HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Antimicrobial resistance (AMR), HC 848

Wednesday 8 January 2014

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Written evidence from witnesses:

- Public Health England
- Royal College of Physicians
- Imperial College London
- Novolytics
- Novartis
- University of Southampton Medical School
- British In Vitro Diagnostics Association (BIVDA)

Watch the meeting

Members present: Andrew Miller (Chair); Jim Dowd; Stephen Metcalfe; David Morris; Stephen Mosley; Pamela Nash; David Tredinnick

Questions 39-111

Witnesses: **Professor Anthony Kessel**, Director of Public Health Strategy, Public Health England, **Dr Michael Moore**, National Clinical Champion for Antimicrobial Stewardship, Royal College of General Practitioners, **Professor Alison Holmes**, Director of Infection Prevention and Control, National Centre for Infection Prevention and Management, Imperial College London, and **Dr Susan Hopkins**, Chair, Healthcare Associated Infections Working Group, Royal College of Physicians, gave evidence.

Q39 Chair: Welcome to everyone here this morning. Thank you very much for coming. The subject of our inquiry has coincidentally captured some media attention, with a piece on regional BBC news the night before last and on the BBC "Inside Out" programme on TB in London, and today the Wellcome Trust on Radio 4 was talking about antimicrobial resistance as well. From discussions we have had with Dame Sally Davies, we realise that this is an area

of some concern, so we want to cover a number of aspects this morning. Just for the record, I would be grateful if the four of you would introduce yourselves very briefly.

Professor Kessel: I am Professor Anthony Kessel. I am director of public health strategy and the responsible officer at Public Health England. I also have a chair at the London School of Hygiene and Tropical Medicine.

Dr Moore: I am Michael Moore. I am a general practitioner. I have been a GP in Salisbury for 26 years. I also hold a research post at the University of Southampton. I am here today as I am representing the Royal College of General Practitioners. I am their national clinical champion for antimicrobial stewardship.

Professor Holmes: I am Alison Holmes. I am professor of infectious diseases at Imperial College London, and I am also a director of infection prevention and control within the NHS.

Dr Hopkins: My name is Susan Hopkins and I am a consultant in infectious diseases and microbiology at the Royal Free Hospital in London. I also work with Public Health England as a healthcare epidemiologist. I am here today representing the Royal College of Physicians as chair of their HCAI working group.

Q40 Chair: Thank you very much. First of all, a straightforward question: who is currently accountable for ensuring adherence to the Department of Health policies for reducing antimicrobial resistance?

Dr Hopkins: At an NHS level—from the point of view within the NHS—the Health and Social Care Act 2008, updated in 2011, clearly gives responsibility for health care-associated infections, antimicrobial resistance and antimicrobial stewardship to the chief responsible officer, the chief executive of those organisations. There is also a personal responsibility within the Health and Social Care Act for everyone working in health care to prevent infection spreading from one patient to the other and to make sure that they use antibiotics as prudently as possible.

Professor Holmes: Within acute care and acute hospitals, the structure is such that the chief executive is responsible for the delivery of that, but there is a director of infection prevention and control who reports directly to the chief executive, with the responsibility of addressing infection prevention and antibiotic stewardship within that trust.

Q41 Chair: We hear of clinician-focused initiatives like "Start Smart—Then Focus". How effective are initiatives like that in dealing with issues like antimicrobial resistance?

Professor Holmes: We welcome such initiatives.. I particularly welcome initiatives such as that, because it actually focuses on the principles of good prescribing rather than the kind of technical expertise of which drug, what type of organism; it actually focuses on safe and best practice, which means that it is much more amenable to all of those involved in prescribing antibiotics, administering antibiotics or caring for patients on antibiotics. That type of approach is extremely welcome, but we must remind ourselves that it is not a

policy; it is a guideline. It is a framework that can be adopted to promote best practice within acute care. I welcome the fact that it emphasises best practice and principles of good prescribing. We have used it locally to promote multi-professional engagement, so it is not just for doctors who prescribe; it is for nurses who look after, and it is for pharmacists who are involved in the managing of drugs. It has been a useful external reinforcement.

Dr Hopkins: One of the key things is ensuring that we get the best agent to the patient up front to reduce morbidity and mortality from sepsis, so we often start broadly. One of the key things in "Start Smart—Then Focus" is focusing down after two to three days of treatment into a narrow agent that has less impact on both the microbiology in the individual patient and the microbiology in the environment of the hospital that can then lead to onward transmission events within hospitals. One of the things about "Start Smart—Then Focus" is that it focuses the need for good microbiology and diagnostics up front and requires people to think about what they need at the start. It requires education and training of individuals to know the right tests to do when an unwell patient comes into hospital.

Professor Holmes: It is altering the message slightly, which I think is really important. This is not all about control of antibiotics; it is access to effective antibiotics, so starting smart is a critical component. What we need, though, is teeth around these things. This is a very useful guideline, but it would be useful to have a little bit more regulation. I am speaking for acute trusts, and my colleague can talk about primary care, but in terms of acute trusts it would be quite useful if we started to look at process indicators and best practice, and got a bit more teeth around what is good practice. At the end of "Start Smart" there is a variety of guidelines, but it would be useful if we could tell trusts that they need to deliver on this.

Q42 Chair: Is the message the same in primary care?

Dr Moore: It is complicated in primary care because you are talking about individual practitioners who are self-employed. They sit in their office, and they are the people controlling the prescription pad, as it were. They are much more distant from these kinds of initiatives and regulation. It is much more difficult to influence them. We have obviously made attempts with the TARGET website, which is a collection of educational tools for GPs to teach them about more rational prescribing, but we cannot force people to do these things and we cannot force them to change. It is much more difficult to influence individual GPs, and at the moment there are not any regulatory approaches that do that.

Q43 Chair: Have the new structures that have been established in the NHS helped or hindered this process?

Dr Moore: It has disrupted continuity and it is less clear now on the mechanisms for influence than it was before. I am sure things will sort themselves out with time, but when there were PCTs there were prescribing advisers within them and they communicated with the GPs in their patch, whereas now they have been made homeless; they are finding

themselves, I think, back in Public Health England. A big organisational change is disruptive, so I do not think at the moment we are quite clear how to influence GPs. They are contracted through the area teams, which is NHS England working through the area teams. I anticipate that in time they will be looking at things like antimicrobial stewardship, but at the moment that is not at the top of their priority list.

Q44 Chair: Who has the responsibility overall to pull that together?

Dr Moore: I guess that resides with NHS England, which then contract GPs through the area teams.

Q45 David Tredinnick: Do you think that current undergraduate medical courses focus enough on antimicrobial resistance, and, if not, what should be done about it, please?

Dr Hopkins: The first thing to say is that undergraduate medical courses are at the moment both regulated and have standards applied by the General Medical Council. I reviewed the curricula for those courses recently, and what the GMC says is that they should have some training in microbiology, and microbiology obviously includes looking at micro-organisms and resistance. It also mentions that it is important to understand the principles of infection prevention and control, and antibiotic prescribing. We know that there is variability in the number of hours of training that are given to medical students across the country. It is an area that has had various amounts of attention, depending on the skills that the university set. Potentially there is an opportunity now with the AMR strategy to bring this to the fore, both with the General Medical Council and with Health Education England, and talk to them about strengthening that area of their curriculum. Obviously every area of the curriculum fights for its support and its necessary niche, but it is an area that cross-cuts all the delivery of medicine, in that we know that every individual who works as a doctor will prescribe an antibiotic during their day-to-day life. It could be strengthened, but it is in the curriculum at present.

Q46 David Tredinnick: Who do you think should be responsible for the curriculum content of medical degrees?

Dr Hopkins: The General Medical Council is a very good place to start with the curriculum content, as they are responsible for doctors and for their revalidation in the future. Health Education England's new role of delivering an effective work force has to start to develop what it wants undergraduate curricula to look like across the board for health work force delivery. The GMC set the standards and review the universities—attend universities and review whether they are meeting the minimum standards that are required—but the question is whether those standards need to be enhanced at the moment to make sure that we bring this, as an area of patient safety, across the board and improve it for undergraduate health care.

Q47 David Tredinnick: Much of the Government's antimicrobial resistance strategy, perhaps naturally, focused on increasing supply—looking at new ways of finding antibiotics and looking at encouraging drug companies to produce them. Would you agree that we should be looking at reducing demand much more and looking at some of the other options that are currently available, perhaps not tested as much as other drugs, such as acupuncture, herbal medicine and possibly homeopathic medicine, which is used widely outside this country? What do you think about reducing demand through looking at other options, and should more research money be spent on these topics?

Professor Kessel: One of the good opportunities in the new strategy is co-ordination around professional education and public awareness. That goes not just for doctors, both undergraduate and postgraduate—we have only talked about undergraduate medicine here—but across other health care professionals who are all involved in antimicrobial resistance and play a part. Public Health England will play a big role in the co-ordination of that improved professional education. In relation to your question about other ways of reducing demand, I think, yes, one of those includes greater public awareness, so that the public—patients—make fewer unnecessary demands, or inappropriate demands, for antibiotics. It is important in terms of what is provided that it is evidence based—that you are providing treatment or interventions that are evidence based. Some of the things that are encouraged in the strategy around alternatives to antibiotics include vaccines against bacteria and more work on diagnostics that can assist in appropriate prescribing and those kinds of things.

Professor Holmes: Could I pick up on the education questions and expand on what my colleague was saying? The GMC is responsible, but the universities can deliver that in a variety of ways, and some UKCRC-funded work has just demonstrated the enormous variability in the education provided in our medical schools, from a range of five hours to over 240 hours in this domain. It is there, but there is a huge amount of variability, and this is looking at antibiotic safety and antibiotic use as a kind of core aspect of training that maybe goes across all people involved in health care. We are talking about medical students here, but we should also be talking about our pharmacists and nurses as well, perhaps having some kind of core principles, and then, on top of that, different types of education depending on the profession and the type of development the individual needs. There is enormous variability, but we can do a lot more to improve it, and look at innovation and how we teach as well.

Dr Moore: I want to come back to the alternative treatments for symptoms. Most antibiotics in this country are prescribed in primary care—80% is the estimated amount—and most of those are for respiratory tract infections, which are self-limiting. It has been shown that antibiotics make very little difference to the outcome from those infections. People still go to see their doctor because they are very uncomfortable and have distressing symptoms, which last two or three weeks, and at the moment the doctor's dominant strategy is to issue a prescription. Around 80% to 90% of the time, a prescription for antibiotics is still issued. Obviously there are alternative things that we have looked at, like using delayed prescriptions, but another potential strategy is to offer something for symptom relief. There is an urgent need to look for alternative ways of providing symptom relief. People go to their doctor with symptoms and they anticipate getting something to help them. At the moment there is not much in the cupboard and people go to antibiotics,

although we really are pretty sure that they do not make any difference—or very little difference—to the duration of symptoms.

Q48 Jim Dowd: Just to make sure I understood it correctly, the most common use of them, you said, is for respiratory infections.

Dr Moore: Yes.

Q49 Jim Dowd: Everybody knows, apparently, that they do not work, so who is prescribing them?

Dr Moore: They are being prescribed by GPs in their surgeries.

Q50 Jim Dowd: Are they not aware of what everybody else knows?

Dr Moore: It is a complicated interaction and at the moment there are few alternatives. You might say, "Why don't people just stop prescribing them?", but that does not happen, so we have to find other ways of helping that happen. You can do it by saying, "There is a different way. Wait a few days. We are using a delayed prescription." We can use near-patient tests, which perhaps focus on the people who need antibiotics, and we can find alternative symptom relievers.

One of the things people worry about is complications; I think there was something in the paper today about somebody who did not get antibiotics and then died as a result of pneumonia. When people go to the doctor with a bad cough, feeling pretty terrible, they are worried that they are going to get pneumonia. The doctor really does not know if they are going to get pneumonia or not. It is the same if you have a very bad sore throat: are you going to get an abscess in your throat? One of the drivers of that continued prescribing is being risk averse, worrying about potential complications, so, "I will give you these antibiotics because I do not want you to get one of those bad complications." We need to get much more sophisticated about spotting the people who really need the antibiotics and the majority who simply do not need them. Another focus for research is to try and do that, but it is difficult. It is not as easy as you might think to spot those people.

Dr Hopkins: It is appropriate versus inappropriate antibiotic prescribing; we talk about this a lot. It is very easy in retrospect to describe inappropriate prescribing, because you have seen how the patient has gone over a few days. In a way, managing antibiotics in hospital comes under that measure, because we monitor the patient daily for a few days. That is why "Start Smart—Then Focus" works; at two days, you can make that intervention. Where the majority of antibiotics are prescribed, in general practice, you have a 10-minute interaction, you will not see the patient again and they can potentially get much worse. It is about understanding, first of all, which patients are likely to get worse and, secondly, delivering strategies that are acceptable to patients. Patient acceptability is quite important in all of this as well. The aspect where we need research, outside of development of new drugs, is point-of-care tests that are acceptable to patients that will help us diagnose a virus from a bacteria, because you cannot do that simply by

looking at a patient. We know that 80% to 90% are viruses, but we do not know the 10% to 20% that are not, when the patient is in front of us.

Q51 Jim Dowd: Is part of it to retain the confidence of the patient? They expect to get a prescription and they get a prescription, even though it is medically dubious.

Dr Moore: Not all of them are expecting a prescription. In fact, one of the things you can do is to explore the expectations of the patient, and we have shown that training in communication skills is one way of reducing antibiotic prescribing. There are ways of dealing with that but you have to get people to pick up and implement these things at practice level.

Chair: We are going to come back to this theme in a moment.

Q52 David Tredinnick: Briefly, just to go back to my suggestion that we should be looking at other options more thoroughly, according to a briefing we have received, "Primary Care Research Projects on Herbal Medicine in Infectious Disease," already "A number of research projects with implications for AMR, particularly around herbal treatment, are in progress at the National School for Primary Care Research." These include one on a herb called Uva ursi for acute urinary tract infection and another relating to probiotics and vitamin D and infections. Do you not think this is the big clue that we should be spending more money on looking at remedies that have been with us for thousands of years, rather than spending so much money looking at new treatments? They are staring us in the face, so why don't we do more research on treatments that have been available for thousands of years?

Dr Moore: I am the chief investigator of the Uva ursi study, so you are trying to convince the wrong person really. I lead that research.

David Tredinnick: So you are very much involved, well recently obviously—

Dr Moore: Yes.

David Tredinnick: Thank you very much.

Q53 Chair: Before we move on, can I ask how involved is Health Education England in respect of the medical curriculum as far as AMR is concerned, and, at the opposite end of the spectrum, are doctors coming into the NHS from other countries sufficiently well versed in dealing with our approach to AMR?

Dr Hopkins: I will take the second part first, as it is easier in my day-to-day job to understand what we do. When doctors come into the UK, they register with the General Medical Council showing that they have standard competencies to achieve that registration. Once they are within the system, every doctor starting within the NHS system in health care, in hospitals or in a training programme—that includes GP training programmes or any training programme within hospitals—has a minimum, mandatory day that they have to cover; it includes infection prevention and control and antimicrobial stewardship as a basic minimum on the day they start. The curricula for all hospital doctors all include basic requirements on microbiology infection control and

antimicrobials stewardship, and it is required that they have this knowledge and awareness as they are progressing through the system. All the postgraduate exams have some aspect of this.

Could it be strengthened? Of course. I am speaking as an infectious diseases physician; I obviously believe it should have great priority on all the postgraduate curricula. We push for that as the Royal College of Physicians, and have pushed to strengthen it throughout all of the curricula at the Royal College of Physicians. It is there; it is present. I would never say it was enough, but that is coming from the area that I am in. Now is an opportunity to make sure that we have raised awareness again with people who are not specialists in this area, to ensure that they understand why they should not prescribe, what are the unnecessary consequences and, in particular, to think about it as a whole-population approach rather than just the individual sitting in front of them. As doctors, we very much think about the individual in front of us; antimicrobial resistance really focuses us to think about the population and the impact a prescription may have on somebody down the line.

With respect to Health Education England, as a new organisation they have been very much focusing on postgraduate training across the health care work force, as their remit is the NHS work force. They are there to help to develop the undergraduate curricula, and I look forward to their impact in this area.

Professor Kessel: The education of professionals is complex and multifactorial. On top of the educational packages for doctors, nurses, pharmacists and others involved, there are—and the new strategy has provided—a range of other educational materials being developed already. In Public Health England, we are preparing prescribing quality guidelines for primary and secondary care. NICE, the National Institute for Health and Care Excellence, along with Public Health England, are already preparing new good practice guidance, clinical guidance and public health guidance—three sets of guidance—on antimicrobial resistance. The strategy has enabled us to ramp up the priority attention that has been given to antimicrobial resistance, and provides us with an excellent opportunity.

In terms of Health Education England and its role on the professional education strand of the new strategy, the overall co-ordination is falling to Public Health England. I am the policy lead for Public Health England, so I chair the co-ordination group, and Health Education England is on that group. Just as the strategy is only relatively new—a few months—Health Education England and indeed ourselves are relatively new, so we are settling down, but we, Public Health England, are absolutely dependent on working with partners like Health Education England to ensure further improvements in prescribing education.

Professor Holmes: Could I expand on the perspective from the acute NHS trust side of things? Echoing what Susan says, acute hospitals have a framework, so it does not matter where doctors join them from; they should have an infrastructure and a framework that actually supports, encourages and drives good prescribing around the principles of good prescribing. The other thing is that prescribers and doctors are not doing this in isolation. There is a multidisciplinary programme for how we look after antibiotics, monitor them and ensure that best practice is there. If the systems are there—the trusts should have these systems in place—it really should not matter where doctors come from.

Q54 Stephen Metcalfe: Dr Moore, you talked about the distance between initiatives and GPs. Is one way of narrowing that distance through the use of continued professional development—CPD—and how much control is there over what is studied as part of your continuous professional development? Could antimicrobial resistance form a greater part of it?

Dr Moore: That is the way forward. GPs are mandated to continue professional education. They have an annual appraisal process at which their educational attainments are discussed with an appraiser, but at the moment they are independent contractors and they choose, or choose with their appraiser, what their development needs are. I do not think at the moment that antimicrobial resistance and rational prescribing are high on the agenda. There are lots of other new things, huge pressures and a massive curriculum for GPs to try and keep up with, and they are probably pretty comfortable with their day-to-day stuff. They have been in practice for 20 years prescribing antibiotics; people do not come back because they get better. They are not really thinking about looking in a critical way at their prescribing practice and doing educational activities. One of the difficulties is that there will be 100 other things GPs will be asked to look at, and they will not be critically looking at their antibiotic prescribing. Dame Sally Davies's annual report highlighting antimicrobial resistance is really helpful and the strategy is helpful, but these are words on paper in Government offices and they do not really filter down to the man or woman behind the desk with the prescribing pad.

Q55 Stephen Metcalfe: How do you change that—by the assessor making it more of a priority?

Dr Moore: The mechanism for change would be somehow to raise the priority level so that it is discussed in the appraisal process and people take up educational initiatives.

Q56 Stephen Metcalfe: Who is responsible for raising that priority?

Dr Moore: I do not know the mechanism, but you have someone here who knows the answer to that.

Professor Kessel: One of the points being made is that we have, I believe, an ambitious and very important strategy, but we must not underestimate the enormity of the challenge of implementing it, and making the changes required nationally and internationally for what is a very significant problem. What Dr Moore has also highlighted is the gap between the strategy and its ambitions and the greater opportunity with implementation at ground level. I echo some of that as a former GP myself. The new system of revalidation for doctors in this country that the General Medical Council introduced earlier this year—which in the responsible officer part of my role I am responsible for in Public Health England—provides a really good opportunity to strengthen the appraisal process. A significant part of that—I am already seeing it through in the new style of appraisals that are required annually for every consultant, specialist and GP—is greater attention to continued professional development. But, to my knowledge at the moment, there is not a

way of specifying, whichever specialty you are in—public health physician or general practitioner—what should be in the CPD, what you should be doing. That is an opportunity. The Royal Colleges and the Faculty of Public Health have a part to play in that, and I think it is an interesting idea.

Q57 Stephen Metcalfe: By mandating it, by making it obligatory.

Professor Kessel: Of influencing, yes.

Q58 Stephen Metcalfe: Revalidation, the appraisal system as it stands at the moment, will be different depending on who is carrying out that appraisal. It does not contain the same—

Professor Kessel: Yes and no. The appraisal process, whichever specialty of medicine you are in—whether you are a microbiologist, a general practitioner or a public health physician—covers the same domains of medical practice and areas of importance. When you go into the details of it with your appraiser, you will focus on the area relevant to your specialty. Antimicrobial resistance is obviously important whether you are a paediatrician, a public health physician, or a GP and so forth.

Professor Holmes: There are enormous opportunities to use the appraisal and revalidation processes. We are talking just about medics here, but I think we can look at the roles of all health professionals in this. One opportunity is also framing this in terms of patient safety and the quality of care. It does not need to be a technical, separate little bit of expertise. It can be about the overall delivery of quality of care and patient safety, and you can frame that bit of the appraisal to fit in addressing antimicrobial resistance as an aspect of patient safety and quality of care. You can use that, and I think there are enormous opportunities. In fact, that addresses one of the issues about stakeholder engagement, which is not just all about stakeholder engagement with the public, but stakeholder engagement with other health care professionals. The appraisal and CPD mechanism may be a great opportunity.

Q59 Stephen Metcalfe: Thank you for that. I take it, therefore, from your answers that there is at the moment no effective way of monitoring the use of antimicrobials within GP practices. There is no national monitoring going on.

Dr Moore: To some extent, there has been a policy to reduce the prescribing of some antibiotics that are associated with C. diff infections—quinolones and cephalosporins. Those things have been monitored and fed back to practices and there has been quite a dramatic change in the prescribing of those antibiotics in primary care. It is possible to specifically focus on an antibiotic and to deliver that through the quality mechanisms for primary care, and to implement change. It is not entirely true that there is no mechanism. It is simply that general antimicrobial stewardship has not been part of one of those approaches.

Q60 Stephen Metcalfe: It works on individual specified drugs at the moment, rather than taking a wider view of use generally.

Dr Moore: Yes.

Q61 Stephen Metcalfe: With the examples you used for C. diff, were there or are there any consequences if you discovered that someone was continually overprescribing that particular antimicrobial?

Dr Moore: The feedback takes the form of a traffic-light chart, and you are green, amber or red. I guess it is up to your professional standards, if you are persistently showing red on the traffic light, to change your behaviour or not, but there are not any sanctions for people who do not change their behaviour.

Q62 Stephen Metcalfe: Do you think there should be?

Dr Moore: The new mechanisms with CCGs are an opportunity, because they are slightly more grounded in practice, and I think that there will be greater pressures brought to bear as a result of being in a CCG rather than a PCT. I am not a great fan of regulatory big-stick approaches, but there may be a case for some kind of sanction for people who persistently do that. People will always say, "I did it in this instance," and you do not know what the drivers are; you are not the clinician in the consultation, and I think it is a mistake to have absolutes.

Professor Kessel: It is a complex picture that you get in primary care—the same goes for secondary care, to get a picture for us—on the amount of antimicrobial resistance. We will want to look at antibiotic prescribing, but also antibiotic usage, which might not be the same as prescribing. Also the real end result, the amount of resistance in infections in primary care, which will be different from secondary care, is equally important. Again, we do not have at the moment all those surveillance systems set up optimally, but the strategy provides us with the opportunity to work towards those, and we are. My experience has been that, thankfully, in this country we are not at a standing start in terms of our general surveillance systems for health care-associated infections and antimicrobial resistance. We have one of the best sets of systems in the world, and my experience, travelling to other countries, is that often we are the envy. But we are thinking about ways that we can share good practice. I was recently with the chief medical officer at the World Innovation Summit for Health conference. We were talking about ways that different countries could share their good practices, for instance around surveillance—both high income and low income countries—which is I think something we have to do.

Professor Holmes: I want to raise an issue about the critical role of pharmacists. With some of the changes, it is not quite so clear what their roles are now in primary care. Within secondary care, the role of our pharmacists is absolutely critical in working in a multidisciplinary way to address this issue, looking at prescribing, monitoring prescribing and being involved in the feedback within the organisation so that prescribing can be performance-monitored at the level of directorate, division, unit and individual. We

completely rely on our pharmacists to work with us in this, and with the changes that will become clear in primary care.

The other thing that is going to be important for us is that we address this as a whole health care economy, so that we are not addressing it in acute care and primary care but really bringing it together. It is completely artificial and nonsense to do it completely separately.

Q63 Pamela Nash: Dr Moore, you mentioned the horror story of someone contracting pneumonia after not being prescribed antibiotics, and we know about the effect resistance is having on TB, here in London, and gonorrhoea—the two that we talk about. Are there other examples? Are these just horror stories? I am thinking of my family. I am sure everyone in this room was either ill or had a family member who was ill over the Christmas break, and many were running to the doctor. As a result of this inquiry, I spent a lot of time persuading my family members that they did not need to go to the doctor, and I even had a pharmacist trying to tell me to go to the doctor and get an antibiotic. Are these horror stories, or could you give us a better understanding of what the dangers are of not prescribing antibiotics?

Dr Moore: If you compare areas with high and low antibiotic prescribing in England, the evidence shows that if you move to a lower prescribing area there are more episodes of infection such as quinsy, which is a throat infection that is a complication of a sore throat. They are very rare complications, but if you prescribe less you will see more of those complications. The same applies to prescribing for chesty coughs or bronchitis. If you do less prescribing, there will be a few more cases of pneumonia seen as a result. Those complications are rare and are usually treatable rather than untreatable. If you move to a lower prescribing environment, you will see, as a result, a small increase in more serious infections. That will be a kind of consequence of that public health strategy. The positive side is that you are going to reduce antimicrobial resistance in the future, and the future we might be looking at in 20 years' time is that, if you develop pneumonia, you will have an untreatable infection, and that may be fatal. There is a kind of a pay-off, but it is a difficult place to be, to say, "If we do this globally now, there will be a few more cases of pneumonia and serious infections, but in the future we will have antibiotics which still work. If we just prescribe indiscriminately now, we will prevent a few of those infections, but in the future we won't be able to treat people." We need to be honest about that in the public debate about antibiotic prescribing, and we need to be smarter about spotting the people who really need antibiotics.

Q64 Pamela Nash: So some of this could be mitigated with better or alternative treatments.

Dr Moore: There are various approaches to doing that, and one of them, as I mentioned before, is the delayed prescription, where you say to somebody, "You do not need an antibiotic now, but, if you do not get better in four or five days' time, you do not have to come back and see me but you can take this prescription at that point." That reduces prescribing in sore throats, say, from 90% down to about 40%. You get much less antibiotic uptake by using that. You need to use strategies where you have what we call a safety net, which is that you say to people, "You do not need an antibiotic now, but these are the things that you need to look out for and I would want you to re-consult for." In

other words, if people are deteriorating or getting worse, they should seek further medical advice. Another strategy is to use near-patient tests. For instance, in people who present with chest infections, there is a near-patient test available that moderately increases your ability to detect or determine who does and does not need antibiotics, although there is a grey area in the middle; people with very high scores almost certainly do need antibiotics and people with very low scores almost certainly do not, but there are still a number of people in the middle, on whom you are uncertain.

We can get smarter and we can use delayed prescribing, we can use effective safety net advice and we can use near-patient tests. With all of these things complications are rare but they are serious, and that is one of the things that worries the prescriber and the patient with bad symptoms who is seeing the doctor.

Professor Holmes: Moving from primary care into acute care—I am sure Susan will support me on this—this is not something way in the future; it is something we are seeing now. It is really important that we start shifting the public debate away from MRSA bacteraemias and C.difficile to looking at how we address antimicrobial resistance in our hospitals, particularly the rise in E.coli infections and some of the other gram negative infections and the resistance rates. We need to shift that so that we can actually start addressing this within our health care services and have a whole-systems approach around it, but we really need to move from looking at those two to looking at antimicrobial resistance in a more comprehensive way.

Professor Kessel: That is absolutely right. Working in public health, we are constantly having to weigh up that balance between what might be in the population's health interests—nationally but also the global population—which is undoubtedly to reduce antimicrobial resistance, which will involve reducing antibiotic prescribing and certainly reducing inappropriate antibiotic prescribing, against the individual person's interests. Arguably, on an individual person basis, actually not receiving an antibiotic which is of no use to you is probably a good thing anyway, but there will be cases where that does not happen, albeit thankfully rare. The near-point diagnostics that could tell you in the doctor's surgery whether the infection the patient next to you has is viral and will not benefit from an antibiotic, or is bacterial and will, will be invaluable, hence the importance—it is mentioned, I think, in the strategy and in our submission—of more research around that.

Q65 Chair: In a hospital environment is there not a tension between the clinical desire to deal with every patient as an individual and the big corporate view that, "We must not have our statistics look bad"?

Professor Holmes: That is spot on. That is why we need these processes, structures and leadership within trusts to understand the risks and that tension, but it is also why—as we were discussing earlier—we should not be talking just about antibiotic control. It is about access to effective antibiotics, so we need to make sure that our sick patients get antibiotics immediately when they need them. There can be no blocks to that. But then we have the opportunity to review, step down, narrow the spectrum, stop, IV to oral, all those things, and they need to be part of the process. Earlier on, we were talking about the risk at

the individual level in terms of antibiotic resistance and the risk at the societal level of antibiotic resistance.

The other issue for us within hospitals of course is C.difficile—antibiotics driving C.diff—and the risk-benefit. We have a variety of ways of making sure that we minimise the amount of antibiotics we expose people to. But you are absolutely right; that is a tension and it is managed every day in complex patients. It is something that has to be thought through. You cannot walk away and think, "Actually, what I'll do is just leave this person on so many antibiotics that I cover everything. It doesn't matter that we'll drive resistance, give the patient C.diff and when they next have an infection we won't be able to treat it." You have to weigh up all of that at the time you are treating the patient, with the possible collateral damage you will do to that patient then and in the future, as well as to the society and people around them.

Dr Hopkins: There is an important role for pharmacists, nurses and infection specialists in hospitals. You help to arbitrate the individual clinician who is responsible for the patient into looking at the big picture and basically say, "Yes, I understand that you have treated this patient aggressively, but now it's two days later, they are doing fine, and we could do this." It is about being able to have structures in a hospital that help to bring down antimicrobial prescribing into the narrower spectrum that will treat the patient effectively, using the epidemiology that we know is occurring in the hospital and the best for the patient. It is about having those external-internal people, if you like, who do not, potentially, have the same doctor-patient relationship but are looking at the best for that patient and also the best for the population.

Q66 Pamela Nash: In the evidence that we have received so far, and indeed you mentioned it this morning, there is variation across England in terms of doctors prescribing antibiotics. Could you give us an idea of how much—what is the range of that variation—and, if any of you know, whether that variation exists across the United Kingdom as well, not just England?

Dr Hopkins: I will take a little bit of this, if that is okay. I have recently taken over the oversight group looking at the English surveillance programme for antimicrobial use and resistance. As part of that, we have been gathering information at a CCG level from primary care and also from hospitals, but as a larger grouping of hospitals together, to understand what is happening in ecological levels across the country. We can see that there is about a fivefold variation in prescribing across practices. Some of that can be explained by the age structure of the populations, but some of it cannot. What we are looking at is trying to understand this information better: what particular antibiotics are being prescribed across the country? Is it related to deprivation? There is some evidence that the more deprived populations have higher prescribing levels, and that may be related to their co-morbidities and smoking and so on.

We also know that we can help drive down prescribing if we are open and transparent about the data. We need to understand it at Public Health England and at prescribing levels across the country, and then we need to feed that back, to explain to people, "If one practice can do this, can we look and see what that practice is doing to drive down prescriptions?" Very much part of our aim at Public Health England is to be open and

transparent in looking at antimicrobial prescribing data across CCGs and across hospitals over the next year, and the AMR strategy is helping to drive that.

Professor Holmes: The funding that has been made available to look at some of these interesting aspects in the strategy—particularly to develop applied research—will drive some of the research and address some of these important questions. The creation of health protection research units in this area will also help to address some of these questions.

Professor Kessel: It is across different countries. We are obviously not the only country that sees this kind of variation in practice. Public Health England's counterpart in America, the CDC—the Centers for Disease Control and Prevention—produced their report on antimicrobial resistance late last year, in autumn 2013, and one of the quite striking maps shows almost double the problem of antimicrobial resistance antibiotic prescribing between states in south-east United States and the west coast and California. There are various reasons discussed, but again you see a variation in practice and in seriousness, which reminds us that the factors that influence prescribing and antimicrobial resistance are complex. They are professional factors about doctors and their prescribing and lots of other factors, but also public awareness. I think we touched on it in the previous question. I believe there is a responsibility on the public around demands for antibiotics, and we experience this in the general practice room where you have a very short consultation and can be pressed on receiving an antibiotic. That is a real ground-level issue, hence again the importance in the strategy of greater improving of awareness and understanding among the public of antimicrobial resistance.

Q67 Pamela Nash: Professor, you just touched on my next point. We have discussed the variation in prescription and the fact that in areas with more prescription there is some increased infection, but the Society of Biology has given us evidence that resistance is still increasing across the country. Is there variation in resistance, and do we have enough information yet to say that in areas where prescribing antibiotics has been curtailed resistance is receding, or is it still continuing to rise at the same rate?

Dr Hopkins: The first thing to say is that, predominantly in the UK and in England over the last 10 years, we have monitored bacteraemia surveillance, which is the tip of the iceberg, and bacteraemias do not occur in primary care. By and large, if somebody is sick with a blood culture infection or sepsis, they are in hospital.

More recently, over the last couple of years, we have developed a surveillance system to look at all microbiology samples from microbiology laboratories, and we have now almost achieved a 60% uptake of laboratories across the country reporting centrally to Public Health England. That is from samples such as urine, which are a really good marker for what is happening in the community, and sputum samples as well. That is the surveillance system that will help give us the early warning signals. In some areas, such as the west midlands, 100% of the laboratory data are being reported, so we know exactly what is happening in that. In other areas, there are resources being put in by Public Health England to improve surveillance.

Until we have robust surveillance systems collecting laboratory data, we do not know where our gaps are. Our priority over the next year is to improve that, to make sure that

60% of labs are reporting and to get that to 70% to 80%, so that we know we have good coverage and that we have developed our early warning systems. But with that, we need hospitals and laboratories to work with us to make sure that they can give us the data. We need hospital laboratory systems to be updated to modern IT so that they can transmit the message to us. We cannot have outdated systems; if we have old IT systems, they will not communicate with more modern ones. It is everyone working together, so that Public Health England can develop a surveillance system. Hospitals need to help us engage with that so that we know what is happening at the ground level.

Pamela Nash: Thank you. That is important.

Dr Moore: In primary care there is not a history of sampling. For most people who come, we do not take microbiological samples. When you do take samples, it is when there are complicated cases, where people have had a course of antibiotics, the infection has not improved and they have come back with a urine infection, say, for a third time, and you send a sample off at that stage. The routine samples that come from primary care are not representative of the global picture. One of the missing pieces of the jigsaw is a systematic sampling of all routine cases, and I think that is something we could develop for the future so that you used a number of sites across the UK to routinely sample everybody who presented with particular conditions, which would give you a much better idea of the rates of antibiotic resistance in the bacteria isolated in the general population, whereas at the moment your sample is from complicated cases, so you will not get a true picture of the antimicrobial resistance. That is a gap that could be filled.

Professor Kessel: Measuring the amount of antimicrobial resistance in primary and secondary care is complex. There are definitely gaps, and Dr Moore has highlighted one. From an already good start in terms of our surveillance in this country, I am confident, because we have already made a significant start in Public Health England, that in a relatively short period of time—a few years—we will have even stronger systems in place. They will not necessarily have answered all the questions, and this particular one may take longer, but there will be even stronger surveillance systems, so we can speak even more clearly about the amount of the problem in this country. I do not know about the Society of Biology's report, but if you could share it with us we could respond in a written manner to the Committee because I do not know what they are referring to.

Q68 Pamela Nash: I think there is someone in the room who might be able to do that. Just before I move on to my last point, Professor Kessel, you mentioned the US. There was evidence that, where there was a variation in areas where antibiotics, the prescription, had been curtailed, there was a reduction in resistance. Is that correct?

Professor Kessel: There is almost a twofold difference between states in the amount of the problem of antimicrobial resistance and prescribing practice between states in the south-east.

Q69 Pamela Nash: But those two figures correlate. The data where resistance exists correlate with prescribing.

Professor Kessel: That is right. I have that here in my pile of supporting material, and I am happy to share it or send the report through afterwards. It came out as the CDC's publication came out in the autumn of last year.

Q70 Pamela Nash: My final point covers the fact that there is variation across the world, as we have touched on, in antibiotics; indeed, in many countries we can buy them over the counter. How will that affect us in the United Kingdom, and how significantly will it undermine our efforts here in the UK?

Professor Kessel: The scope of the problem internationally is absolutely huge. It is not only our own strategy; one of the things the work of the chief medical officer over the last three or four years has done, which has been hugely influential, has been to dramatically raise the profile of antimicrobial resistance as an issue internationally. Last year at the World Health Assembly, which I attended, there was a session on AMR that there had not been before. There is planned to be a new resolution at the World Health Assembly next May. There is a whole range of other international activities going on. We are doing a lot of work with Public Health England and the CMO and her team with the Commonwealth about twinning countries—higher income, lower income countries—around laboratory and antimicrobial resistance issues. There is a huge amount of attention that did not exist to the degree it does now just three or four years ago, even when I started at the Health Protection Agency. That attention internationally was not there.

Q71 Chair: On the BBC programme on regional television the night before last that I referred to in my introductory remarks, a clinician was arguing in favour of screening for the resistant form of TB from certain populations. Do you think that is a serious proposition—people moving into the country from particular countries?

Professor Kessel: I might ask a colleague on that. I realise I did not quite answer your question about over-the-counter medicines; we know that it is a significant issue in a number of countries—some of the high population, lower resource countries. In India, they have been doing a lot of work to change over-the-counter provision of medicines, but of course it is a problem. If you can just go and get an antibiotic over the counter, it may well be an antibiotic that is not necessary. One of the huge challenges there is that in those kinds of settings that might be your only way to get a valuable treatment. So the work that needs to be done has to be done in conjunction with improving primary care infrastructure and so forth, but there is a huge amount of work going on internationally to raise that in the agenda, which is incredibly valuable.

Professor Holmes: Could I just say one other thing about over the counter, and then talk about screening, but bring it to the screening of antibiotic resistance particularly in bacterial infections rather than TB? First, in the UK, we have very tight regulation about over- the-counter prescribing, but your question was on the impact of over-the-counter prescribing around the world when it is a global problem. We are talking locally and nationally but it is a global problem. There has been a huge amount of work done on this, particularly in India with the Chennai Declaration. Their first proposal for antibiotic control was unpragmatic and not deliverable, because of the issue about tight control of

over-the-counter antibiotics. When we actually talk about access to antibiotics, that might be the only place people can access antibiotics, so the more pragmatic approach was a step-wise progression of the antibiotics that had to be regulated and the ones that were still over the counter, and that has now been introduced. I think it was introduced in August. The work in India has been quite extraordinary.

In terms of the question about screening, we are particularly concerned about severe antibiotic resistance being brought in; indeed there is a document that has been released recently advising hospitals what best to do about screening. We are very conscious of the issue when patients come in from intensive care units from other places, from hospitals from other places, or even when they are just involved in health care in other places, and the need to screen is being recommended, but Susan may want to say a bit more about the policy.

Dr Hopkins: Yes. Public Health England has generated screening guidelines for carbapenem resistance, which is really important for people coming from overseas, seeking health care here, or after having health care abroad in one form or another. Those are the patients who can transmit and cause an epidemic of multidrug resistant bacteria within a hospital setting, and that is where we have been focusing a lot of our attention, because obviously that would be a new transmission event and a very dangerous form of infection—gram negative infections—within hospitals, rapidly developing resistance to, essentially, all first, second and third-line available antibiotics, leaving us with old and poor available drugs.

You also mentioned TB. I think tuberculosis has had a long history in the UK of slow, simmering rates, and higher rates in London where there are higher populations from overseas, so we have about 3,500 cases a year in London, and about 1.5% to 1.7% of those are multidrug resistant, so resistant to two of our major first-line drugs. That has not changed that much over the last 10 years actually; we have had a slow, steady rate, between 1% and 2%, of drug resistance. It is important that we ensure that patients with symptoms are screened as necessary. Port health screening is organised for individuals who have symptoms of TB coming into the UK, and there is a questionnaire for those from countries that are high risk. It is important that we have good microbiology services, so that if people present we diagnose multidrug resistant TB fast and accurately. That is available through Public Health England's tuberculosis national reference lab to any laboratory in the country, so any laboratory can request that test for a fast turnaround on any patient with suspected tuberculosis.

Chair: We are running a tad behind time, so can colleagues speed things up a bit?

Q72 David Morris: I think a lot of what you have already said has probably answered this, but, in relation to antimicrobial resistance, are existing diagnostics tests used effectively across the NHS? If not, why not? Do you think that the diagnostic tests used for looking into diseases are actually pertinent to what we are doing to dish out antibiotics, or do you think we are not doing a good enough job of the diagnostics in the first place?

Dr Hopkins: There are two elements of diagnostics. Once a sample gets to the microbiology department, we can say that the microbiology departments are accredited to perform the microbiology tests. They have minimum standards so that they can do it. If

they are unsure about the result, they can send it to a national reference laboratory. The question is if there is no sample sent; as we have heard already, 80% of prescribing happens in primary care where the majority of patients have no samples performed at all, and actually even if they did have a sample sent it would have little impact on that patient's antibiotic prescription because the result would take three to five days to get back to the general practitioner.

There needs to be new development of easier point-of-care testing—testing that will give rapid results. Some of that is happening to diagnose viral infections. For example, we know that there are now tests that we can use where we take a nose swab and see if someone has a virus, and if they have a virus you can say that they do not need an antibiotic. We need to develop it such that the GP can do that quite easily, at a cheap cost that is not going to massively influence health care costs across this country, and deliver that at a primary care level. A lot of development work is required on that. From a hospital level, once the sample gets into the laboratory, and it is an approved, accredited laboratory in a hospital, we can be pretty sure that that laboratory is performing the right tests.

Q73 David Morris: Is there a central database that these tests can be fed into, to give you a mapping of where and when antibiotics should be used, or certain treatments?

Dr Hopkins: Antibiotics are used according to the clinical syndrome about the patient—when the patient presents, what signs and symptoms they have. The microbiology helps focus our treatments down to narrow treatments, or widen them as necessary, so it helps us in "Start Smart—Then Focus," but it does not change what happens to the patient and the patient-doctor interaction on the front line.

Professor Holmes: The issue about the point of care is not just one for primary care. With the centralisation of microbiology laboratories, it is becoming more and more important sometimes that we get the diagnosis at the point of care, particularly in intensive care. Point of care is very important in acute care as well as primary care, so that we can get the results fast, rapidly, where we are looking after the patient. Investing in research in this technology is absolutely critical. It shapes how we treat patients and improves outcomes, and there is a lot more we could do there.

Q74 Stephen Mosley: Most of the focus so far has been on the clinical and on the professional side, but Professor Holmes, you mentioned there was a need for public debate. Do you, as a panel, think that UK patients understand the threat posed by antimicrobial resistance and how their own actions contribute towards it?

Professor Holmes: I think some of them do. We have touched on some of the issues, and perhaps we need to consider the issue about health literacy and be a little more analytical about that in its broader sense, not just about the antimicrobial resistance issue. I mentioned before that there is a lot of work around public engagement. We may need to look more critically at how we measure whether it is effective enough, but I also think we need to look at not just public engagement but engagement across everybody who is involved in delivering health care. We still need to work on engagement within health care, as well as looking at public engagement. I think we are looking more and more into

aspects of qualitative research and social science and so on, to get the messages right and to calibrate them a little more effectively. That is taking place now.

Q75 Stephen Mosley: Whenever anyone says, "We need to look at doing this," I ask more specifically what needs to be done.

Professor Holmes: I will start with what I was saying about people within health care. We need to make sure as technical experts that we are not just talking to each other. We need to engage with our clinical and professional colleagues. It is really important that we recognise the effect of the power of hierarchies within specialities, and work with leaders across a range of specialities and work with our professional bodies. We must include nurses here. There needs to be much more talk about the role of nurses in the delivery of antibiotic safety. There needs to be much more talk about the critical role of pharmacists; quite a bit of work has been done already with the development of a masters programme for pharmacists. I think Anthony might be able to say a bit more about the work that is being done critically and academically looking at behavioural change strategies and getting the message right. There is investment in research to do this, but there is also a programme of work that Public Health England is involved in.

Q76 Stephen Mosley: It is the public awareness side of things that I am particularly interested in.

Professor Kessel: I think the answer is yes; in my view, there is a need for further public engagement or public awareness. Again it is not straightforward: how do you raise public awareness? One could say we will run an awareness-raising campaign, but it is very important, in so doing, that you run something that is effective. They cost a lot of money and they take time. One does not want to do something that is not effective in terms of raising the public's knowledge, understanding, or even, most importantly, their behaviours in terms of going to a GP and asking for antibiotics.

We in Public Health England have from 1 April this year taken from the Department of Health the team responsible for running those kinds of campaigns, and I and my team have been asked to look at whether we can run a broader public health campaign around antimicrobial resistance in this country. We have started to look at how we can do that in a targeted way that is effective and cost-effective. The research draws on some of the work that the World Health Organisation has done, called TAB, which is about targeting appropriate antimicrobial resistance strategies around, first of all, doing some qualitative work to find out where such a campaign might be most effective—which groups, so it could be age groups; which sectors, whether it is schools or residential sectors, and those kind of things—and then running a tailored campaign accordingly. You ask what should be looked at, and that is something we are looking at, but we have just started doing it. That is very much part of the strategy in terms of raising the level of discussion and debate.

Dr Hopkins: This is an important release, I think, to start us having those conversations. Eurobarometer, which is a European-wide survey, has just released the results of the 2013

survey, which focused on antimicrobial resistance because obviously this is a big attention area throughout Europe. That survey showed that one in three people in the UK, and roughly the same across Europe, had an awareness of some antibiotic campaign in the previous year. There are campaigns out there that people are becoming aware of. Interestingly, one in two people in the UK knew that antibiotics were not right for colds, flu and viruses, but that means 50% do not, so we still have a lot of work to do out there to convince people that viruses do not need antibiotics.

What I thought was really important in those results was to know that actually the main place where people seek advice and where they will get advice that they believe in is from health professionals. That comes back to the engagement of health professionals, and looking at health professional strategies rather than just looking at all-encompassing campaigns. When people are ill and seek health advice, that is the moment when they will listen to the important piece of advice that can change their behaviour, not only for this episode but potentially for the next episode and the one thereafter. It is about resources, education campaigns and interventions that can be rolled out across GP practices that can change those behaviours in the future, not just for now.

Q77 Stephen Mosley: We have focused on the prescribing of medicines. It is also important that once a member of the public has these medicines they complete the course and use them properly. How can medical professionals make sure that patients actually complete the course they are given? People go to the doctor, get given the antibiotics and then that is the end of the story as far as that connection with the GP is concerned. How can you make sure that the link continues and they complete the course?

Dr Hopkins: There are two things that are quite important. The first thing is that a lot of the research about the length of course happened a long time ago; often it was predefined 30, 40 or 50 years ago. Actually we need research about what is the shortest length of course. Can we let the courses be shorter so that people do not take antibiotics on day 7 when they are better, because they do not need them?

We also know that, if people do not have an infection in the first place, they do not need antibiotics. If they were in hospital, they would have stopped antibiotics on day 2 when we decided they did not have an infection, so perhaps we need to reinvent this a bit and get better at understanding when patients do not need them. That is about stopping the prescriptions in the first place, but it is also about trying to see if we can come up with a way that we can shorten the durations of courses so that they do not take them for such a long time. If they are feeling better after two days, and it was thought to be a virus at the beginning but it was a delayed prescription, perhaps they should stop it at that point. I would like to turn that on its head a bit; we need to look at that in the future in a different way, because the more antibiotics people take, the more the microbiology inside their body will change.

Professor Kessel: If a patient ultimately decides when they have a five-day treatment that they are feeling better after three or four days and they want to throw the rest in the bin or not continue, it is quite hard to influence that. The way we do it is by awareness raising, public debate, discussion with the public, but also with professionals about how they convey the importance of those messages. I was just reminded by a note about a very good

educational material called e-Bug, electronic bug, which is an online tool that we developed in the Health Protection Agency—now Public Health England—which has won awards and is used multiply in schools across this country. Indeed, it has been used in a number of countries overseas, having been translated into different languages. It covers areas pertaining to that understanding—which bugs respond to antibiotics, why antibiotics should be used and for what duration and so forth.

Q78 Jim Dowd: I think all of you have made reference during the course of the morning to the differences and discrepancies, or the different ways matters are treated in secondary as opposed to primary care. I want to look briefly at the antimicrobial resistance strategy, the five-year plan for 2013-18. It has been criticised from a number of quarters for being far too concerned with the clinical environment, principally the secondary acute sector, at the expense of primary care, and not mentioning the environment in nursing homes at all. I wonder if any of you would care to respond to that.

Dr Moore: I can talk to that. I have recently done some work looking at antibiotic prescribing in nursing homes; it is not yet published, but it shows that if you take into account the other co-morbidities—the other illnesses that people have—the rate of antibiotic prescribing in nursing homes is around double what you would expect for that population. There is a problem with antibiotic prescribing in nursing homes and it is, I think, often misdirected. This is a high-risk population; these are very frail, elderly people usually, who are at high risk of bacterial infections and serious infections. Managing that risk in primary care is difficult because you are worried that people may have more serious infections, but there is still overtreatment.

My particular focus has been on urinary infections. It is very common for people in nursing homes to carry bacteria in their urine. Probably about a third of people, if you do a random sample, would have bacteria in their urine; there is a kind of a paradigm, where somebody becomes more unwell and then somebody else will dip their urine and show that there is protein and blood in it, which suggests an infection, and then they will get an antibiotic, but actually the link between the bacteria in the urine and the illness is very tenuous. That is one of the drivers of antibiotic prescribing, so it is an area that I have been looking at and will be focusing on to try and intervene and get better targeting. Again, it is about identifying the people that really need the antibiotics, but we are talking about a high-risk environment with the frail elderly.

Q79 Jim Dowd: Your view would be that the resistance strategy is seriously deficient in this area.

Dr Moore: It is an area which warrants more attention, and I think it has not been an area that has been looked at. There are high levels of prescribing, probably greater than you would expect even for the frail elderly population who are in there, and I think more work needs to be done, yes.

Professor Kessel: As I mentioned earlier, I think this is an ambitious and important strategy; it is an overarching strategy. We talked earlier about the enormity of the challenge and the fact that implementation at ground level has other elements, which

cannot be, and would not be, covered in an overarching strategy. The issue around community settings is vitally important for all the reasons that have been mentioned. I cannot recall whether that is specifically mentioned, but I can be absolutely sure that it does not stop Public Health England, as part of our work on surveillance and our roles and responsibilities there—roles on surveillance, education and practice—from attending to community settings, nursing homes and residential homes. In fact only last year—Dr Hopkins might correct me if I get the date wrong, but I think it was last year or the year before—we produced an important pack on community nursing homes, residential care settings and advice for practitioners on health care-associated infections and antimicrobial resistance. It is an area that is already being addressed.

Q80 Jim Dowd: But the huge increase in recent years in resistance, and attention given to resistance, has been in the community rather than in clinical environments. The position in hospitals, in the acute sector, has not really changed that much over time. Infection levels are effectively under control and now reducing, but the huge explosion in this has taken place in the community sector. Should that not be where the attention is being placed?

Dr Hopkins: We can say that we have seen a rise in E.coli bacteraemia across the country. We know that you are more likely to have resistance if you have had a health care setting intervention in the previous three months. The infection may start in the community, but it is more likely to have been related to your previous health care event. Nursing homes are really important. There are more than 30,000 nursing and residential homes across England, and they have a very vulnerable population. I do not think they are excluded from the strategy, because the strategy encompasses the whole health care economy and primary and secondary care, and nursing home residents are involved. The delivery of their care is via primary care, so their prescriptions that we gather—the resistance that we gather—are being gathered by the same mechanisms as everything else. As something that could be strengthened, explicitly stating what is required in long-term care facilities would be beneficial. Long-term facilities are also covered by the Health and Social Care Act. They are also regulated by the CQC. They fall under everything else that we have talked about in primary and secondary care as well, so they are not excluded by any means by what it says in the strategy, though it does not, I agree, explicitly state, "This applies to long-term care," but primary and secondary care physicians and nurses are the same people who deliver care in long-term care facilities.

Chair: That was an extremely informative session. We are extremely grateful for the contributions you have made. I realise there will be one or two follow-up documents—the ones you referred to, Professor Kessel. Dr Moore, if you are able to flesh out a little more about the paper you are about to publish—I recognise the sensitivity of that in the science environment—that would be helpful, and also if there are any further bits of information the rest of you would like to add as well. Thank you very much for your attendance this morning.

Examination of Witnesses

Witnesses: **John Hardcastle**, Chief Executive Officer, Novolytics, **Dr David McIntosh**, Global Scientific Affairs Senior Expert, Novartis, **Professor George Lewith**, Professor of

Health Research, University of Southampton Medical School, and **Doris-Ann Williams**, Chief Executive, British In Vitro Diagnostics Association, gave evidence.

Q81 Chair: Thank you very much for attending this morning. It would be helpful if you could introduce yourselves.

Doris-Ann Williams: I am Doris-Ann Williams. I am chief executive of the British In Vitro Diagnostics Association, the industry association representing manufacturers and distributors of diagnostic products in the UK.

Professor Lewith: I am George Lewith. I am a professor in the department of primary care. I work very closely with Mike Moore on a number of studies, which David Tredinnick just mentioned. I am a GP and a consultant physician. I have 30 years of experience in researching herbal medicines and hold a variety of roles. One of the things I have been involved with very recently is getting the National School for Primary Care Research—part of the NIHR—to develop a really powerful working group looking at alternatives to antibiotic prescribing both in care homes and in primary care, using a variety of nutritional and herbal approaches, particularly in relation to urinary and lower respiratory tract infections. I do not represent anybody other than the University of Southampton and the NIHR.

Dr McIntosh: I am David McIntosh. I am a paediatric infectious disease specialist. I am also an honorary clinical senior lecturer at Imperial College in London. I act as the global scientific affairs senior expert for Novartis Vaccines, and I teach at a number of universities around the world.

John Hardcastle: I am John Hardcastle. I am the chief executive of Novolytics, which is an SME company in Daresbury; we research into bacteriophage therapeutics. Prior to that, most of my career has been spent in the venture capital industry.

Q82 Chair: In different ways, you all propose alternatives to antibiotics. Could you each outline what your approach is? Let us go down the line again.

Doris-Ann Williams: The diagnostics industry sees the tools that our products produce as a way of appropriately differentiating patients' treatment. In primary care there are simple tests, as we heard in the last session, which are in common use in the Nordic countries, Germany and Switzerland and also in the USA, to differentiate between viral and bacterial infections, and allow a debate or a discussion between the primary care physician and the patient as to whether an antibiotic is appropriate for that condition or not. In secondary care, it is a way of targeting antibiotic therapy to make sure that the correct antibiotic is used for the correct infection. Increasingly, there are products available that will look at more than one parameter in one sample type, and they are reducing the length of time to get the results. In the traditional microbiology lab, it would take five to 14 days to culture up micro-organisms; you can now do it within five hours using molecular technology.

Professor Lewith: My background is as a clinician, a GP, so I can add to some of the comments made by Dr Moore and I can certainly expand any that may be relevant to this part of the meeting. As a primary care physician, you are in a very difficult position; you

are in a one-to-one situation with a patient who may want or demand an antibiotic. Education works to a point, and we discussed the strategies in the previous part of the meeting, but GPs very much feel they need alternatives. The evidence we have from the research is that they would look at things like herbal and nutritional medicines if they were thoughtfully evidence based. Within the EU, particularly in Germany, 20% of the OTC prescriptions are for herbal medicines. There is a real good track record of herbal medicines being better produced and us getting better quality herbal medicines in the UK, and better herbal practitioners, particularly since the 2001 House of Lords report.

My main approach would be to try and see how we can use these kinds of approaches, looking at good science but perhaps understanding that we are not after a magic single chemical. Herbals work differently. They work synergistically and often through several different immuno-modifying mechanisms. One herbal, which may have 40 or 50 different biologically active chemicals, may be working through several different systems, and nutritionals may be as well. They modify many different systems in the body, so it is a different kind of approach, which requires a slightly different understanding of science. I think we can use those approaches to manage symptoms and mitigate antibiotic prescribing in primary care very effectively when we know that there is good preliminary evidence and we do not need to make many of the antibiotic prescriptions that we are making.

Chair: Thank you. We are going to pursue that a little further later on.

Dr McIntosh: Antibiotics are used for treatment generally, and vaccines are used for prevention. We have had a golden age of antibiotic development, and I believe that golden age is coming to an end. I believe we are at the beginning of a golden age of vaccination and discovery of vaccines. Vaccination has the potential to prevent patients from being admitted to hospital, thereby preventing their exposure to organisms in the hospital. Vaccination also has the potential to prevent disease in the community; in fact, vaccination can prevent large epidemics. Vaccination can prevent the long-term consequences and sequelae of infections. I believe that vaccination is now the best approach for looking at organisms, both resistant and multi-resistant and susceptible in that fashion, by targeting multiple targets on these organisms. Antibiotics just target one aspect of the organism. Vaccines have the potential to target multiple targets on the organism. I also believe that with effective vaccines against community and healthcare-associated pathogens, and effective implementation, we have the potential to reduce antibiotic resistance by up to 50%.

John Hardcastle: We are trying to develop bacteriophage therapeutics. Phages are viruses that kill bacteria, and you will be drinking them as you drink your water. They have been around for longer than bacteria. They are used regularly in the eastern bloc, but they are not used here yet because we have not done clinical trials that are to western standards. Our belief is that they will form a complementary approach to the use of antibiotics. They are very narrow spectrum. Typically, any one phage will only kill a number of strains within a bacterial species, so you need to know what bug you are dealing with before they are effective.

Q83 Chair: That response, from your point of view, answers one of my next questions: are other countries ahead in your particular fields and are the procedures for adopting alternatives in the NHS easy ones to deal with?

Dr McIntosh: With vaccination, the United Kingdom has set an extraordinary example over many years of introducing new, innovative vaccines. We have now not completely conquered, but are getting towards conquering, the great killers of the 20th century, and before that. We now face somewhat rarer infections in the community, such as meningococcal infection, and in the hospital, such as Staph and E.coli. With its extraordinary track record of vaccination, the United Kingdom is in fact right at the sharp end of being able to develop new vaccines. Of course, other countries are using various vaccines, and the United Kingdom is using those and other vaccines, so it does depend somewhat, but my point is that the United Kingdom is really very advanced with the implementation of most vaccines.

Professor Lewith: My response is that you need all of us in a co-ordinated way. You need phages when you have really bad infections in hospital. You need vaccinations for prevention. You need simple primary care approaches that stop over-prescription and you need near-patient testing, so you need the technology. You need to implement the near-patient testing by making private contractors in general practice do it so that it is feasible, so that they do not lose money. At the moment, they would be paying for the tests themselves out of their own wages. You need better research for symptom-relieving remedies, and we need a better structure to manage that research within the NIHR. We need the vaccinations preventatively, and we need better strategies when we have serious overwhelming infections in secondary and tertiary care environments. You cannot have one of us without the other. I am sorry I am in the middle. I am the GP, you see, and I am always in the middle.

Doris-Ann Williams: I agree that we are not talking about one of our approaches against all of them. There is room for everything to fit into the health care picture. One of the problems, which George just alluded to, was the cost of doing testing in primary care. It is an added cost, but there are ways around it. Outside of antimicrobial infection, GPs have started doing simple tests, which stop referring to secondary care, and the money is recouped in other ways. Companies are quite innovative at doing risk-sharing projects on costing, so I do not think that is beyond the wit of us to do. Much more important, I think, is awareness among GPs of what tests are available commonly and are being used in northern Europe and in the US.

Q84 Stephen Mosley: I wanted to discuss vaccinations in particular, so I guess this is mainly aimed at Dr McIntosh, but if anyone has any comments, please add in. In your initial answer, you covered the broad areas and I want to be a bit more specific. We have had recent news in the London press about TB and the incidence, or rates, of TB in London in particular. The current TB vaccinations that we all had as teenagers are 70 years old now. I think you said that we are entering a golden age of vaccination. How can that be so when the vaccines are so old?

Dr McIntosh: Of course, we have had an unfortunate failure of the development of a new tuberculosis vaccine from the Jenner Institute, and this was sad because we do need to

replace the BCG vaccine for tuberculosis. The approach that has been used for the Bexsero meningococcal serogroup B vaccine is called reverse vaccinology, and this is what I mean by a new golden age of vaccine development. By looking at the genetics of the organism, we now have the potential to identify targets that can be used for vaccine. The serogroup B meningococcal vaccine—the Novartis Bexsero vaccine—was developed along those lines. For the nosocomial infections—to be specific, Staphylococcus aureus—there has also been a failure, or two failures, of vaccines. E.coli, Acinetobacter, Enterobacteriaceae, Klebsiella and so on: we need to use this new sort of technology to develop specific vaccines for Staph, E.coli, Staph epi and so on. When I say golden age, we are going to have great difficulties in developing new antibiotics unless there are some miracles. But we have the potential now to use genetics, looking at these very resistant organisms, to develop vaccines, not necessarily to use them throughout the whole community for everyone, like we generally do, but to use these new vaccines in a more targeted approach, especially for people going into hospitals, people who are at risk of these serious infections.

Q85 Stephen Mosley: Is one of the problems you face—going back to the BCG—that it only protects against certain strains of the TB virus, or bacteria? Is there a problem that, if you are just vaccinating against certain strains, actually you can encourage the other strains to develop?

Dr McIntosh: The beauty of this new approach is that one can attack or prevent as many potential strains as possible, and again I refer to the meningococcal serogroup B. Until now we have had a vaccine in Córdoba, a vaccine in Normandy and a vaccine in New Zealand, because that is where there have been particular strains of this organism. But in fact there are hundreds of different strains of this organism around the world, the meningococcal B, and now we have the potential to have a vaccine which can cover the majority of those strains. Similarly with Staph, similarly with tuberculosis; in fact, what I would also like to mention—this might come as a surprise to you—is the role of viral vaccines in preventing antibiotic consumption and antibiotic resistance. For example, influenza may result in secondary super-infection, bacterial infection, and this is why the influenza vaccine has the potential to prevent antibiotic usage. I think we should be talking about bacterial vaccines and about viral vaccines as well.

Q86 Stephen Mosley: Why is vaccine development so much behind antibiotic development? Again with TB, it is 70 years since it was developed. There must be some sort of failure in the system.

Dr McIntosh: With vaccine development we have been using, let's call them, old-fashioned approaches, mushing up the organism or breaking up the organism, using bits of the organism, intuitively trying them out. Now we have the potential to look at the genetics of the organism, do various tests after that, using bioinformatics and computer systems, and really identify the targets that will be successful vaccine targets.

Q87 Stephen Mosley: Why hasn't that come along in the past? Is it a technology thing or is it because of the market situation? Drugs companies have a vaccine on the market, it does 90% of the job, so, hey, it is not really worth their economically developing a new vaccine. Is that the case?

Dr McIntosh: No.

Q88 Stephen Mosley: Why has it taken 70 years?

Dr McIntosh: It is a long process to develop a new antibiotic. It is also a long process to develop a new vaccine. It is very expensive. Once you have done that particular process of discovery of an antibiotic or a vaccine, then you have to run it through human clinical trials, you have to get it approved and so on, so it is very costly. I think that the process of reverse vaccinology will reduce the costs of developing new vaccines. I do not see any new techniques available for developing new antibiotics. I think the discovery process there is fixed. We now have a flexible, new approach to developing new vaccines.

Q89 David Morris: Ms Williams, you said you wanted Government action to ensure existing diagnoses were taken up more widely in the NHS. Is there ready evidence that this would be cost-effective?

Doris-Ann Williams: There is some evidence. There are studies done on certain tests. There are international audits; there is an audit on a C-reactive protein, which is a test to show rise in infection. There are some studies, with cost-effectiveness related, available from a global study. Cost savings within the NHS are hard. There is never a bag of cash that is released. With diagnostics, it is more that you are shifting resources to be used elsewhere, or releasing capacity, much more than actually turning up with money at the chief executive's door, and it is quite hard to track that through the system. It is not quite as clear; it is not as simple as taking a pill and someone gets better, or they don't, and they release a bed. Diagnostic tests produce information which is used, but it is only one step in the pathway. It is quite complex.

Professor Lewith: If we use a CRP, which is C-reactive protein, you can use it as a near-bedside test. That is what GPs can use. It is reasonably effective at differentiating between viruses and bacteria. It is something that is used outside the UK quite widely. We do not use it here, as I said, because it costs the GPs three quid each time they do it, and they might be spending a lot of three quids in a winter. We are about to pilot a large study in Southampton—Mike Moore is running that. It will be piloted through our clerk and we will look at the cost-effectiveness of offering that remuneration within primary care. That is a process that is in the planning stages at the moment. It is a very good question, and it is one we need to answer for the NHS, but we need rigorous evidence, which we do not have yet.

Dr McIntosh: There is great potential for synergy between diagnostics and vaccination. I refer to the previous session in terms of the fear of medical practitioners that the patient could have some underlying serious infection, and therefore the wish to prescribe antibiotics. With diagnostics and successful vaccination, we can reduce the fear level—not

only in the medical practitioners but also in the public—that the patient will have a severe infection. I think there is a great potential for synergy between diagnostics and vaccination.

We mentioned influenza diagnostics. We should mention the great success of the pneumococcal conjugate vaccine, which has really reduced the fear of people having pneumonia, because it has reduced pneumococcal pneumonia, and the great success obviously of measles, mumps and rubella, measles being associated with pneumonia as well. The synergy between effective diagnostics and effective vaccination can certainly impact on compliance, the number of prescriptions, the fear of patients that there is a serious infection and also on this public debate about whether or not antibiotics should be used.

Professor Lewith: David, I agree with you that it could impact, but it is not, because it is not getting into primary care. It is not happening. The science is right, but the dissemination and the activity are not happening from the GP's seat. We have real issues—Mike Moore and some of the other guys were talking about it this morning—about a co-ordinated process of making this happen in primary care where the prescriptions are happening.

Q90 David Morris: Presumably information on the incidence of infection and resistance would be useful to companies producing diagnostic tools. Should these companies be doing more to facilitate gathering the information, to aid their product's production?

Doris-Ann Williams: Access to that sort of information is quite tricky. As an industry, we are small with limited resources, and it is a bit of a vicious circle to drive production of a product when you have limited resources to pay for the data and the information. But companies are quite happy to work in combination with the NHS wherever possible to produce that sort of data.

Q91 David Tredinnick: This is really to Mr Hardcastle and Professor Lewith first and foremost. What advantages do your approaches have over other traditional antimicrobials?

John Hardcastle: The thing that gets me about this discussion is that there is lots of talk about "potential", and the thing that Dame Sally Davies keeps emphasising is that we are running out of time. The critical thing for us is that we know that phages work; it is just that we cannot make them available in this country. The reason we cannot make them available in this country is that we have more rigorous regulatory standards. First, we know that there is evidence that they work. Secondly, they are harmless in man and they are inert; therefore, the rate at which you can bring them through the regulatory regime should be quicker. Thirdly, there are lots of them. One of the issues that the antibiotic development arena has is that there are lots of possible candidates and very few of them actually get through to being useful drugs. From our perspective, we have a lot of good putative candidates already.

Professor Lewith: I think that the nutritional and herbal approaches have some preliminary evidence behind them. We need some further investment in research, so we

need some harder studies to demonstrate that they really do control symptoms, and that they can be prescribed by GPs, or over the counter and made available by pharmacists, so that the GPs can feel they are doing something. It is very difficult when somebody comes to ask you for help to say, "Go away and put up with it for five days." We do not have that kind of culture.

We need to be able to do something that is safe and does not actually load up antimicrobial resistance for the future. There is huge potential with herbal remedies, but I think we need to move away a little bit from the drug-mining element of herbal remedies, where we are looking for the wonderful chemical in the way they looked for the new malarial with Artemisia. We need to see them in a slightly different context, as more complex mixtures of chemicals. We need to understand much more about herbal safety, because herbs generally are much safer than conventional medicines—the evidence is pretty overwhelming around that—and we need to have thoughtful levels of regulation with the MHRA. I share with John that we need a better process within our regulatory and safety processes, to take account of things which are not standard pharmaceutical agents, and a process which allows us to have good, critical and thoughtful scientific review that is relevant to the disciplines, so that these new and old medications may be reviewed properly and scientifically.

John Hardcastle: Our dealings with the MHRA have been pretty good, but, as far as I am aware, we are the only company on the planet that has regulatory approval in the way we make our product, and that is where most of our money has gone to date. It is not that the MHRA are difficult, or the FDA or any of the rest of them for that matter, but the mentality makes it very difficult to bring new antimicrobials through quickly.

Q92 David Tredinnick: The UK Five Year Antimicrobial Resistance Strategy 2013 to 2018 states that the development of novel therapies is an important element of the multifaceted approach to tackling ARM. Do you then feel that more resources should be dedicated to your work, and that this falls into the category so described here?

John Hardcastle: It certainly falls into that category. I get very nervous about suggesting that more money from Government should be placed behind our company or our initiative, but what you should think about is changing the landscape so that both big pharma and the venture capital community will put private money behind potential new antimicrobials.

Professor Lewith: The answer to that, I would add, is that the MHRA has been really helpful, but they are surrounded by a regulatory system that makes it sometimes difficult for them. The situation with herbals is very difficult because herbals are not easily patentable, and also many nutritionals, which may equally be effective. We have a big trial that is in debate at the moment about using nutritionals in care homes—vitamin D and probiotics—to diminish or cause antibiotic prescribing. You have talked about care homes, and it could have a big impact if we could do that. They are very simple, cheap supplements, but they are not patentable, so it is very difficult for us to combine with industry to do that. We need to do that with Government-funded research boards, and that is difficult with the present structure.

Q93 David Tredinnick: Developing this theme for a second, according to a submission from the Chinese Medical Institute, research in China tells us that the "immunomodulatory actions of traditional Chinese medicine formulations have a stimulatory effect on immune cells, immune organs, cytokine production as well as inhibitory effect on inflammations, allergies and autoimmune diseases. Studies on acupuncture have shown that this treatment can increase the release of endogen opioid peptides—"

Professor Lewith: Endogenous opiates.

David Tredinnick: Thank you, Professor. "—that affect the immune system. Indeed, acupuncture can strengthen the immune system. The effect can be further enhanced with acupuncture when combined with Chinese herbal medicine"—and western medicine. Is this not something that we should be looking at more carefully? They have a body of knowledge there that has been developed over thousands of years.

Professor Lewith: We are. First, we are looking at it. Secondly, that is a bit of a claim, and I will just leave it at that. Thirdly, you are unlikely to go to your GP in London and get acupuncture for your chest infection. That is not going to be cost-effective. That is not a reasonable thing to expect the NHS to pay for. But, for instance, we are currently doing a study in Southampton on recurrent urinary tract infections in older women, which is a big problem for a significant minority of older women, in which we are using Chinese herbal medicines instead of antibiotics. We think that they act in several ways. Interestingly, they act to block the cell membrane pumping the antibiotic out. One of the ways that the body becomes resistant to antibiotics is that it gets rid of them from the bacterial cells very quickly; synergistically, the herbs appear to stop that membrane transport pump, so the antibiotics can stay in the cells for longer. One of the actions of the particular concoction of herbal medicines we are using does that. It also has direct antibacterial effects. The whole point of this process is that we can do this, and we can do it very scientifically and very thoughtfully, but we cannot do it in an easily patentable way, and commercialisation is difficult.

Dr McIntosh: One needs to remember that there is an overwhelming body of scientific evidence in favour of immunisation and vaccination, and that immunisation and vaccination is preventative. To crystallise your point, do you want to go down the path of treatment or do you want to go down the path of prevention? I think prevention is, ultimately, in the short term and the long term, going to be the way to combat antibiotic resistance.

John Hardcastle: I am a big fan of vaccines, but all I would point out again is the time line. Traditionally, vaccines work better against viruses than bacteria, and I am not sure it makes commercial sense to develop vaccines against all bacteria that cause problems, simply because not everyone gets infected.

Q94 David Tredinnick: I have just one more question. I think I am right in saying that none of you are qualified as homeopaths, but, Professor Lewith, I think your submission was in conjunction with Dr Peter Fisher, who is the Queen's physician.

Professor Lewith: He is.

David Tredinnick: He also runs the London hospital for integrated medicine. He draws attention in your submission—I assume it is him—to a health technology assessment commissioned by the Swiss Federal Government which found that "29 clinical trials of homeopathy for upper respiratory tract infection or allergies found 29 clinical studies of which 24 were positive for homeopathy." He also refers to a study supported by the Indian Ministry of Health, which "involved collaboration between conventional ear, nose and throat specialists and homeopathic doctors in a randomised controlled trial of homeopathy versus conventional treatment in acute otitis media." It suggests that the numbers of antibiotic prescriptions in the homeopathically treated group were much lower. Although this is not particularly your field, would it not be sensible for us to make further investigations in this field to establish whether its usage is effective?

Professor Lewith: There are two things. First, I agree that vaccinations are very important preventatively, but you are not going to stop every virus or bacteria with vaccinations. We need some interventions. Secondly, as far as homeopathy is concerned, this Committee has been around the corner very publicly with homeopathy previously and I do not want to get involved in that. The biggest impact a general practitioner has in a consultation is the consultation. When you consider that we have an ageing population with multi-morbidity, pain, arthritis, hypertension, irritable bowel, headaches and all sorts of things, for the vast majority of those chronic illnesses, except perhaps hypertension, the biggest response is to the consultation, not the medicine. If you go to a GP and get a homeopathic medicine, it may well be a placebo, but you may go away without using your antibiotics. That happens quite a lot in France and it seems to be quite an effective way of minimising antibiotic prescribing. If you wanted to know whether homeopathy really worked for these infections, then you would need to do more clinical trials, because the trials are promising but small. There are about 80,000 medically qualified homeopaths, mainly in France and Germany, who use homeopathy in this situation quite regularly, and the evidence is that they use many fewer antibiotics. Whether that is all placebo or real effect, we do not know yet.

Q95 Chair: Before we move on, to help my understanding, could micro-organisms develop resistance to either the bacteriophage approach or indeed the herbal approach?

Professor Lewith: Resistance in micro-organisms is very interesting. If you go back to the genome of the micro-organism, you note that they evolved with fungi. Most of our antibiotics are fungi. There is an interesting theory that quite a lot of the current antimicrobial resistance is the reawakening of old evolutionary genes. If you remember Fleming's experiment in St Mary's, the fungi flew in from the window, sat on his plate and the penicillin fungus killed the bacteria. Our antibiotics largely come from fungi that have co-evolved with bacteria.

Q96 Chair: So the answer to my question is yes.

Professor Lewith: Yes. The argument here around vaccination and stimulating the immune system becomes very powerfully preventative if you look at the evolutionary context of antimicrobial resistance.

John Hardcastle: Just for a bit of background, phages have been around for about 3 billion years and bacteria just afterwards. There has been, for want of a better expression, an arms race going on between the pair of them for a long time. Every day about a quarter of all bacteria are killed by phages worldwide. To be clear, the way they apply them is as a cocktail, so that you do not get that concern practically.

Q97 Stephen Metcalfe: Further research seems to be key to finding future developments. Who should be the main funders, or who are the main funders of the various types of research that are going on?

Dr McIntosh: This is obviously relevant to a big question for vaccination, because vaccine-developing companies invest hundreds of millions of dollars and pounds in developing new vaccines. Universities and biotechs are often involved at very early stages, but then you get to the very expensive part of doing the big clinical trials, which we have all referred to. To get these products approved one has to do clinical trials. The question then comes on to the value that the particular product—the phage, the homeopathic, the vaccine, obviously, or the antibiotic for that matter—will have to the NHS in reducing cost. The balance is the amount of investment being put in and the cost-benefit to the national health service that will come out—the reduction in antibiotic prescriptions, the reduction in antibiotic resistance. My quick answer really is that in appraising vaccines—I am not going to comment on the phages or homeopathy—we now need new ways of appraising using health technology assessment to assess the cost-effectiveness of vaccines, not only in the community but also within the hospital setting.

John Hardcastle: Stephen, did you mean as in who should be picking up the tab for the development of new antimicrobials?

Stephen Metcalfe: No, non-chemical antibiotics. Who is funding the research that is going on at the moment?

John Hardcastle: I would say that any antimicrobial—it does not really matter whether it is a vaccine, a phage or a new drug—for the most part should be funded by the private sector. The reason I say that is that you need to ensure that everyone is appropriately incentivised. The reason there are few new antibiotics coming along is that it is not worth big pharma's while to put their effort there. That is why, if you look at the top selling drugs, they are antidepressants, cholesterol reducers and the like. What you need to do is change the landscape to encourage those with very deep pockets to take advantage of the good work that is done in academic centres already. It is not an issue about a lack of good ideas. The real issue is when it gets expensive and you have to make it worth while for those with deep pockets to make a turn.

Professor Lewith: I agree with that completely.

Q98 Stephen Metcalfe: I was just going to use you as an example of why you may not agree with that.

Professor Lewith: Thank you. We can always turn the arguments round the other way. I think what John is saying is that we need different kinds of processes to incentivise companies. There are lots of big herbal companies in Europe—unfortunately not in this country because we seem to be in the process of destroying that industry at the moment—that produce very good quality products and want to work with us, and we need to make that easier and more feasible. We need to understand that if they are going to invest £1 million in a clinical trial they need to have something out of that. That then comes back to the process of patenting and how we manage that institutionally. People are willing; we just need to create the right environment for that to happen.

Q99 Stephen Metcalfe: That was my point. You were saying how difficult it was to patent herbs. Can you give us some direction that we should go in, to try and resolve this, rather than saying "This is the problem"? We can all see that. What is the resolution to that problem?

Professor Lewith: The resolution is to have commitment from both public and private joint ventures that work well, because if you incentivise people they work harder and they do not sit on their bums and expect the Government to pay. I think that is really important. The other thing is that we can create patented remedies around two or three herbals that might do this, and they might be very effective mechanisms of symptom control; some of the big Chinese companies are really interested in this. We need to reach out to them and get our MHRA inspectors going into China to make sure that these products are produced to good manufacturing practice. We need to be more open in our universities and incentivise them to set up joint ventures, and we need to have facilities within the MHRA so that they can understand and facilitate—not drop standards—and bring in the skilled people who understand these processes and can let us work. I think if we can do that, it is not expensive: it needs legislation and a few people.

Dr McIntosh: Could I give you a concrete example of why big pharma might not want to invest in antibiotics or vaccines? The concrete example is the vaccine I referred to before, Bexsero, the meningococcal B vaccine, which has had a huge amount of investment and approval in Europe but recently got knocked back by the JCBI. Now of course the JCBI is reviewing that decision and putting some new inputs into their model, but for big pharma, let us say, the investment that one has to make in a vaccine such as Bexsero, or a vaccine for Staphylococcus aureus, E.coli or Acinetobacter, is huge, and the tools we have for measuring the potential benefit for the NHS and the health system in general are not the best tools. That is a concrete example where I think a big pharma company may think twice about investing huge amounts of money in any intervention if there is not more of an assurance of it being recommended—whether it be a phage, homeopathy or a vaccine such as Bexsero, which is now available to prevent the most common cause of childhood infectious death in the UK. One thinks, "This is a huge investment, but is this product or vaccine going to be recommended?"

Q100 Stephen Metcalfe: It strikes me that barriers to the research are the regulatory framework and the tools that are used to work out that cost-benefit analysis. Funding is an

issue because of some of that. Are there any other barriers to people investing? The will? Is there a will to research?

Professor Lewith: There may not be a will to research certain things like phages or herbal medicines; there may not be enough investment academically to do that. Setting up one or two centres of excellence would be really helpful and can be done relatively cheaply in joint ventures with specific universities that express interest. Small amounts of money can be used to seed things. If you get the academic interest and get people on side, in the clinical professions, you can begin to make things change.

John Hardcastle: My experience on this has been that we have had to go outside the UK to tie up with centres of excellence in our business, but really there are three things you need to think about. First, you need to think about changing when the patent time starts ticking. Rather than it being when you apply for a patent, you need to tie it to when you can sell the medicine. Secondly, you need to think about why it is that those folk who set the drug tariffs believe it is worse to die of cancer than it is to die of pneumonia, because right now you can get a heck of a lot more money for a new drug against, let's say, bowel cancer than you can against a new antibiotic or antimicrobial. Thirdly, you might think about supercharging EIS relief, which should be relatively straightforward. You are not going to be able to pick winners, so what you should be thinking about is saying that those folk who are prepared to back companies in our situation need to be encouraged to divert more of their spare cash away from, let's say, a bricks and mortar deal or a software development company into antimicrobials.

Q101 Stephen Metcalfe: Thank you. There is a proposal for a Diagnostics and Stratified Medicine Catapult Centre. Do you think that is the right approach, or do you think we should have one that specialises in antibiotics research and things associated with that—diagnostics?

Doris-Ann Williams: We were delighted in the diagnostics industry that the TSB recognised the importance of having a Catapult to get diagnostics used, and that stratified medicine is across the whole health care continuum, diagnosing, ruling out, monitoring and managing disease as well. I would be highly in favour of that continuing along the plans that they have got going at the moment.

Q102 Stephen Metcalfe: Does anyone else have a comment on that?

John Hardcastle: It would probably be no bad thing to align those kinds of initiatives with the import that Dame Sally gives, but I would say that the diagnostic aspect is absolutely critical.

Q103 Pamela Nash: You have covered quite extensively the barriers to research in the UK. Could you tell us a bit more about barriers to introducing new techniques to the market, apart from research?

Dr McIntosh: First, I will make a broad comment, not necessarily about vaccines. We do value more, I think, interventions for the elderly end-of-life type of approaches which may

extend life perhaps by a few months or improve quality of life in older people and the elderly, and there is nothing wrong with that at all.

Q104 Pamela Nash: I am sorry, Dr McIntosh, when you say "we", who are you referring to?

Dr McIntosh: I am saying "broadly speaking".

Professor Lewith: Are you making a comment about the age of politicians now?

Dr McIntosh: I am speaking as a paediatrician; we could spend more investment and resources at the beginning, in childhood, in paediatrics. I am speaking, I guess, as a paediatrician more than anything, again not devaluing what is done for elderly people and older people, but I think we could perhaps start to transfer the focus to earlier times in life, childhood, paediatrics and even neonatology, with vaccines coming in for that area as well, where we can really improve not only the quality of life but the length of life by preventing childhood infections. Secondly, preventing childhood infections with vaccines has been shown to have a benefit for adult and elderly populations as well; the pneumococcal and influenza vaccination programmes are cases in point where an intervention in childhood has an extreme benefit in the adult and elderly population. I think we can start to link up a little bit the beginning of life and the end of life.

Q105 Pamela Nash: I would be quite interested to hear, Ms Williams, about the barriers that BIVDA feel are prevalent in the UK, particularly within the NHS.

Doris-Ann Williams: One of the barriers is the financial flows around the NHS systems in both England and the developed nations. Pathology generally has a budget to provide the testing for all of the hospital care and local community care as well, and that means that there is a restriction on the amount of testing that can be done. One of the things we would like to see, wherever tests are specific to a patient pathway, is that the relevant department actually picks up the costs of that, because, as we have said, the cost of a diagnostic test is relatively cheap on the whole and the value it provides is much higher. But if you have a restricted silo budget for numerous tests on respiratory infections—respiratory infections are the second of the main causes of admission to hospital—and if you have an old-fashioned microbiology lab, which will very effectively pick up the cause of the infection but will take time to culture those plates up, it is very difficult to introduce a new technology that will be slightly more expensive but means that the patient could get the right antibiotic therapy within five hours of being admitted.

Q106 Pamela Nash: I know we are running short of time, but I am interested in everyone's view on this, particularly yours: do you think that the new structures within NHS England are going to be a help or a hindrance to getting new techniques through?

Doris-Ann Williams: At the moment, it does not look like the situation for us has changed significantly. Maybe it will and commissioning may help in that, but one of our problems

is the lack of awareness as well; we need to make physicians aware of the tests that are available. We have talked about CRP, but there are simple swab tests that could be used in primary care that are routinely used elsewhere, which just give a colour-change reaction in the same way as a pregnancy kit. They take seconds to do and cost maybe £1 or £2. We have to find a way of financing that, but it is about educating GPs. I even thought that having a biomedical scientist working in the community would be a way to support GPs' workload for that sort of point-of-care testing.

Professor Lewith: We have a uniquely refined primary care research structure in the UK which is probably the best in the world, and it is really well funded. It has not been dramatically affected by the NHS changes, because it is mainly an academic and NIHR-funded structure. There is a huge amount that we could do if we took co-ordinated and thoughtful action on this. It is very attractive to large pharma to do that kind of work in the UK, because they know it will be high quality. We could do a lot of these things here, within the community, very effectively and earn money from them.

John Hardcastle: You asked about the barriers, as I understood it, in relation to the NHS. The issue for us is cultural. There is a real familiarity with using antibiotics to sort out infectious disease, and it is not necessarily easy for clinicians to have to deal with a number of different approaches to killing a troublesome bug, so there is going to be a cultural issue.

Q107 Pamela Nash: When you say a "cultural issue", who is this affecting? It is the same with what you were saying about BIVDA; there is a high recognition within this place, for instance, about what BIVDA does.

John Hardcastle: Say, for example, that someone comes in and they have an infection, the typical response would be a broad spectrum antibiotic, initially. If you have rapid diagnostics and you know exactly which version of a bug is causing you difficulty, you could apply a narrow spectrum treatment, which would give you a better outcome, but it would require a different approach by the clinicians treating the patient.

Professor Lewith: The medical culture, not the culture in the House of Commons.

Q108 Chair: Can we pin this down a bit more? There is a UK antimicrobial resistance strategy 2013-18. Does that strategy encompass fully the approaches that each of you is adopting? If not, what amendments would you recommend? I will just go down the table and ask that.

John Hardcastle: I know phages are mentioned on page 18, so yes is the short answer. The key issue is the funding.

Chair: Dr McIntosh?

Dr McIntosh: The strategy is a good document but it does not explicitly or implicitly state that vaccination has had a role in reducing antibiotic consumption or antibiotic resistance,

and does not implicitly or explicitly state that in the future vaccination has a role in reducing antibiotic resistance.

Chair: Can we leave Professor Lewith till last?

Doris-Ann Williams: I think the strategy is excellent. It does mention diagnostics. I was quite surprised in the earlier session to hear that GPs are not considering prescription of antibiotics. When you think that must be the most common prescription they write, you would think they would look for a tool and that that would still be at the forefront of their mind.

Q109 Chair: The reason I left you till last, Professor Lewith, is that I want to split the answer in two from you, one in respect of what you said about herbal and the other in response to David Tredinnick's question, your response on homeopathy, because I guess there must be two separate answers.

Professor Lewith: Yes, there are.

Q110 Chair: Professor Davies is on record to this Committee and talking to the Lords as saying that "outwith the placebo effect, homeopathy has no impact. I am very concerned when homeopathic practitioners try and peddle this way of life to prevent malaria or other infectious diseases. I am quite clear about where I believe the evidence is." I am presuming you might have two separate answers.

Professor Lewith: Let's answer the difficult one first. I do not think you should be using homeopathy with malaria; I think that is outrageous. In dealing with acute infections, the actual evidence, if you look at it, is unclear as to whether it is a placebo or not. With the greatest respect, I do not think Dame Sally Davies has perhaps studied that evidence in any detail, but I think the jury is very much out on that. I do not think it is conclusive. I would support that by saying that you can look at the same data in two separate *Lancet* systematic reviews about homeopathy and come to entirely opposing conclusions, which, to me, means there is not enough data.

As to the second, in terms of herbal medicine, I agree that the policy is a great policy. I have read it and I think it covers most of the issues. I think that the issues around herbal medicine are around regulatory issues and facilitating expertise in the UK, and within that context, with very small changes, we could do some quite interesting things in the same way as they are doing in continental Europe.

Chair: I thank the panel for their presentations this morning. It has been a very interesting morning all round. If you have any additional information you would like to submit, please feel free.

Q111 Jim Dowd: I have one brief question, if I may, Chair. If phages are killing a quarter of all the bacteria in the world every day, how come there is still so much of it about?

John Hardcastle: It is those pesky bacteria that go and breed the next day.

Chair: On that point, thank you very much for your attendance.