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# The Spring Lecture: "Antimicrobial resistance: global threat to health and economy" by Professor Dame Sally C. Davies

## Abstract of the discussion

[Institute and Faculty of Actuaries, London, 27 April 2017]

**The President (Mr D. C. E. Wilson, F.I.A.):** It is my great pleasure to welcome you to this lecture. The autumn and spring lectures that we organise are part of the Institute and Faculty of Actuaries (IFOA's) commitment to promoting thought leadership and advancing actuarial science. They are intended to be useful resources for members and non-members alike, and on subjects of relevance not only to actuaries but also to those outside our profession.

I am delighted to introduce Professor Dame Sally Davies. In her lecture this evening she will be sharing her thoughts on antimicrobial resistance (AMR) and the impact that this has on economics and society.

Dame Sally is Chief Medical Officer for England. She qualified as a medical doctor but also has vast experience in public health, advising governments on health and social care issues.

Before becoming the Chief Medical Officer, she held responsibility for research and development and was the Chief Scientific Adviser for the Department of Health. She provides professional leadership for Directors of Public Health and was actively involved in NHS Research & Development from its establishment, and founded the National Institute for Health Research.

Dame Sally also sits on the World Health Organisation (WHO) Executive Board and advises many governments on health and policy.

In 2011 Dame Sally published her Chief Medical Officer's annual report on infectious diseases. That focussed on the increasing threat of antimicrobial resistance, or AMR, calling for national and international action to address the key areas of stewardship, monitoring and surveillance, and of course antibiotic development.

Since then, she has continued to advocate globally on AMR and has spoken at many events around the world. Dame Sally will also be playing a leading role in the new UN inter-agency co-ordination group for AMR. The first meeting will be held next month, and the group is going to be responsible for reporting back to the UN General Assembly in November 2018 on progress and the next steps.

Dame Sally received her DBE in 2009. She was elected a Fellow of the Royal Society in 2014 and a Member of the National Academy of Medicine USA in 2015.

**Prof Dame Sally Davies:** I am going to talk about AMR and why it is appropriate for you as actuaries. It is not too bad a problem at the moment. We calculate probably only about 5,000 people a year die in England of drug-resistant infections. But across the world, it is worse. If we do not take action, it is going to be much worse.

If you want to model it, I cannot tell you who is going to catch the infection that is resistant to drugs. We have no markers for those who will not respond to drugs because that is specific to the bug.

I want you to imagine a world in which modern medicine does not work. A caesarean section generally has some antibiotics to protect the mother. For hip replacements, which are big operations, the patients are protected by antibiotics. For cancer patients, I can imagine a day, if we do not get this right, when I go to the doctor and he says, "Well, Sally, I can give you a treatment and it might well cure you, but you are going to get an infection and I may not have the antibiotic". I might choose my bucket list and palliation.

Put that beside the impact that it could have on our food chain, a shortage of pork and chicken because of uncontrollable infections, for instance, and you will think that this is a dystopian future. I want to show you how this story is beginning to unfold. Infectious diseases are fighting the treatments that we have and so we have to do something about it. I had not understood this fully until I did my annual report 4 years ago.

I am going to talk briefly about AMR and its complexity. I found one only this week that I had not uncovered in the last 4 years. I will mention how we misuse antibiotics, and the current and the future impact; and then I will talk about what we are doing nationally and globally to try to make this a problem that does not kill more people.

Let me start with what AMR is: drug resistant infections, or superbugs not responding to drugs. Clearly, it is a natural phenomenon.

I find a lot of the public, when we talk about this, think that it is they that develop the resistance and therefore they need to take more precautions and have more antibiotics rather than understanding that it is the bacteria.

It is a Darwinian, natural selection issue, that if you have a bacterium, and it has one of the routine changes in its genes, a mutation that gives it an advantage in the presence of a drug, then it will multiply. The generation time for one common bug, E. coli, is 20 minutes. So, one bug getting that selection advantage multiplies very quickly.

If it were just that, it would be a problem but it would not be too bad. But these bugs are very clever. I am going to talk mainly about bacteria. Clearly, you can also have resistance in viruses; indeed, 7% of HIV viruses are resistant now to first line drugs. Malaria, which is a big problem of resistance in the Burma, Indo-china and Vietnam area, is spreading. This is a problem for all infections and it is the same natural selection.

I am focussing particularly on bacteria and what bacteria do as it is acute and killing people. They can not only pass resistance to their children, they can also pass little circles of DNA with the resistant gene from one bug to another which is called conjugation.



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They can go hunting in their environment and find the gene that gives them resistance and ingest it. It protects them. They will pass it on to their progeny. That is transformation. Also, you can get genetic material called plasmids transferred by these infective organisms, which are a kind of virus that attacks bacteria.

If you think about it, those are three ways where they can catch resistance from another bug or their environment and then pass it on to their cousins, their sisters, their aunts and uncles; and all of them will have that resistance. You can see how horrible this is.

If you think about these three different methods, you will understand that it is really easy to pass resistance from one type of bacteria to another type of bacteria. That happens in our guts. As we are improving our understanding of this, we are also understanding more about how important bacteria are to our health. We have more bacterial cells in us and on us than we have human cells. When they are disturbed, we can become ill. These bacterial cells are called a microbiome. We partially inherit our microbiome from our mothers.

I want to mention this issue of complexity and how every time I lift a stone I discover more.

When I started on this journey four years ago and discovered that it had become much worse than it had been when I looked after children with leukaemia or people with sickle cell disease, I thought it was a problem of humans. But it is not. It stretches to aquaculture — that is, fish farming.

Do you know what they do in fish farming around the world? They tip antibiotics into the fish farms in order to protect the fish from infection. That is washed out as they clean the fish pens. I am pleased to tell you this is not so in Scotland where Scottish salmon and trout are fine, or in Scandinavia, where they have individual vaccinations with a mixture of three vaccines.

But you can see how, with normal aquaculture, the antibiotics leach into the water and sewage, and then they can reach wildlife. Here we are surrounded by bacteria and we are exposing them to antibiotics that drive the development of resistance, and once resistance develops, drive its proliferation and expansion.

It also happens with food animals. Over 70% of antibiotics across the world go into food animals because it is a cheap way of making them grow, and it is cheaper than good hygiene and sanitation. Then it gets into the food chain. Actually, it is not just eating animals using antibiotics that affects us. Of the antibiotics eaten by animals, including us, only 70% pass straight through and out into the urine.

There was a study in China of primary schoolchildren who had not had antibiotics in the preceding 3 months. They found 21 different antibiotic residues in their urine. Those children were being exposed through the water that they drank, the water that they washed in and swam in and the food that they ate.

The average grown pig in China excretes 175 mg of antibiotics every day. That is equivalent of an adult antibiotic pill a day. So, we are damaging our environment. This is worrying.

In 2014, researchers from Newcastle University and the Indian Institute of Technology tested water from the Ganges. The levels of resistant bacteria genes, which we call NDM-1 (originally named



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New Delhi Metallo-Beta-Lactamase-1) makes bacteria resistant to carbapenems, one of our last resorts, a really strong class of antibiotics. They found the levels of this NDM-1 resistant bacteria 20 times higher in the water of the Ganges during the pilgrimage season than at other times. The sewage is in their water from overloaded waste handling systems.

But it happens in Britain, too. In 2014, the University of Exeter found that 6.3 million water sports sessions in the preceding year had been exposed to — and probably ingested —at least one type of resistant bacteria. The overflows of discharging raw human sewage into the rivers and seas of this country — there were 31,000 overflows last year — put bugs into the rivers and seas, and many of those will have resistance.

What have we done to make this worse? It should come to us as no surprise. When Alexander Fleming went to collect his Nobel Prize, he said, "The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to non-lethal quantities of the drug, make them resistant".

Fleming recognised the problem. But we have used antibiotics far too easily, far too inappropriately, not just in healthcare but in agriculture, as I have mentioned, in crops and livestock across society. I am told that one antibiotic, tetracycline, is put into the paint of some warships because it stops barnacles sticking.

So you can see why people do it. But it is one of those areas where we have not recognised the long-term effects. There is a direct correlation between antibiotic use and resistance.

If you look at total antibiotic consumption per capita, you will see Australia, America and Europe are the hot spots.

Australia is particularly worrying. I have just been there for a couple of weeks at some conferences on AMR. It was interesting that they did not have a big push on it, as their levels of resistant organisms are much higher than ours. Maybe as actuaries, as you give advice, you can look at the maps to see where this is worst. The maps are all on the web and are fascinating to look at. In Europe the best maps of resistance are produced by the ECDC, the European Centre for Disease Control.

In one world map you can see how the developing countries are expanding their use of antibiotics. We may be the largest consumers, but it is a sign of development and improved health services that other countries are starting to use them.

I want to highlight that, at the moment, more people die from a lack of access to antibiotics than die of resistance. What I am trying to prevent is flipping to more dying of resistance. It is a long haul, because we do not have new drugs and new drugs take 20 years to produce.

I also want to highlight that antibiotics are not a good substitute for public health. Diarrhoea claims 1.1 million lives a year across the globe. It is the second most important cause of death in children. 60% of those deaths could be avoided by access to safe water and sanitation. We can reduce our use of antibiotics, all of us, let alone across the world, if we use good hygiene, hand washing and sanitation.

Clearly, drugs are not good enough on their own. We need investment in education, good hygiene and sanitation. I could have shown you some of the impacts of President Modi's lavatories



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across India. A wonderful move. Millions are being built but in many villages the men have used the lavatories as storage because they do not mind going in the fields, which is worrying.

If you want to control the use of antibiotics, then surely you reduce prescriptions. But, as Alexander Fleming said in his acceptance speech, penicillin can be bought in shops. Many of you may have, like me, gone into a pharmacy in Italy, France or Spain and just bought them over the counter. But it is even worse in other parts of the world. If you go to Bangladesh and Nigeria, for example, you can buy them at a kiosk in a market.

If you are poor, as most are, first of all, you will not have a prescription, so you do not know whether you are getting the right antibiotic, and often in India you can buy injectable ones. Second, you probably cannot buy a whole course. You can probably buy enough for a day, or two, so you are going to stimulate the development of resistance.

We have a problem, which is getting worse in Britain, too, because hard as the regulatory agency (the Medicines and Healthcare Regulatory Produces Agency (MHRA)) work, internet pharmacies are still sending antibiotics through the post in this country. There are regular prosecutions of internet pharmacies from the MHRA and the police.

Another reason for people overusing antibiotics and driving resistance is using them when they are not needed, such as for a virus, a cold or the "flu".

But the pressure many of our public put on our GPs is sometimes overwhelming. It is difficult for GPs: GPs are estimated to distribute at least 10 million unnecessary prescriptions a year in England alone. It is possible to get on top of this, but it needs a lot of public education and work. We have done some behavioural work with GPs and steadily the use of antibiotics through our GPs is going down, but it is not easy because we have to take the public with us.

Two-thirds of antibiotics are used routinely in livestock for growth promotion. I am happy to tell you that since 2006 this has been illegal in the EU. It has also been phased out in the United States. In the States, this is consumer-led. Many restaurants now advertise that they use antibiotic-free chickens and pork. It is seen as an important consumer issue.

As incomes rise across the world, the demand for meat is rising and if antibiotics give this growth promotion, you can see why people carry on using them. What we need are new technologies to increase growth, but without the antibiotics. There are technologies being worked on but they will have to be cheap. One of the reasons that people use antibiotics is that, in general, they are cheap.

Before I move on further, I want to address this access versus excess issue. As we try to solve this problem globally, I do not want us to get into the position that we are in with climate change, where two things have happened. One, people dispute the science — I have yet to understand why. The second is the South says: you, the North, did it. You are now saying we cannot have that development opportunity. They see it as the North bashing the South. I think in solving this problem of AMR — drug resistant infections —it is incumbent on us to try to solve the access issues as well, so that more are used appropriately and there are fewer deaths because people did not receive the antibiotics that they needed.

40% of deaths in low-income countries are from treatable infectious diseases. Bill Gates is developing a strategy at the moment. He did a study that showed that if we gave antibiotics to all the



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children in Africa we would save 75% of children who would otherwise have died. That is very powerful. We do not want those children to die.

How do we balance all of that and get it right? We are going to have to do it by using rapid diagnostics and new drugs and so on.

Many of the cheap, old antibiotics are off-patent, so they are called "generics". They are not easily available in this country, let alone in Africa. What I thought was a problem of logistics and cost in some of these African countries is compounded by the fact that they are selling the more expensive ones rather than the ones that are dirt cheap. They have a much smaller selection of antibiotics. We are going to have to bottom out what is available and what is not and how to get the drugs manufactured and distributed in order to be fair.

The final area in which we are going to have to do some work is counterfeit and substandard antibiotics. Counterfeit and falsified antibiotics are common on the internet. This is an issue. The WHO estimates 50% of drugs sold on the internet are counterfeit. I was told recently about a country that thought it had resistance to the antimalarial drug it had bulk bought. Someone thought to check the drug. It was chalk. They did not have resistance. People were dying because some profiteers had sold chalk to that country.

In developing countries, counterfeit drugs account for between 10% and 30% of all drugs sold, but can, in some parts of Africa, be up to 60% of the drugs tested. If you take a sugar pill or a chalk pill, you are not going to get better. If it just has a bit of the antibiotic in it, it is more likely to drive resistance.

Let us have a look at the current position. I want to tell you about the last drug, which is called colistin. Colistin is a nasty drug. It was developed in the 1940s. When it came into use, we decided not to use it in humans because it damages the kidneys and liver. We put it aside and it was used in animals instead.

Unfortunately, because of other resistance, we are now having to use colistin in humans affecting their kidneys and livers en route. You hope you can kill the bug before it has done that damage. But, unfortunately, because of inappropriate use of it, mainly in animals, but also probably in humans, in 2015 a Welsh group working with Chinese scientists discovered resistant E. coli in the guts of pigs. It was called MCR-1. It gave resistance to colistin. That was in China.

They predicted that it would spread globally. What we do not know is whether it became global spread after this finding in China or whether it was there beforehand. But it was found in Denmark. Then in the United Kingdom. Then in the United States.

By the end of June 2016 it was in 32 countries. There are plenty more that we do not know about. Resistance is low to colistin. It is not that common. But it is out there and it surely will spread. It will get worse. If it combines with another resistance gene, then we will be at the start of a post-antibiotic era. What would that look like?

You, as actuaries, may well be aware that the WHO calls us the TB capital of Europe. Eight of our London boroughs exceed their high incidence threshold of 40 cases of TB per 100,000. In 2014, 126 of those cases were resistant to at least one first line drug. You probably thought that it



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had been eradicated. It is a very unpleasant illness. TB causes a cavity in the lung. People cough up the gunk from there and bleed. When I was a young doctor I sat by the bedside of a man through the night as he bled to death from one of those cavities. There was nothing that we could do.

If you have multi-drug resistance, you have to take quite a lot of tablets. It amounts to 19 pills a day for 2 years. You are going to have to take 14,000 pills to get better. How many people can afford 14,000 pills? How many people will adhere to 14,000 pills?

Let us take another issue. Gonorrhoea can give you pain in urinating. It can give you arthritis and neonatal eye problems, which can lead to blindness. Until recently, this was treated with a single pill. Since 2011, we have had to use two pills to treat cases in England because we have had an outbreak of gonorrhoea that is highly resistant to an important drug called azithromycin.

So what happens when we get resistance to that? We are going to have to go for the old-fashioned treatments. You could do urethral irrigation. They used to put mercury or iodine into the bladder to wash out the germs. Or you could try getting into a hot box and being heated to 43° in the hope that that would kill off the disease.

We have rising resistance levels, which we are making worse by our behaviours. Like climate change, this is a generational transfer. We will probably be all right, but our grandchildren will not, unless we take action.

At a conservative estimate, AMR is claiming at least 25,000 lives in Europe every year. That is about the same as a Boeing 747 crashing each week. If it were a Boeing crashing each week, we would hear about it. The problem, which is why you do not hear about it, is it does not have a face. The death certificate does not say that the cause of death is a drug resistant infection or AMR. It says it is pneumonia or an E. coli infection.

It is because there is not a WHO code for it. I have been pushing hard sending the Office of National Statistics and Public Health England to meetings around the world to try to get a code for it. It is difficult to get the numbers.

At least this number die in the States every year, too. It is already a real cause of disease. When I came across all of this back in 2013, I thought that we should do something about it. I persuaded our then prime minister that we should use the model of climate change. The debate around the world changed when Lord Stern looked at climate change through an economics lens. Prime Minister Cameron commissioned Jim O'Neill (now Lord Jim O'Neill) to review it. Jim used to be the chief economist at Goldman Sachs.

What he found was that, at the moment on a conservative estimate, there are probably around 700,000 people dying a year of drug resistant infections. I can tell you that the work from India suggests that at least 60,000 babies die every year of drug resistant infections. 700,000 a year is a death every 45 seconds round the world.

If we do not act, this is only going to get worse. The O'Neill review team showed that by 2050, if we do not take action, we will have 10 million deaths a year — more deaths of drug resistant infections than of cancer. Many of the cancer and diabetes deaths will be down to drug resistant infections. That is going to cost rather a lot, too — somewhere between $60 trillion and $100 trillion to the global economy.



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This data was pooh-poohed. I chivvied the World Bank for a couple of years and eventually, last autumn, they produced a report and essentially they arrived at much the same figure. The global GDP, if we did not do something about it, would go down between 1% and 4%. Global trade would drop by about the same amount. Global livestock outputs would drop by more. That would throw 28.3 million people across the globe into poverty as well as, of course, increasing the cost of healthcare.

We know in this country that when someone has a drug resistant infection it doubles the hospital stay, it doubles the cost and it doubles the mortality. Just imagine that. We would then lose chemotherapy, organ donations, caesarean sections, big operations and treating infections of diabetes and much more.

I have a picture of children with TB in 1932 receiving the best possible treatment of their day, fresh air and sunshine, with a mortality rate at 50%. I am concerned that if we do not win this fight against drug resistant infections, we are going to be back to fresh air, sunshine and hygiene.

Of course, part of winning the fight is hygiene, sanitation and vaccines. But we are at risk of losing the modern miracles.

I have photos of a little girl who, in the 1940s, bit the inside of her cheek 6 days before the photos were taken. She had a temperature of 40° and was having difficulty breathing. She was one of the first patients treated with penicillin. The photos show her recovery over a period of 9–10 days.

Why do we not just make some more antibiotics? We have had no new classes of antibiotics discovered and coming into clinical practice since the late 1980s. Essentially, we have market failure because everyone takes antibiotics for granted. We pay very little for them, we treat them with disregard and they are difficult to find. The whole world has disinvested in microbiologists and basic scientists who look at how bugs work and therefore could find new antibiotics. Most of the pharmaceutical companies have disinvested because there is no money to be made.

I went to see one of our big drug companies. They agreed that we will need the new antibiotics but they are leaving that for other companies. They are going to make much more money through cancer treatments. I pointed out that I thought they had a social responsibility. But, as I explained to you at the beginning, would we want to buy the cancer drugs if we could not be treated for it?

In the O'Neill report, you can see there are now some drugs in the pipeline. One of the problems is that the nasty bacteria at the moment are called gram-negative. They have two cell walls. You have to get the drug in through two walls and there are pumps that are busy pushing it out, and other things destroying it. The most successful antibiotics that we have are not synthetic small molecules like most modern drugs. We have either small molecules or biologics, which are big and complex. They are products that came from nature, which are quite big molecules and work in multiple ways on bacteria. They are complex, low hanging fruit, as the expression goes, and we have as a world disinvested. It is particularly worrying when you think about how long it takes to find a drug, make it, get it through regulation and market it. It takes on average about 20–25 years. We have a business model that is broken. Clearly, we have to address this globally, and we are beginning to do so.

We have compounded this by the fact that infections do not respect borders. A mathematical colleague in Berlin, Dirk Brockmann, did a model that shows that we in London, because of



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Heathrow, are actually, for infections, closer to Hong Kong and JFK than we are to Birmingham and Glasgow. We cannot say that it is not a problem for us.

So, what do we need to do? We need to use the antibiotics we have much more wisely. We need to make sure that people who do not have antibiotics receive them. That is the access issue. We need to do good infection prevention. Did you know that when you have used the lavatory you should wash your hands with soap and water while singing "Happy Birthday" twice? No? It takes an abominable long time.

I did a Friday evening lecture at the Royal Institution and we got permission to have a colleague in the ladies' and the gents' to see how many people wash their hands properly. After all, as they were coming to a science talk, we thought they would be science aware. I have to say that the results were abysmal. I knew I was being watched so in my mind I sang "Happy Birthday", but it does take a long time.

We need to understand the interaction between humans, animals and wider environmental aspects. You have the farmers and the vets asking, "Where is the evidence that what I use kills humans"? Actually, there is very limited evidence. My argument is that we have not looked for evidence, but do we really want our environment contaminated with the overuse of antibiotics? That cannot be good.

That reminds me of a book, Rachel Carson's "Silent Spring". It is about how we are slowly poisoning our planet. Going up through the food chain these things become more concentrated.

We need better diagnostics. GPs and the public find it difficult to know when to have antibiotics because we do not know for sure whether that sore throat is a bacterial or a viral infection. We can make good, educated guesses. We need to work to sort this out, which means we need much more evidence.

The evidence was thin when I started out. People had disinvested in all of this. I am pleased to say that that we are moving on. We have to have good governance about how all of this works. We need some leadership. I asked our Government to place AMR on our national security risk assessment. It is right up there with pandemic "flu" and terrorism. We did the modelling. We did the Jim O'Neill review, raising public awareness. Indeed, in the north-west at the moment there is a pilot of a television advertisement. What the advertising company found was that, in this country, if their doctor says he does not think they need an antibiotic, people thought that the doctor was trying to save money. This advertisement tells people to save antibiotics for when they really need them.

It was worth highlighting Jim O'Neill's ten recommendations.

The first is a massive global public awareness campaign. It has to suit the culture and the system of the country. Number five is about surveillance. We have improved our surveillance; it is as good as anywhere in the world. But across the world, in most countries, they do not know what problem they have and how big it is. Fortunately, Chancellor Osborne gave us a fund of £265 million worth of official development assistance to support low-income countries, to develop their laboratories and their capacity to do this. Clearly, we have to find a way to overcome the market failure, and everyone now agrees that we need what is called delinking. We need a new market mechanism. We need some incentives.

I set out to build a global coalition for real action (recommendation number ten). As I started working internationally to build that coalition, I kept coming back to this country saying: I know we



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have a strategy across government working with the vets, etc., but I do feel a little exposed internationally if we are not doing really well. I chaired a meeting recently and we are turning the corner — reducing our use and being much more careful — in this country.

We are getting much better data. We do an annual point prevalence study. That is, every patient in the country is looked at on one day. The Public Health England Fingertips website is wonderful. We can look up how our local GP is doing. We are also doing what we have asked the whole world to do, a "One Health" report, which means it is not just about humans, it is about animals and the food chain as well. We are making good progress and we are underpinning it with data.

The global coalition has made sure that we increase the amount of research. Some of the UK funding is from the Cross Research Council initiative and the National Institute for Health Research. We have a "funders' forum". I can report that across the world more and more people are putting in money. An American company is spending £250 million on new drugs and innovations, and the Innovative Medicines Initiative from the EU is spending £700 million. We are going to have to do things differently and be innovative.

I went on holiday to Flores, which is an island south of Bali, because they have Komodo dragons. I had wanted to see them all my life. They are the biggest lizards in the world. They grow to 3.5 m. I am particularly fascinated with them at the moment because they kill their prey by biting it and leaving it to die of untreatable infections. Then they go back and gobble them up in 17 minutes. Then they do not need to feed again for 19 days.

What is it that they have that allows them to live with bugs that when people are bitten by them and taken off to hospital they are not treatable? Some Americans went and took some bloods and they found 48 novel potential peptides. They are a totally new class. They have evaluated eight of them and all eight killed some really nasty infections. So they are looking into those.

I went to a meeting and discovered a German group working on beetles. Beetles live in the soil. There are piles of bugs there, yet they do not die of infection. So we have some people being innovative looking at interesting places. We need to take that data into policy.

I have already told you about MCR-1 and China. The advantage of a benevolent dictatorship such as China is that when they realised what was happening in 2015, in July 2016 they banned colistin. They have taken out more than 8,000 tonnes of colistin as a growth promoter in a year. That means that they may be using other antibiotics or Chinese traditional medicines, but at least they have stopped using colistin. So it can be done, although it is not so easy in our environment.

To finish, I will highlight the international work that we have all been doing because Britain has played a massive leadership role in this. We have had to do so because, when we started on this journey, nothing much was happening. It is clear that we cannot just be in an island and close our boundaries; we have to work globally.

There have been a couple of actions and efforts, but they have not got very far. We decided we would get a WHO Assembly Resolution and that that would lead through, in the following year, to an action plan for the whole world. We got 194 countries to sign up to an action plan to take it through the Food and Agriculture Organisation and the World Organisation for Animal Health. We got everyone signed up to a global action plan and then we took the whole issue to the UN General

Assembly last September. Next week we have the first meeting of a coordination group, for which I am the convener, set up by the new secretary-general of the UN to try to take the global work forward, and to help make sure that there is support for poor countries to make the changes that are needed, and to chivvy the pharmaceutical industry into producing new drugs, and the medical devices industry into making some rapid diagnostics. It is only by doing all of this that we will save our children and grandchildren.

**The President:** Dame Sally, thank you for that fascinating talk. I am going to start by asking one of the questions from social media and then throw the event open to the floor for others.

**The question is:** As actuaries, how can we model the potential range of impact and outcomes, given all the uncertainties about how fast the spread is happening, about how some of the mitigations might happen and the possible new treatments?

The slightly simpler version of this question is: what do you think the worst-case scenario on global mortality might be?

**Dame Sally:** We see the worst-case scenario, from the O'Neill Review, as the 10 million deaths every year by 2050 if we do not solve the problem, a conclusion that was mirrored by the World Bank. We did not go for that figure to shock people; we set out to work out, based on what we know now and modelling it, where we will end up.

**The President:** Is there anything in the modelling that has been done which would indicate what the range of possible outcomes around that might be?

**Dame Sally:** There is. For the financial modelling, I did mention a range of trillions of pounds that it could be. There is a range in that work — and we will have to go back and see what the figures were. But I would also point out that it is likely to be worse than that because only four of the concerning drug bug combinations of the WHO were looked at. The WHO had, at that time, seven of concern. And now there are nine of concern. They did not bother to add the others in.

**The President:** Thank you. I am now going to ask for questions from the room.

**Ms Oliver:** I sit on the working party in the IFoA for antibiotic resistance. We are looking into some of the outputs that might come as a result of modelling.

My question is about mitigation. You covered the main points around good stewardship and public understanding. One of the areas that was raised in the O'Neill Report is whether or not we are going to see any kind of policy change around the purchase and distribution system of antibiotics to help stimulate drug development. As you quite rightly pointed out, the remunerative return to pharmaceutical companies is much poorer than for, say, a chronic disease drug.

**Dame Sally:** We are beginning to get some traction on the need for a new model. The innovative medicines initiative of the EU has funded a programme called Drive-AB. They have come up with a similar model — though it is not yet public — to the O'Neill one of delinkage and push and pull incentives. The Boston Consulting Group has done a background paper for the German presidency of G20, which also said we need a delinked model and has also come up with the estimate that it will cost about £1 billion per antibiotic per year. We are waiting for July, when the G20 heads of



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government meeting is, for an Organisation for Economic Co-operation and Development paper. Work with them suggests that they are going to come up with much the same.

Meanwhile, the World Economic Forum has said that it will work with a few countries and drug companies to see if it can pilot some experiments of this kind of delinkage, and the stewardship that needs to go with it. When we talk about stewardship, what we mean is that the drug will be used appropriately.

The market failure is even more complex than I explained. It is not just that antibiotics are cheap; most companies earn their money by selling the drug for the patent life. The more they can sell, the bigger the profit. They like selling drugs that you will take every day, like high-blood pressure tablets or diabetes ones.

There are a couple of problems with antibiotics. One, you do not take them every day. With a bit of luck, you will not have a week in a year. You take them short and sharp. That does not make lots of money. The other is the more you use them, the more resistance will happen and you could end up with the resistance before the end of the patent. So you do not even get the patent life to make money. That is even if they could raise the price of them, which presumably they could.

We need to have a model where the R&D is paid for and the drugs are available. Actually, as Chief Medical Officer, I can lock them up in a cupboard and let them out only when they are really life saving. That does not make money either, so we are looking at models such as the one Gordon Brown developed for vaccine pre-advancement commitments.

It is a complex area of modelling. I am glad that I am not in charge of it. I am not an economist. There is now a lot of work going on, I am pleased to say. We also need more vaccines for types of fish other than salmon and trout. We need vaccines for animals; and different growth promotion.

**Mrs C. Nolan, F.I.A.:** I am particularly interested in this because I now work part-time as an actuary and I am doing a biological sciences degree with a particular interest in microbiology.

As well as trying to develop new antibiotics, how much progress is there in using bacteria or viruses to fight bacteria?

**Dame Sally:** Bacteriophages are a type of virus that infects bacteria and kills them. They look quite hopeful. The Russians used to use a lot of those, and there are a couple of companies in Leicester developing them. I used to talk about my expectation that when I went in for a hip operation instead of having antibiotics I would drink a soup of many different phages because they are specific to the type of bacteria. It is not just the strain, it is the sub-type.

It may come to pass. I met the man who is in charge of AMR in the Russian Federation, and he was very glum about bacteriophages. He did not think it would pay off. I do not know whether it will work.

We are going to have to try all sorts of different methods. It is interesting. As I learn more about this, I discover that most people's nasty infections, in the case of leukaemia or cancers, or just a debilitated old person, come from their own guts.

If we can keep the gut microbial flora healthy and clean, that would be another way of approaching it.



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**Ms C. Richards:** I am here from a responsible investment organisation, ShareAction. Over the course of the past year, we have been working with the FAIRR Initiative (Farm Animal Investment Risk and Return Initiative) to coordinate a large investor group to try to encourage fast food companies to introduce more stringent policies on prophylactic use; that is, using antibiotics to prevent rather than to treat sickness. There are signs of progress. That investor group now has 70 members and more than $2 trillion of assets under management. Companies are tending to make small positive steps, but they are limited to poultry in the US market. There is a tendency to do it where civil society pressure and media attention is higher and then stopping there.

**My question is:** What more can be done? The stats you are presenting and that have been shown down the years are shocking. It is an apocalyptic scenario, yet food companies are not stepping up sufficiently to take responsibility for what they can do to mitigate this risk.

**Dame Sally:** Let me start by saying thank you, Claire Richards. I know about your work and I applaud it. We have yet to wake up consumers and investors in this country as much as in the States.

It is going to be a long haul because no government wants to regulate and then find that people are cheating. It is difficult. I am told by the Chief Veterinary Officer — we are co-chairing a meeting tomorrow with people from the agriculture sector — that just as in humans we are beginning to make steady progress, but this is a long, slow haul. It is difficult to regulate, even if a government were inclined to do so. Consumer and investor pressure become more and more important.

**Ms M. Henriques:** I am a science reporter for the International Business Times. I was interested in what you said about there being no code you can put on a death certificate to start appreciating the scale of the problem.

Do you also think the fact that people who are older, immuno-compromised, or perhaps vulnerable in some other way, are the most likely to have this kind of infection? Is that a problem as well in terms of understanding it?

**Dame Sally:** Yes, absolutely. They are more likely to get an infection. If it is a resistant one, they will not throw it off as well as someone who is young and healthy. Our modelling of the 5,000 deaths happening a year in England at the moment are those from E. coli, generally, and elderly women in care homes.

**The President:** We will have to draw the meeting to a close there. I am particularly struck by the similarities between our climate change debate and the issues that are being established there. It sounds as though we have many of the same issues around engagement of the public and internationally. But maybe we have got further with intergovernmental cooperation here than in the climate debate. But it is a long way to go, nonetheless.

Thank you all for participating here at The Royal College of Physicians and for those on the social media feed. Dame Sally thank you very much for your interesting and thought provoking presentation.



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