INTRODUCTION

BMA Cymru Wales is pleased to provide a response to the Welsh Government consultation on its Antimicrobial Resistance Delivery Plan.

The British Medical Association (BMA) is an independent professional association and trade union representing doctors and medical students from all branches of medicine all over the UK and supporting them to deliver the highest standards of patient care. We have a membership of over 153,000, which continues to grow every year. BMA Cymru Wales represents over 7,500 members in Wales from every branch of the medical profession.

RESPONSE

The BMA view on the issue of antimicrobial resistance, and how it should be tackled, was the subject of a briefing published by the BMA Board of Science in 2015. This is attached for information as Appendix 1 to this response.

In relation to the views being sought as part of this consultation, whilst we will not be providing a response to all of the questions posed, we would nonetheless wish to present a number of observations which have been put forward by our members.

BMA Cymru Wales members have a generally positive view of the contents of the proposed delivery plan, but some have expressed disappointment that it relies too much on a top down approach rather than seeking to follow an approach which is more based on the principles of co-production – something which might be seen as better fitting in with the Welsh Government’s supported ethos of prudent healthcare. Greater thought could perhaps therefore be given to how members of the general public might play a greater role than at present in working with health professionals in the fight to stave off the increasing challenge of antimicrobial resistance. We would therefore like to see a strengthening of those aspects of the plan relating to public education. This needs to deal with issues such as public expectation, as well as...
the importance of patients completing a prescribed antibiotic course. It should also be considered how we can make better use of data derived from patients through the use of various treatment regimes in order to better ascertain their true cost benefits.

Whilst we observe there are references in the plan to patient engagement and public education, a key challenge will be to ensure that this is done meaningfully and sufficiently comprehensively. As part of this, we feel it is important to ensure that doctors can be adequately supported when they make appropriate decisions not to prescribe antibiotics in order to help them in dealing with any resultant patient dissatisfaction.

Another issue highlighted by a number of our members is the lack of any reference to the impact of the use of antibiotics within agriculture. Overuse of antibiotics within agriculture is clearly a major contributor to the problem of antimicrobial resistance, and it is therefore very surprising that there is no mention of this issue whatsoever within the delivery plan. Such a glaring omission clearly needs to be rectified before the plan is finalised.

On a similar note, it has to be recognised that tackling antimicrobial resistance requires co-ordinated international action, as well as action that can be taken within Wales. We would note that in a number of countries, antibiotics can be purchased without the need for a prescription. Often what is viewed as the ‘best’ antibiotic may be that which is the most expensive and ‘strongest’ and this can mean that second- or third-line drugs are over-used for the treatment of minor ailments. Whilst we understand that international action may lie outside the scope of this draft delivery plan, it would be helpful to for it to show that actions to be taken locally must play their part within a wider, global strategy.

Some members have highlighted concerns with the way data has been presented within the introductory section of the document. For instance in the graph showing a comparison of antibacterial usage between GP clusters (Figure 3), the data has been presented in a manner which only takes into account differences in the age or gender balance of patient cohorts. However, it doesn’t take into account differences which may exist in the socioeconomic make-up of different cluster populations, or of variations in chronic disease prevalence. In certain geographical areas, such as those with a more industrial heritage, there may be a higher prevalence of certain chronic diseases such as chronic obstructive pulmonary disease (COPD) with sufferers of those diseases being more prone to acquiring bacterial infections. Such factors mean that there will inevitably be variation in the need to prescribe antibiotics between different cluster areas. One GP member has advised that certain of his COPD patients are currently provided with ‘rescue packs’ of antibiotics and steroids for use in appropriate circumstances. As such, they may be seen as significant consumers of antibiotics but evidence from the use of this approach over a five-year period would suggest it has also led to a reduction in secondary care admissions.

We believe there needs to be more evaluation of such approaches and greater use of best practice sharing. This can also help in reducing the incidence of unnecessary or ineffective practices. For instance the vast majority of asthmatics admitted to hospital in status (i.e. suffering from a severe acute asthma attack) are given antibiotics despite the existence of guidance that this is not required. The action plan therefore needs to make sure that such issues are addressed.
Antimicrobial resistance

A briefing from the BMA board of science - March 2015
Doctors have expressed significant concern about the threat of a 'post-antimicrobial age', where current antimicrobials will be ineffective due to increasing levels of resistance. This represents a major public health issue, and has the potential to severely limit the effectiveness of many routine and complex medical treatments. In light of increasing rates of resistance and MDR (multi-drug resistance), as well as the lack of new drugs in development, doctors have called for:

- improved antimicrobial prescribing in medical practice in the UK and internationally, with the aim of preserving antimicrobial sensitivity for as long as possible
- the introduction of tighter regulation to significantly reduce the inappropriate use of antimicrobials in farming practices.

The aim of this briefing is to consider ways to support action in this area. It has been informed by discussions at an expert focus session hosted by the board of science in September 2014.

Background

Antimicrobials\(^a\) are designed to inhibit the growth of, or kill, microorganisms, and are used in the treatment and prevention of infection by bacteria, viruses and fungi.\(^1\) Since the discovery of penicillin in 1929, antimicrobial agents have significantly reduced morbidity and mortality throughout the world,\(^2\) and modern health systems rely on the availability and effectiveness of a range of antimicrobials.\(^3,4\) They are also important for the treatment and prevention of infection in animal medicine, as well as fishing and farming practices.

Over the past 75 years, antimicrobial resistance has become increasingly wide spread in terms of incidence and geographical distribution.\(^3\) Approximately 70 per cent of known bacteria across the globe have developed resistance to one or more antimicrobial.\(^5\) In April 2014, the WHO (World Health Organization) released its first global report on the surveillance of antimicrobial resistance, warning that antimicrobial resistant bacteria have reached alarming levels in many parts of the world.\(^6\) Although there are significant issues surrounding the development of antimicrobial resistance in viruses, protozoa and fungi – including the development of drug-resistant malaria, HIV and influenza\(^a\) – resistance in bacteria has received most attention. In the UK, the CMO (Chief Medical Officer) for England, Professor Dame Sally Davies, and the House of Commons Science and Technology Select Committee, have highlighted bacterial resistance to antibiotics as a major area of concern for public health and modern medicine, and the UK five-year antimicrobial resistance strategy is principally focussed on bacterial resistance to antibiotics.\(^7,8,9\) The development of resistance to antibiotics threatens to reverse the substantial reductions in mortality and morbidity achieved during the nineteenth and twentieth centuries.\(^2\)

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\(^a\) Antimicrobial is an umbrella term that includes antibiotics, antivirals, antiprotozoals and antifungals.
UK Five Year Antimicrobial Resistance Strategy 2013-18

Published in 2013 by the Department of Health, the UK Five Year Antimicrobial Resistance Strategy has been developed in collaboration with the Veterinary Medicines Directorate of the Department for Environment, Food and Rural Affairs, the Northern Ireland Executive, the Scottish government, the Welsh government and the UK Public Health agencies. The report identifies the following seven key areas for action: improving infection prevention and control practices; optimising prescribing practices; improving professional education, training and public engagement; developing new drugs, treatments and diagnostics; better access to and use of surveillance data; better identification and prioritisation of AMR research needs; strengthened international collaboration. The first annual progress report on the UK Five Year Antimicrobial Resistance Strategy was published in December 2014. The report lists key achievements over the first full year of the strategy, which include the publication of antimicrobial prescribing quality measures, the launch of public awareness initiatives and the development of a new WHO resolution on AMR.

What is causing the development of antimicrobial resistance?

Exposure of microbes to antimicrobials drives the development of resistance. Prudent use of antimicrobials is therefore important to minimise the development of resistance. While it is generally accepted that the development of resistance in human infections is mainly accelerating due to increasing antimicrobial use in humans, non-human usage of antimicrobials is also an important contributory factor. In 2003, an expert group – gathered by the WHO, the FAO (Food and Agriculture Organization), and the OIE (World Animal Health Organization) – reached a consensus that ‘...there is clear evidence of adverse human health consequences due to resistant organisms resulting from non-human usage of antimicrobials’. In particular, farm animal antimicrobial use has been implicated in the development of resistance in a number of bacteria capable of causing human infections including Salmonella, Campylobacter, E.coli (Escherichia coli) and enterococci.

The science of antimicrobial resistance

Antimicrobial resistance is a natural phenomenon, and resistant strains of bacteria existed even before the discovery of penicillin. The ability to develop resistance to antimicrobials has been demonstrated in viruses, fungi and bacteria. Microbes gain resistance through changes in their genetic material; either through random genetic mutations, or the transfer of genes between microbes (including between different species). The use of antimicrobials creates selection pressure in favour of resistant microbes, by targeting susceptible organisms and creating a competitive advantage to resistant strains. Over time, natural selection favours these resistant microbes, which come to dominate.
How are antimicrobials being used?

A number of healthcare professionals may prescribe antimicrobials including doctors, dentists, nurses and other non-medical prescribers. According to ESPAUR (the English Surveillance Programme for Antimicrobial Use and Resistance), antimicrobial prescribing increased in England from 25.9 DDDs (daily doses) per 1,000 inhabitants in 2010 to 27.4 in 2013. Similar levels of antimicrobial consumption have been recorded in Scotland through SAPG (the Scottish Antimicrobial Prescribing Group), with 25.8 DDDs per 1,000 inhabitants being prescribed across primary and secondary care in 2012. In Scotland there was also a trend of increasing antimicrobial use between 2009 and 2012. Public Health Wales provides data on antimicrobial consumption in Wales. While not directly comparable – due to different units of measurement – total antimicrobial consumption in Wales increased marginally between 2005 and 2011. Similar data for Northern Ireland are not available, although a surveillance programme is being established. Data from ESPAUR also provide a breakdown of prescribing by type of healthcare professional. In 2013, 78.5 per cent of prescribing in England occurred in general practice, 9.1 per cent and 6.2 per cent for hospital inpatients and outpatients respectively, and 6.2 per cent was related to other community prescribers (predominantly dentists). While there are little comprehensive data on why antimicrobials are prescribed, it has been estimated that respiratory tract infections account for approximately 60 per cent of antibiotic prescribing in primary care.

There are limited data on antimicrobial prescribing in UK veterinary practice. The UK VMD (Veterinary Medicines Directorate) provides data on the volumes of antimicrobials sold annually, which has varied little between 2006 and 2012. It is worth noting that these sales data do not provide an accurate measure of actual use and therefore need to be interpreted with caution. Aside from sales data, it is estimated that in the UK in 2010 over 80 per cent of antimicrobials sold for animal use were intended for prophylaxis (routine prevention) or treatment of infection in food producing animals.

What is accelerating the emergence and spread of antimicrobial resistance?

The increasing levels and spread of antimicrobial resistance in the UK and worldwide is primarily linked to their increasing use in medicine, veterinary practice and modern farming.

Inappropriate use of antimicrobials in medicine

There are a number of common scenarios where antimicrobials may be inappropriately used in medicine. Antibiotics may be prescribed for viral infections (and therefore have no effect), or for self-limiting infections. Where a bacterial infection is present, the wrong type of antimicrobial, or ineffectual dosage, may be prescribed. Broad-spectrum antibiotics – those effective against a wide range of pathogenic bacteria – are commonly overused. Increasing the exposure of bacteria not sensitive to broad-spectrum antibiotics facilitates the development of resistance. Narrow-spectrum antibiotics – those active against specific families of bacteria – are recommended for use where possible, though this relies on efficient and accurate diagnosis of

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b This provides data on antimicrobial prescribing across NHS community and hospital pharmacies in England.
infection. Between 2010 and 2013, the use of narrow-spectrum antimicrobials within hospitals decreased in the UK, with the use of broad-spectrum antimicrobials increasing over the same time period.

Reasons that inappropriate prescribing practices may take place include:

- a lack of appropriate guidance and support to clinicians when prescribing antimicrobials
- concerns that not prescribing antimicrobial medications may result in an undetected infection going untreated and a worse outcome for the patient
- diagnostic methods that are inadequate to distinguish a bacterial infection from a viral infection, or for a bacterial infection, the exact type of bacteria
- pressure from patients to prescribe antibiotics for viral or self-limiting infections
- workload pressures, including short consultation times in general practice
- fear of complaint, litigation, or adverse publicity or feedback, including via the NHS friends and family test.

Inappropriate prescribing is most common where prescribing takes place without adequate information regarding the nature of the infection or the results of diagnostic testing. This underlines the importance of accessible patient records, strong microbiology services, and guidance and support for clinicians, to ensure appropriate antimicrobial use. The impact of regional and local variation in antimicrobial prescribing on the development of antimicrobial resistance is unclear, and more research is required to understand the significance of such variation.

Patients failing to complete or follow a course of treatment as prescribed can also contribute to antimicrobial resistance, by providing an opportunity for microorganisms with varying levels of resistance to survive and multiply. Patients may intentionally stop treatment early, so as to save treatment for later self-medication. A 2006 UK study found that nearly six per cent of households had leftover antimicrobials, and half of those had kept them with the intention of treating future illness.

Inappropriate use of antimicrobials in veterinary practice and modern farming

The widespread inappropriate prescribing of antimicrobials for routine prevention of disease is a significant area of concern in animal medicine. Antimicrobials may be appropriately administered to a group of animals following diagnosis of infection or clinical disease in part of that group, to prevent the spread of infection (metaphylaxis). However, antimicrobials are also commonly administered prophylactically to large numbers of healthy livestock without a diagnosis of infection. This may be driven by prescribing to animals ‘at-risk’ of infection due to poor hygiene or animal husbandry, a practice that is likely to facilitate the emergence and spread of antimicrobial resistant organisms capable of causing infections in animals and humans. The use of antimicrobials in food animals also threatens to facilitate the transfer of antimicrobial resistance genes to human pathogens.
A further concern is the inappropriate use in animal medicine of antimicrobials that are critically important in human medicine. These include the fluoroquinolones and modern cephalosporins which are vital for treating serious infections including *Salmonella* and *E.coli*, as well as macrolides which are one of few available therapies for serious *Campylobacter* infections. Fluoroquinolones, cephalosporins and macrolides have been classified by the WHO as the highest priority critically important antimicrobials for human use. While there are no specific data on prescribing patterns for these critically important antimicrobials, data from the UK VMD show that the total sales (in gross tonnage) of fluoroquinolones, cephalosporins and macrolides all increased between 2008 and 2012.

**Other factors**

A number of other factors may also contribute to the emergence and spread of antimicrobial resistance including poor infection control (screening and isolation of high risk patients, and basic hygiene practices); increasing international trade in food of animal origin, and increased travel and medical tourism (which can facilitate the spread of antimicrobial resistant organisms).

**What are the implications for healthcare?**

The consequences of increasing levels of antimicrobial resistance, combined with the slow pace of development of new antimicrobials, are stark. The emergence of resistance for example has created a barrier to the control of gonorrhoea. Treatment failures due to resistance to third generation cephalosporins – the ‘last line of defence’ against gonorrhoea – have been reported in a number of countries, including the UK.

Progression to a post-antimicrobial age would fundamentally change the provision of healthcare, as the risk of infection associated with many routine and complex medical procedures could not be controlled through the use of antimicrobials. Almost every medical discipline would be affected. In a post-antimicrobial age, the risk of infection might be so high that routine surgical procedures would be deemed too great a risk to life to undertake. The same could be seen in oncology, where antimicrobials are used to prevent infection during chemotherapy. Antimicrobials also aid the survival of pre-term babies, and those with autoimmune diseases.

As well as threatening to reduce treatment options and significantly increase rates of morbidity and mortality in the future, treatment failure caused by antimicrobial resistance already contributes to increased costs, not only in terms of care, but through increased societal and economic costs. Treatments for MDR infections are often more intensive, and frequently require significantly longer hospital stays (see **Box 1**).
**Box 1**

- The treatment of MDR tuberculosis strains requires two years of medication with toxic and expensive medicines.\(^3\)
- Across Europe 25,000 people die each year as a result of hospital infections caused by resistant bacteria, adding an estimated €1.5 billion in additional hospital treatment and societal cost.\(^2\)
- Up to 5,000 patients a year are estimated to die from gram-negative blood poisoning in the UK.\(^10\) Of these half are thought to be from an antimicrobial resistant organism.\(^2,10\)
- The rate of mortality for patients with septicaemia due to resistant *E.coli* bacteria, is double that of the non-resistant strain.\(^7\)
- Bacteria, including some strains expressing the enzyme NDM-1 (New Delhi metallo-beta-lactamase), have become resistant to all types of antimicrobials.\(^7,25\) In secondary care settings, an outbreak of a MDR bacteria can spread rapidly and have potentially severe consequences.\(^3\) Although rates of MRSA (methicillin-resistant *Staphylococcus aureus*) infections have reduced significantly over the last decade, a significant threat is posed by the increase in infections by *E.coli* and *Klebsiella* (types of gram-negative bacteria for which there are very limited treatment options).\(^34\)
- It is estimated that a continued rise in antimicrobial resistance, by 2050, would cost the world up to $100 trillion in lost economic output.\(^35\)

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**How can the problem be addressed?**

While the threat of antimicrobial resistance cannot be eradicated, it can be better managed to mitigate its impact on human health.\(^6\) Doctors have identified improved antimicrobial stewardship\(^7\) in human and animal medicine as a vital measure for reducing the emergence and spread of antimicrobial resistance.

**Promoting and supporting good medical practice**

In light of the requirement for doctors to follow GMC (General Medical Council) guidance on prescribing,\(^36\) there is a need to focus on supporting and promoting good medical practice in this area. This is with a view to reducing inappropriate antimicrobial prescribing while ensuring doctors continue to prescribe antimicrobials when clinically appropriate, and should be achieved through action in the following areas.

- **Improving medical education and training** – medical curricula and continuing professional development should include sufficient training on the diagnosis and treatment of infection, to ensure that individuals are competent in the appropriate prescribing and stewardship of antimicrobials.\(^37\)

Training and professional development should also highlight the negative impact of inappropriate antimicrobial prescribing on future medical practice.\(^8\) Timely feedback regarding individual doctors’

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\(^{3}\) This has been defined by the National Institute for Health and Care Excellence as ‘...an organisational or healthcare-system-wide approach to promoting and monitoring judicious use of antimicrobial drugs to preserve their future effectiveness.’
prescribing – requiring the introduction of a unique prescribing number – would help ensure appropriate prescribing of antimicrobials is maintained throughout clinical practice. If doctors are unsure about appropriate prescription of antimicrobials they should consult the latest relevant local or national guidelines or formulary.

- **Implementation of evidence-based guidance** – a number of initiatives have been taken aimed at improving guidance with a view to reducing inappropriate antimicrobial prescribing. There is now a need to identify mechanisms to ensure that this guidance is successfully implemented, so that it is adhered to by all clinicians when prescribing antimicrobials. Clinicians should be aware of what guidelines are available and how to access them. All guidance on antimicrobial prescribing needs to be continually updated to remain relevant, supported by ongoing research and surveillance.

- **Ensuring adequate microbiology services and improved diagnostics** – the diagnosis of infection is essential for informing doctors’ decision-making when prescribing antimicrobials. Mechanisms that facilitate accurate and timely diagnosis of infection are key to improving antimicrobial prescribing in primary and secondary care. This includes providing adequate resources for effective microbiology services and diagnostic tests, as well as developing better diagnostics where required. In particular, the development and implementation of rapid point-of-care diagnostics, such as testing for biomarkers of infection, may have an important role to play in supporting appropriate antimicrobial prescribing in primary care. Improved direct communication between microbiology services and doctors, especially in primary care, also needs to be developed. This would enable microbiology services to provide in-consultation advice to GPs when prescribing antimicrobials.

- **Better information sharing** – increasing the availability and accessibility of patient information, particularly regarding the nature of infection, or the results of diagnostic testing, is necessary for improving antimicrobial prescribing. There is a need to ensure that the results of diagnostic testing are accessible to clinicians and can be integrated within patient records. Ongoing antimicrobial surveillance and stewardship programmes require more comprehensive information, particularly relating to why different antimicrobials are being prescribed. There is also limited understanding of the impact of antimicrobial use on patient outcomes. Improved surveillance of patient outcomes

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4 Current initiatives to improve antibiotic prescribing include: ‘Treat Antibiotics Responsibly, Guidance and Education Tool’ (TARGET) for GPs, developed by the RCGP; ‘Stemming the Tide of Antibiotic Resistance’ (STAR), an educational programme for GPs developed by a number of stakeholders; antimicrobial stewardship ‘Start smart - then focus’ for hospital prescribers, developed by the Department of Health; Public Health England’s antimicrobial prescribing and stewardship competencies and guidance for managing common infections in primary care; guidance from the National Institute for Health and Care Excellence on antimicrobial prescribing for self-limiting respiratory tract infections in primary care, and on prescribing of quinolones and cephalosporins. A number of Clinical Commissioning Groups have also developed guidance for antimicrobial prescribing.
requires better linking of GP and hospital records. While the majority of GP records are electronic, greater utilisation of electronic prescribing records is required in hospitals, to improve the availability of patient-level prescribing data.\textsuperscript{24}

- **Supporting general practice** – the majority of antimicrobial prescribing in the UK occurs in general practice.\textsuperscript{24} While efforts are being made across primary care – including through medicines management teams – to improve antimicrobial prescribing, it is important to consider the environment in which antimicrobials are being prescribed. There is a need to ensure adequate investment and resources are provided to properly support GPs when prescribing antimicrobials. Consultation times need to be sufficient to allow GPs to properly assess patients, and if necessary to give explanations as to why antimicrobials have not been prescribed. Better access to timely diagnostic tests in primary care is also required to improve antimicrobial prescribing. The fragmentation of primary care – whereby services are delivered by numerous providers – risks undermining efforts made by GPs to reduce antimicrobial prescribing. Reducing this fragmentation and preserving list-based general practice would help ensure improvements in antimicrobial prescribing by maintaining continuity, trust and consistency.

- **Greater accountability for antimicrobial stewardship in hospitals** – it is often unclear in hospitals which staff have ‘ownership’ of antimicrobial prescribing and responsibility for minimising resistance. Effective local leadership is a key factor in improving the quality of antimicrobial prescribing.\textsuperscript{40} There is a need to identify clinical infection specialists who can ‘champion’ appropriate antimicrobial prescribing locally, and take ownership of antimicrobial resistance. These ‘antimicrobial champions’ would ensure that all hospital doctors had access to support when prescribing antimicrobials, and help ensure that best-practice guidance on antimicrobial prescribing is followed.

- **Effective infection control** – improvements in infection prevention and control practices are required to reduce the spread of infection and the demand for antimicrobial therapy.\textsuperscript{4,8} There is a need for coherent and consistent infection control practices across health services.\textsuperscript{8} The BMA’s 2009 report *Tackling healthcare associated infections through effective policy action* reviews the evidence for infection control policies and explores specific action that hospitals can take to reduce the burden of HCAIs (healthcare associated infections). The report recommends that infection control practices are evidence-based, adequately resourced and implemented in partnership with clinicians.\textsuperscript{41}

- **Enhancing patient and public information** – the UK Five Year Antimicrobial Resistance Strategy 2013-18 highlights the responsibility patients have for reducing antimicrobial consumption,\textsuperscript{4} and includes necessary recommendations for promoting wider understanding of the need for a more sustainable approach to antimicrobial use. The strategy indicates the need for patients to understand when
antimicrobials are necessary and not to expect antibiotics for self-limiting viral infections. It also highlights the importance of patients taking antimicrobials appropriately when prescribed, including the requirement to complete any prescribed course.\textsuperscript{4} Alongside these recommendations the importance of basic hygiene in reducing the spread of infection needs to be promoted to the public. Public information should include clear, uncomplicated messages about the way in which antimicrobial use leads to resistance. While a number of public awareness initiatives are ongoing,\textsuperscript{9} there are no definitive targets or measures of success in raising public awareness. As the Science and Technology Select Committee have recommended, the introduction of robust national targets for improving public awareness of antimicrobial resistance would be an important policy development.\textsuperscript{8}

\textit{Reducing the inappropriate use of antimicrobials in modern farming}

The UK Five Year Antimicrobial Resistance Strategy 2013-18 includes a range of recommendations to improve antimicrobial conservation and stewardship in livestock. These include:

- measures to improve the knowledge and understanding of antimicrobial resistance in farming practice, including prioritising antimicrobial resistance in veterinary training
- provision of clear guidelines to animal keepers and veterinarians for conserving the effectiveness of current treatments
- promoting good hygiene in animal husbandry, to prevent unnecessary reliance on antimicrobials
- improving surveillance of antimicrobial use and resistance in livestock, including the collection of prescription data.\textsuperscript{4}

These actions need to be implemented and built upon. Two important aspects not covered in the strategy that need consideration are restrictions on the prophylactic (routine preventative) use of antimicrobials, and the use of critically important antimicrobials – including cephalosporins, fluoroquinolones and macrolides – in UK farming practices.\textsuperscript{4} The lack of specific recommendations on these aspects has been criticised for not going far enough to prevent antimicrobial resistance.\textsuperscript{11,42} Some countries, such as the Netherlands and Denmark, have restricted the use of critically important antimicrobials in animals.\textsuperscript{29} In 2014 the EU commission adopted proposals – for consideration in the EU parliament – to prohibit the preventive use of antimicrobials in medicated feed.\textsuperscript{43} Further action on reducing the inappropriate use of antimicrobials in veterinary medicine in the UK should focus on ensuring framework is in place that:

- prohibits routine prophylactic use of antimicrobials in veterinary medicine

\textsuperscript{9} Current public awareness activities include the annual European Antibiotics Awareness Day organised by the European Centre for Disease Control; Antibiotic Action, a UK-based public awareness initiative, funded by the British Society for Antimicrobial Chemotherapy; ‘Take care not antibiotics’ – a series of videos produced by NHS Choices; PHE’s ‘Antibiotic Guardian’ initiative. Various BMA activities have supported this approach of raising public awareness about the need to use antimicrobials appropriately, including as part of the BMA’s winter pressures campaign, and the BMA PLG (patient liaison group) guidance ‘Working together for better health’.
- restricts veterinary use of classes of antimicrobials (including fluoroquinolones, modern cephalosporins and macrolides) that are critically important in human medicine.

Facilitating the development of new antimicrobials
Alongside better stewardship of existing antimicrobials, preserving the sensitivity of antimicrobial therapy in the long-term requires the development of new antimicrobials. Between 1929 and the 1970s, emerging resistance was met with the development of more than 20 new classes of antimicrobials, or analogues of existing classes.² By the late 1970s, more than 270 antimicrobials were in clinical use.⁴⁴ The development of new antimicrobials has subsequently stalled, with no distinct classes of antimicrobials discovered since 1987 entering clinical use. At the current rate of development, it may not be possible to discover and market enough new antimicrobials to keep up with the spread of resistance.²

One of the key problems in developing new antimicrobials is that the current business model provides little financial incentive for doing so. Antimicrobials have a much lower potential investment return for pharmaceutical companies in comparison to medications used to treat or manage long-term conditions.⁴⁵ In 2004, antimicrobials accounted for less than two per cent of all drugs in development by the world’s largest 15 pharmaceutical companies.⁴⁶ The CMO’s 2011 second annual report (published in 2013) highlighted several of the key economic considerations dissuading pharmaceutical companies from investing in antimicrobial development, including that:

- antimicrobials are used for short treatment courses compared with drugs for chronic conditions
- where antimicrobials are reserved for future use, their effective patent period – and investment return – is reduced
- antimicrobial drugs have challenging clinical trial requirements.⁷

The report called for a focus on new ways to incentivise innovation, as well as engaging the private sector, public institutions and academia in a programme of research and development of new antimicrobials.⁷ In July 2014, the UK Prime Minister, David Cameron, announced a review into why so few antimicrobials had been developed in recent years, and ways to encourage and accelerate the discovery and development of new generations of antimicrobials.⁴⁷

The UK Five Year Antimicrobial Resistance Strategy 2013-18 also recognises the need to address issues of commercial viability and market failure to encourage investment in antimicrobials. It includes a number of specific recommendations that need to be taken forward, including:

- fostering international collaboration in antimicrobial development, such as public private partnerships
- developing the UK’s research and development capacity
- exploring new approaches that would provide greater incentives for antimicrobial research and development
• reforming regulatory requirements relating to the licensing and approval of antimicrobials, to facilitate development.\textsuperscript{4}

While these recommendations are welcome, there is a need to ensure they are fully implemented and effective in facilitating research and development of new antimicrobials.

**International cooperation on tackling antimicrobial resistance**

Tighter international regulation is required to reduce the use of antimicrobials globally in medical practice and modern farming.

Unlike most of northern Europe and North America, consumption of non-prescribed antimicrobials is commonplace in many countries.\textsuperscript{48} Doctors have raised particular concern about the availability of antimicrobials over-the-counter in some European countries. The supply of substandard, counterfeit antimicrobials is a growing problem in all regions of the world.\textsuperscript{49} Direct sales of antimicrobials on the internet are increasing and are difficult to regulate and control.\textsuperscript{50} In addition, international medical tourism has the potential to facilitate the global spread of antimicrobial resistant infections, especially healthcare associated infections.\textsuperscript{51} Increased international trade in food of animal origin is also likely to facilitate the spread of antimicrobial resistance, a situation that is compounded by insufficient controls on the use of antimicrobials in global farming practice.\textsuperscript{29}

While international networks for antimicrobial surveillance and stewardship exist\textsuperscript{4}, they have not yet resulted in a collaborative framework sufficient for tackling the problem of antimicrobial resistance. Coordinated action is urgently required to properly identify, track and manage the emergence and spread of antimicrobial resistance globally.\textsuperscript{6} This should involve surveillance of the development of antimicrobial resistance and the consumption of antimicrobials across medical and veterinary practice. More comprehensive data on the burden of resistance and the consumption of different classes of antimicrobials is needed to inform the development of effective policy for tackling the spread of resistance. The ‘one health’ concept is a strategy for expanding collaborative multi-disciplinary work at local, national, and global levels to attain optimal health for people, animals and the environment.\textsuperscript{6}

Various calls have been made for the further development and expansion of international partnerships to tackle the threat of antimicrobial resistance.\textsuperscript{4,43,51,52} This has extended to a proposal for creating an international legal treaty, equivalent to the IPCC (Intergovernmental Panel on Climate Change).\textsuperscript{53} The development of an international legally binding treaty would be a proportionate response to the scale of the global threat posed by antimicrobial resistance. It would also provide an important platform for the global

\textsuperscript{4} Current international networks aimed at tackling antimicrobial resistance include Re-Act (Action on Antibiotic Resistance); The Alliance for the Prudent Use of Antibiotics; The Transatlantic Taskforce on Antimicrobial Resistance; The World Alliance against Antibiotic Resistance: The Global Antibiotic Resistance Partnership.
implementation of policies for improved antimicrobial stewardship in medical and farming practices, and surveillance of resistance and antimicrobial consumption.
Reducing antimicrobial use in medical practice and modern farming, and preserving antimicrobial sensitivity – action areas

- Improved antimicrobial prescribing in medicine should be facilitated through:
  - adequate provision of medical education and training that ensures individuals are competent in the appropriate prescribing and stewardship of antimicrobials
  - greater adherence to national evidence-based prescribing guidance
  - provision of adequate local microbiology services and the development of improved diagnostics, in particular rapid point-of-care diagnostics
  - improved information sharing – especially regarding the nature of infection, or the results of diagnostic testing – in order to inform and support doctors’ decision-making when prescribing antimicrobials
  - sufficient investment and resources to support prescribing in general practice
  - identification of clinical infection specialists who can champion appropriate antimicrobial use in hospitals and provide greater accountability for antimicrobial stewardship
  - implementation of effective, evidence-based infection control practices.

- There should be a continued focus on programmes aimed at raising awareness about the appropriate use of antimicrobials among healthcare professionals, veterinarians and the public, supported by ambitious targets for improving public awareness of antimicrobial resistance.

- Tighter regulation to reduce the use of antimicrobials in veterinary medicine and modern farming practices should focus on:
  - prohibiting the routine prophylactic use of antimicrobials
  - restricting the use of classes of antimicrobial that are critically important in human medicine.

- A comprehensive research agenda should be a priority nationally and internationally, focusing on:
  - incentivising innovation and engaging the private sector, public institutions and academia in a programme of research for the development of new antimicrobials
  - improving surveillance of antimicrobial resistance and prescribing, and developing novel diagnostics to support antimicrobial prescribing.

- Greater international cooperation should be facilitated through the development of an international legally binding treaty on antimicrobial resistance. This should include global policies for:
  - improved antimicrobial stewardship in medical and farming practices
  - surveillance of antimicrobial resistance and antimicrobial consumption.
References


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51 Department of Health, Foreign & Commonwealth Office press release (20.05.13) UK calls for international action on antimicrobial resistance.

52 World Health Organization press release (10.04.14) WHO’s first global report on antimicrobial resistance reveals serious, worldwide threat to public health.