taking into account the animal productivity compared to other countries.

Figure 11: Antibiotic sales for food-producing animals, including horses, by country for 2013 (mg/PCU).



Source: ESVAC[30], 2015; AMR review, 2015

The VMD has engaged across a number of species sectors and other non-governmental groups to develop guidance on the responsible use of antibiotics. Sector-specific engagement fora were first established in November 2013 by the VMD bringing together representatives from academia, animal keepers, veterinarians and retailers. Intelligence from these groups and sector trade bodies has informed the VMD's work on strengthening surveillance on antibiotic use and resistance and is helping target engagement work on promoting responsible use. In

29 http://amr-review.org/sites/default/files/Antimicrobials%20in%20agriculture%20and%20the%20environment%20-20Reducing%20unnecessary%20use%20and%20waste.pdf

30 http://www.ema.europa.eu/ema/pages/includes/document/open_document.jsp?webContentId=WC500195687

December 2014, the VMD published a reference document for keepers of livestock on the responsible use of animal medicines[31].

The VMD is also working with the Responsible Use of Medicines in Agriculture Alliance (RUMA) to provide educational tools and qualifications, raising awareness of resistance and promoting responsible use of antibiotics. Non-governmental organisations also have a key role in achieving the societal shift needed to tackle AMR. Two examples of professional bodies and other groups taking action to tackle AMR in their sectors are the Red Tractor Farm assurance scheme that imposed new requirements regarding antibiotic use in chickens[32] and Arla Food which introduced new standards on the use of antibiotics in dairy cows[33] to its 3000 supplier dairy farms.

Forward look

We continue to work towards identifying optimal antibiotic prescribing levels and to make year on year safe reductions in the use of antibiotics in both human and animal sectors. To that end in response to Lord O'Neill's report we have set clear England-wide ambitions to reduce inappropriate prescribing by half by 2020 and to reduce antibiotic use in livestock and fish farmed for food to the level recommended by Lord O'Neill by 2018. This is covered in more detail in the Government's response to the report, published alongside this progress report. We will also aim to standardise data reporting in the coming year to give a clearer picture of the overall UK position.

We will improve diagnostic testing to support better prescribing. C reactive protein (CRP) testing and urinalysis are readily available to many general practices and CRP has been shown to reduce antibiotic prescribing for respiratory tract infections by 25%[34]. We will develop example patient centred care pathways for diagnostic testing and describe commissioning models of provision for diagnostic services, identifying the costs and benefits of diagnostic tests across the pathway to ensure that the business case is made for investment in new technology, and for commissioning the right tests.

Initiatives that began in early 2015 using behavioural change interventions and financial incentives have had a positive effect on prescribing. We will do more work to understand and make use of all the levers we have available to ensure that professionals and the public follow best practice advice. We will bring work on improved prescribing and on infection prevention and control together to see where we can best bring pressure to raise standards, and to identify how we can best support local teams to identify local issues and put plans in place.

Key to making progress will be empowering local teams to set levels of ambition for improvements in prescribing that are appropriate for their populations. Data for human health is now available on a single site in England so that prescribers can compare infection rates and antibiotic prescribing levels of their own local hospitals and GP practices with others. These data will inform local action on AMR and encourage local teams to set ambitious goals for the reduction in infections and inappropriate prescribing. These data will also be accessible to patients and the public, aiding transparency and accountability. On the animal side, we intend to supplement sales data with livestock sector use data as the data collection systems are gradually put into place.

31 https://www.gov.uk/government/publications/responsible-use-of-animal-medicines-on-the-farm

32 http://assurance.redtractor.org.uk/rtassurance/schemes/Standards%20home/Standards2014.eb

33 http://www.arlafoods.co.uk/overview/about-us/company/news/2015/pressrelease/arla-foods-launches-arlagaarden-in-the-uk-1228817/

34 PHE Health Matters /https://publichealthmatters.blog.gov.uk/2016/01/07/health-matters-your-questions-on-antimicrobial-resistance/

We know that antimicrobial resistance genes (ARGs) can transfer between bacteria and that bacteria can pass between animals, humans and the environment. Key to addressing the problem of the maintenance and spread of ARGs in the environment is understanding better the factors and their relative role in selection for, and maintenance of resistance and contribution to dissemination routes. Monitoring of some of these factors will commence soon.

More widely, we will continue to raise awareness amongst the public of the simple steps they can take to reduce the risk of them and their loved ones acquiring infections in the first place through the Antibiotic Guardian campaign and utilising other campaigns to include messages on AMR such as the Stay Well this winter campaign.

PROMOTE the development of new drugs

The third pillar in slowing the growth in AMR is to **PROMOTE** the development of new drugs and alternative treatments.

The Review on AMR, announced by the Prime Minister in July 2014 and led by Lord O'Neill[35], has published a series of discussion papers. These papers have addressed the economic and health burden of AMR, potential solutions to reinvigorate AMR research and the drugs pipeline, diagnostics and One-Health, agriculture and the environment, alternative treatments and infection prevention, control and surveillance. The final report and recommendations were published on 19th May 2016.

While the Review had an international focus, there are areas where the UK, working with international partners, is well placed to take a lead. In October, during the Chinese state visit, David Cameron announced that the UK and China agreed to develop a new fund to support vital research and development on antimicrobial resistance. We will encourage other countries to contribute funding and address the need identified by the Review for significantly more investment in research in AMR.

At the same time, the Department of Health (DH) and the life science industry have been working collaboratively to explore what might be done in the UK, alongside the completion of the Review and in the light of its interim outputs, to boost the development of new antibiotics and diagnostics. The focus of this engagement over the last year has been on the scope for, and development of, a potential antibiotic pricing and reimbursement model that would take account of the unpredictable nature of usage over the life course of a product. The AMR Funders Forum and the UK government's international work on AMR continue to ensure collaboration between academia, industry and the NHS to both build the underlying knowledge about AMR, for both human and animal health, and support the development of new treatments.

We commissioned the Wellcome Trust to undertake a review of alternative treatments[36]. While many approaches have potential, the report concludes that there is a continued need for conventional antibiotics to treat the majority of infections for the foreseeable future. We continue to work with the Medical Research Council, Business, Energy and Industrial Strategy (BEIS), the Office for Life Sciences and Innovate UK to ensure that we have the capability and capacity required to develop potential new treatments over the next decade.

Forward look

The final report from the Independent Review on AMR was published on 19 May 2016. The recommendations in the report have a global focus but, as promised in the UK Government's manifesto, have we will continue to lead the global fight against AMR, taking forward those recommendations in collaboration with our international partners. We will work with the Chinese Government on a global innovation fund and we are exploring options to work with other countries to pilot new funding models.

35 http://amr-review.org/

36 Lancet Infect Dis 2016; 16: 239–51 Published Online January 12, 2016 http://dx.doi.org/10.1016/ S1473-3099(15)00466-1

Underpinning work programmes

The three pillars of preventing infection, protecting the antibiotics we have and promoting the development of new ones, are underpinned by surveillance, research and international collaboration. Better surveillance will support the collation of information about infections, prescribing and rates of resistance, and enable those at local, regional and national level to take the right action and work to improve our understanding of resistance and the best means of tackling it. Research underpins the effort to strengthen AMR control through the application of new knowledge and approaches. Our national work is also underpinned by action taken internationally, ensuring that tackling AMR is prioritised by governments across the globe.

Surveillance

It has only been possible to provide the data included in this report because of the comprehensive surveillance programmes on bacterial resistance and antibiotic use in both human and animal medicine in each of the four nations of the UK. These systems improve year on year, resulting in what is one of the most comprehensive **surveillance** systems for AMR in the world.

For human health in 2014, while resistance rates have remained relatively stable overall, the incidence of resistant infections has increased. Antibiotic use in the UK has also increased. Animal use, based on sales data, has remained stable over the lifetime of the strategy for both livestock and companion animals, and resistance in veterinary pathogens has remained low (VARSS, 2015).

In July, we published the first UK One-Health surveillance report spanning human and animal health encompassing antibiotic resistance and consumption data across the human and animal sectors across England and the Devolved Administrations, providing recommendations for actions required. We will build on this first report to include more detailed data in future reports, starting with the next report, planned for 2017.

The One-Health report represents an important first step in aligning data across both sectors and includes recommendations to address current data limitations and to improve integrated analyses of human and animal antibiotic consumption and resistance data[37].

PHE rolled out the second generation surveillance system for the reporting of infectious diseases and antimicrobial resistance in humans in December 2014. It has also developed an electronic system for reporting infections with carbapenemase-producing organisms, to allow demographic and clinical risk information to be captured and analysed[38].

Scotland has introduced a framework for local surveillance of antimicrobial use, which details reporting requirements for hospital and primary care which was added to the mandatory national Healthcare Associated Infection surveillance programme. Surveillance data for primary care has been available for several years and more recently has included patient level data, allowing reporting by age group, sex, and also for patients in care homes. Systems are in place

37 https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals

38 https://www.gov.uk/government/publications/carbapenem-resistance-implementation-of-an-enhanced-surveillance-system

for national, health board and GP Practice level reporting and a suite of primary care prescribing indicators are available.

In Northern Ireland, surveillance of device-associated infections in critical care settings has continued, with validation of CLABSI (central line associated bloodstream infections) completed in 2015. Priority areas for implementation of the Strategy for Tackling Antimicrobial Resistance (STAR) include the development of infrastructure and arrangements to deliver antibiotic usage and resistance surveillance. It is anticipated that systems supporting region-wide surveillance will be further developed during 2016. Enhanced surveillance of Carbapenemase producing organisms continues and programme outputs are regularly shared with all Health and Social Care Trusts.

During the year, we were one of the ten EU countries to participate in a pilot to determine methods of collection of actual use data in the pig industry to identify a scheme that could be adopted across the EU. We have since built on this. Working with the pig industry, we are developing a pig medicine hub, the e-MB (electronic Medicine Book for the pig sector), for the routine collection of such data. Further, the poultry industry has provided, for the first time, usage data collected from British Poultry Council (BPC) members, (representing 90 % of the commercial meat poultry industry).

Forward look

Good data are core to targeting our efforts most effectively. In England, we aim to publish the ESPAUR reports each year with increasingly comprehensive data and targeted in depth areas of focus. We want to get to the point where we know which antibiotic has been prescribed and for what infection. We will then be able to see the impact of changes in infection rates on prescribing and resistance and match this to patient outcomes to enable better decision making locally about appropriate treatments and responses to outbreaks.

We will also work to ensure that the data collected in the four nations are reported in the same way, so that we can have a clearer picture of the overall UK position in the next annual report. We will build on the pilot work of collecting antibiotic use data in pigs, reporting of use in the poultry industry and work with the dairy industry to develop similar capability for dairy cattle use.

Research

We now have unprecedented levels of research collaboration, coordinated by the AMR Funders Forum, supported by the Medical Research Council (MRC). This includes a £40m AMR cross-council initiative, led and managed by the MRC on behalf of all seven research councils, which set up four themes to tackle AMR (specifically antibacterial resistance).

These aim to:

Understand resistant bacteria
Accelerate therapeutic and diagnostics development
Understand AMR and the real world interactions
Understand behaviour within and beyond the health care setting

The MRC on behalf of the Joint Planning Initiative on AMR, has undertaken an exercise in mapping AMR research (specifically anti-bacterial research) publically funded across 21 participating countries, including the UK, and European Union(EU) from 2007-2013 and a full report and database is available through the Joint Planning Initiative on AMR website[39]. A paper was publsihed in the Lancet in December 2015.A paper on alternatives to antibiotics (a pipeline portfolio review) was also published in the Lancet in January 2016[40].

The National Institute for Health Research (NIHR) AMR themed calls are now closed and 16 projects will be funded at a cost of £15million. Some additional proposals are under consideration and further projects have been funded by VMD. A full list of the projects is included in Annex G. At the same time, the Scottish government has funded a consortium of researchers to look at the prevention and control of HCAIs and the challenge of dealing with AMR. A Northern Ireland AMR network has also been established, bringing together multi-sectoral, multi-disciplinary researchers, policy makers and practitioners. The vet schools council has also established an AMR group.

Forward look

Ensuring that the research councils, academia and industry continue to collaborate is essential, but we also need to ensure that the outcome of research is effectively disseminated and used to inform policy and practice.

The requirement for research continues to evolve as we learn more. We therefore need to feed in new research requirements as they arise. In April 2016 the Wellcome Trust hosted an international One-Health AMR Science Summit which brought experts from around the world together to test whether we are asking the right research questions to reduce AMR.

International work

AMR is a global problem, and no single country can tackle it alone. Effective control requires action at both domestic and international levels. In our first annual report we said that the WHO had adopted a resolution on AMR. In the second year, more progress has been made as we moved from raising awareness to galvanising action, with the UK showing global leadership on AMR. The World Health Assembly adopted a Global Action Plan (GAP) on AMR in May 2015. All countries are required to develop national AMR action plans within two years. Resolutions on AMR were adopted by the Food and Agriculture Organisation (FAO) and the World Organisation for Animal Health (OIE) which cross-refer to the WHO's global action plan, reinforcing the One-Health approach to tackling AMR.

We have continued to strengthen international engagement through project and programme work in a number of countries and promoted the work of the internationally focused Review on AMR lead by Lord O'Neil.

In 2015, the G7 Leader's Summit declaration included a strong statement on AMR, further supported by the G7 Health Ministers meeting in October, with the G20 leader's communique underscoring the importance of a coordinated international response. The UK continues to

39 http://www.jpiamr.eu/

40 Published Online January 12, 2016 http://dx.doi.org/10.1016/S1473-3099(15)00466-1

encourage and support international action on AMR through the Global Health Security Agenda (GHSA). The UK is one of six countries leading the AMR action package within the GHSA, alongside the Netherlands, Sweden, Canada, Germany and Japan. This work is focused on supporting implementation of the GAP by facilitating sharing of evidence in both human and animal sectors, and expertise in implanting strategies to tackle AMR. Following a productive meeting of the leading and contributing countries of the AMR Action Package in Seoul in September, we have been working closely with WHO, FAO and OIE to focus on GAP implementation, establishing three subgroups within the action package and influencing country thinking ahead of the United Nations meeting in September. The UK also contributes to six further action packages across the prevent, detect and respond pillars of GHSA; zoonotic disease, biosafety and biosecurity, nationwide laboratory systems, surveillance, emergency operating centres and countermeasures.

Although the UK has an excellent surveillance system, many parts of the world do not. This puts those countries at a huge disadvantage in taking forward action to tackle AMR, as they do not have the core data upon which to base a robust action plan. That is why the UK government has committed £265 million over five years to launch a new Fleming Fund that will support AMR surveillance world-wide. The fund will focus on enhancing laboratory capacity and surveillance networks in developing countries.

In October 2015, the UK Prime Minister and the Chinese President, Xi Jinping, announced the intention to create a Global AMR Innovation Fund. The aim of the fund is to increase investment to stimulate global research in AMR. The UK has committed £50m to set-up this Global AMR Innovation Fund to target and coordinate investment globally. In addition to the partnership with China, the UK will continue to engage internationally with other governments, third-sector, and industry to leverage the additional global investment required for AMR R&D.

AMR remains a priority for the Foreign and Commonwealth Office (FCO), particularly through the Science and Innovation Network (SIN), based in 28 countries, as well as through the cross-government health teams in India and China. Two SIN AMR programmes have been developed for 2015-16. PHE and the AMR Research Funders Forum has helped with programme design, to ensure coherence with wider UK activities.

More widely, SIN and cross-government health teams in India and China have helped the National Endowment for Science, Technology and the Arts (NESTA) promote the Longitude Prize, including at events and engagements in Brazil, India, China, the US, Germany and Switzerland. It has also supported international engagement by the independent Review on AMR including outreach visits to China, India the US and Brazil. A UK-Japan SIN programme was supported by the VMD and Animal and Plant Health Agency (APHA) in 2014 with follow-up visits and agreed future engagement; and the VMD supported the UK-Russia SIN meeting (2015).

The Newton Fund is being used to support two joint UK-India global AMR research centres focussing on new diagnostic tools and treatments to address the sharp rise in cases of multidrug resistant tuberculosis (MDR-TB) and finding solutions to the inappropriate use of antibiotics. In addition, a joint fund of £4.5 million from the UK with matched funding from China to support research on AMR between the MRC, the Biotechnology and Biological Sciences Research Council (BBSRC), the Economic and Social Research Council (ESRC) and the National Natural Science Foundation of China (NSFC) was announced during the October China State visit. Further Newton Funded research calls on wider themes such as infectious diseases may support AMR. The VMD contributed to an OIE workshop on identifying vaccine opportunities that would support reduced use of antibiotics in livestock and aquaculture.

Forward Look

We will continue to work to foster and strengthen existing international collaboration to tackle AMR in the context of the final recommendations of the independent review on AMR.
Our overarching goal is to reach international agreement on a framework for combating AMR that will support implementation of the WHO GAP and promote the development of new drugs. Following progress at the WHO, FAO and OIE, and as mandated by the WHO GAP and the FAO resolution, we will now work to secure a successful meeting on AMR at the UN general assembly meeting in 2016.

In animal health, further enhanced surveillance will be implemented. The presence of resistance mechanisms in E. coli and Campylobacter obtained from broiler chickens and turkeys at slaughter will be monitored. More specifically, tests for ESBL, AmpC and carbapenemase producing E. coli will be undertaken. Work has also been initiated by the Food Standard Agency in 2016 to check for the presence of resistant E. coli obtained from chicken and turkey meat samples at retail.

The Year Ahead (2016)

We have made considerable progress in tackling AMR at a national level by putting in place the building blocks of better and more accessible data, new guidance and an enhanced antimicrobial stewardship framework. Internationally, the adoption of Resolutions in multilateral organisations is a significant achievement. But we know that we have yet to see definitive evidence that our interventions are working, and we will do more in 2016.

We will shift from developing strategy and disseminating guidance at the **national level** to supporting action at the **local level** in England, empowering and supporting change driven in local teams. We are ensuring that local teams have the detailed data they need to understand their own performance. We will also ensure that local data are transparent, simple to understand and accessible by both local teams and members of the public. We will develop a network of AMR leaders to ensure that awareness levels are raised and to lead the development of local action to improve antibiotic stewardship at every level in every healthcare setting.

This does not mean that there is nothing to be done at the national level. A common thread running through the strategy is the need to change behaviour, both of professionals and the public. For example, professionals need to be supported in not prescribing antibiotics and the public need a better understanding of symptoms, how to manage self- limiting illness at home, and when they should visit a GP or seek advice from the local pharmacist. They also need to understand when antibiotics will help, and the risks and possible side effects of taking them. We will explore how we can use behavioural tools to drive these positive changes.

We will make recommendations to deliver improvements in diagnostic systems so that diagnostics tests are carried out at the most appropriate place and time, and ensure that appropriate tests that are available now are being used to support treatment decisions. We will be working to implement the recommendations of the Review on AMR led by Lord O'Neill, as set out in the response to the review published alongside this progress report. The focus of the UK's **international work** is now directed towards **three** main areas. **Firstly**, we will continue to build support to take forward the recommendations of the Review on AMR, including through efforts to promote a focus on AMR during China's G20 Presidency in 2016. These steps will be critical towards a sustainable global response to the AMR threat. **Second**, we are actively leading and contributing to work with other countries, supporting development of national action plans in the next two years in order to implement the WHO GAP. This includes work through the GHSA. **Thirdly**, following progress at the WHO, FAO and OIE, we are working to secure a successful high level meeting on AMR in the UN General Assembly in 2016.

We will continue to build support for a positive global response to the recommendations of the Review on AMR, including through efforts to promote a focus on AMR during China's G20 Presidency in 2016. These steps will be critical towards a sustainable global response to the AMR threat.

We will also look into potential drivers of dissemination of resistance genes in the environment along with the potential dissemination routes.

The second year of the UK AMR Strategy has been a year of substantial achievement in terms of delivery. We now have the building blocks in place to make a real difference. We are acutely aware, however, that we have yet to see conclusive evidence that we are making a difference in

levels of resistance. While initiatives begun in 2015 are beginning to demonstrate impact, we consider it vital in 2016 that we focus on action at a local level in order to embed good practice in the prevention and control of AMR in every part of the health system.

Projects in 2016/1017

The UK HLSG that oversees and drives implementation of the Strategy has reviewed the implementation plan published last year in the light of new data and other emerging information and research findings. The focus of the coming year's programme is on the key projects set out below. These will help us make progress towards our England-wide ambitions set in response to the Lord O'Neill's review to halve inappropriate prescribing by 2020; halve the number of healthcare associated bloodstream infections that pose the biggest risk – such as E-coli - by 2020; and setting an overall target for antibiotic use in livestock and fish farmed for food, cutting use to the level recommended by Lord O'Neill by 2018.

No	Project title	Key action area reference	Aim/ descriptor
1	Local AMR action	1 - IPC 2 - prescribing 3 - training 5 - use of surveillance	Making the integrated indicated data set available and supporting local AMR action, empowering local teams in England
2	Improved use of diagnostic testing	2 - prescribing 4 - new diagnostics	To support good antibiotic stewardship across the human and animal health system.
3	Supporting Behavioural change	1 - IPC 2 - prescribing 3 - training	Supporting good stewardship of antimicrobials through evidence based interventions.
4	Promoting the development of new drugs, diagnostics and alternative treatments	4 - new drugs, treatments and diagnostics	To support stewardship and promote a sustainable supply of new antimicrobial drugs
5	Expanding surveillance for human health	5 - surveillance	Measuring the impact of initiatives on antimicrobial use and resistance.
6	International work	7 - strengthened international collaboration	Supporting countries to build capability and capacity and working towards a high level meeting at the United Nations
7	Education and training	1 - IPC 2 - prescribing 3 - training	To ensure that antimicrobial stewardship is a core part of training for all working in human and animal health and social care
8	Expanding	5 - surveillance	Measuring the impact of surveillance

	surveillance for animal health		systems and antimicrobial stewardship on antibiotic use and resistance.
9	Engagement for animal health.	1 - IPC 2 - prescribing 3 - training	To improve stewardship through education and training, working across species sectors.
10	Improved biosecurity to reduce incidence of infection.	1 - IPC	To improve livestock productivity, welfare and industry resilience.
11	FSA systematic literature review	1 - IPC 5 - surveillance	To increase understanding of the role of food production, processing and consumption in the development and spread of AMR.

Key action area 1: Improving Infection Prevention and Control (IPC) practices in human and animal health, both through enhanced dissemination and implementation of best practice and better use of data and diagnostics.
Key action area 2: Optimising prescribing practice through implementation of antimicrobial stewardship programmes that promote rational prescribing and better use of existing and new rapid diagnostics.
Key action area 3: improved education, training and public engagement to improve clinical practice and promote wider understanding of the need for more sustainable use of antibiotics.
Key action area 4: developing new drugs, treatments and diagnostics, through better collaboration between research councils, academia, industry and others; and by encouraging greater public-private investment in the discovery and development of a sustainable supply of effective new antimicrobials, rapid diagnostics and complementary tools for use in health, social care and veterinary systems.
Key action area 5: better access to and use of surveillance in human and animal sectors through new arrangements that facilitate greater consistency and standardisation of the data collected across the system and encourage improved data linkage.
Key action area 6: better identification and prioritisation of AMR research needs to focus activity and inform our understanding of AMR. This may identify alternative treatments to new drugs as well as new or improved rapid or point-of-care diagnostic tests for humans and animals.
Key action area 7: strengthened international collaboration working with and through a wide range of governmental and non-governmental organisations, international regulatory bodies and others to influence opinion, galvanise support and mobilise action to deliver the scale of change needed globally.

Annexes

Annex A - summary of key work and achievements in 2015

A detailed implementation plan was published in the first annual progress report. The following is a summary of the key pieces of work that have been completed and achievements in 2015.

Infection Prevention and Control
The Health and Social Care Act 2008 Code of Practice on the prevention and control of infections and related guidance was revised and published in July 2015; links to AMR, antibiotic stewardship, including IPC, were strengthened.
The NHS Standard Contract, published in March 2015, included amendments to require compliance with the Code of Practice.
A Carbapenemase-producing Enterobacteriaceae (CPE) toolkit for the non-acute and community sector was published in June 2015.
The NICE urinary tract infection in adults quality standard was published in June 2015.
A structured three year training programme for medical infection trainee doctors in England is now in place covering all aspects of infection and control.
Publication of Healthcare Associated Infection Standards in Scotland.

Optimised Prescribing Practice
The behavioural insights randomised control trial targeting GPs with high antibiotic prescribing rates showed a reduction in antibiotic prescribing of over 3.0%.
The National Institute for Health and Care Excellence (NICE) published guidance on Medicines Optimisation in March and on Antimicrobial Stewardship in August 2015.
The NHS England 2015/16 AMR Quality Premium, published in March 2015, required a reduction in antibiotic prescribing in primary care and the validation of secondary care prescribing data.
The Trust Development Authority (TDA) included measures to address AMR in non-Foundation Trusts in 2015/16 annual planning and technical guidance.
In Scotland, pharmacists who have developed a personal e-Portfolio of evidence have completed the process of becoming educational supervisors in the Scottish antimicrobial stewardship programme launched in 2014, and will be supporting the next tranche of learners.
In December 2014 the Veterinary Medicines Directorate (VMD) published a reference document for keepers of livestock on the responsible use of animal medicines.
In May 2015, 2 Sisters Food Group removed all antibiotics considered “critically

important to human health" by the WHO from its poultry production.

The Veterinary Schools Council established an AMR Group with the primary aim of raising awareness amongst students about resistance and appropriate prescribing. The Group will also promote research on AMR.

A RUMA- VMD conference on responsible use was held in November. This conference was for anyone involved or interested in the use of medicines in food producing animals. RUMA announced (Dec 2015) voluntary restrictions on colistin use in the UK livestock.

Health Education England, in collaboration with PHE and NHS England, launched an introductory level module on antimicrobial resistance.

Since October 2015, over 3000 dairy farmers supplying Arla Food UK have had to comply with new standards on the use of antibiotics in dry cows as part of their quality assurance programme. A transition from blanket prophylaxis to selective dry cow therapy is expected to be outlined in the farm health plan (a tool designed to assist farmers to maintain accurate records of animal health and management).

Public engagement

European Antibiotics Awareness Day (EAAD) 2015/ Antibiotic Guardian plans have consolidated and built on the approach and learning from 2014.

World Antibiotic Awareness Week, launched in 2015 by the WHO has enhanced the national EAAD AMR campaign.

Guidance on LA-MRSA for people who work with livestock was published on gov.uk and distributed at the London Vet Show[41].

Developing new drugs

DH funded the Centre for Evidence Based Medicine at Oxford to produce a review of Antimicrobial Resistance Diagnostics; this was published on their website on 15 July.

PHE undertook a national microbiology laboratory survey; the survey showed a significant variation in use of tests between laboratories.

A report commissioned to look at emerging technologies for alternative treatments to antibiotics was completed.

The independent Review on AMR, led by Lord O'Neil, published a series of short reports during late 2014 and 2015 addressing the burden of AMR, potential solutions to reinvigorate AMR research and the drugs pipeline, diagnostics and one health.

Surveillance

41 https://www.gov.uk/government/publications/la-mrsa-information-for-people-who-work-with-livestock

In July 2015 the first UK One-Health report was published encompassing antibiotic resistance and consumption data across the human and animal sectors, providing recommendations for actions required.

PHE published the ESPAUR annual report in November, expanded to include additional data.

Trust validation of antimicrobial consumption data was included as part of the 2015/16 CCG Quality Premium.

PHE developed an electronic system for reporting carbapenemase-producing organisms, to allow demographic and clinical risk information to be captured and analysed.

The VMD published the third combined report of the UK veterinary antibiotic sales and antibiotic resistance data in November (VARSS 2014).

The British Poultry council (BPC) published their usage data 2015 in February 2016. Data showed a 28% drop in overall antibiotics usage and fluoroquinolones usage was reduced by 53% compared to 2014.

Scotland introduced a framework for local surveillance of antimicrobial use, which details reporting requirements for hospital and primary care which was added to the mandatory national HAI surveillance programme.

In Northern Ireland, surveillance of device-associated infections in critical care settings has continued, with validation of CLABSI (central line associated blood stream infections) completed in 2015.

Research

The National Institute of Health Research (NIHR) announced that 16 projects are being funded at a cost of approximately £15million following the AMR themed calls.

The MRC has undertaken mapping of AMR research on behalf of the European Joint Programme Initiative on AMR (JPIAMR); a full report and database is available through the JPIAMR website with a link from the MRC website.

The AMR cross council initiative has supported multidisciplinary proposals at a cost of £36m bringing different research communities and skills together to tackle AMR (http://www.mrc.ac.uk/research/initiatives/antimicrobial-resistance/tackling-amr-a-cross-council-initiative/

The Scottish government has funded a consortium of researchers to look at the prevention and control of HCAIs and the challenge of dealing with AMR.

In 2015, a Northern Ireland AMR network was established, bringing together multi-sectoral, multi-disciplinary researchers, policy makers and practitioners.

International Collaboration

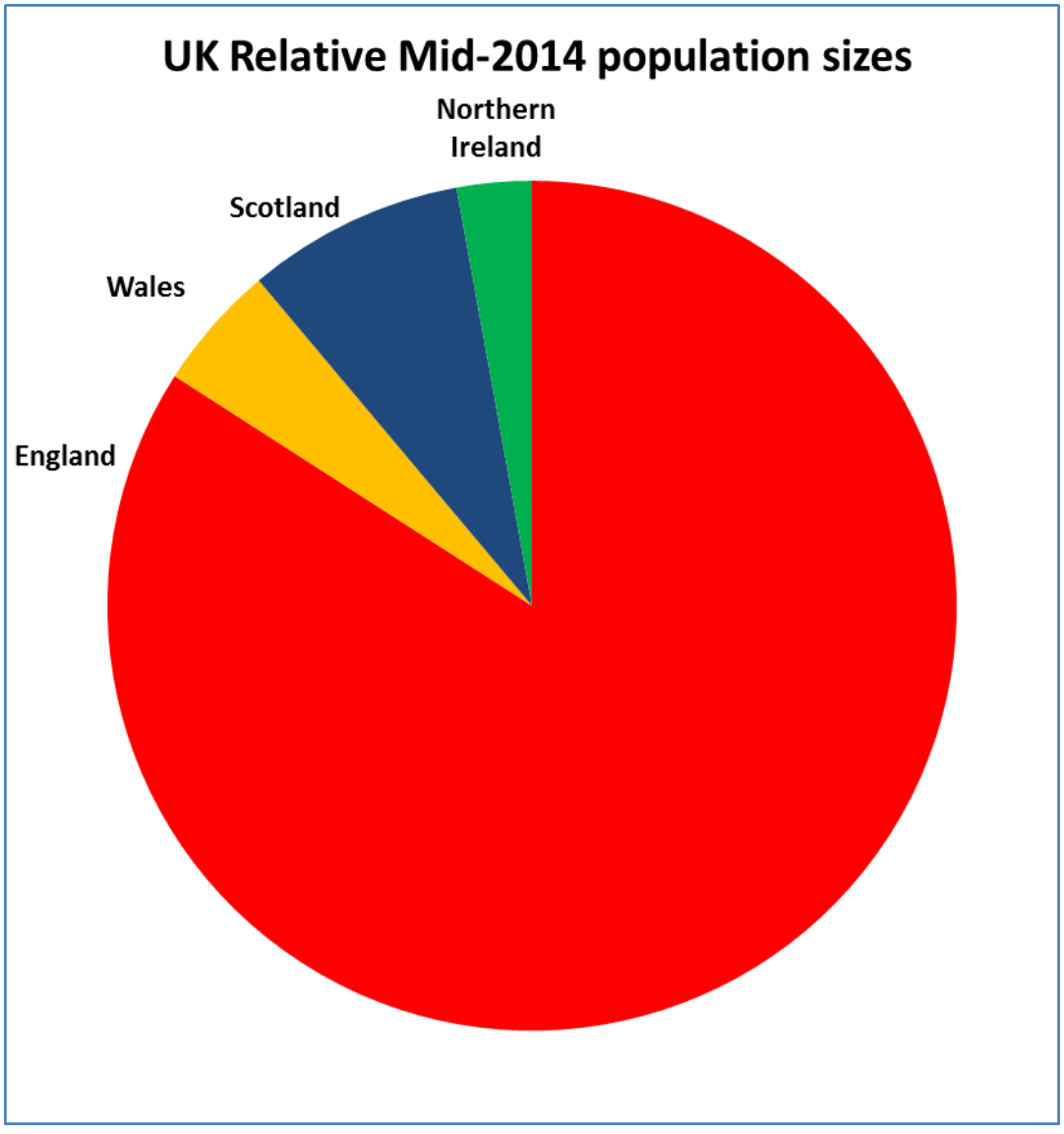
The World Health Assembly adopted a Global Action Plan (GAP) on AMR in May 2015. All countries are required to develop national AMR action plans within two years.
Resolutions on AMR were adopted by the FAO and OIE; both cross-refer to the GAP, reinforcing the One-Health approach to tackling AMR.
The G7 Leader's Summit declaration included a strong statement on AMR, further supported by the G7 Health Ministers meeting in October. The G20 leader's communique underscored the importance of a coordinated international response.
The Government announced a commitment of £265m over five years to launch the new Fleming Fund to support antimicrobial and infectious disease surveillance world-wide.
The UK continues to encourage and support international action on AMR through the Global Health Security Agenda, by supporting Science Innovation Network activities and as a founding member of an international "group of champions" on AMR.

Annex B - population sizes for the four UK countries.

Population Estimates Summary for the UK, mid-2010 to mid-2014

ALL PERSONS (units)	Mid-2010	Mid-2011	Mid-2012	Mid-2013	Mid-2014
United Kingdom	**62,759,500**	**63,285,100**	**63,705,000**	**64,105,700**	**64,596,800**
England	52,642,500	53,107,200	53,493,700	53,865,800	54,316,600
Wales	3,050,000	3,063,800	3,074,100	3,082,400	3,092,000
Scotland	5,262,200	5,299,900	5,313,600	5,327,700	5,347,600
Northern Ireland	1,804,800	1,814,300	1,823,600	1,829,700	1,840,500

Source: Annual Mid-Year Population Estimates for the UK, Office for National Statistics, 2015
Figures may not add exactly due to rounding.



Annex C - drug bug combinations for 2014 and 2015.

Outcome measure - Drug/ bug table for 2014 (with 2015 additions set in bold)

Table 1: drug/bug combinations for national surveillance of AMR

Bacteria	Antibiotic class	Metric
E. coli	Fluoroquinolone	% NS to ciprofloxacin
E. coli	Cephalosporin	% NS to cefotaxime and/or ceftazidime
E. coli	Aminoglycoside	% NS to gentamicin
E. coli	Carbapenem	% NS to imipenem and/or meropenem
E. coli	**β-lactam**	**% NS to co-amoxiclav**
E. coli	**β-lactam**	**% NS to piperacillin/tazobactam**
K. pneumoniae	*Fluoroquinolone*	*% NS to ciprofloxacin*
K. pneumoniae	Cephalosporin	% NS to cefotaxime and/or ceftazidime
K. pneumoniae	Aminoglycoside	% NS to gentamicin
K. pneumoniae	Carbapenem	% NS to imipenem and/or meropenem
K. pneumoniae	**β-lactam**	**% NS to piperacillin / tazobactam**
Pseudomonas spp.	Cephalosporin	% NS to ceftazidime
Pseudomonas spp.	Carbapenem	% NS to imipenem and/or meropenem
S. pneumoniae	β-lactam	% NS to penicillin
N. gonorrhoeae	Cephalosporin	% NS to ceftriaxone
N. gonorrhoeae	Macrolide	% NS to azithromycin

NS, non-susceptible (comprises both intermediate and full resistance)
Note: for Northern Ireland, coverage for some of the newer combinations for inclusion may not be at 100% of clinical laboratories
Data for a secondary (shadow) set of drug/bug combinations (Table 2) will be considered to potentially expand the list of infections to be reported.

Table 2: Secondary "shadow" list of drug/bug combinations for possible inclusion in national surveillance in the future

Bacteria	Antibiotic class	Metric
K. oxytoca	Fluoroquinolone	% NS to ciprofloxacin
K. oxytoca	Cephalosporin	% NS to cefotaxime and/or ceftazidime
K. oxytoca	Aminoglycoside	% NS to gentamicin
K. oxytoca	Carbapenem	% NS to imipenem and/or meropenem
S. aureus	β-lactam	% NS to methicillin
Enterococcus spp.	Glycopeptide	% NS to vancomycin
Acinetobacter spp.	Polymyxin	% NS to colistin
Pseudomonas spp.	β-lactam	% NS to piperacillin/tazobactam

Animal Health

In line with statutory EU requirements, the animal health side actively monitors resistance in Salmonella spp. and E. coli obtained from poultry and pigs at slaughter, and in Campylobacter jejuni from poultry at slaughter. Drug-bug resistance data are being collected for the combinations listed below:

Table 3: Drug/bug combinations for national surveillance of AMR in livestock in the UK,

Bacteria	**Antibiotic class**	**Metric**
*Salmonella and Commensal E.coli**	β-lactam	% resistant to ampicillin
	Cephalosporin	% resistant to cefotaxime or ceftazidime
	Carbapenem	% resistant to meropenem
	(Fluoro)quinolone	% resistant to ciprofloxacin or nalidixic acid
	Tetracycline	% resistant to tetracycline
	Polymixin	% resistant to colistin
	Aminoglycoside	% resistant to gentamicin
	Sulphonamide/trimethoprim	% resistant to trimethoprim or sulfamethoxazole
	Glycycline	% resistant to tigecycline
	Amphenicol	% resistant to chloramphenicol
	Macrolide	% resistant to azithromycin
Campylobacter jejuni.	Macrolide	% resistant to erythromycin
	Fluoroquinolone	% resistant to ciprofloxacin or nalidixic acid
	Tetracycline	% resistant to tetracycline
	Aminoglycoside	% resistant to streptomycin or gentamicin

*** Salmonella or commensal E.coli isolates that are resistant to carbapenem or cephalosporin classes of antibiotics will be tested against another panel of antibiotics which includes additional antibiotics from these two classes**

These antibiotic sensitivity data were published in the VMD Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) annual report in November 2015 in a way which permits comparability of data between human and veterinary reports. In addition, there is an extensive programme of passive surveillance which tests over 5000 animal bacterial pathogens a year, inclusive of zoonotic pathogens, for antibiotic susceptibility. These data are also published in the VARSS annual report.

From 1st of January 2016:
The presence of resistance mechanisms in E. coli and Campylobacter obtained from broiler chickens and turkeys at slaughter will be monitored. More specifically, tests for ESBLs, AmpC and carbapenemase-producing E. coli will be undertaken. Work has also been initiated by the FSA in 2016 to check for the presence of resistant E. coli obtained from chicken and turkey meat samples at retail.

Annex D - outcome against drug bug combinations in 2014, UK.

Humans

Bacteria	Antibiotic class	Metric	UK Baseline Resistance (2013)	UK Resistance (2014)	Infections monitored in surveillance
K. pneumoniae (Klebsiella pneumoniae)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	11.1%	11.3%	Blood stream infections
K. pneumoniae	Carbapenem	% NS to imipenem and/or meropenem	0.8%	1.3%	
K. pneumoniae	Aminoglycoside	% NS to gentamicin	7.9%	7.2%	
K. pneumoniae	Fluoroquinolone	% NS to ciprofloxacin	10.7%	10.5%	
E. coli (Escherichia coli)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	10.3%	10.9%	Blood stream infections
E. coli	Carbapenem	% NS to imipenem and/or meropenem	0.1%	0.1%	Blood stream infections
E. coli	Fluoroquinolone	% NS to ciprofloxacin	18.3%	18.8%	Blood stream infections
E. coli	Aminoglycoside	% NS to gentamicin	9.6%	9.8%	Blood stream infections
Pseudomonas spp.	Cephalosporin	% NS to ceftazidime	6.8%	7.2%	Blood stream infections
Pseudomonas spp.	Carbapenem	% NS to imipenem and/or meropenem	8.9%	11.5%	Blood stream infections
Neisseria gonorrhoeae	Macrolide	% NS to azithromycin	1.6%*	1.0%*	Gonorrhoea
Neisseria gonorrhoeae	Cephalosporin	% NS to ceftriaxone	0.2% *	0.0%*	Blood stream infections
Streptococcus pneumoniae	β-lactam	% NS to penicillin	4.0%	4.4%	Blood stream infections

The data show that the proportions of isolates of each species resistant to each antibiotic are generally stable between 2013 and 2014 (either the same or a marginal increase). However, as the incidence of bacteraemia has continued to increase, the denominator for the proportions increases giving an increase in the actual numbers of resistant infections. This highlights the importance of initiatives focussing on infection prevention and control. Please note, these estimates of numbers are based on voluntary reporting.

Source of data: Guy R , Geoghegan L, Heginbothom M, et al. Non-susceptibility of Escherichia coli, Klebsiella spp., Pseudomonas spp., Streptococcus pneumoniae and Staphylococcus aureus in the UK: temporal trends in England, Northern Ireland, Scotland and Wales
J Antimicrob Chemother, 2016 doi:10.1093/jac/dkw018

Animals

Bacteria	Antibiotic class	Metric	UK Baseline Resistance (2013)	UK Resistance (2014)	Examples of some infections caused by the bacteria
Klebsiella pneumoniae (K. pneumoniae)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	low isolates**	low isolates	Mastitis in cattle.
K. pneumoniae	Carbapenem	% NS to imipenem and/or meropenem			
Escherichia coli (E. coli)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	Pigs: 0.6% Chickens: NT Turkeys: NT	Pigs: NT Chickens: 0% Turkeys: 0%	all E.coli cases reported are from the EU harmonised monitoring programme which collect samples from healthy animals and therefore less likely to be pathogenic strains.
E. coli	Carbapenem	% NS to imipenem and/or meropenem			
E. coli	Fluoroquinolone	% NS to ciprofloxacin	Pigs: 1.3% Chickens: NT Turkeys: NT	Pigs: NT Chickens: 3.8% Turkeys: 7.1%	
E. coli	Aminoglycoside	% NS to gentamicin % NS Streptomycin (pigs)	Pigs: 3% (gent) Pigs: 37% (Strep)	Pigs: NT Chickens: 19.5% Turkeys: 4.2%	
Pseudomonas spp.	Cephalosporin	% NS to ceftazidime	low isolates	low isolates	all cases reported are mastitis in cattle.
Pseudomonas spp.	Carbapenem	% NS to imipenem and/or meropenem			

**** Statistics not available due to very low number of isolates tested (<10).**
NT: Not tested

UK drug bug table – combined outcome for 2014 for animals and humans

Humans

Bacteria	Antibiotic class	Metric	UK Baseline Resistance (2013)	UK Resistance (2014)	Infections monitored in surveillance
K. pneumoniae (Klebsiella pneumoniae)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	11.1%	11.3%	Blood stream infections
K. pneumoniae	Carbapenem	% NS to imipenem and/or meropenem	0.8%	1.3%	
K. pneumoniae	Aminoglycoside	% NS to gentamicin	7.9%	7.2%	
K. pneumoniae	Fluoroquinolone	% NS to ciprofloxacin	10.7%	10.5%	
E. coli (Escherichia coli)	Cephalosporin	% NS to cefotaxime and/or ceftazidime	10.3%	10.9%	Blood stream infections
E. coli	Carbapenem	% NS to imipenem and/or meropenem	0.1%	0.1%	Blood stream infections
E. coli	Fluoroquinolone	% NS to ciprofloxacin	18.3%	18.8%	Blood stream infections
E. coli	Aminoglycoside	% NS to gentamicin	9.6%	9.8%	Blood stream infections
Pseudomonas spp.	Cephalosporin	% NS to ceftazidime	6.8%	7.2%	Blood stream infections
Pseudomonas spp.	Carbapenem	% NS to imipenem and/or meropenem	8.9%	11.5%	Blood stream infections
Neisseria gonorrhoeae	Macrolide	% NS to azithromycin	1.6%*	1.0%*	Gonorrhoea
Neisseria gonorrhoeae	Cephalosporin	% NS to ceftriaxone	0.2% *	0.0%*	Gonorrhoea
Streptococcus pneumoniae	β-lactam	% NS to penicillin	4.0%	4.4%	Blood stream infections

*** these figures are for England and Wales**
**** Statistics not available due to very low number of isolates tested (<10).**
NT: Not tested

The data show that the proportions of isolates of each species resistant to each antibiotic are generally stable between 2013 and 2014 (either the same or a marginal increase). However, as the incidence of bacteraemia has continued to increase, the denominator for the proportions increases giving an increase in the actual numbers of resistant infections. This highlights the importance of initiatives focussing on infection prevention and control. Please note, these estimates of numbers are based on voluntary reporting.

Annex E - revised antibiotic prescribing quality measures for 2015/16

England revised antibiotic prescribing quality measure for 2015/16

	Primary care	Secondary care
Total prescribing measures	Total antibiotic prescribing to be reduced by 3% per year at CCG level as measured by number of antibiotic prescriptions ("items") per 100 patients per year	Total antibiotic consumption to be reduced by 1% per annum 2015-2019 as measured by DDD per 1000 admissions per year.
Measures to encourage narrow spectrum prescribing	Proportion of antibiotics from cephalosporin, quinolone or co-amoxiclav classes to be reduced to less than the current median for English CCGs as measured by the number of prescriptions ("items") from target classes in comparison with the total number of antibiotic prescriptions per year.	Total carbapenem consumption to be reduced by 1% per annum 2015-2019 as measured by DDD per 1000 admissions per year Total piperacillin-tazobactam consumption to be reduced by 1% per annum 2015-2019 as measured by DDD per 1000 admissions per year

NHS Scotland Antibiotic quality indicators 2015/16

Primary care	Secondary care
Antibiotic use (expressed in items/1000/day) in at least 50% of practices in each NHS board will be at or below the 25th percentile of Scottish practices or will have made the minimum acceptable reduction toward that level (using January-March 2013 as the baseline)	1. All prescribed doses administered or reason for omitting dose(s) documented 2. The indication for antibiotic treatment documented 3. A) For oral antibiotics, the anticipated duration for treatment documented B) For IV antibiotics, the anticipated duration of treatment or a review within 72 hours documented 4. Antibiotic treatment is compliant with local prescribing policy or the reason for deviation is documented

Annex F - data supporting figures 3,6,7,8.

Supporting data figures 6,7

	Antimicrobial Usage - DDDs per 1,000 population per day							
	England				Scotland			
Year	2011	2012	2013	2014	2011	2012	2013	2014
Primary Care	17.8	19.0	18.4	18.8	21.1	22.1	21.5	21.4
Secondary care	3.8	3.9	4.1	4.2	3.6	3.8	3.9	4.1
Country total	21.6	22.9	22.5	23.0	24.7	26.0	25.4	25.5

	Wales				Northern Ireland			
Year	2011	2012	2013	2014	2011	2012	2013	2014
Primary Care	20.3	21.8	21.5	21.9	26.42	28.3	27.5	27.6
Secondary care	a	a	a	a	b	b	b	4.5
Country total	a	a	a	a	b	b	b	32.1

a Wales does not collect the data in a manner comparable with England & Scotland
b Northern Ireland has had difficulties with providing the data for earlier years.

Supporting data figure 8

	United Kingdom			
	2011	2012	2013	2014
DDDs per 1,000 popn	18.4	19.7	19.1	19.4
% change on 2011	0.0%	6.5%	3.4%	5.3%
population (millions)	63.3	63.7	64.1	64.6

Data supporting figure 3

Bacteraemia reports for England, Wales and Northern Ireland

2010 - 2014

	2010	2011	2012	2013	2014
Total bacteraemia reports	98,352	99,459	101,537	103,808	106,708
increase on **2010**	-	1,107	3,185	5,456	8,356
increase as a % of 2010	0.0%	1.1%	3.2%	5.5%	8.5%
population (thousands)	57,497	57,985	58,391	58,778	59,249
% increase on 2010	0.0%	0.8%	1.6%	2.2%	3.0%
reports per 1000 population	1.71	1.72	1.74	1.77	1.80
% increase on 2010	0.0%	0.3%	1.7%	3.2%	5.3%

Selected bacteraemia reports for Scotland

2010 - 2014

Selected gram negative	**2010**	**2011**	**2012**	**2013**	**2014**
E. coli	3,602	3,839	3,924	4,321	4,539
Klebsiella pneumoniae	715	697	718	688	753
Pseudomonas aeruginosa	295	242	234	292	238
Acinetobacter baumannii	36	34	24	28	34
sub total	**4,811**	**4,812**	**4,900**	**5,329**	**5,564**
% increase on 2010	0.0 %	0.0 %	1.8 %	10.8 %	15.7 %

Selected gram positive	**2010**	**2011**	**2012**	**2013**	**2014**
MRSA	310	194	173	141	128
MSSA	1,317	1,258	1,187	1,327	1,269
Streptococcus pneumoniae	486	446	419	506	394
Enterococcus faecalis	459	434	419	405	396
Enterococcus faecium	251	236	250	261	320
sub total	**2,823**	**2,568**	**2,448**	**2,640**	**2,507**
% increase on 2010	0.0 %	-9.0 %	-13.3 %	-6.5 %	-11.2 %
Total selected	7,634	7,380	7,348	7,969	8,071
% increase on 2010	**0.0 %**	**-3.3 %**	**-3.7 %**	**4.4 %**	**5.7 %**
Population (thousands)	5,299	5,300	5,314	5,328	5,348
% increase on 2010	0.0%	0.0%	0.3%	0.5%	0.9%

Annex G - NIHR and VMD funded research projects, November 2015.

Projects funded as part of the Antimicrobial Resistance Themed Call

Programme NIHR Number	Application Title	Lead Applicant	Grant Value
EME 13/95/10	Probiotic to Reduce Infections in Care Home Service Users (PRINCESS)	Chris Butler, University of Oxford	£1,872,938
HTA 13/88/10	Electronically delivered, multi-component interventions to reduce unnecessary antibiotic prescribing in primary care. A cluster randomised trial using electronic health records (eCRT2)	Martin Guilford, Kings College London	£533,580
HTA 13/88/11	Efficacy, safety and impact on antimicrobial resistance of duration and dose of antibiotic treatment for children with Community-Acquired Pneumonia (CAP): a randomised controlled Trial - CAP-IT	Mike Sharland, UCL	£2,532,730
HTA 13/88/13	Children's local anaesthetic drops to reduce ear pain and antibiotic use in acute otitis media: the CEDAR randomised controlled trial	Alastair Hay, Bristol NHS CCG	£1,508,809
HTA 13/88/21	Alternatives To prophylactic Antibiotics for the treatment of Recurrent urinary tract infections in women (ALTAR study)	Chris Harding, University of Newcastle	£956,481
HTA 12/33/12	General Practitioner (GP) use of a C-Reactive Protein (CRP) Point of Care Test (POCT) to help target antibiotic prescribing to patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) who are most likely to benefit (The PACE Study)	Chris Butler, Cardiff University	£1,355,679
HTA 13/82/04	Accuracy of a rapid intrapartum test for maternal group B streptococcal colonisation and its potential to reduce antibiotic usage in mothers with risk factors (GBS2)	Khan Khalid, QMUL	£983,153
i4i II-LA-0214-20007	Characterisation, commercialisation and clinical studies of a long-term antimicrobial urinary catheter	Roger Bayston University of Nottingham	£335,612
i4i II-LA-0214-20008	Enhanced, Personalized and Integrated Care for Infection Management at Point of Care (EPIC IMPOC)	Alison Holmes Imperial College London	£687,740
i4i II-LA-0214-20009	Breath Analysis in Intensive Care: Proof of Concept for Non-Invasive Diagnosis of Ventilator Associated Pneumonia	Stephen Fowler University of Manchester	£454,694

i4i II-LA-0214-20010	A Single Tube Point-Of-Care Test for detection of Carbapenemase Producing Organisms	Dr Paul Martin Enigma Diagnostics Limited	£1,560,825
i4i II-LB-0214-20004	Clinical development and evaluation of advanced prototype for in situ microbial sensing, providing early antimicrobic susceptibility data for organisms colonising chronic wounds	Curtis Dobson University of Manchester	£558,269
i4i II-LB-0214-20005	A Point of Care antimicrobial resistance test for Neisseria Gonorrhoeae and Mycoplasma Genitalium infection. Ensuring accurate therapy and antibiotic stewardship in sexual health medicine.	Syed Tariq Sadiq St. George's, University of London	£1,481,876
Fellowships PDF-2014-07-008	Improving the management of drug resistant tuberculosis in the UK.	Helen Stagg, UCL	£307,715
Fellowships PDF-2014-07-072	Developing a personalised approach to the treatment of fever with neutropenia (FN) for children and young people with cancer	Bob Phillips, University of York	£533,655
HS&DR 13/97/24	Interventions to improve antimicrobial prescribing of doctors in training: A realist review	Geoff Wong, University of Oxford	£187,260

In addition, the following projects are funded by VMD

VM0506	The molecular biology of antimicrobial bacteria affecting food producing animals in England and Wales.	APHA	£967,399
VM0509	Motivations and drivers of antimicrobial prescribing practices in farmed animals.	U of Liverpool	£200,414
VM0516	Exploring the molecular basis for antimicrobial resistance in Brachyspira hyodysenteriae using whole genome sequencing.	APHA	£465,178
VM0518	Molecular signature (MOLSIG) of antibiotic resistance in pigs as a potential source of antibiotic resistance.	APHA	£401,605
VM0520	National surveillance of antimicrobial prescription and resistance in companion pet animals	U of Liverpool	£58,922
VM0529	Characterisation of ESBL/ampC/carbapenem resistant Escherichia coli from pigs and poultry to identify antimicrobial resistance genes, circulating plasmids and fitness attributes	APHA	£337,581

Annex H - Antibiotic consumption data – sources, caveats/ limitations.

Human consumption data - primary and secondary care data by country:

England. Primary care; Data source: NHS Business Services Authority (national Prescription Cost Analysis) *Includes*: all antibiotic prescriptions dispensed in the community from GP, out-of-hours, dentists, non-medical prescribers and prescriptions written in hospitals dispensed in the community. **Secondary care**: Data source: IMS Health. Includes: 99% of secondary care providers dispensed prescription for hospital inpatients, outpatients and ambulatory care

Northern Ireland. Primary care: Data source: Health and Social Care Board Medicines Management Information team, using information contained on prescription forms received and paid through the Business Service Organisation's FPS Pharmaceutical Payment System *Includes*: Prescriptions written by GPs, dentists and non-medical prescribers for antibiotics and dispensed from community pharmacies or by dispensing doctors. **Secondary care:** *Includes*: All Secondary care Trusts using the pharmacy tracking systems

Scotland. Primary care: Data source: Prescribing Information System (PIS) database, maintained by Information Service Division (ISD), of NHS National Services Scotland (NSS). The information is supplied to ISD by Practitioner and Counter Fraud Services strategic business unit of NSS who is responsible for the processing and pricing of all prescriptions dispensed in Scotland. *Includes*: Prescriptions written by GPs, dentists and non-medical prescribers and from prescriptions written in hospitals dispensed in the community. **Secondary care**: Data source: Hospital Medicines Utilisation Database (HMUD). This database held by ISD collects information from hospital pharmacy systems across Scotland and presents standardised information on use of medicines using a web-based system. *Includes*: Data on antibiotic use in secondary care

Wales. Primary care: Data source: Prescribing Services Unit (PSU), NHS Wales Shared Service Partnership. The data are collected from prescriptions that are submitted to PSU by dispensing contractors at the end of each month from prescriptions that have been dispensed. *Excludes*: private prescriptions. **Secondary care**: Data source: Welsh national medicines database, Medusa. *Includes*: stock data for all acute hospitals in Wales. Excludes: Singleton hospital; non-acute, or community hospitals.

Veterinary antimicrobial sales data

Sales data do not permit accurate analysis of antibiotic consumption by animal species or production category. Some formulations of antibiotics are authorised with indications for use in more than one species, e.g. pigs and poultry. It is not possible to ascertain from sales data in which species the product was used.

A volume of antibiotic may represent many doses in small animals or few doses in large animals. Therefore it is not possible to predict the number of doses (consumption) that the sales volume represents. Even within a species group there may be variations in animal size.

Changes in volumes of sales data should be considered in parallel with changes in the UK animal population over the corresponding time period. The populations of animal species are an important denominator and may vary quite markedly from year to year depending on market conditions for livestock derived food; the greater the number of animals, the greater the potential need for antibiotic treatment. Similarly variations in the size of the animals being

treated should be taken into consideration as larger animals will require a larger total volume of antibiotics over a treatment period.

To try and address the variation in animal populations and demographics, over time and between countries, the ESVAC project has developed a Population Correction Unit (PCU), a calculation that estimates the weight of the animal (or group of animals) receiving an antibiotic at the most likely time of administration. This unit is now used across EU member states and is currently the best approximation of consumption. We have used this form of analysis in this report.

Sales data in general over estimate use, as not all antibiotics sold will be used. There is natural wastage resulting from pack sizes that do not meet dose need, and from drug expiry.

The sales data represented in this report do not take into account imports or exports of products. For the purpose of this report it is assumed that all products sold in the UK remain in the UK and nothing is imported.

Medication sold for use in humans may be used in animals under certain circumstances, according to the prescribing cascade; figures on such use are not included in the data presented.

Annex I - Glossary

Antimicrobial	An antimicrobial is 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.
Antimicrobial resistance (AMR)	The ability of a microorganism to grow or survive in the presence of an antimicrobial at a concentration that is usually sufficient to inhibit or kill microorganisms of the same species and that exceeds concentrations achievable in the human / animal / patient.
Antimicrobial stewardship	The use of co-ordinated interventions to improve and measure the use of antimicrobials by promoting optimal drug regimen, dose, duration and route. The aim is for optimal clinical outcome and to limit selection of resistant strains. This is a key component of a multi-faceted approach to preventing antimicrobial resistance.
Broad-spectrum antibiotics	These are effective against a wide range of bacteria. For example, meropenem is a broad-spectrum antibacterial.
Carbapenems	Carbapenems are broad-spectrum antibiotics, often used as the last line of treatment for hard to treat human infections caused by Gram-negative bacteria.
Carbapenemases	These are enzymes produced by bacteria which destroy carbapenems and other beta-lactam antibiotics.
Cephalosporins	Types of broad-spectrum antibiotics.
Cephalosporins – third-generation	Cephalosporins like cefotaxime and cefixime are particularly active against Gram-negative bacteria.
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.
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	These are bacteria that are stained dark blue or violet in the Gram-staining procedure. They include Staphylococcus aureus and Clostridium difficile.
Healthcare associated infections (HCAI)	Infections acquired via the provision of healthcare in either a hospital or community setting.
Multi-drug resistant	Resistant to multiple classes of antimicrobial.
Meticillin-resistant Staphylococcus aureus	MRSA - A strain of Staphylococcus aureus that is resistant to beta lactam antibiotics which include penicillins (eg meticillin and oxacillin) and almost all cephalosporin antibiotics.
"One-Health" approach	Collaborative multi-disciplinary work at local, national, and global levels to attain optimal health for people, animals and the environment.
Pathogen	An infectious agent (bug or germ), a microorganism such as a virus, bacterium, or fungus that causes disease in its host.
Prevalence	A snapshot at a particular point in time of the total number of cases, or proportion of resistant cases, in a given population.
Primary care	Services provided by GP practices, dental practices, community pharmacies and high street optometrists.

Quinolones	A family of antibiotics, includes broad-spectrum agents like ciprofloxacin.
Responsible prescribing	The use of antimicrobials in the most appropriate way for the treatment or prevention of infectious disease.
Secondary care	Covers acute healthcare, either elective care (planned specialist medical care or surgery, usually following referral) or emergency care.
Susceptibility testing	Testing to detect possible drug resistance in common pathogens and to assure susceptibility to drugs of choice for particular infections.