Health and Social Care Committee

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Committee reports are published on the Committee’s website at www.parliament.uk/hsccom and in print by Order of the House.

Evidence relating to this report is published on the inquiry publications page of the Committee’s website.

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Antimicrobial resistance (AMR) poses a grave threat to health. Quite simply, if action is not taken to address this growing threat, we are told that modern medicine will be lost. By 2050 it is estimated that AMR will kill 10 million people per year, more than cancer and diabetes combined. Antimicrobial treatments make previously life threatening illnesses such as TB, pneumonia and malaria treatable; they enable surgery to be carried out safely; make childbirth far safer for both mother and baby; and protect cancer patients whilst their immune systems are weakened by chemotherapy. Without effective antimicrobial treatments, the risk of death from infectious disease becomes substantially higher, and weighing the risks of complications or death through infection against the benefits of proposed treatment will become increasingly challenging. We are seeing a rise of resistant infections across healthcare and even where these are not currently life threatening, they are causing serious harm for example sexually transmitted infections such as gonorrhoea and chlamydia.

Visible and active Government leadership needs to be restored to tackle AMR. We therefore urge the Prime Minister to work closely with her relevant ministers to raise the profile of AMR both at home and on the international stage. Given the severity of the threat, AMR needs to be firmly established as a ‘top five policy priority’ for the Government as a whole, and a dedicated budget should be made available to enable work in this area to make more rapid progress across all relevant departments.

No new classes of antibiotics have been discovered for decades. This is the result of market failure–pharmaceutical companies are concerned about the profitability of new antimicrobial drugs, and investment in their development has therefore been limited. Because of the need to protect new antibiotics from overuse in order to reduce the emergence of resistance, new approaches are required to encourage research and development in the public interest. Investment in basic scientific research is essential but so too is the investment by pharmaceutical companies in further development and bringing products to the market. Options to address this market failure include changes to patent law and changes to the ways that pharmaceutical companies are reimbursed for new antimicrobial medicines. We want to see tangible progress within six months on implementing practical policies to reverse the worrying exodus from this area of research and development and both government and industry should play their part in tackling this issue.

It is also essential to conserve the effectiveness of current antimicrobials by improving infection prevention, and by reducing inappropriate and unnecessary prescribing. We are supportive of public education campaigns to promote antibiotic stewardship. Improvements to date in prescribing practices are a step in the right direction but more needs to be done including to address unwarranted variation. This should be supported by rapid diagnostic tests, where these are recommended by NICE but in many cases there are already evidence-based decision support tools that are under-used.

Digital health tools for clinicians and policymakers have the potential to greatly increase the quality, safety, and cost effectiveness of clinical care and reduce the threat of antimicrobial resistance. The variation in uptake of best practice is unacceptable and there is good evidence of how this could be addressed. A single organisation should be
given responsibility for co-ordinating clinical decision support systems across the NHS, and ensuring they prompt evidence based prescribing of antimicrobials, as well as other medicines.

There should also be a clear message about the value of vaccination programmes in preventing both primary and secondary infection; encouraging uptake also helps to reduce antimicrobial use and AMR.

Antibiotic use in farming is an important contributor to AMR and DEFRA must ensure that progress in reducing the use of antibiotics in animals is embedded and in some areas extended, including keeping targets under close review. Serious concerns remain about the prophylactic or metaphylactic use of antibiotics in animals, and the use of antibiotics of last resort that may as a result lose their effectiveness for humans more quickly. Strict controls on these practices are essential and attention must be paid to this following the UK’s departure from the EU. The Government must make a clear commitment that post-Brexit, any future trade deals will require any meat and dairy produce imported into the UK to meet at least the same standards relating to antibiotic use which apply to meat and dairy products produced in the EU.

The strategy should include commitments to establish safe discharge levels for human waste, agricultural waste and pharmaceutical manufacturing waste, and to introduce systems to monitor and enforce them.

We recognise that AMR is a global issue requiring co-ordinated international action, including on environmental contamination by antimicrobials. We expect the Government’s new strategy to give greater focus and emphasis to this area and we urge a clear commitment to provide global leadership.
Introduction

1. Antimicrobial resistance (AMR) poses a grave threat to health. Professor Dame Sally Davies, the Chief Medical Officer, told our inquiry quite simply that if action is not taken to address this growing threat, ‘modern medicine will be lost’.1

The “bedrock of modern medicine”

2. We heard that before the discovery of antibiotics and other antimicrobial2 treatments, 43% of people died from infections, and life expectancy was on average 20 years lower.3 Since antibiotics first came into widespread use in the 1940s, they have played an increasing role in underpinning modern medicine, being described as ‘the bedrock of many of the greatest medical advances of the 20th century’.4 Antimicrobial treatments have a key role in tackling infections—making common but previously life threatening illnesses such as TB, pneumonia and malaria treatable. Before their advent even a simple cut had the potential to kill if it became infected. Antimicrobials play a far wider supporting role in medicine than this, making it possible to carry out life-changing surgery safely—from hip replacements to organ transplants—and making childbirth far safer for both mother and baby. Cancer patients often depend on antimicrobial medicines to protect them whilst their immune systems are weakened by chemotherapy. Without effective antimicrobial treatments, we face a “being cast back into the dark ages of medicine”,5 where simple infections will once again kill people, and people will be faced with agonising decisions over whether or not to have cancer treatment or surgery, as risks of death through infection may outweigh the benefits of treatment.

What is AMR and what causes it?

3. Current antimicrobial treatments are becoming less effective because bacteria and other pathogens have evolved resistance to the medicines used to treat them, through processes of spontaneous genetic mutation and natural selection. The development of AMR is an inevitable and expected development—indeed it was predicted by Alexander Fleming, the scientist who discovered antibiotics, over 70 years ago.

4. The eventual development of resistance is inevitable, but the speed at which it develops is accelerated by excessive, inappropriate and unnecessary use of antimicrobial treatments. Antimicrobial use is rising across the world, with global consumption of antibiotics increasing by nearly 40% between 2000 and 2010, increasing the rate at which resistance is developing. International travel has created new opportunities for antimicrobial-resistant diseases to be spread globally.6 Evidence also suggests that far more antimicrobials are used than need to be, both in the UK and abroad. Although only 10 per cent of sore throats benefit from antibiotic treatment, as most are viral, antibiotics

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1 Q4
2 Antimicrobials refer to all chemicals (including heavy metals) and drugs that can kill microorganisms (bacteria, fungi, parasites and viruses). Antibiotics are a subset of antimicrobial drugs that kill or inhibit the growth of bacteria.
3 Q2
6 The Review on Antimicrobial Resistance (launch paper), Lord Jim O’Neill, December 2014, p4
Antimicrobial resistance are still prescribed in as many as 60 per cent of cases.\textsuperscript{7} A recent study found that nearly a third of antibiotics prescribed by doctors in the US were prescribed for conditions that do not respond to antibiotics, translating to 47 million unnecessary prescriptions each year.\textsuperscript{8} In some countries, antimicrobial medicines are available without a prescription at all.

5. Antimicrobial resistance can also develop in animals and the environment. Over 40\% of the UK’s total antibiotic use is in animals.\textsuperscript{9} In some countries antibiotics are widely used in farming both for growth promotion and to prevent infection, with antibiotics either being used to prevent infection developing, or being given to a whole herd or flock when one animal develops an infection, rather than isolating and treating only the affected animal.

6. Although antimicrobial resistance has been developing since the introduction of antimicrobial medicines, clinical problems have emerged relatively recently, and are escalating. Until the end of the 1980s, so many new types of antimicrobial medicines were being discovered that when an infection became resistant to one drug, alternatives were usually available. However, the era of rapid drug discovery has now come to an end, partly because the ‘easy discoveries’ have already been made and partly because the business model for antimicrobials does not incentivise the pharmaceutical companies to invest in drug discovery in this area. This issue is discussed in more detail in Chapter 2. Many of the medicines used to treat infections are based on chemical structures discovered 30 or more years ago.

7. Action to tackle the growing threat of AMR therefore needs to be on two fronts—firstly through reducing the inappropriate use of existing antimicrobials to preserve their effectiveness for longer and slow the development of AMR, through more targeted prescribing and action to prevent infections in the first place; and secondly through the development of new antimicrobial treatments.

The scale of the problem

8. Antimicrobial-resistant infections currently claim at least 50,000 lives each year across Europe and the US alone, and 700,000 lives globally—but these figures are set to rise dramatically over the next 30 years. The estimate of global mortality from AMR across the world by 2050 is a staggering 10 million per year. This would represent a greater death toll than cancer and diabetes combined.\textsuperscript{10}

9. While in developed health systems it is currently often possible to access alternative second or third line treatments when patients develop a resistant infection, mortality rates and costs of treatment are likely to be approximately double for a drug-resistant infection, generating an estimated cost to the NHS of £180 million per year.\textsuperscript{11} Especially in poorer countries there is a growing prevalence of drug resistant strains of TB and malaria, increasing danger to individuals and communities as well as the cost burden of dealing with those critical diseases.\textsuperscript{12}

\textsuperscript{7} What if antibiotics were to stop working? King’s Fund blog authored by Professor Dame Sally Davies, 2017
\textsuperscript{8} What if antibiotics were to stop working? King’s Fund blog authored by Professor Dame Sally Davies, 2017
\textsuperscript{9} Reducing UK antibiotic use in animals, Parliamentary Office of Science and Technology, October 2018
\textsuperscript{10} The Review on Antimicrobial Resistance (launch paper), Lord Jim O’Neill, December 2014, p5
\textsuperscript{11} O2
\textsuperscript{12} The Review on Antimicrobial Resistance (launch paper), Lord Jim O’Neill, December 2014, p4
10. Public Health England publishes data on resistance rates in key infections, including E coli, K. pneumonia, K. oxytoca and Pseudomonas SPP. The most recent data shows that for all of these, the percentage of cases involving antibiotic resistance was higher in 2016 than 2012:

11. Gonorrhoea has developed resistance to all classes of antibiotics used to treat the infection.

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13 These are gram-negative bacteria that can cause septicaemia and pneumonia, and which are increasing in incidence in healthcare settings.
In the past year cases of multi-drug resistant gonorrhoea—for which there is no effective treatment—have been detected in the UK and elsewhere.

**Previous action to tackle AMR**

12. The Government launched its five year UK strategy to tackle antimicrobial resistance in September 2013. The strategy takes a ‘one health’ approach, addressing AMR in humans, animals and the environment. A number of Government departments and agencies are involved in steering and delivering the strategy, which is led by PHE, DHSC and DEFRA. The Government’s assessment of its progress against seven key areas for future action is set out in its written evidence. Around the same time as the strategy was published, the House of Commons Science and Technology Committee launched an inquiry into AMR, focusing on whether the proposals would contribute enough to tackling this threat. Its report and the Government’s response to its recommendations were published in 2014. Also in 2014, the then Prime Minister announced an independent review of the issue, chaired by Lord O’Neill of Gatley. This report, published in 2016, looked beyond the UK and took a global view, made ten recommendations, many of which dovetail with the aims of the UK strategy. In response to the report, the Government set out five new ambitions, listed in their written evidence.

**Our inquiry**

13. The Government’s updated AMR strategy, due to be published early in 2019, will be an opportunity to renew the impetus for tackling this extremely serious threat. We therefore call not just on the Department of Health and Social Care, but on the Government as a whole, to incorporate the recommendations of this report within the strategy. We intend to take follow up evidence from the Government shortly after publication of its strategy. This report makes recommendations in five key areas:

- Priority and political leadership
- Pharmaceutical market failure
- Antimicrobial use in healthcare
- Antimicrobial use in animals
- Antimicrobials and the environment.

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14 The UK strategy was developed collaboratively with the devolved administrations of the UK, and each of the devolved administrations has responsibility for its implementation within their own jurisdictions in relation to human health. The control of veterinary medicines, including antimicrobials, is currently a reserved power, and the Department for Environment and Rural Affairs (Defra) has UK-wide responsibilities in relation to animal health.

15 Department of Health and Social Care (AMR0043) paras 7–57


17 Government response, September 2014

18 Department of Health and Social Care (AMR0043) para 5
1  Priority and political leadership

14. We recognise that important steps towards tackling AMR have been made in the past five years. Professor Mike Sharland, Chair of the Government’s Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection, told us that the UK is ahead of many other countries in even having an AMR strategy in place, and Lord O’Neill gave us his view that progress was now being made in many of the areas his review highlighted. Two of the targets set out by the Government in response to Lord O’Neill’s report relating to reductions in antibiotic use in both humans and animals have now been met. However, little progress has been made in some other very important areas.

15. Both Professor Dame Sally Davies and Lord O’Neill told us that strong, visible political leadership at the highest levels is urgently needed. Lord O’Neill argued that in previous years, “Britain had a fantastic voice, power and influence globally on this topic …”.19 Asked if we were losing that leadership role, he replied that in his view, we were.20 Under the Cameron Government, it was a top-five policy priority. I am not aware of it being publicly mentioned in any international forum by any of our leading Cabinet Ministers, never mind the PM, since.21 He went on to argue that “policymakers around the world are seemingly presiding over an accelerating car crash.”22

16. Professor Dame Sally Davies told us

I would like more visible and active Government leadership, not just from our Department and the Prime Minister… we need it from DEFRA around animals and the environment, and from DFID continuing its global work … and the Foreign Office as well.23

17. When asked what her sense was of how important AMR was at the top of the DHSC and NHS England, she said ‘it is recognised.’24 She went on to ask for our support in prioritising AMR more widely across government.25

18. Dr Susan Hopkins, a Deputy Director of Public Health England leading on healthcare associated infections and AMR, highlighted the priority and leadership that has been given at an official level, by Professor Dame Sally Davies herself. Her evidence also gave insight into the difficulties faced in prioritising AMR amongst other disease areas also competing for funding, particularly given that AMR is perceived as a ‘future threat’ rather than ‘a serious threat right now’:

I think it is given a lot of priority. Dame Sally has really championed the issue. There has been a lot of discussion and a lot of momentum behind the AMR strategy. I think funding could always be greater across all the areas. There are many different disease areas that are equally demanding of attention.
and funding so the money has to be spread out. Obviously antimicrobial resistance is a future threat, particularly for this country, compared with a serious threat right now. I think we have given it substantially more funding in the last five years than we did before that, but we will need to continue with at least that, if not more, funding if we are to tackle the problem in the future.

19. Dr Sheuli Porkess, Deputy Chief Scientific Officer at the Association of the British Pharmaceutical Industry, suggested that AMR should be a key priority in the NHS 10 year plan.26

20. Professor Dame Sally Davies was clear that more funding was needed in this area.27 However, she argued strongly for a central, cross-Government budget:

You will not solve this from the Department of Health and Social Care budget. This is a wicked problem that is cross-sectoral. It takes in animals and the environment. It will have to be solved with Treasury funding rather than funding from the Department of Health and Social Care, and no one country can do it on its own.28

21. The DHSC minister with responsibility for AMR, Steve Brine, rejected Lord O’Neill’s assessment that the UK has lost its international presence on this issue and told us that the Prime Minister had raised the issue herself in a number of international forums, including last year’s G20 summit.29 We welcome the minister’s recent work on this issue at the G20 summit in Argentina. However, he also told us that he had had no official inter-ministerial meetings on the subject of AMR with his opposite number in DEFRA, DFID or with the Prime Minister during the 15 months he has held the portfolio for this issue.30

Conclusions

22. Antimicrobial medicines are critical not only in treating infections but also in enabling safe childbirth, as well as healthcare interventions that we take for granted, such as surgery, transplants and cancer treatments. Without them, quite simply, modern medicine will be lost. Yet diseases are rapidly becoming resistant to existing antimicrobial drugs, and there are insufficient new drugs being developed to replace them. This makes AMR a critical risk for current as well as future generations.

23. The evidence we have received has suggested that despite the severity of the threat posed by AMR and its potential to affect every area of healthcare, AMR is now struggling for priority and needs political leadership at the highest level of Government. The fact that no inter-ministerial meetings have been held to discuss AMR in the past 15 months speaks not only of a lack of priority, but also of a lack of join-up across Government to tackle this.

24. Two of the Government’s key advisers on AMR have independently called for ‘more visible and active Government leadership’ on this issue. We therefore urge the

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26 Q95
27 Q5
28 Q37
29 Q181
30 Q204
Prime Minister to work closely with her relevant ministers to raise the profile of AMR both at home and on the international stage. Given the severity of the threat, AMR needs to be firmly established as a ‘top five policy priority’ for the Government as a whole, drawing together the work of DHSC, DEFRA, DFID, the Foreign Office and BEIS. A dedicated budget should be made available to enable work in this area to make more rapid progress across all relevant departments.
2 Pharmaceutical market failure

25. As noted above, one of the most serious issues in the fight against AMR is the fact that no new class of antibiotics has been introduced for over thirty years. According to Professor Dame Sally Davies, this is in part because the ‘easy wins’ have been made; but there is also now a fundamental failure of the market for new antibiotics.

26. New medicines have a patent of 20 years during which the market dictates the price paid for them—it is during this period that new medicines make a high profit and pay back the investment that has been made in their development. After their patent expires they can be produced by any manufacturer and are sold far more cheaply as ‘generic’ medicines.

27. However, given the growing threat of AMR, and the need to conserve and use current and future antibiotics very carefully to preserve their effectiveness for as long as possible, pharmaceutical companies are aware that any new antibiotic they bring to market will only be prescribed very sparingly rather than as a first line treatment during its patent life, thereby reducing its profitability. Other factors cited as contributing to a lack of commercial appeal for antibiotic development include the unpredictable nature of emerging resistance, and shorter courses of use, compared with for example, a medication to treat high blood pressure. Addressing this market failure was a key strand of Lord O’Neill’s recommendations.

28. During the past 5 years, we heard that there has been increased investment in the early scientific research needed to discover new antimicrobials. Between 2015–16 and 2017–18, DHSC funding for research on AMR has risen from £11.6 million to £30.6 million. However the number of pharmaceutical companies involved in the further development and clinical trials to then take new antimicrobials to market has decreased. The latest company to exit this market, in June of this year, was Novartis, bringing the total number of companies involved in antimicrobial drug development to six.

29. The Access to Medicines Foundation’s 2018 Benchmark report sets out current levels of industry involvement in AMR development, and identifies eight companies involved in
research of this type–GSK, Johnson and Johnson, Merck, Novartis, Pfizer, Roche, Sanofi and Shionogi. Since the publication of the report however, two of these eight companies, Sanofi and Novartis, have left the market.

30. Lord O’Neill told us he was very concerned about this market failure. He argued that the market

… does not function, and it is getting worse. Somebody I respect said to me about a month ago that, if they were a betting person, they would think that there might be no major pharmaceutical company left seriously attempting to produce antibiotics within two years. Since our review finished, more have left than have got involved.35

31. Professor Dame Sally Davies argued that industry needed to step up and act in a socially responsible way, pointing out that tackling AMR is also in their interests:

Although many of these companies are colleagues, and many of their members are doing their best to work with us, I am disappointed by the number of them who have said quietly over a drink, “Well, Sally, we know you’re going to solve this. The Government will have to pay, so we’re waiting until you pay”. There are two issues. First, where is social responsibility? They should be putting in their money too. The second is short-sightedness. To go back to the point about losing modern medicine, what is the point of developing the world’s greatest cancer portfolio if there are not antibiotics to rescue the patients? Yet they expect that we in the Government and the public sector will fund this, or that it will happen by someone else being corporately responsible.36

32. In the view of the ABPI, however, sufficient investment is already being made by industry:

[Dr Paul Williams MP] We heard from the previous panel that industry seems to be waiting for the Government to stump up the cash. Is there collective investment from industry as well?

[Dr Sheuli Porkess, ABPI] Yes. The investment from industry has been made, in that we already have five candidate products that have been put forward to the Department of Health and Social Care for consideration for the pilot. Industry has already invested in developing those, and we now need to work together on how we get the pilot early next year.37

33. The market for antimicrobial drugs is a global one, and we were told that the UK accounts for only 3% of this market.38 Therefore this is not a problem that the UK should have, or indeed will be able, to solve unilaterally. However, as we heard from the ABPI, if the UK leads by example in this area by intervening to stimulate or regulate the market here, other countries may follow its example.39
34. We heard evidence of a number of different possible options to tackle this problem:

- “Play or pay”—Lord O’Neill’s report suggested the introduction of an “antibiotic investment charge” to be paid by pharmaceutical companies, but with exemptions for those which are participating in antibiotic development.40

- Changes to patent law, including the possibility of extensions, or of a transferable patent voucher, currently under consideration in the US.41

- Upfront payments to drug companies who develop new antimicrobial drugs—like advance purchase orders—so that a certain level of profitability is guaranteed within the patent life, even if the product is held back as treatment of last resort and not extensively used.

35. The Government has been working with the ABPI on developing a pilot scheme of this last option. We heard that this will require Government funding now to take it to the next stage. When questioned about progress developing the market for antibiotics, the Minister did not seem as concerned by lack of progress in this area as previous witnesses.42

Conclusions

36. The market failure for antimicrobial drugs must be resolved, or modern medicine will be lost. As well having a profoundly damaging effect on the health and lifespan of people in all parts of the world, and the world’s economy, this will have a clear financial impact on the pharmaceutical industry, if, for example, chemotherapy stops because there are no antibiotics to support it. The government needs to re-engage with the seriousness and urgency of this problem.

37. We expect to see tangible and rapid progress in this area within six months. Efforts to pilot the Government and industry’s current preferred option of an upfront payment scheme should not be delayed. Both government and industry should invest in this scheme. We recommend that other options to address market failure, including changes to patent law for antimicrobials and Lord O’Neill’s ‘play or pay’ proposals, should also be considered by Government.

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41 Q37 [Professor Dame Sally Davies]. A transferable patent voucher would grant a patent extension to the successful developer of specified antimicrobials; this patent extension could be used to extend the patent on another product, or could be sold on to another company.
42 Q218
3 Antimicrobial use in healthcare

38. Progress in developing new antimicrobial treatments is urgently needed. But as our witnesses pointed out to us, the development of new antimicrobials will not change the situation within the next five years, the lifetime of the new AMR strategy, and it is therefore essential to maintain a strong focus on looking after and preserving the effectiveness of existing antimicrobials.

39. Prevention is key. Prevention includes vaccination, as well as stopping or reducing transmission, both in hospital settings—through measures to improve cleanliness and control MRSA—and also in the community. Our evidence emphasised the importance of continued focus on prevention. Variation in practice also needs to be addressed.

40. We also heard that progress was also being made in reducing antibiotic prescriptions. The Government’s advisory Committee has estimated that around 20% of UK prescriptions are inappropriate. The Government aims to halve inappropriate prescribing. However, it is not clear that this target is sufficiently challenging, as we were told that antibiotic prescription rates in the UK remain approximately double those seen in the Netherlands, Sweden and the Baltic states.

41. In primary care, there has been a 13% reduction in prescriptions in the past five years. However, in secondary care there has been less progress. PHE report that:

Secondary care, despite some progress observed in 2015, has not had a sustained reduction in total antibiotic prescribing. However, from 2015 to 2016 hospitals reduced their use of the ultra-broad spectrum antibiotics piperacillin/tazobactam and carbapenems (both -4%). This is the first step in reducing antibiotic use in hospitals and focusing on using these antibiotics appropriately is key to preventing the emergence and spread of carbapenem-resistant Gram-negative bacteria.

42. Efforts to educate prescribers have included the Antibiotic Guardian campaign, run by PHE, and supported by public awareness campaigns, which are designed to support prescribers in reducing antibiotic prescription. NICE has also developed guidance in this area. We are supportive of public education campaigns to promote antibiotic stewardship.

43. We heard that in secondary care much lower target reductions, of around 1–2%, have been set. This is because many people requiring hospital admission are acutely ill and are prescribed an antibiotic on admission as an appropriate safety measure while tests are run. The focus of efforts to change antibiotic prescribing in secondary care will be on encouraging prescribers to review antibiotic use at 24 hour intervals to check that the
antibiotic is still needed and that the correct one has been used.\textsuperscript{49} Given that there is also rightly a focus on rapid recognition and treatment of possible sepsis, it is important that staff are not deterred from early action.

44. Many decisions to prescribe antimicrobial medicines are made in the absence of a positive diagnosis of the cause of the infection, potentially leading to inappropriate prescriptions. For example, as we note above, although only 10 per cent of sore throats benefit from antibiotic treatment as most are viral, antibiotics are still prescribed in as many as 60 per cent of cases. Lord O’Neill argued strongly for the increased availability of rapid diagnostic testing, and, ultimately, for all antimicrobial prescribing to be tied to diagnostic testing.\textsuperscript{50} Practical difficulties were raised with this, including the fact that it is far cheaper to prescribe an antimicrobial than to carry out a diagnostic test.\textsuperscript{51} We also heard that the widespread use of diagnostic tests could in fact increase rather than decrease inappropriate prescribing. This is because, even if a patient tests positive for a certain bacteria, that does not mean that antibiotics are required, as in many cases the illness will be self-limiting and the person’s own immune system will manage to fight it off without antimicrobial treatment.\textsuperscript{52}

45. We were told that decision-making algorithms could in some cases be as effective or more effective than diagnostic tests in improving prescribing, and far cheaper.\textsuperscript{53} However, implementing evidence-based best practice in this area appears to be a major challenge, even when the evidence base is long established and well known. Professor Michael Moore, Professor of Primary Health Care Research at the University of Southampton, told us:

The research is published, but it just does not get into practice. You are saying ‘why isn’t there a thing coming up on my screen to say ‘is it an antibiotic? What are you prescribing it? Is there a clinical score?’ Then you do not label it properly. NICE guidance said that all antibiotic prescription should be associated with an indication. That is just a simple programming thing, and it has not happened to date.

There is a how body of work around delayed prescribing: why isn’t that easy to do? It was around the mid-1990s when we first published on delayed prescribing. There is no delayed prescribing button on your IT system that says ‘how long do you want to delay the prescription for?’ and prints the information on the other side of the prescription.

We know that for one [diagnostic test]–CRP testing–there is good evidence that it reduces prescribing. The NICE guidance for pneumonia recommended the use of that, but it is simply not being implemented. It is three and a half years since the NICE pneumonia guidelines came out. What happens is that the costs of those tests are met in primary care, and the antibiotics are paid for at the CCG level. If you say to a general practice, which is a small business, “We want you to use this test,” they say that it costs £10 a go, whereas it costs them nothing not to use it. If they are doing

\textsuperscript{49} Q140
\textsuperscript{50} Qq13–14
\textsuperscript{51} Q90
\textsuperscript{52} Q91
\textsuperscript{53} Q91
100 of those tests a year, you are asking them to spend £1,000 on that testing. That is an implementation problem. It is about getting the resource in the right place to get these things implemented.54

46. When we put this issue to Public Health England, they told us that best practice evidence on responsible prescribing of antimicrobial medicines—including the use of delayed prescriptions—was now at the forefront of newly available NICE guidelines, and that work was taking place to improve IT systems.55

47. Digital health tools for clinicians and policymakers have the potential to greatly increase the quality, safety, and cost effectiveness of clinical care and reduce the threat of antimicrobial resistance. Technology can and does exist to support prescribing. For example OpenPrescribing.net56 is a suite of tools that shows prescribing in every individual NHS practice, every month. Research carried out by DataLab using prescribing data shows that when PHE guidance on treatment of urinary tract infections was published, recommending a change in the first line antibiotic, and a quality premium was introduced to promote the change, changes in prescribing rates did occur, and were more rapid after the introduction of the quality premium. However there was considerable variation in the implementation of new guidance between CCGs. These graphs show the changes in the three highest and three lowest CCGs (all marked in red, with the blue dotted line representing the median):

48. DataLab argue that whilst software exists that supports prescribing, its use to support antimicrobial and other prescribing is variable, and that better co-ordination is needed at a national level:

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54 Q90
55 Q151; Qq153–154
56 https://openprescribing.net/
The NHS invests heavily in ‘Clinical Decision Support Systems’. They are, put simply, computer software that aims to prompt a clinician at the point of prescribing to ensure the prescription they give to a patient works, is as safe as possible, and gives the best value to the NHS and tax-payer. Practically this is normally done by generating a pop-up box for the prescriber before they finally issue a prescription.

Despite extensive knowledge and work in this area it is unclear to us where the ultimate responsibility for the content of these systems lies in the NHS. It appears that there are diverse arrangements and diffuse responsibility for procurement and assuring that these systems are high quality, and providing front line health clinicians with support based on the best evidence and latest national guidance. We believe that there could be better national coordinated approach by the NHS and arms-length bodies for ‘Clinical Decision Support Systems’ to implement change and help eliminate the kind of wide variation we have identified through OpenPrescribing.57

Conclusions

49. In order to preserve the effectiveness of current antimicrobial medicines for as long as possible, it is essential that they are prescribed appropriately. Improvements to date in prescribing practices are promising but need to continue. As UK prescribing levels are still approximately double that of the Netherlands, Sweden and the Baltic states, more challenging targets for primary care, and for rapid review and withdrawal of clinically unnecessary secondary care prescribing are needed.

50. Despite a growing body of research about the appropriate use of antimicrobials, and the availability of NICE guidance in this area, we were told that there are still fundamental problems with implementation—the guidance ‘just does not get into practice’.

51. As prescriptions are now issued electronically, introducing prompts to prescribers which require them to ensure that correct algorithms, diagnostic tests and reviews have been followed before antimicrobials are prescribed should be a simple matter, making appropriate prescription of antibiotics the default option. Instead, we heard that 20 years on, simple, low cost interventions such as issuing delayed prescriptions, which have proven efficacy in safely reducing antibiotic use, can still be very difficult to put into practice on standard GP prescribing systems.

52. Antimicrobial resistance has not been sufficiently addressed in a joined-up way—although research and guidance is clear, frontline clinicians still lack the tools to implement it easily because it has not been included in IT specifications. We welcome NICE’s development of evidence-based guidelines on antimicrobial prescribing, but we expect to see rapid and concerted action by NHS England to ensure that prescribing systems in all care settings make responsible prescribing of antimicrobials the default option.

53. Digital health tools for clinicians and policymakers have the potential to greatly increase the quality, safety, and cost effectiveness of clinical care and reduce the threat of antimicrobial resistance. The variation in uptake of best practice is unacceptable

57 DataLab written evidence (AMR0075)
and there is good evidence of how this could be addressed. A single organisation should be given responsibility for co-ordinating clinical decision support systems across the NHS, and ensuring they prompt evidence based prescribing of antimicrobials, as well as other medicines.

54. We heard a range of views about the importance of rapid diagnostic testing in antimicrobial prescribing, with some arguing that no antibiotic should be prescribed without one, while others felt that this could have unintended consequences, and that in some cases algorithms were a better aid to prescribing. Rapid diagnostic tests are already recommended by NICE for certain infections, but we heard that often these are not used because the cost of the test—which is far higher than the cost of antibiotics—falls on individual GP practices rather than the CCG.

55. Encouraging the development of rapid diagnostic testing should be considered alongside the action to promote the development of new antimicrobials, but use of diagnostic tests should be based on NICE guidance. Where testing is clinically appropriate and recommended by NICE, action should be taken to address the perverse financial incentives which may discourage their use.
4 Antimicrobial use in animals

56. The widespread use of antibiotics in animals is of concern because it is likely to lead to accelerated development of AMR, leading to welfare issues for farm animals and commercial issues for farmers. This also contributes to the development and spread of AMR in human pathogens. In 2016, agriculture accounted for 33% of total UK antibiotic sales, and companion animals accounted for 8%. We heard that good progress has been made in reducing antibiotic use in agriculture. Total UK antibiotic use in agricultural animals dropped by 27% between 2014 and 2016, to 45 mg of antibiotic per kg of livestock (mg/kg), exceeding the Government target of 50mg/kg by 2018. In comparison UK human antibiotic use was 129 mg/kg in 2014.58

57. Antimicrobial medicines are used differently in animals than in humans. For humans they will be used to treat or prevent infection in an individual. In the past, antibiotics were routinely added to animal feed as growth promoters—this practice was banned in the EU in 2006, although it persists in many other non-EU countries. Antibiotics are also used for routine prophylaxis59 and for metaphylaxis.60 However, all meat, eggs and milk sold in the EU have to pass tests to ensure that any antibiotic residues left from previous treatment are at levels that are considered safe for human consumption, and below a concentration that inhibits bacteria.61

58. Our written evidence expressed persisting concerns about the prophylactic use of antibiotics in animals, and also about the use of antibiotics of critical importance—antibiotics that are defined by the European Medicines Agency as vital in maintaining human health, including fluoroquinolones, 3rd and 4th generation cephalosporins and colistin. Some called for a ban on both of these practices. Witnesses from DEFRA argued that a ban was not necessary, as substantial reductions in both of these practices had already been achieved. Total sales of critically important antibiotics in agriculture have fallen to 1.5% of sales. Moreover, Christine Middlemiss, the Chief Veterinary Officer, told us that new EU medicines regulations would tighten practices significantly. She told us that this EU legislation will be mirrored in domestic legislation, with these specific provisions included.62

59. We heard that new trade agreements post-Brexit had the potential to introduce meat and dairy products to the UK market from parts of the world which are not subject to the same level of controls on antibiotic use as the UK and the EU.63 Government officials and ministers told us that the Secretary of State for DEFRA was clearly and strongly opposed to any reduction in food standards as a result of Brexit.64 We welcome this assurance.

60. Witnesses from DEFRA and RUMA argued that UK consumers themselves would object to a lowering of standards and would reflect this in their purchasing choices, should products from other countries become available. Our witnesses argued that current

58 Reducing UK antibiotic use in animals, Parliamentary Office of Science and Technology, October 2018
59 The practice of giving antimicrobials to a group of livestock to prevent illness occurring, even when there is no illness currently present.
60 The practice of giving antimicrobials to a group of livestock to prevent the further spread of an illness, once an illness has been detected in an individual animal.
61 Reducing UK antibiotic use in animals, Parliamentary Office of Science and Technology, October 2018
62 Q55
63 Qq78–79
64 Q237; Qq260–261
assurance marks used in the UK such as the Red Tractor assurance scheme could play a key role in helping consumers choose products from farms which adhered to the UK’s stringent standards in this area.\textsuperscript{65} However, we are not convinced that this is the case, as for many people price will be the driving factor; equally, labelling may not be obvious, and may not apply in all sectors, including the take-out sector. We discussed the possibility of changing labelling to inform consumers about antibiotic use standards, and we were told that labelling products as ‘antibiotic-free’ was in fact misleading as it does not mean that the animal involved had not received antibiotics during the course of its life.\textsuperscript{66}

Conclusions

61. Progress has been made in reducing the use of antibiotics in animals. DEFRA must ensure that this progress is embedded and in some areas extended, including keeping targets under close review. Serious concerns remain about the prophylactic or metaphylactic use of antibiotics in animals, and the use of antibiotics of last resort that may as a result lose their effectiveness for humans more quickly. It is essential that tight controls on these practices are introduced and maintained following the UK’s departure from the EU.

62. We have heard concerns that when the UK leaves the EU, imported meat and dairy produce will enter the UK market which has not been produced to the stringent standards relating to antibiotic use which currently apply to meat and dairy products produced in the EU. We were told that assurance schemes such as the ‘Red Tractor’ scheme would provide assurance to UK consumers, but we are unconvinced that the absence of such an assurance mark will provide sufficient information and protection to UK consumers.

63. We welcome the Secretary of State’s clear and strong opposition to any reduction in food standards as a result of Brexit. However, we do not regard those assurances as sufficient to guarantee that UK consumers will continue to be able to choose meat and dairy products which have been produced responsibly and in a way which will not undermine efforts to tackle AMR. \textbf{We invite the Government to make a clear commitment that any future trade deals will require any meat and dairy produce imported into the UK to meet at least the same standards relating to antibiotic use which apply to meat and dairy products produced in the EU.}

\textsuperscript{65} Qq265–270
\textsuperscript{66} Qq263–264
5 Antimicrobials and the environment

64. Antimicrobials can enter the environment through waste—including human, animal and farming waste, as around 70% of antibiotics are excreted in urine.

65. Waste can also come from pharmaceutical companies producing antimicrobial medicines, and is a particular concern in some countries, as our witnesses described:

Dr Williams: What is happening? Is a company flushing out the tanks and discharging antibiotics into the environment, and then bacteria breed in that environment?

Dame Sally Davies: Some of it is active pharmaceutical ingredients, the preliminary ingredients that are made generally in China and India, and some is the manufacturing. I do not believe it is our big companies. Much of it is generics companies in those countries.67

66. AMR is no respecter of international boundaries - therefore this has implications for the UK, just as overuse of antimicrobials in humans and animals abroad does.

67. We heard from many of our witnesses that not enough attention has been paid to this area. Sally Davies said that more research was needed,68 a view which was echoed by the Chief Veterinary Officer:

We need to understand more about how that interaction between the animal, waste, the environment, water and humans drives resistance and what the key pathways are.69

68. Professor Peter Borriello, Chief Executive of the Veterinary Medicines Directorate at DEFRA agreed on the need for better surveillance:

In terms of integrated surveillance and surveillance particularly in the DEFRA areas of responsibility we need to do more. What is particularly true for AMR is that monitoring certain compounds in the environment was not something that was considered that important in the past, so there are not systems to build on; we are having to start de novo …70

69. He added that from 2019, the Environment Agency will be measuring two more commonly used antibiotics, as they will be a better marker than those currently being measured.71 We also told that the pharmaceutical industry has agreed discharge targets which will be formally announced shortly.72 Professor Dame Sally Davies highlighted particular concerns relating to the environmental impact of fish farming,73 although Professor Borriello argued that concerns about fish farming in the UK in this regard were unfounded.74
70. Perhaps the most striking illustration of lack of progress in addressing issues relating to AMR in the environment was given by Gwyn Jones, Chairman of the Responsible use of Medicines in Agriculture Alliance (RUMA). He told us that after dairy farmers had been issued with advice not to feed calves with milk from cows who have been treated with antibiotics, they then faced questions on how the milk should be disposed of—there was no scientific evidence available to guide them on how best to do so.  

71. We recognise that AMR is a global issue requiring co-ordinated international action, including on environmental contamination by antimicrobials. We expect the Government’s new strategy to give greater focus and emphasis to this little-understood but important area. The strategy should include commitments to establish safe discharge levels for human waste, agricultural waste and pharmaceutical manufacturing waste, and to introduce systems to monitor and enforce them.
Conclusions and recommendations

Priority and political leadership

1. Two of the Government’s key advisers on AMR have independently called for ‘more visible and active Government leadership’ on this issue. We therefore urge the Prime Minister to work closely with her relevant ministers to raise the profile of AMR both at home and on the international stage. Given the severity of the threat, AMR needs to be firmly established as a ‘top five policy priority’ for the Government as a whole, drawing together the work of DHSC, DEFRA, DFID, the Foreign Office and BEIS. A dedicated budget should be made available to enable work in this area to make more rapid progress across all relevant departments. (Paragraph 24)

Pharmaceutical market failure

2. We expect to see tangible and rapid progress in this area within six months. Efforts to pilot the Government and industry’s current preferred option of an upfront payment scheme should not be delayed. Both government and industry should invest in this scheme. We recommend that other options to address market failure, including changes to patent law for antimicrobials and Lord O’Neill’s ‘play or pay’ proposals, should also be considered by Government. (Paragraph 37)

Antimicrobial use in healthcare

3. In order to preserve the effectiveness of current antimicrobial medicines for as long as possible, it is essential that they are prescribed appropriately. Improvements to date in prescribing practices are promising but need to continue. As UK prescribing levels are still approximately double that of the Netherlands, Sweden and the Baltic states, more challenging targets for primary care, and for rapid review and withdrawal of clinically unnecessary secondary care prescribing are needed. (Paragraph 49)

4. We welcome NICE’s development of evidence-based guidelines on antimicrobial prescribing, but we expect to see rapid and concerted action by NHS England to ensure that prescribing systems in all care settings make responsible prescribing of antimicrobials the default option. (Paragraph 52)

5. Digital health tools for clinicians and policymakers have the potential to greatly increase the quality, safety, and cost effectiveness of clinical care and reduce the threat of antimicrobial resistance. The variation in uptake of best practice is unacceptable and there is good evidence of how this could be addressed. A single organisation should be given responsibility for co-ordinating clinical decision support systems across the NHS, and ensuring they prompt evidence based prescribing of antimicrobials, as well as other medicines. (Paragraph 53)

6. Encouraging the development of rapid diagnostic testing should be considered alongside the action to promote the development of new antimicrobials, but use of diagnostic tests should be based on NICE guidance. Where testing is clinically appropriate and recommended by NICE, action should be taken to address the perverse financial incentives which may discourage their use. (Paragraph 55)
Antimicrobial use in animals

7. Progress has been made in reducing the use of antibiotics in animals. DEFRA must ensure that this progress is embedded and in some areas extended, including keeping targets under close review. Serious concerns remain about the prophylactic or metaphylactic use of antibiotics in animals, and the use of antibiotics of last resort that may as a result lose their effectiveness for humans more quickly. It is essential that tight controls on these practices are introduced and maintained following the UK’s departure from the EU. (Paragraph 61)

8. We invite the Government to make a clear commitment that any future trade deals will require any meat and dairy produce imported into the UK to meet at least the same standards relating to antibiotic use which apply to meat and dairy products produced in the EU. (Paragraph 63)

Antimicrobials and the environment

9. We recognise that AMR is a global issue requiring co-ordinated international action, including on environmental contamination by antimicrobials. We expect the Government’s new strategy to give greater focus and emphasis to this little-understood but important area. The strategy should include commitments to establish safe discharge levels for human waste, agricultural waste and pharmaceutical manufacturing waste, and to introduce systems to monitor and enforce them. (Paragraph 71)
Formal minutes

Thursday 18 October 2018

Members present:
Dr Sarah Wollaston, in the Chair
Luciana Berger Andrew Selous
Dr Lisa Cameron Dr Paul Williams

Draft Report (Antimicrobial resistance), proposed by the Chair, brought up and read.

Ordered, That the draft Report be read a second time, paragraph by paragraph.

Paragraphs 1 to 71 read and agreed to.

Summary agreed to.

Resolved, That the Report be the Eleventh Report of the Committee to the House.

Ordered, That the Chair make the Report to the House.

Ordered, That embargoed copies of the Report be made available, in accordance with the provisions of Standing Order No. 134.

[Adjourned till Monday 22 October at 1.30pm]
Witnesses

The following witnesses gave evidence. Transcripts can be viewed on the inquiry publications page of the Committee’s website.

**Tuesday 4 September 2018**

**Professor Dame Sally Davies**, Chief Medical Officer for England, Department of Health and Social Care; **Christine Middlemiss**, UK Chief Veterinary Officer, Department for the Environment, Food and Rural Affairs; and **Lord O’Neill of Gatley**.

**Gwyn Jones**, Chairman, Responsible Use of Medicines in Agriculture Alliance; **Professor Michael Moore**, Professor of Primary Health Care Research, University of Southampton; and **Dr Sheuli Porkess**, Deputy Chief Scientific Officer, The Association of the British Pharmaceutical Industry.

**Tuesday 11 September 2018**

**Professor Mike Sharland**, Chair, Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection; and **Dr Susan Hopkins**, Healthcare Epidemiologist Consultant in Infectious Diseases and Microbiology, Public Health England.

**Professor Peter Borriello**, Chief Executive, Veterinary Medicines Directorate, Department for Environment, Food and Rural Affairs; **Steve Brine MP**, Parliamentary Under-Secretary of State, Department of Health and Social Care; and **Dr Susan Hopkins**, Healthcare Epidemiologist Consultant in Infectious Diseases and Microbiology, Public Health England.
Published written evidence

The following written evidence was received and can be viewed on the inquiry publications page of the Committee’s website.

AMR numbers are generated by the evidence processing system and so may not be complete.

1. ABPI (AMR0018)
2. Age of Autism (AMR0034)
3. AHDB (AMR0044)
4. Ainsworths (AMR0051)
5. Alliance of Registered Homeopaths Ltd (ARH) (AMR0041)
6. Alliance to Save Our Antibiotics (AMR0052)
7. AMR Centre Ltd (AMR0062)
8. AMR Centre Ltd (AMR0064)
9. Andrew Ward (AMR0001)
10. Anthony McDonnell and Flavio Toxvaerd (AMR0006)
11. Antibiotic Research UK (AMR0003)
12. BD (Becton, Dickinson and Company) (AMR0019)
13. BGMA (AMR0036)
14. Biochemical Society (AMR0016)
15. Bioindustry Association (AMR0039)
16. BIVDA (AMR0061)
17. Bloodwise (AMR0027)
18. Boots UK (AMR0057)
20. British Poultry Council (AMR0030)
21. British Society for Antimicrobial Chemotherapy and British Pharmacological Society (AMR0032)
22. British Veterinary Association (AMR0048)
23. Caroline Ford (AMR0004)
24. CUTIC (AMR0025)
25. Cystic Fibrosis Trust (AMR0045)
26. DataLab (AMR0075)
27. David Tredinnick (AMR0015)
28. Deb Group Ltd. (AMR0002)
29. Department of Health and Social Care (AMR0043)
30. Dr David Jenkins (AMR0072)
31. Dr Rony Armon (AMR0049)
32. Dr Yubraj Sharma (AMR0022)
33. East and North Herts CCG (AMR0007)
Edinburgh Infectious Diseases (AMR0024)
GSK (AMR0047)
HCA Healthcare UK (AMR0010)
Healthcare Infection Society (AMR0069)
Homeopathy International (AMR0012)
Infection Prevention Society (AMR0070)
Institute and Faculty of Actuaries (AMR0031)
Institute for Global Innovation (IGI) (AMR0042)
Johnson & Johnson (AMR0014)
Matoke Holdings Ltd. (AMR0013)
Medical Research Foundation National PhD Training Programme in Antimicrobial Resistance Research (AMR0066)
Microbiology Society and the Society for Applied Microbiology (SfAM) (AMR0060)
MSD (AMR0028)
MSD Animal Health (AMR0037)
National Office of Animal Health Ltd (AMR0020)
National Pig Association (AMR0009)
Pfizer Ltd (AMR0056)
Professor Michael Ferguson (AMR0053)
Professor Xiaoning Xu (AMR0063)
Prospect Diagnostics Limited - Distribution Partner for RPS Diagnostics the manufacturer of FebriDx (AMR0026)
Quadram Institute (AMR0040)
RESULTS UK (AMR0055)
RESULTS UK (AMR0058)
Roche Products (AMR0023)
Royal College of Nursing (AMR0054)
Royal College of Physicians and Surgeons of Glasgow (AMR0017)
Royal College of Physicians of Edinburgh (AMR0011)
Royal Pharmaceutical Society (AMR0059)
RUMA (AMR0033)
STOPAIDS (AMR0050)
Stuart Calimport (AMR0074)
SULSA (AMR0038)
TB Alliance (AMR0073)
The Bureau of Investigative Journalism (AMR0071)
The College of Medicine, London (AMR0005)
The Hygeia Project (AMR0068)
The Society of Homeopaths (AMR0008)
71  The Wellcome Trust (AMR0065)
72  UK Research and Innovation (AMR0046)
# List of Reports from the Committee during the current Parliament

All publications from the Committee are available on the [publications page](#) of the Committee’s website. The reference number of the Government’s response to each Report is printed in brackets after the HC printing number.

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