HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: Science in emergencies: UK lessons from Ebola, HC 469

Tuesday 20 October 2015

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Written evidence from witnesses:

- National Institute for Health Research (NIHR) Health Protection Research Unit in Emerging and Zoonotic Infections (Professor Tom Solomon)
- Professor Trudie Lang
- Wellcome Trust
- Institute of Development Studies

Watch the meeting

Members present: Nicola Blackwood (Chair); Victoria Borwick; Chris Green; Dr Tania Mathias; Carol Monaghan; Graham Stringer; Derek Thomas; Matt Warman

In the absence of the Chair, Dr Mathias was called to the Chair

Questions 1-106

Witnesses: **Professor Tom Solomon**, Director, National Institute for Health Research, Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, **Professor Melissa Leach**, Director, Institute of Development Studies, University of Sussex, and **Professor George Griffin**, former Chair, Scientific Advisory Committee on Dangerous Pathogens, gave evidence.

Q1 Chair: Our usual Chair Nicola Blackwood is slightly unwell. She might be coming in later. I am Dr Tania Mathias and I will be chairing today. Before we begin, I want to say on behalf of everybody on the Committee, and I am sure everybody in the room, that we are very humbled by the volunteers who put their lives at risk to tackle the Ebola epidemic. Our thoughts today are particularly with Pauline Cafferkey and her family. We hope that, like all other victims, she will recover. I want to put that on the record. Welcome to our eminent guests. Before we ask questions, could each of you give an introduction on your work on the Ebola crisis and your involvement, bearing in mind that today we are focusing on UK lessons from that crisis?

Professor Griffin: My name is George Griffin. I am professor of medicine and infectious diseases at St George's in south-west London. I am a practising clinician and a research bioscientist in the field of how humans respond to infection. For eight years I was chair of the Government's Advisory Committee on Dangerous Pathogens. I came to the end of my eight-year rotation about four months ago. There is a new chair of that committee, but I was involved very heavily in this outbreak.

The ACDP is a very interesting committee. It is tripartite and involves the Department of Health, the Health and Safety Executive and DEFRA. We all meet together, so there is ease of communication between human health and animal health and how that interacts, and health and safety to protect the workforce and the population. An important part of today's hearing is that the ACDP, if I may use the abbreviation—

Q2 Chair: I will often ask you, if you are using an acronym, to refer to it in full.

Professor Griffin: The Advisory Committee on Dangerous Pathogens had a pre-emptive document on the management of severe containment level 4 infections in humans. It was started about 25 years ago. When I was chair I was very keen to revise it in great depth, and that was exactly what we did. I have the dates of the revision and will give them to the secretary. The revision looked in particular at the clinical care of patients who may come into the UK with what are called viral haemorrhagic fevers, of which Ebola is one. We had that document produced, and when the outbreak happened it formed the basis of the Department of Health's response, ready in the UK.

Q3 Chair: We will probably come on to more detail later.

Professor Griffin: We have had substantial revisions in light of what was evolving and happening and what I thought was excellence in the way we disseminated the information to clinical front-line hospitals and doctors, but we will come on to that.

Q4 Chair: Did I hear the word "excellence"?

Professor Griffin: Yes, you did.

Chair: Good. Thank you. That is very helpful.

Professor Leach: My name is Melissa Leach. I am director of the Institute of Development Studies, which is a global research and policy institute based at the University of Sussex. I am also a social anthropologist who has worked for the last 30 years in the tri-border region of Sierra Leone, Liberia and Guinea, where the Ebola outbreak hit. Together with colleagues at the IDS and partners round the world, I have been working for the last decade or so on epidemics, pandemics and zoonoses, which are diseases transmitted from animals to people.

When the Ebola outbreak hit, I had multiple reasons for getting involved. I became involved in a way that I think represents a huge success story for the UK. It is a success story about the role of social sciences in shaping and improving pandemic responses,

where I think the Ebola crisis brings us positive lessons that we can take into the future. What my colleagues and I did in the context of Ebola was to set up what we called an Ebola response anthropology platform, which was funded by the R2HC, the—

Chair: Acronym.

Professor Leach: I do not think it spells out; it is research in humanitarian crises. The platform is also funded by the Wellcome Trust, DFID and Save the Children, and worked with the London School of Hygiene and Tropical Medicine to bring anthropological and social advice and knowledge about the region to all the things that proved to be critical in handling and responding to Ebola: people's practices in care and funerals; why the disease was transmitting in the way it did; and how to make responses socially effective. I also served as a social scientist on the scientific advisory group for emergencies—SAGE—on Ebola, and was part of the World Health Organisation's Scientific Advisory Committee and part of the ethics advisory committee and a number of platforms for helping to devise clinical trials.

Q5 Chair: I hope that in the questions you will be able to expand where you think it appropriate. I might come back to you at the end of the questions if we have missed things.

Professor Solomon: My name is Tom Solomon. I am a doctor and researcher. I do research on emerging and zoonotic infections. As you have heard, zoonotic infections are those that spread from animals to humans. I am director of the Institute of Infection and Global Health at the University of Liverpool, which does quite a lot of work in these areas. In 2014 I became director of the National Institute for Health Research, which as you will know is Government-funded through the Department of Health, a health protection research unit on emerging and zoonotic infections—they are often known as HPRUs, but I will try to describe them as health protection research units. Essentially, the Government invested nearly £50 million in a whole range of health protection research units on various emerging threats, including respiratory infections, gastrointestinal infections and ours, which was emerging zoonotic infections. These units are teams that comprise a university, in our case the University of Liverpool and the Liverpool School of Tropical Medicine, in partnership with Public Health England, the idea being that the units do research needed to answer the questions that Public Health England faces to deal with whatever the unit is working on. We had a whole range of work in terms of the risks to the UK of this virus being brought to the UK by airline passengers. We did a bit of work on screening at airports, healthcare workers' attitudes to the infection, what stops people going out to West Africa and treatments for Ebola; and also some work on virus evolution and spread. This is work done by the whole unit rather than me.

Q6 Chair: Thank you. All of that is very useful. Out of curiosity, have all of you been in the field, although it is not necessary to your work? Have you all been in the area as well?

Professor Griffin: Yes.

Q7 Chair: We will be asking different questions. Professor Griffin, Public Health England tell us that they identified the Ebola outbreak at the outset. Do you think the UK and the international community were slow to respond?

Professor Griffin: The international community was definitely slow to respond. The WHO has been pilloried very hard on this.

Q8 Chair: From your point of view.

Professor Griffin: From my point of view, they were definitely slow to respond. I did a public inquiry into an outbreak of severe gastroenteritis in petting farms about four years ago. We decided at that point that as soon as there was a single case of a severe E.coli infection it was an orange light; as soon as there were two cases it was a red light and it had to be investigated. Similarly, you could easily argue that for something like Ebola with a couple of cases red lights should start flashing, and then the geography and so on needs to be sorted out. It took several months for a robust response from WHO.

Q9 Chair: What about the UK response?

Professor Griffin: I apologise for using the word "excellence" because nothing is excellent; one strives for excellence, which is what I was aiming for. The UK's response was guided by the document, which I hope has been circulated to you, on the management of haemorrhagic fevers. That document was revised three times during the epidemic but was republished in 2012, not in anticipation of an epidemic but so that we were ready, in terms of a structure to follow. It was down to quite small detail—what do you do with the body when somebody has died of one of these viral haemorrhagic fevers?

Q10 Chair: You believe that the UK was ready at the outset.

Professor Griffin: Yes. That was all written and easily available. When I was talking about excellence, I meant that in the end as a practising doctor I was very keen to make sure that people at the coal face had the document. We achieved that by putting it on to the websites of Public Health England, the Department of Health and the Health and Safety Executive. It was right at the top. You got into PHE, you saw advice on viral haemorrhagic fever, pressed a single button and the document came up.

Q11 Chair: I might come back to that.

Professor Griffin: If I may say one other thing, I insisted, not with difficulty but with great attention, that the document had a single-page algorithm which was ready to be photocopied. It is in the document. That could be put on the wall in casualty, in a doctor's office and so on, so that if somebody came in with a fever from those countries you could follow the trail.

Q12 Chair: At the outset.

Professor Griffin: With phone numbers, e-mails and so on ready for use.

Q13 Chair: Excellent. We need to find that algorithm. Professor Leach, from your point of view do you feel that the UK and the international community were different in their response?

Professor Leach: Yes, I do. I would also draw to the Committee's attention the fact that I submitted written evidence that covers some of these points but I believe it is not on the website.

Q14 Chair: We will amend that.

Professor Leach: I absolutely agree that the international response was very late. There are reasons for that, which go to some of the deeper-rooted structures in the World Health Organisation and the way its funding has been related to bilateral disease-specific programmes over the last years. That has undermined the capacity to do the kind of broad-based response that an unexpected pandemic requires. I believe that the UK responded quickly and was ready in terms of the threat of a case and an outbreak reaching the UK, but, equally, I believe it was late in responding to the outbreak in West Africa. Once the UK started, we had major aid resources going in from DFID and the Government. The UK took over and took the lead on the response in Sierra Leone, and did it in many ways very effectively, and in a way that was very science-informed, but none of that began until September, by which time the outbreak in West Africa was already exponential.

Q15 Chair: It was way beyond your orange.

Professor Leach: It had gone way beyond orange, and we were looking at the doubling of case loads every 30 days. By that stage there was a science-informed response through the scientific advisory group on Ebola working up through the chief medical officer and the Government chief scientist to inform what the Ministry of Defence and the Department for International Development were doing, and then we saw a big influx of volunteers. But that was all done on the hoof without planning; it was done to try to bend the curve of an epidemic that was already out of control. It could have been much better if done earlier.

Q16 Chair: That is down to WHO.

Professor Leach: It is down to WHO and international recognition of the pandemic. I would argue that it is also down to the UK being interested in responding only once there was a potential threat to the UK, whereas for the future, in the context of a globally interconnected world, the UK should be interested in what is happening in origin countries for their own sake and their own public health, and because heading off an epidemic at source is the best way to protect our population too.

Professor Solomon: I would endorse that. The outbreak in West Africa was confirmed in March 2014, but UK activity really started in July 2014. It seemed to follow the first case that was transmitted by an airline passenger, from West Africa to Nigeria. That seemed to be the trigger for the rest of the world to wake up and say, "Oh, this outbreak could affect

us." To some extent the response of individual countries, like ours, is limited if the WHO has not recognised it as an international emergency. One of the challenges is how to get greater international recognition so that individual countries can embark on a response. I do not think there is any doubt that once the UK got started its response was phenomenal and made an enormous difference.

Q17 Chair: Were there UK colleagues in the field who would have told you way before the WHO did that this was happening?

Professor Solomon: Messages were coming back that this was bigger than we had seen previously in any other outbreak.

Professor Griffin: This was a very unusual epidemic. Previously, Ebola had often been in very rural settings—half a dozen cases in a village; a ring called a cordon sanitaire was put around the village and that contained the outbreak. This outbreak was multi-centric and was in the capital cities of all three countries.

Q18 Chair: But there were no cordon sanitaires even then.

Professor Griffin: No. It is very difficult to do that in a shanty town situation. It was a unique situation of intense severity.

Q19 Chris Green: Professor Solomon, you have previously stated that there was no formal process for your unit to communicate research findings on Ebola to Government. Did that lead to any evidence being overlooked?

Professor Solomon: The health protection research units were relatively newly established in 2014. I think that is part of the reason why the channels of communication may not have been as strong as they could have been. From our point of view, we were feeding in the information we were discovering in terms of flight risk, screening and so on, but going forward one might want to make sure that, given that there is big Government investment in research in all these areas and you are establishing a group of experts to address research questions, you look to those units and see if there is anything they can contribute.

Q20 Chris Green: Do you think there should be more formal arrangements, or given the nature of different pandemics do you have to address them in this way?

Professor Solomon: I think that the nature of the way these things happen means that when various Government groups are set up—I do not understand all the different Government groups; I am not even sure I understand all the abbreviations—inevitably to some extent it will be in an ad hoc way, depending on what the crisis seems to be and what expertise is available, but at some point you would say, "We are funding research specifically to help Public Health England address some of these questions. How do we make sure?" All those units are set up. When they were set up, they were told they had to be able to divert their activities quickly to deal with any urgent research questions that came up, so we all had the capacity to do that. We have the capacity to do that. It just seems surprising that nobody asked us to do it, but we actually did it; we spent time on

those issues. Having set up the system, you would think they would want to take advantage of it.

Q21 Chris Green: If these pandemics, these incidents, happen more frequently, you will have the experience and familiarity to get off the ground far more quickly, whereas if they are very infrequent those connections will become rusty.

Professor Solomon: The units are doing research anyway on various diseases. For example, one of the current threats people are worried about is a respiratory disease called MERS. If that became a bigger problem, you would like to think that if there were unanswered questions they would be addressed to the respiratory health protection research unit, the emerging infections unit and perhaps some of the others, because that is what they are there to do.

Q22 Derek Thomas: Professor Leach, thank you for your positive introduction. It was great to listen to you. During that, you mentioned your membership of SAGE—the Strategic Advisory Group of Experts; I am taking my hint from the Chair. Would you say that there was broad enough expertise on that group from the outset?

Professor Leach: I would. It was the first time I had been part of one of those groups, and I was impressed by the breadth of expertise. It linked together people who came from a clinical medicine and an epidemiological background and people who could do modelling and look at how the disease was playing out in the source countries with those from the UK side, from Public Health England and others. What was exciting and different about it was that it also connected up medical science with social science, which from a very early stage proved vital to understanding what was going on in West Africa and, therefore, the implications for the UK in a number of different ways. This was a very different Ebola outbreak from previous ones because it was spreading in a high population region—a very mobile population—with a history of inequalities and economic policies that had left people very distrustful of foreigners and the state in many areas. Those things needed to be understood.

We also learned very early that the ways Ebola transmits are through social routes: caring for the sick and dead, burial practices and the ways people moved around in everyday life. If we did not understand those things, it was going to be really difficult to halt the outbreak. Thirdly, it became clear that local institutions had an enormous amount to bring to the response, whether it was chieftaincy institutions putting in place local quarantines or secret societies in the region managing funerals—people you had to get on side in an effective response. Fourthly, from the very outset, the humanitarian agencies who got in there early—Médicins sans Frontières and others—and those who came later were resisted. One of the reasons why the epidemic got out of control so quickly was that in the early outbreak responses sometimes vehicles were stoned and villagers kept response teams out.

Understanding those things, which were rooted in the history of a deeply exploited region, and turning them around required social science knowledge to work with proper community education and local institutions. Bringing that kind of insight, in conjunction with medical and epidemiological scientists and policymakers, SAGE was able to come up

with policy suggestions that were implemented in practice, things like the community care centres as an alternative to the large alienating Ebola treatment units. There were some very positive things about the breadth, and that is a lesson for the future.

Q23 Derek Thomas: We remember seeing on our TV screens the challenge of communicating with a small village community. In terms of social scientific advice, the contribution you made and the battle you won on finding and owning your place in that group of experts, have you added to our understanding of future disease outbreaks? Do you think the future is much brighter because of this experience?

Professor Leach: The Ebola crisis, for all its horror, has been a positive turning point for the recognition of social science, particularly qualitative social science—anthropology and sociology—not just in pandemic response but in preparedness. There are now strong arguments from the American Institute of Medicine, the Commission on Global Health Risk, the World Health Organisation and certain voices within the UK Government that we need some kind of platform for the future that could enable this kind of social science advice to be ready to mobilise much more rapidly.

What we were able to do, with colleagues, was to get together a global network. People devoted a huge amount of volunteer social science labour to the Ebola response, but what was most effective was where we were able to connect up universities in Sierra Leone, Liberia and Guinea and local organisations. That took longer to get going because the capacities were not there. Future effective emergency response preparedness capacity needs to have done some groundwork to have local institutions and scientists ready to engage in this way in future.

There is also a strong argument for investment in the kind of science for pandemic preparedness that would look at the drivers of potential disease emergence in origin countries, because as we saw with Ebola, and as has been the case with other pandemic threats, whether highly pathogenic avian influenza, SARS or MERS, we are looking at a combination of drivers that are economic, political, environmental and social. There have been good examples of UK funding of interdisciplinary science under a one-health banner which have begun to look at those drivers and build the knowledge that we need to be prepared, but we need more of that.

Q24 Derek Thomas: What you are saying is that social scientists should be routinely asked about these things, but we are not there yet. You are suggesting that we have work to do to achieve that.

Professor Leach: We have work to do, because it has not been the history. It is not necessarily even known. The reflex response of social scientists is to whinge, frankly, about being marginalised from science and technology debates and policy. You have one or two written evidence statements on your website that are exactly of that kind. I suggest that they are not evidence-based, because they have not looked at what happened in this response. If we could look hard at the evidence of how social scientists helped to make this response as effective as it was, we could take it forward to bring this kind of model routinely into future pandemic preparedness.

Q25 Victoria Borwick: To bring us back to the UK, how do you think the Ebola SAGE interaction could avoid duplicating the work of the Advisory Committee on Dangerous Pathogens?

Professor Leach: I find it hard to respond to that because I do not know very much about the Advisory Committee on Dangerous Pathogens.

Q26 Victoria Borwick: Maybe Professor Griffin could help.

Professor Griffin: I am sorry; I missed the point of the question.

Q27 Victoria Borwick: I was asking how the Ebola SAGE committee interacted with and avoided duplicating the work of the Advisory Committee on Dangerous Pathogens. We need some guidance as to how the two roles are performed.

Professor Griffin: There was no formal interaction between SAGE and ACDP. The formal interaction was between ACDP and the Department of Health in setting up the logistics for the response within the UK, and then advising on the medical response within the developing countries. SAGE was formed quite late in the outbreak. I was not on SAGE, but I was leading ACDP and integrating that with the Department of Health.

Q28 Victoria Borwick: Continuing with our response, do you think that the number of units we have—the two at the Royal Free—are sufficient? Do we have a view on that?

Professor Griffin: The number of units where?

Q29 Victoria Borwick: We have a high level isolation unit at the Royal Free with two beds in it. Is there a view as to whether that is sufficient?

Professor Griffin: This is something ACDP has had responsibility for, and in the evolution of the guidelines I have been very involved in it. There was a unit in Newcastle that had two beds, and we were very keen to have a new unit at the Royal Victoria Infirmary. That has run into planning problems. When the old unit, which was in a different hospital, had to close down because everything moved to the Royal Victoria Infirmary we lost those two beds in the north of England. That is still subject to planning permission and the Royal Victoria Infirmary in Newcastle getting going. The Department of Health has already given money for that, and just before this meeting I contacted John Newbold in the Health and Safety Executive, which is leading the charge on that. He is actively negotiating.

Q30 Victoria Borwick: We have the current two-bedded unit.

Professor Griffin: In the Free, yes.

Q31 Victoria Borwick: Do you think that for the moment we are, fortunately, coming to the end of this particular problem?

Professor Griffin: What we then did was to decide that two beds could easily be saturated, so as part of the UK response we started what we call surge capacity, and units within Newcastle, Sheffield, Liverpool and the Royal Free were commandeered that could take over should there be 30 or 40 patients in the country. One of the revisions I had to make to the guidelines was to make very clear what was safe personal protective equipment, or PPE, for doctors, nurses, social workers and so on to have within the hospital.

Q32 Victoria Borwick: Was there a view that transporting people around each of these units would be more dangerous than just keeping them in one?

Professor Griffin: One of the best components of the whole response was the ambulance service. I was very impressed by their attitude and professionalism in organising the potential transfer of patients who were very ill. That was all designed and ready, and they had vehicles ready to do it. In the event, the Royal Free was the only place needed for clinical care, but there was surge capacity throughout the country and each of those places had at least five beds that would have been available.

Q33 Victoria Borwick: The resilience was there.

Professor Griffin: Yes.

Q34 Victoria Borwick: But although in this particular instance the ambulance service very much came up trumps, do you have a view about the safety of transporting people around to smaller units rather than keeping them in one location? That is what we are looking at.

Professor Griffin: Yes. The challenge is that when patients get very ill, as we have seen at the Free, it is not safe for them to be in small units. It is also not safe for them to be nursed and looked after by doctors who are not used to using personal protective equipment, so training is crucial.

Q35 Victoria Borwick: A specialist unit is therefore the best.

Professor Griffin: Yes.

Q36 Victoria Borwick: I think we touched on Pauline Cafferkey. As a quick follow-up to that, do you think adequate systems are in place to continue to monitor, because it was a bit of a shock to the system that she ended up having to go back?

Professor Griffin: It is tragic, as the Chair said at the beginning. What has happened since the outbreak is that we are beginning to understand the disease. We did not before. For example, we did not appreciate that the virus would linger around in patients who had recovered and were well, so that is a bit of a surprise—it is more than a bit of a surprise. When Pauline was discharged the first time, I was part of a nationwide teleconference

involving, I think, six people. We had seen her clinical recovery. We saw the amount of virus in her blood drop to undetectable, and just before she was going to be discharged there was a tiny blip—a signal that there could be virus present. We had a long teleconference to decide whether it was safe to allow this lady to go home. She was perfectly well, afebrile and so on. What happened was that she was discharged to a safe house and followed by Public Health England very closely, for a month, I think, before she went back to Scotland. We have been very surprised that the virus can be detected so long after apparent clinical recovery.

Q37 Matt Warman: When it comes to responding to an outbreak such as Ebola it is all about data and evidence so that we do the right thing. I am not quite clear who is ultimately responsible for collecting the data and evidence. Is there one body?

Professor Griffin: It would be Public Health England. They have responsibility for surveillance, the collation of data and the system of orange and red flags. The person who chaired the Department of Health committee I worked with in terms of getting things organised was the head of surveillance in Public Health England, John Simpson, a clinical doctor who understood how to keep all those things together.

Q38 Matt Warman: Do you think that response was as good as it could have been?

Professor Griffin: I think it was very good; Public Health England responded valiantly in terms of sending technical and medical staff to Sierra Leone. One of the major features of this epidemic, which will be a learning point for the future, is just how important rapid, accurate diagnosis is. A febrile patient in Sierra Leone could have one of many diseases.

Q39 Chair: I can plug LGC—the Laboratory of the Government Chemist—in my constituency, which has a DNA kit for fast diagnosis of Ebola.

Professor Griffin: Yes.

Q40 Matt Warman: That is now on the record. Is that real-time analysis of who was where and when adequate? Does it need to be better?

Professor Griffin: It is developed and works well. When the epidemic started, samples had to be transported for 12 hours on a rough road.

Q41 Chair: Now it can be done within the hour.

Professor Griffin: It is possible to have accurate near-patient bedside diagnosis which will distinguish malaria, typhoid and viral haemorrhagic fever.

Q42 Matt Warman: Are there any barriers to that data-sharing that concern you?

Professor Griffin: No.

Professor Solomon: You asked who was responsible for data. In this country it is Public Health England, but the challenge is about who is responsible for data internationally. Who owns the data? It is a challenging area. How we get people to share data is a challenge. Public Health England certainly does not own data that come out of countries in West Africa. The general consensus would be that the data belong to the countries. Often though, those data are acquired with the support of research teams, and then the question becomes how we make sure the data are shared so that they are available to everyone who needs them to develop the response. I do not think there is a simple answer. It is an area of ongoing discussion.

Chair: I know we are overrunning, but this information is really good, so we will carry on.

Q43 Carol Monaghan: Professor Griffin, in October 2014 at the height of the outbreak the World Health Organisation was saying that entry screening to the UK was not recommended. A couple of days later Public Health England said they had no plans to screen people coming into the UK, and then the Prime Minister announced that there would be screening. I think you made a statement that the diversion of resources to that was not really helpful. How much do you think that announcement and the consequent actions were grounded in strong scientific evidence, and how much was a reaction to public opinion?

Professor Griffin: I made a statement on Radio 4 at lunchtime and was asked to go back the next day after Cobra had decided to change the plan I had been told about the day before. There was little clinical evidence that the screening involved in terms of body temperature would be either sensitive or helpful. We know that Pauline was missed. However, it raised public awareness. When you came in through Heathrow, and eventually through Eurostar, you saw a sign: "If you have been to these countries and you are not well, please be aware." In terms of being a medically good action to take, it was an incredibly blunt and insensitive tool, but in terms of something that raised and kept up public awareness I think it was reasonable. Undoubtedly, there were difficult decisions to make. You're damned if you do and damned if you don't. Had it not been in place and Pauline had been missed, there would have been a huge outcry about why we were not testing temperature. I think most clinicians felt it was a very blunt tool.

Q44 Chair: Can I turn to the other clinician? Professor Solomon?

Professor Solomon: That is a good example where you did not have to guess. We did the maths and looked at the numbers, and we could tell exactly what the benefit was of screening people as they left West Africa and what the additional benefit was likely to be in terms of how many people you would pick up. It is a very small number. There is added benefit, but it is very small, so the information was there.

Q45 Carol Monaghan: The incubation period can be quite significant. I think it is up to three weeks.

Professor Solomon: Yes, and most flights were 12 or 24 hours, so the question is about who would be febrile 24 hours later when they got off the plane, but not febrile when they got on the plane, and picked up. It was a small number. We did the numbers. It is not

worth going into, but the data are available. The question becomes how you use those data and what decision you make.

Q46 Carol Monaghan: Did you feel you were able to express those views openly and freely to the Government, and were you listened to?

Professor Griffin: I expressed them on Radio 4.

Q47 Carol Monaghan: Was that when they started listening?

Professor Griffin: There was no further discussion. The decision was made. PHE were told to implement this thing, and I understand from my contact with PHE that they were given extra funding to do it. Very quickly, they instituted the screening programme. It was not a question of whether we were going to do it; it was going to be done.

Q48 Chair: Is there any major point that you think we have missed? We will be putting stuff on the website that you have submitted. We thank you for that.

Professor Solomon: No. I am sure other issues will come up this afternoon, based on the people I have seen who are due to join you.

Professor Leach: The only point I would like to make is that we need to balance the discussion of science in emergencies when they hit the UK, which we have talked about quite a lot this afternoon, with scientific inputs and responsibilities to potential countries of origin, which is actually the way to head off potential disasters that hit here. There are many scientific opportunities for the UK in being part of a global community that deals with things where they occur.

Q49 Chair: That is why I am very pleased about your field experience and that of your colleagues.

Professor Griffin: I think it got too complicated and too bureaucratic. The Department of Health, for example, had about 30 people working on this in Richmond House. It seemed to me to be going rather bureaucratic, but it happened. A smaller number of people working sharply would have got things organised more quickly.

Chair: You give us great confidence in how you have relayed what worked and what did not. I wish you were working with WHO as well. I think we would then be better off. Thank you very much for what you have contributed this afternoon.

Nicola Blackwood resumed the Chair.

Examination of Witnesses

Witnesses: **Dr Ripley Ballou,** Vice President and Head, GSK Vaccines Research and Development Centre, Rockville, Maryland, **Professor Adrian Hill,** Director, The Jenner Institute, University of Oxford, and **Professor Trudie Lang**, Head, The Global Health Network, University of Oxford, gave evidence.

Q50 Chair: Can I welcome the second panel? I apologise for my lateness; it was unavoidable and it is no indication of the importance of this inquiry, which I think the evidence has already shown has very important lessons for all of us to learn. I am going to dive right in and put to all of you some comments made by the British Society of Immunology. It has submitted written evidence to the Committee that in its view, "With the exception of influenza, we lack a truly effective and co-ordinated platform for the research, development, and manufacturing of new vaccines and treatments against novel or emerging disease threats, such as Ebola". Does that concur with your views? What do you think needs to be done to address those concerns? Could I start with Professor Hill?

Professor Hill: Broadly, I agree. I am Adrian Hill, director of the Jenner Institute, which is based at the University of Oxford. We are involved purely in vaccine design and early stage development. We partner with the Pirbright Institute, which is involved in veterinary vaccine development. We were very engaged in testing new Ebola vaccines. In the last year we have tested a total of five of those so far, some in collaboration with Dr Ballou from GSK.

The British Society of Immunology is correct, in that we do not have a complete platform going from vaccine design and discovery, if you like, to animal studies, early stage clinical trials and larger-scale manufacturing and deployment, but then again hardly any country does. Vaccinology is a very broad discipline that requires a whole range of skill sets and facilities, and we need to be able to link labs like our own, which do very early stage research, early clinical trials and some manufacturing, with large companies that are in a position to manufacture large amounts—millions of doses—of vaccine.

The central challenge on Ebola and other outbreak pathogens is that the business case for large pharma becoming involved in marketing or developing those vaccines is very weak. Take Ebola, which we have known about since 1976. There have been maybe 20 or 30 outbreaks, all in central Africa, over that period of 40 years. All were well contained until the outbreak in West Africa at the beginning of last year. What is the business case for making a vaccine that is unlikely to be used in any of those outbreaks? We need a system whereby public and foundation money is used to work with academics and industry to develop Ebola vaccines and other vaccines for which the business case is weak. This is not a new problem. We have identified the solutions before. For malaria, on which I work a lot, HIV and TB there are public-private partnerships that are pretty well financed by foundations and by Government to develop vaccines for those very difficult diseases.

To me, the irony with Ebola is that it was not a disease where it turned out to be difficult to make a vaccine. We could have done it five years ago and had the vaccines ready. I suspect that many other vaccines we need—for MERS or Marburg, which were mentioned earlier; I could give you a list of 15—are probably relatively easy to make. We need to get on with those, but somebody has to finance it. It is very difficult to look to large industry

and say, "Do all of these," because vaccine development is expensive. The society is right; we need a solution to answer this issue.

Q51 Chair: Before I was Chair, I heard excellent presentations from the Jenner Institute previously, and I have visited the Oxford vaccine centre and know of the very important work that went on at Oxford to try to accelerate progress towards a vaccine. Professor Lang, what are your reflections on the comments made by Professor Hill, particularly his point that we could have come up with a vaccine five years earlier? Do you think that prior to the outbreak the UK did not have processes in place to identify and develop vaccines against the most serious disease risks facing the UK?

Professor Lang: I come to this from the therapeutic side. Your comment about the immunology paper talked about drugs and vaccines. On the panel there is vaccine development on either side of me, and I can talk about the drug situation. I agree with everything Adrian says, and it is exactly true of therapeutics as well.

By way of introduction, I work for the Centre for Tropical Medicine in Oxford and have spent 20 years running clinical trials in their root source settings. We run an organisation called the Global Health Network which tries to strengthen research capacity in those settings. It is exactly the same story. We lack treatments and evidence-based treatment care for all sorts of neglected diseases. It is the 90/10 gap. Most of the research that happens in the world is concerned with diseases that are not diseases of poverty; they happen in places in the world where we work. I come to this from a tropical medicine background. Many of us in the room and on the panels today know each other because we all come from tropical medicine and work in that area. We have faced the same thing for years. You are working against the background of no commercial viability, but there are also fantastic examples of public-private partnerships and corporate social responsibility activities that many pharmaceutical companies are engaged in. That has led us to develop quite a strong research capacity and the ability to develop products like this in those settings, which we have been doing for years. Not many of us working in this area had any Ebola expertise before last year, and we were called up to the plate. Based on our experience, we were asked by the Wellcome Trust, and awarded a grant, to set up a clinical trial platform to evaluate potential therapeutics.

Against the backdrop of disease outbreaks like this, there has never before been a clinical trial to evaluate a drug for Ebola; nor for MERS, which Tom mentioned earlier, or for H1N1 or the respiratory viruses that are emerging. There are never any clinical trials, and you have a very narrow window to set up a trial, get it going and get your answer, which is an extremely tall order. It usually takes 18 months to set up a clinical trial; we managed to do it within six weeks for this, but that was everybody pulling out all the stops and making it incredibly agile and streamlined. We have learned a lot.

Those are the cumulative reasons why we do not have therapeutic agents or vaccines in this situation. You are on the same spectrum of it not being necessarily commercially viable and the odd setting for the disease outbreak. It is a very challenging space to work in, because it is usually impossible to set up a trial at that speed.

Q52 Chair: Dr Ballou, Professor Lang has made a number of points: the length of time it normally takes to set up a trial—I think on average it is 621 days in the UK; and the lack of commercial viability in general when normally you have such a small cohort who would be exposed to a disease, until there is an outbreak on the scale we saw with Ebola. She mentioned that there had been some success with public-private partnerships. What is your answer to the point about how to prevent this and needing a big outbreak in the future, given some of the other challenges we are facing at the moment, because we know Ebola is not the only disease on the horizon?

Dr Ballou: I am Ripley Ballou and I represent GSK, which is a global pharmaceutical vaccine and consumer products company headquartered in the UK. I am currently the head of the research and development centre based in Rockville, Maryland. A year ago I was responsible for clinical programmes in GSK Vaccines Belgium, and it was in that context that I played a leadership role in the development of GSK's candidate vaccine.

Before getting involved in Ebola, I spent most of the last 30 years working on malaria with my colleagues here. One of the reasons we were able to respond very quickly was that there was a network in place built largely around malaria, HIV and TB. We were able to pick up the phone and call colleagues, and within days have, essentially, a group of willing participants who could check down: "We need to do this, this and this, and these are the people we are going to call. We need funding. We need access to trial sites." It evolved very quickly, but that is an ad hoc situation; it is not really a plan. We were able to respond very quickly when WHO said, "Can you help us?" It took them a long time to ask for help, but when they did we were able to respond quickly.

The comments you have heard are absolutely spot-on. I would like to put one nuance on why we do not have Ebola vaccines, beyond the obvious fact that there is a small market. An interesting fact is that there has been Ebola vaccine development for the last 15 years, driven largely by researchers in the United States who were funded by the US Government worrying about Ebola being weaponised, so for a very different purpose there was vaccine development. We understood pretty much how to make an Ebola vaccine at the time. GSK happened into a situation, through the acquisition of a biotech, where one of the candidate vaccines landed in our portfolio. It was in my portfolio in the company. When I became aware of the data and then was aware that we had an outbreak, it was easy to put two and two together and say, "Should we potentially advance this in the context of potentially assisting in the control of this outbreak?"

One of the problems that led to slow development of vaccines like the Ebola vaccines, which for more than a decade have been under research, is the fact that there is not a clear path to licensure. If you cannot license a vaccine, you cannot commercialise it. This is true of a number of the other disease threats we are worried about. They are very rare events. When they occur they may do so explosively but in a very short period of time. To be able to put together clinical trials designed to gather the kind of evidence base that regulators require to register vaccines or drugs as being safe and effective is not compatible with an outbreak setting. On top of that, this occurred in a very resource-poor environment where essentially social government was dissolving in front of our eyes. There was nobody to talk to about getting authorisation for a clinical trial. If it was not for WHO, Public Health England, and Sierra Leone and others coming in and helping to shore up those institutions, it would have been even more difficult.

Q53 Dr Mathias: Our previous panel commented on some problems of WHO. What is your opinion of WHO and its advantages and disadvantages in the recent outbreak?

Dr Ballou: From the vaccine side, to me the major problem was that they had no policy that even contemplated the use of a vaccine in an Ebola outbreak. On 23 March, when I read on the internet that there was an outbreak in Monrovia, as an infectious disease physician my immediate response was that this was very unusual. It was clear that there was a big impact on healthcare workers. I called the WHO and spoke to colleagues there I knew from malaria. I said, "We've got a vaccine. It's not been in the clinic yet. How could we accelerate it?" Essentially, the response was, "We manage Ebola through contact tracing, isolation and taking care of patients. We don't have any policy for how we might use a vaccine."

Q54 Dr Mathias: That was in March.

Dr Ballou: Yes. I called back in June and in July, and finally in August they came back and said, "We have a major problem. Can you do something?"

Q55 Dr Mathias: They weren't looking at the news, were they?

Dr Ballou: I do not mean to be critical of WHO. What was missing was a proactive policy that vaccines, which might not be licensed and ready in the pharmacy today but are in development in some place, might be used as a tool in these kinds of outbreaks. Thinking along those lines was simply not there.

Professor Hill: I fully agree. The key word we need to focus on is "stockpile"—stockpiles of vaccines. We do this on the veterinary side. The UK has a stockpile in case there is a foot and mouth outbreak. Why doesn't the world have a stockpile in case there is an Ebola outbreak? We have no licensed vaccine; we have one vaccine that has been shown to work, but it has not been licensed yet. It will take a little time for this and for GSK's and other vaccines to be licensed. What do you do then? Who has the stockpile, and who controls it? We have done this before in Africa for meningitis A. There was a stockpile and it was flown out to wherever outbreaks happened.

What I am advocating is a halfway house to full licensure of vaccines for all these threats. There are more than a dozen. Typically, vaccine development costs hundreds of millions of pounds. Where are we going to get the billions to do all of that? You may not need that in the short term if you can make investigational stockpiles, which is after all what we did for Ebola. We did not know that the vaccines would work until we tried them. The one that was tried was 100% effective, so the science underlying that was good. Can we do the same for Marburg and for MERS? I am in an institute where we make these vaccines very routinely. The challenge is to take them forward and have them ready in a stockpile, manufactured not to millions of doses but tens of thousands. Once there is an outbreak, not only do you have the opportunity to control it when it is tens of people, not thousands, but you also get a chance to test your vaccine and show that it is efficacious. That needs to be co-ordinated globally.

The UK has made a good start by beginning the UK vaccine network—a £20 million investment from the Government. There are other international partners who have to come together and come up with an agreed plan. I do not think that is happening fast enough. It is all doable, but we have to decide to do it and execute it. That is urgent. It would look extremely bad if next month there is a Marburg outbreak and we are in the same situation, with a vaccine made but not tested.

Q56 Dr Mathias: As Jenner led the way, is the UK still leading the way? I mean Jenner the physician.

Professor Hill: We were in an unusually fortunate position to test the Ebola vaccine, because we have tested vaccines of that type and we have a strong working relationship with several partners, including GSK. We had fantastic support from the chief medical officer, the Government and the regulators to get trials started quickly. That was why we were able to take a vaccine into the clinic in weeks rather than months. That situation could happen again, but I am not advocating that. We should not have been rushing to catch up; we should have done this a few years beforehand, and had the vaccine stockpiled and ready to test, knowing that it was fairly safe in hundreds of people and knowing the dose of the vaccine and how many doses we needed to give. All of that can be done now before the next outbreak, and we would be prepared. It is not happening, because it is nobody's clear responsibility internationally to do that.

Q57 Chair: Emerging infectious diseases have been on the national risk register since 2008 when it started, but Ebola appeared on it only in 2015 after the outbreak. You are advocating stockpiles. Who would identify which diseases to stockpile for and making sure that we have the right stockpiles and are not expending lots of money on stockpiles for the wrong diseases?

Professor Hill: That is a key question. Remember that the WHO and other international bodies had diseases of poverty—HIV, malaria and TB kill lots of people; and they had neglected tropical diseases, and many elements in others. Ebola and the outbreak pathogens did not even make the list of neglected, so they were not even in the bottom division; they were being ignored. That will not happen, fortunately, any more after Ebola, so something will have to be done.

The UK is very strong in surveillance internationally and in mathematical modelling and imaging of where diseases are, using satellite imaging and so on. I do not think it will be difficult to get consensus about what the top five or 10 target diseases should be. Those discussions are ongoing. That is not the difficult bit; you can get a committee to do that. The difficult part is the next bit: make the vaccines, manufacture them, test them and have them in stockpiles, and that needs funding.

Professor Lang: Obviously, it is really important to have vaccines, but we need to remember that we need drugs to treat these diseases, especially in outbreaks, and vaccines to prevent them. Our experience with WHO in trying to establish whether there were any therapeutics that could treat this disease was that they did a remarkable job at pulling us all together and holding key meetings to discuss things like the ethics of running clinical trials in these situations, and how to design the trials and operate them. Where the WHO needs a

significant amount of support and strengthening is in the ability to take a leadership role and co-ordinate us. There were probably four or five key groups running clinical trials in this outbreak: our group, funded by the Wellcome Trust to set up a clinical trial platform; groups looking at convalescent plasma; and other groups elsewhere in Europe and the US looking at other therapeutics. There were four or five of us. We all communicated very well and the WHO facilitated that effectively, but we were left to lead our own charge in talking to the aid agencies who were setting up medical relief, and in where and how we worked with local organisations. There could have been much, much better co-ordination and leadership from WHO, but they do not have the mandate, the strength and probably the finance to do that. That is a significant gap. The other side was selecting the products that went into trials, making sure the right products went in and we were not competing for sites, and having a very co-ordinated approach that needed an international neutral leadership that was not there.

Q58 Derek Thomas: Professor Lang, you said in the past that there was no on-the-ground research seen as needed in the emergency response. Why do you think that was? How would that research have helped to develop the vaccine?

Professor Lang: What I meant by the bit you are quoting is that there was a strong medical and humanitarian response to Ebola at the beginning to put in treatment. That was absolutely needed and perfectly correct. We were able to add research later, so we were fitting that into the care-giving setting that was already established. Where we could do better next time, which we are already working on quite effectively with lots of groups, is to work much better with the humanitarian and medical aid organisations to put research into their thinking, co-ordination and planning. Research should not be an afterthought. We need drugs and vaccines and we need to be able to implement research. Research is really different. A good question was raised earlier about data-sharing. Of course we need to share data. The data should come right at the beginning as soon as you are beginning to understand what is happening to the virus in the patient, when patients are dying, who is dying, and what is happening. Those are observational data. Then we need trials to evaluate interventions. That is protocol-driven research, which needs to be questioned in an ethics committee. That is a very different step and it needs to be thought about in a different way. People need to be taught and to learn how to do that. There is an amazing amount of research capacity in these regions—this is where we have all worked for years—but we do not share it and harness it. We need to put in place systems to harness it effectively in these outbreaks.

Q59 Derek Thomas: When the Ebola epidemic was on our TV screens and there was enormous pressure from the world's media about how people were responding and what was happening, what assessment do you think the Government were making about where the gaps were in research, taking the horse has bolted approach and looking at the gaps and how we could quickly plug them?

Professor Lang: I can only answer that from my experience. There was an amazing amount of press coverage. I have worked on malaria and things like diarrhoeal disease for years and years and I have never been on "Newsnight" or the "Today" programme, wheeled out, as we were, but for us it was a good opportunity to explain why we needed

clinical trials in that setting. There was a lot of concern, quite rightly, about the risk of ill people coming back to the UK, quite rightly, as there is now concern about Pauline. We were able to say that this was very difficult and challenging in the UK, but unless we could run the research in those settings and find out what therapies and vaccines worked we would never get anywhere. We used that as an opportunity to explain the difference between managing an individual in the UK, as we were, and assessing therapeutics in the rigour of a clinical trial and the importance of research. I hope we were plugging the knowledge gaps on why we need research in these settings.

Q60 Carol Monaghan: Professor Lang, in your article in *Nature* you talked about "a chaotic land-grab for…patients" when you were carrying out clinical trials. In what way did the competition for patients affect the research that has been carried out?

Professor Lang: It is what I alluded to earlier. If you are doing a clinical trial in an infectious disease, it is different from working in, say, hypertension where you can go through a list of patients and have 100 patients eligible for a clinical trial. In an infectious disease, which is our background, you have to wait for patients to walk in the door, so that is even worse. In this very narrow window of disease outbreak we did not know how long it was going to last, or how many patients would be available for the studies. With the huge benefit of hindsight, that is where we could have done with better co-ordination, because it probably was not an overly sensible approach to have five different groups testing five different things and splitting it. It was left to Médicins sans Frontières, Save the Children and other organisations that had the sites to say, "You work here, you work here and you work here," when actually we should have decided where the best intervention was and gone for it to answer that question, because you can do vaccine trials in the general population, but for testing therapeutics we need ill patients. We did not know how many we had or how long we would have them for. We need to do that better next time, and that is where we need neutral international leadership to help it happen.

Q61 Carol Monaghan: We are hopefully getting to a situation where Ebola has been eradicated, but that creates other challenges because there are fewer patients available for clinical trials. Has that been an issue as well?

Professor Lang: Absolutely. We only got our trial started at the end of the epidemic curve. You can see when patient numbers went up, and we were starting our trials as those numbers were coming down. This is why there have never been trials in an outbreak before, because you have a very narrow window within which to answer your question. Research should be built in, embedded in the immediate response. We should have systems ready to go and we need to strengthen local research capacity. We worked with amazing local partners; it was very much a partnership with African scientists, but we need to strengthen that local research capacity so that we can use the expertise on the ground and start trials earlier next time. We did an amazing job in getting trials set up in weeks rather than months, but it needs to be in days.

Q62 Carol Monaghan: To ask the panel generally, were any particular trials prioritised, and were data shared among the other trials that were going on?

Professor Hill: I believe a total of seven vaccines were tested over the last year for Ebola. Two of those were available early in the first stage. Data became pretty widely available initially at scientific meetings at WHO. Some journals published those data very quickly. I think that was pretty good in terms of making safety and immunological data on how the vaccine was performing available to the community.

What was not in place—I would like to see this as a learning point—was a mechanism for independently comparing the immune responses the vaccines were producing. Given that we ended up with only one country where a vaccine could effectively be tested by the time we were ready to test, did we choose the best vaccine to test? You could argue that it was very effective and therefore we did, but you do not know that. The other ones could have been safer, at least as effective and so on, but there was not a system in place that was widely known, with a reference laboratory. One was identified but it did not have all the samples. I would like to see that much more rigorously and neutrally regulated in a future situation.

To be fair to WHO, which has had a lot of criticism, they were very active and committed to co-ordinating vaccine development in particular once they got started in August, and did a very good job from there on. They were led by a very experienced vaccinologist at the helm who did a good job. They were in a situation that they were relatively unfamiliar with, trying to develop a vaccine to control an outbreak. It has never been done before. It happened this time right at the end of the outbreak, so that was an achievement.

Professor Lang: I can add to that from the point of view of drug trials. This was something we did well. In the WHO meetings everybody who was running trials got together. We talked about making sure we were all collecting data in the same way. Everybody talks about data-sharing, but unless you have standards for what you are measuring and how you are recording it, it is very difficult to share data later. We shared all our data record forms and talked about how we were going to do that. An initiative is now being set up for a single platform where all of us put the trial data we gather. That will be open and available for people to share. I think we did that quite well for therapeutics.

Dr Ballou: From my perspective, the data-sharing went as smoothly as it could, given the limits we had. In order to get data from vaccine trials you have to immunise and wait to collect the samples and then they have to be run in some kind of standardised process. None of these assays was set up beforehand. Within the limits of what we were working with, there has been pretty good transparency. Relative to other programmes which do not have that kind of urgency this went very fast.

Q63 Chris Green: Professor Hill, during the outbreak the necessary clinical trial protocols were expedited for the University of Oxford vaccine trials. Can you talk us through how that rapid response was made and give a bit more detail?

Professor Hill: We were contacted by WHO in early August and at about the same time by the Wellcome Trust, who expressed an interest in supporting clinical trials. We were very lucky to have access to a vaccine from the NIH in the United States, which had been working with GSK on the development of that vaccine for bio-defence, as you heard. It had been designed for that purpose, so a mixture of strains was being prepared. Lots of

pre-clinical work and excellent data were published showing efficacy in animal models of Ebola, so that was a great starting point. The problem was that it had not been given to any human being, so it was waiting there in a very large bag having been manufactured.

What do you need to start a clinical trial? You need lots of approvals. The University of Oxford took on the job of being the clinical trials governance agency and sponsor for that particular trial in partnership with GSK, NIH, WHO and others. An application was made to the regulator in London, the Medicines and Healthcare Products Regulatory Agency, who turned this around in four business days. It is usually pretty good; it takes two or three weeks to review our applications—in other countries it is much longer—but four days is absolutely exceptional. The ethical committee met specially to review the application, and I think it made a decision that day. There was lots of work on formulating the vaccine, transporting it, relabelling it and so on, all of which happened in a few weeks, and we were able to start about a month after that telephone call, which is quite exceptional.

Q64 Chris Green: It seems to have been an incredibly rapid process. Are there any further improvements that can be made now you have that experience and you know what to do and what processes to follow? Could that time be brought down significantly further?

Professor Hill: I would like every trial that we do to take that short period of time, but given how many trials happen in the UK every year, the regulators will explain to you why that is not possible. There may be a case for further investment so that trials happen faster. I think it is relatively good; you can only improve it by a few weeks, if you think about it. The problems are greater beyond that. For example, why was this trial being done in the UK rather than West Africa? We managed to start a trial only three weeks after Oxford in Mali with collaborators at the Centre for Vaccine Development there. That was a very important trial to show safety in West African populations and that the immune response the vaccine was making was as good in West Africa as it was in UK volunteers. That turned out to be the case.

The real challenge is how you set up an efficacy trial in-country in a setting where there is a horrendous outbreak going on, where the infrastructure for doing research did not exist beforehand, and where much of the medical, nursing and other public health capacity is fire-fighting to deal with the outbreak. Who is going to review the clinical trial protocols, and why should that be a priority for them? It is the same problem as Trudie outlined. My own view is that it is a lot to ask in Africa to have 53 authorities capable of doing that in an outbreak. You would like to have regional ethical committees and capacity. We work with some fantastic clinical trial teams in West Africa on malaria: in Burkina Faso and Gambia and an MRC unit in Senegal. Those were the wrong places. They had no obvious role working in Guinea, but they did come in to help. We do not know where the next outbreak is going to be. The real delay is in getting permission to do the phase 3 efficacy trial, not getting the phase 1 trial started, which can happen in weeks, as you saw.

Q65 Chris Green: We heard from the previous panel about concerns local people had that the measures to control Ebola were being done to people and there was a reaction against that, so having more local trials and working with people locally should help to overcome those problems.

Professor Hill: That is always the case. We always work with local people, as my colleagues will explain, but we were unfortunate in that there were no established vaccine trial teams in-country that we could immediately link to, whereas that would have been the case if the outbreak had been in, say, Burkina Faso, Mali or Senegal, so that was unlucky.

Professor Lang: Without question, there is remarkable research capacity in Africa in countries neighbouring those we have worked with for many years, and in other regions of Africa. We could definitely do better at harnessing them and thinking about what we could do next time about transferring the expertise that exists following the amazing efforts that have been made over the years in malaria, TB, HIV and all the other trials that have gone on. The regulatory capacity exists; it is unfortunate that where the disease outbreaks are likely to occur there is often lower research capacity. I think we can work really closely with DFID and other groups to think about how we can do much better. One of the ideas we have is to put a system in place where those experienced clinical researchers are kept on standby for use in disease outbreaks. They are working on existing trials, maybe malaria, onchocerciasis, or something else, but they are on standby to deploy within the region in the advent of the next disease outbreak. That is something we could look at, rather than having to move people from Europe to Africa.

Q66 Chris Green: Dr Ballou, we heard about the difficulties of corporations and pharmaceutical companies engaging in developments and having those vaccines prepared. There is concern about big data and who controls and owns it, and having vaccines stored. If the patent runs out you cannot make any money on it. Has any progress been made to overcome those or other problems?

Dr Ballou: This epidemic has been a huge eye-opener for GSK. Sir Andrew Witty has made this a big area of focus within the company. This outbreak has had tremendous ramifications for our own internal R and D. We have had to stop major programmes in order to focus literally hundreds of people to work on Ebola, and we do not think this is a viable approach going into the future. If I could just elaborate on the concept Adrian mentioned earlier, we think there needs to be a new model. GSK has quite extensively elaborated its ideas about how that might be done. We have spoken with the UK Government, the US Government and others and prepared a White Paper on this. We have referred to an organisation called the bio-preparedness organisation—BPO—with the idea of leveraging key technical platforms that the company believes would be suitable for addressing emerging outbreak threats, including one of the platforms that was used for this particular one, but we have others, and providing them to a stand-alone organisation that would be very closely supported, by GSK in this case, but other industries could use the same model. You would have a group with the wherewithal, knowledge, capabilities and capacity to develop vaccines to the point where they can be tested for safety, to understand the dose, the schedule and their likelihood of working, based probably on animal models, and then manufacture them to a quality that would allow them to be stockpiled in the hundreds of thousands of doses. This BPO concept is now fairly well evolved. We are in the process of looking for support for it. This is something that Governments need to be behind. This kind of investment is to protect populations from emerging outbreaks. We look for a governance model that would allow decisions about how to prioritise, what projects to work on, how the work is being done and who has access to the vaccine stock, and for this to be done in an independent and transparent way. This does not imply

manufacture. The solution to manufacturing for large-scale stockpiling is a separate question, but it is integral to the concept and we would be very open to tech transfer, to allow on a regional basis, for example, manufacturers to develop and maintain large stockpiles of vaccines that are thought to be potentially useful.

Implicit in this is that, first, these are likely to be vaccines that have no commercial value; otherwise, industry would already be working on them and we would have those vaccines. Secondly, it is likely that they will be products that will be very difficult to register. We are talking about stockpiling for emergency use what would still be investigational vaccines. The framework around how you would use them, who gives permissions and what data you collect when you need to test, essentially, investigational products, as we did with Ebola—all of them were investigational vaccines and drugs—needs much more elaboration and strengthening.

Q67 Graham Stringer: Dr Ballou, you said that the regulators wanted randomised control trials but by and large they did not take place; just one took place. Who objected? Why did they object, and on what basis?

Dr Ballou: A meeting was held by WHO on both drugs and vaccines to discuss what should be done in terms of trials that would be used to generate efficacy data that would allow regulators to register vaccines. To have vaccines available in countries they need to be registered at some point. The regulators were very clear that if it is at all possible we should capture data using the most rigorous methods of data collection, data analysis and trial design. At the top of the prioritisation of data quality are randomised control trials. Of course, we proposed several designs, including randomised control trials, but also alternatives, recognising that to do randomised control trials is sometimes not possible. Clearly, in the study where the Merck and NewLink VSV vaccine was tested in Guinea, the decision was taken not to use a randomised control trial; it is weaker in terms of the quality of evidence and data efficacy, but when the signal is very clear, as it was in that study, it was very informative. Non-randomised control trials have their place, but I do not think they should be the first choice out of the starting gate.

Q68 Graham Stringer: My final question may or may not have an answer. Is there a ballpark figure for the cost of stockpiling 10 vaccines for 10 possible outbreaks?

Dr Ballou: There is a ballpark figure for what it would take to have a facility that would be able to do this. To generate and stockpile 10 vaccines will probably take a decade; it is not something that happens overnight. One of the real challenges is that if you are going to do it you need long-term funding. It is not a three-year grant and then you have 10 vaccines. It would require sustained funding over a decade or more to allow you to get to the point where you could work your way down the prioritisation list and have candidate vaccines stockpiled.

Q69 Graham Stringer: Is there a ballpark figure?

Dr Ballou: The ballpark figure is probably of the order of £50 million a year.

Q70 Chair: Dr Ballou, I want to take you back to your first answer to Mr Stringer. You gave us written evidence in which you referred to the meeting about what kind of trial would proceed. You said: "The message was, essentially: 'If it goes the way we are seeing, we are talking about depopulation of West Africa by April 2015'. It was incredibly sobering…This scenario contributed to a sense of desperation which I believe impeded normal scientific debate, especially around study designs." That was not the sense of the answer I got from you just then.

Dr Ballou: That is correct. What I am referring to in that discussion is the fact that at the time we were debating optimal trial designs there were very impassioned arguments coming from parts of the community who felt that any study that involved the use of a placebo or a control vaccine or drug was inherently unethical. This completely dismisses the fact that we were talking about products whose safety profile we did not know and we had no evidence that they actually worked.

As product developers, we come from the perspective that one always has to do the risk-benefit analysis, and there is not always the clear and obvious answer that of course it is going to work because it works in a monkey. We have seen many products that work fine in animal models but do not work in humans, and in fact can steer the discussion and development process in absolutely the wrong direction. I maintain that randomised control trials are clearly the optimal way to do this, but they are not always possible when you do not have the infrastructure and the willingness of the community to participate; we heard from the anthropological side earlier that the whole issue of engagement of communities is critical. In this particular setting, where there were three countries that had gone through decades of civil war, distrust of Government, foreigners and science was a major challenge.

Q71 Chair: Professor Lang, was it also your experience that among the community in the debate about study design there was resistance to certain types of study?

Professor Lang: It was exactly as Rip said. It was a very unusual situation to work in. Normally, you have the luxury of time and calm scientific discussion: here is the question you need to answer; here is the evidence that you can bring to support what design you choose; and then you come to a consensus in the scientific community about what the right design is. In this situation we had to act very fast and quite a lot of players were involved. The backdrop for the therapeutic trials was that we were trying to implement clinical trials in treatment centres where you had very sick, frightened people, and there was no other treatment to give, or nothing else to use as a comparison. We are always told, "Why did you not bring this experience earlier?" We have a huge amount of experience running very difficult trials in vulnerable populations where we are looking at mortality as the end point because it is in awful disease settings. We are used to working with the community to find out how they perceive it and what the risks would be, and working with local anthropologists and social scientists to understand that.

In this situation it was very clear that there was no way you could sit down with a family group. Traditionally, we would randomise and say, "You get the drug, but you will get something else." You would never be able to do that. Médicins sans Frontières and local ethics committees said, "We cannot let you sit there and say that the mother gets the drug

and the daughter doesn't." That was a clear message; but that was okay, we could work within that, because very good scientific designs are used in clinical trials all the time, such as in oncology, where you have a similar situation. You have a desperate situation where no other drugs are available. When you are looking for a very clear outcome—died or didn't die—and a very big difference in survivors, you can use a different type of design. I agree with Rip entirely that ideally we would like to use a randomised control trial where they get one or the other, but that is not always possible, and not always needed. What we need to think about is using the most appropriate design in the most appropriate setting that is scientifically justified. We need to be able to have that debate in a rational scientific way, which was not always the case.

Q72 Chair: It is that bit that is worrying me. It sounds like it was not possible to have a rational scientific debate and there was lots of pressure put on scientists in the process. In the development of any vaccine in an outbreak scenario this set of circumstances would be replicated, so how would you recommend trying to avoid such a fraught scenario in future?

Professor Hill: The easy answer to give is education, but it is not always possible in the short term.

Q73 Chair: You have to pinpoint the location.

Professor Hill: What I think we have learned and should emphasise is that ring vaccination, even though it is not the gold standard, was the design used in Guinea for the successful vaccine trial. It worked really well in that context and gave a very clear result. Ring vaccination had been forgotten about a bit. It was used in Nigeria in the 1970s, but then the gold standard came in and nobody did ring vaccination. I think we are going to see many more ring vaccination trials implemented to test outbreak vaccines.

To return to the point about community buy-in, if you look at that trial, so many people, who were randomised to receive the vaccine immediately, declined vaccination that they formed an additional control group who got a significant incidence of Ebola. You can compare all the people who were randomised to get the vaccine and were vaccinated with those who chose not to be vaccinated and you see a significant difference. That illustrates two things. It is another way of looking at vaccine efficacy, but it also tells you that quite a lot of people—about 20%, I recall—declined vaccination, which illustrates that not everybody was going to buy into the idea of vaccination.

Q74 Victoria Borwick: To go back to Cobra, which we talked about in the earlier session, why do you think Cobra took so long to respond to the request for the Ebola SAGE committee to be formed? Do you have a view on that? It harks back to what we were talking about earlier.

Professor Hill: I don't, no.

Professor Lang: As a research community it is outside our experience. The next panel might be able to answer that.

Q75 Chair: Thank you all for your evidence, which has been very helpful and thought-provoking. We are conducting an inquiry into a very serious matter. We may want to write back to you on a couple of points.

Professor Hill: Can I make a final point? There are two problems. We have talked about one a great deal. How do we get vaccines for these outbreak pathogens? What is the business case, and so on? The second one that I hope will be of interest is the problem of vaccine manufacturing capacity in the UK. It is not a great exaggeration to say that we do not have any. There was a survey at the time. We needed a lot of Ebola vaccine that worked and was available, but we did not have anywhere to make it. Many people are conscious of this. It is not a cheap solution to manufacture, and you cannot create it in weeks; you need years to build manufacturing plant. The UK is lacking in that capacity. It is a national security issue; it is a separate issue but it was very high profile at times during the Ebola outbreak.

Q76 Chair: Professor Hill, can you tell us where vaccines are currently made? I think it is in the Netherlands.

Professor Hill: Dr Ballou would be better able to answer this. Most of the vaccines that we give our children and everybody else are made by a relatively small number of very large pharmaceutical companies that have extensive manufacturing capacity and the experience and know-how to do it, which is slowly acquired. If we go back 25 years, most European countries had somewhere to manufacture their vaccines. Very few do. Private industry controls that today. A lot of new industries and small companies in Asia provide vaccines for the developing world, but what we have lost in many European countries is a national facility for vaccine biomanufacturing. We have some very small facilities; they are not a solution to providing 50 million doses of an Ebola vaccine for the UK population, if we needed that. We should be aware of that. It is not a new suggestion from me; people have looked at this, but it is not one to which we have a solution.

Q77 Chair: Although we had a very effective response, a barrier and so on, had that not been as effective as we hoped and we needed to access a large number of Ebola vaccines in the UK, would we have been able to do that?

Professor Hill: In this particular case GSK was manufacturing vaccines as fast as possible with a new manufacturing process that was rate-limiting. Dr Ballou can say more, but I think the short answer is no. If we had wanted 50 million doses in January we could not have had them.

Q78 Chair: Could you write to us about that, Professor Hill?

Professor Hill: Certainly.

Chair: Thank you so much for your time.

Examination of Witnesses

Witnesses: **Dr Jeremy Farrar,** Director, Wellcome Trust, and **Professor Chris Whitty**, Professor of Public and International Health, London School of Hygiene and Tropical Medicine, gave evidence.

Q79 Chair: Dr Farrar and Professor Whitty, welcome to the panel. I hope you have been enjoying the afternoon. It has been fascinating. Professor Whitty, we saw you in a different capacity a while ago. I want to read a little of the written evidence we received from the Wellcome Trust. Dr Farrar, you described Ebola as an avoidable crisis and said that "a lack of real time data of infection rates and further understanding of the virus significantly impacted on both the ability to make decisions regarding treatment and prevention of spread of the disease," and that "should there be a similar emergency, the availability of vaccines and treatments would still be a critical unmet need." Do you stand by that written evidence today? Professor Whitty, do you agree with that? What do you think we should be doing to try to address those core issues? We have been exploring that a bit this afternoon, but what are your specific views?

Dr Farrar: I do stand by that statement. I think it came out a bit in the previous session, and it is true of every emerging infectious disease. I have been personally involved in most of them, going back to the Nipah and SARS in the last century. The key to intervening is to do it early. If you miss that opportunity, or you do not make the right decisions, things spiral out of control and you lose the ability to keep track of it. That was what we saw in West Africa in 2014. The period between December 2013 and March/April 2014 was when it went from probably a single individual in Guinea to urban transmission across three countries in both urban and rural settings. That is unprecedented in the 40 years since Ebola was discovered. The key is early intervention. In previous outbreaks, where intervention has come earlier and they have been largely rural outbreaks, you have been able to intervene with classic public health, and the numbers have been in the 10s and sometimes 100s, but 30,000 individuals with Ebola is totally unprecedented, and it was in the first six months—what I would call phase l—that the opportunities were missed. In phase 2 from August, when we got into gear, as Professor Hill said—I am sure Chris will talk about this in a minute—things were done that made a big difference. The focus has to be on the first six months in changing that intervention.

Professor Whitty: I broadly agree with that, and I think most people would as well. To be clear, there are some epidemics that you cannot break early on. If there is a big flu pandemic it is going to hit us; there is nothing we can do to nip it in the bud, but while this particular Ebola epidemic happened, several other smaller epidemics happened, including one of Ebola in the Congo area, and a plague outbreak, for example, in Madagascar, and were snuffed out effectively. In a sense, this was the one that wasn't, despite the fact that, as Dr Mathias essentially implied in one of her comments, anyone reading the news could tell that it was not behaving in a normal way. I would say that from about March, a bit later than Dr Farrar, it was pretty clear that it was not behaving in the way you would normally expect, so there was a period between about March and the end of July when there was an opportunity to get on top of it quite quickly and it did not happen.

Q80 Chair: Why do you think it did not? There are examples of other outbreaks where there has been a quicker response. We can point to Cobra being convened in a three-month gap from the SAGE scientific advice being commissioned. It is not clear why there was such a slow response to this from different sources. We have just heard from Dr Ballou, who said he phoned three times to offer vaccine services and got no response until July. What do you think was behind this, Professor Whitty?

Professor Whitty: Let me separate the international response from the UK response, but not quite as starkly as some people do. The international response was extraordinarily slow in the round, but I do not want to go in for a WHO kicking session. We all have to accept that WHO is owned by all of us; it is the international community and, if there is a problem with it, it is our problem as much as anyone else's. There is a danger of thinking it is someone else's fault.

One area where I would part company with Professor Leach on the first panel, before you arrived, Chair, was her comment that the UK could have got on top of this in a sense unilaterally, or at least she implied that. If you think it through logically, I do not think the UK was in a position to be able to do that as an individual country. This had to be either declared by the WHO as an emergency or the countries themselves had to declare their emergency and ask us for help. We cannot just march in and say, "You don't think you've got a problem but you have got a problem, and we are going to sort it out." I am a bit more cautious about the UK acting alone, but there is no doubt that we know how to get on top of Ebola outbreaks. Ebola is not a new disease. Had things been done at any point probably up to the end of April, we could have had good control. The first case recorded in Sierra Leone, which was the country we eventually worked in, was not reported until 25 May, quite a lot later, and if there had been more action at that point it probably could have been slowed right down. It did look as though it was going away at the end of May, and people took their foot off the gas. That was a big mistake, and it roared back again in June.

Dr Farrar: I would agree with that. I very much agree with Chris that WHO is owned by all of us. There was a failure of leadership at WHO, but there was a collective, global failure to respond to what I called the first phase. There must be some lessons learned from that phase. Maybe we will come back to ideas about WHO reform later in the conversation, but we have to change the way that is done.

When you prevent something happening you often get no credit for it because it was not going to happen anyway. In my personal view, there was a hangover from the pandemic in 2009 and a sense in some quarters that there was an exaggerated response to it and it proved to be—not my words—a damp squib, and therefore there was an exaggerated global response. I did not believe that then and I do not believe it now. I would much rather we over-responded occasionally rather than under-responding and ending up with 30,000 Ebola cases. You will not always get it right, but it is much better to over-react occasionally than under-react every so often. Perhaps we will come back to WHO reform in a minute.

We also have to look at Ebola in the context of the 21st century. We tended to look backwards. While I accept Chris's comment that we know how to control Ebola, I am not sure we knew how to control it in the context of the society in which it happened in the 21st century, which was multiple country urban transmission where the dynamics of that

society are very different. Professor Leach talked about that earlier. Outbreaks in the past have been mostly rural, and that is a different community to work with. It is crucial when thinking of these epidemics to look to the future rather than repeat what happened in the past. You will make mistakes if you do that.

Professor Whitty: I absolutely endorse the points Professor Leach made earlier about the importance of social science in this response. It was important in almost every aspect of what we did. The first experience I had in government of a crisis like this was the so-called Mexican flu pandemic. We did not get the social science properly engaged, and the other thing we did not get right was that we did not marry up the international and domestic sides. On this occasion I think we did that a lot better, but in particular social science was much more heavily embedded from the beginning.

Q81 Chair: Professor Whitty, to go back to your previous hat as a Government adviser, one piece of evidence we have received is from Professor Edmunds of the London School of Hygiene and Tropical Medicine. He said that one of the fundamental problems is that, if you respond early and well, what happens afterwards is that people say all the money spent was not well spent because you had only a few hundred cases, yet essentially you have prevented the cases that would have caused the outbreak. How do you deal with that in terms of convincing decision makers that it was well spent, because it is a Catch-22, isn't it?

Professor Whitty: It is a Catch-22. The reality is that people like me in my previous role will appear in front of either your Committee, who are asking, "Why did you not respond earlier?" or the Public Accounts Committee, who are asking, "Why did you spend all this money when it clearly was not needed?" You are damned if you do and damned if you don't, but I do not think that in this case anyone has any doubt that we responded too late. By "we" I do not mean the UK but the international community. I don't think anyone doubts that.

Q82 Graham Stringer: We have heard some quite scientific discussion this afternoon. How important is it to engage the BBC and CNN in getting television cameras there? Is that a critical factor?

Professor Whitty: I will give my answer, but I suspect Jeremy will give a much better one. My answer would be that the media are potentially your greatest ally and your greatest threat. They are the greatest ally because they can get important messages out there and make people realise that this is genuinely serious, and the UK media did a very good job on this occasion. They are your greatest threat because they can hype the thing up and take the wrong things way out of control. Broadly, the UK coverage was pretty measured. I also think that the British political response was extremely measured compared with many other countries, and that made it possible to have a proper operating environment, but it was not a given. There were other countries where the media got seriously in the way of events by making hysterical claims about the risk to well-developed public health systems like the UK and other northern countries.

Q83 Dr Mathias: This might not be appropriate for the time we have. My question is about improvements in the African medical profession, WHO and the UK on co-ordinating and

reforming. If you cannot answer it in a short time, we might have to deal with it after the meeting.

Dr Farrar: I think I can answer it, or at least start with WHO. Publicly, I have called for reform. I think Margaret Chan is in place for another 18 months to two years. As to who the next director general of WHO is, it is absolutely critical. Perhaps we can come back to that. She has a two-year window when it will not be possible to reform the whole of the WHO. That task could take many years, but building on Ebola and Margaret Chan's personal background in H5N1 in Hong Kong, one could establish within WHO a semi-autonomous unit dedicated to the surveillance of and response to emerging infections. It should be properly funded and, to come back to Professor Whitty's point, owned by all of us and it would function even in the inter-epidemic periods, because when you are trying to create such a structure and respond in a crisis you run into real problems. I would have a separate governing board which reported to the director of that entity, and he or she would report to the director general of WHO, but the advice would be transparent and open so we would not be having conversations about who said what to Margaret Chan in corridors in which month and on what date. As with the European CDC, discussions in the morning would be on the website in the afternoon and transparently advised. I think that can be set up in the time Margaret Chan has left at WHO, and it is critical that we do it. That was what came out of the Stocking report; it will come out in subsequent reports, and we need to act on it.

Professor Whitty: I have two points to add. One is on the science and training side. The UK has a very proud tradition of training scientists from Africa in Africa in science as well as in medicine. Building local capacity in all the relevant sciences is absolutely critical. It is more important than surveillance and anything else. On WHO, the only thing I would add is that its regional areas—WHO AFRO is the area where this is—do not always have a good relationship with WHO in the centre. If I could build the capacity of WHO AFRO scientifically, it would be a phenomenal achievement, but I am not sure how easy it would be.

Q84 Victoria Borwick: To go back to the timetable of what happened when, which was referred to earlier, why do you think Cobra took so long to request that the Ebola SAGE be formed?

Professor Whitty: I am not the right person to ask about when the decision formally to form SAGE was made, but I do not think it would be right to think that scientific advice, including formalised scientific advice, was not going in from a very early stage. For example, the SHED mechanism—science in humanitarian emergencies and disasters—was providing advice to the Government in March. I had very close discussions with leading scientists in the UK—social anthropologists, epidemiologists and so on—throughout all the period right up to and beyond the point when SAGE was there. We are very fortunate in the UK to have, in part because of MRC history and the Wellcome Trust in particular, a very large body of some of the world's best tropical health scientists in many different disciplines. For example, the head of our national School of Public Health was one of the co-discoverers of Ebola; the chair of the board of Public Health England was one of the people who worked early on Ebola. Dr Farrar himself comes from an emerging infections background, so we had a lot of the right skills in place. Although it

was not formalised until the Cobra mechanism asked for it to be formalised, the advice was happening well in advance of that.

Q85 Victoria Borwick: Lessons learned?

Professor Whitty: I think the biggest positive lesson—the reason I repeat it over and over again is that it gets missed in almost every other pandemic—was that we got the social science in right at the beginning, along with the modelling, the epidemiology and the clinical. If we had not done that, we would very possibly have failed to get on top of things properly in Sierra Leone. I think we can learn a lot about that for our own domestic responses in the future.

Dr Farrar: In addition to that, similar to my comments about WHO just now, I think it can be replicated within our own system that there is a standing body. So much of this depends, when the proverbial hits the fan, on personal relationships and the fact that you have worked together. Chris and I have known each other for 25 years, so that really facilitated a flow of information, and DFID and the Wellcome Trust have done many things together. That was the mechanism by which we were the first to fund some of the vaccine trials you heard about earlier from Professor Hill. I would like to see that body standing and functional throughout time, so that it does not have to come together just at a crisis. Just as I talked about a semi-autonomous unit within WHO that would be tasked with that, so there would be a standing body doing this on a regular basis and meeting regularly, even in the absence of an epidemic happening today. That is the only way you do the groundwork to respond when something happens; otherwise, you are always trying to catch your tail and be responsive rather than proactive.

Q86 Victoria Borwick: What about the additional resources needed to support the work? What additional resources were needed, and were they provided in a timely manner?

Dr Farrar: Once things got going they were provided. Because DFID, the Wellcome Trust and MRC had been used to working together professionally, we were able to make things happen very quickly, but it depended on some personal contacts. You cannot underestimate how important that is in these chaotic situations. I would like to formalise that more, so that the UK had a standing body that people worked with, whether or not there was an epidemic happening today, similar to what I am asking for at WHO.

Q87 Victoria Borwick: When you talk about additional resources, is that what your recommendation would be?

Dr Farrar: It would be. Part of that structure exists already. There is a body called UKCDS. I cannot remember what CDS stands for, but I am sure Chris will know.

Professor Whitty: Collaborative on Development Sciences.

Dr Farrar: We host it within the Wellcome Trust. That needs to be beefed up and made to function, and it would be the cross-governmental body that could potentially deliver that. I do not think they delivered during Ebola, but potentially they could be the cross-governmental body tasked with doing that.

Q88 Victoria Borwick: To go back to evidence-gathering, assessment and communication, you talked about the personal relationships that facilitated it on this occasion, but how effective was the Ebola SAGE in assessing and communicating information? What lessons can we learn?

Professor Whitty: Professor Leach, who was on it, said earlier that she thought it was very effective. I agree with that, but I reiterate that it was only one formal bit of the mechanism. It was much more long term and in-depth, with many scientists who worked on SAGE itself.[1] SAGE was really to help Cobra formally; it was not the only way in which Government was getting information.

Q89 Carol Monaghan: Professor Whitty, in the previous panel we were talking a lot about vaccine development and trials. You said that insufficient attention was directed towards the clinical response to Ebola. Can you explain what you mean by that?

Professor Whitty: I do not know when I said that, but I do think that, so you have obviously read my mind. There was a very good response on the vaccine; the speed of response on vaccines was admirable from the academic community, from WHO, where they did that well, and from other bodies. The problems on therapeutics were that there were some very simple things that it was clear we should be trying. They were primarily around fluids. How much fluid should you give people, and should you give them antibiotics? They were very simple questions. These were available. We did not need to wait for a drug company to produce them. They were unlicensed.[2] We did not need to do a licence trial; we just needed to test out how best to do it, and we did not do that.

Having been out there in the first few months, the extraordinarily brave Sierra Leonean, international and particularly UK staff were absolutely on their knees, and the possibility that we could have loaded on even a small additional thing was probably not realistic, but once the outbreak had peaked, which was round about December, we could easily have done that and got big enough numbers to get a serious answer, and we did not. That is a collective failure of the academic system. I do not think that belongs to Government; it belongs to all of us in the academic sector. We did not get that right.

Q90 Carol Monaghan: Was that a lost opportunity?

Professor Whitty: It was an opportunity lost.

Dr Farrar: Having lived through very closely SARS, bird flu, MERS, Ebola and a number of other epidemics, we have missed that opportunity in every single epidemic of the last decade. If you go through the diseases I have just mentioned and ask yourself, "Have we pushed through those epidemics therapeutic, diagnostic or vaccine studies?", the answer to all of them is no, with the exception now of Ebola. That is a missed opportunity in each and every epidemic. In 2012 or 2013, I set up, with funding from the MRC in my previous

[1] The witness later clarified that this sentence should say, "It was much more long term and in-depth, with many scientists who did not work on SAGE itself."
[2] The witness later clarified that this sentence should say, "We did not need to wait for a drug company to produce them. They were licensed."

life, the Bill and Melinda Gates Foundation, the Wellcome Trust and the Li Ka Shing Foundation, something called ISARIC, which Trudie is now part of. It sought to change the paradigm by which clinical research is done in the context of epidemics. I think that still deserves support, and it is how we would change the nature of the way we respond to these epidemics.

We must overcome the sense of separation within the response network on the part of those who think everything can be solved with classic public health measures that we might have implemented during John Snow's time in London. I am a great fan of John Snow and those interventions, but diagnostics, therapeutics and vaccines are part of the 21st century public health response and they must be part of the way we think about these epidemics in the future. I do not believe we do that sufficiently today.

Professor Whitty: During the epidemic we in the UK decided that we had to focus on one single strategic goal, which was to get down the force of the transmission, which we call R0, and we would do any form of research, including vaccines, diagnostics, modelling and anthropology, that was around that goal, but we would leave anything that was not around that goal, including therapeutics, to other people, because we just did not have the bandwidth to do everything. Our view was that the epidemic was running out of control. That led to some positive things happening, but there was a deliberate choice made that this was something we did not have enough people to do at the same time. That was just in the nature of the response, but at least we thought about it and felt we did not have the capacity at that point in time.

Q91 Carol Monaghan: There are some fairly strong messages coming from both of you, so I hope we can take note of them. Who had responsibility for deciding which research was going to be undertaken during this outbreak, or any outbreaks, and co-ordinating it?

Dr Farrar: Do you mean on a global scale?

Carol Monaghan: Yes.

Dr Farrar: Ultimately, whether things go forward or not comes down to decisions made in Sierra Leone, Liberia and Guinea, because the Ministries of Health and Governments in those countries have the final say in what happens there. I think that on this the WHO did a reasonable job. In September or August 2014 there was a series of meetings in which WHO sought to establish priorities for both therapeutics and vaccines and to work through the mechanism by which those would pass forward. They were not always listened to, and that is a problem in itself, but there was an attempt to prioritise and say where it would be done. As you know, the United States took on primary responsibility for Liberia, France took on partnership responsibility for Guinea, and the UK took on primary responsibility for Sierra Leone.

Professor Whitty: I agree.

Q92 Carol Monaghan: The Wellcome Trust has spent over £18 million funding Ebola-related research. What is your opinion of the UK's response? Are we overly reliant on charitable funding, or should more funding be put in for such things?

Dr Farrar: I think you should take the figure with a slight pinch of salt, because it is considerably more than that when you add it all together. Almost none of that was done in isolation. That money was provided in partnership with DFID, the MRC, GSK, the NIH and the WHO. The Guinea trial, which was successful, was done in partnership between us, DFID, the WHO in Guinea and the Ministry of Health in Guinea. My own background is in emerging infections, so that may be one reason why the Wellcome Trust put money up very quickly, but it did not do it alone.

Do the UK Government need to do more? Yes, of course. It is on the UK national risk register. I believe there needs to be better co-ordination within the UK about how one thinks about and prepares for these diseases and responds to them. The UK needs to support a stronger WHO and allow it to lead, and give respect to that organisation when it does lead. I absolutely take the points made earlier about vaccine manufacturing. The UK is incredibly vulnerable to a nasty coming from somewhere. The UK has almost no vaccine manufacturing capacity and, if something dreadful happened on a regional or global scale, getting vaccines from other countries would be incredibly difficult. We would be on our own. That is a very worrying situation to be in.

Q93 Carol Monaghan: What steps do you think the UK has to take to make sure it is research ready for any future outbreaks we may experience, of Ebola or other diseases?

Dr Farrar: As I said earlier, I would establish a standing body similar to WHO. If WHO is to have a dedicated semi-autonomous unit with protected funding to look after those activities, I would establish that within the community in the UK. It would bring in industry, academia, Public Health England and the devolved nations, and would allow those structures and, ultimately, personal links to be developed in so-called peacetime, such that, when inevitably something happens that potentially either threatens this country or is somewhere else in the world but we feel the need to respond, we would not be trying to respond to that; we would have prepared properly for it. I would like to see the UK establish that in the inter-epidemic period.

The UK does not have the equivalent of the Centers for Disease Control epidemiological surveillance officer training programme. That has fallen down the priorities in the UK and it should be re-established. Lastly, compared with, say, 25 years ago the UK plays a lesser role in global health diplomacy. When I first started to interact with WHO 20 years ago, the number of people from the UK involved in WHO or in the now European CDC and so on, was more than it is today. That is a critical role to play in trying to influence the way global policies in health work.

Professor Whitty: I would take a slightly different tack, although I agree with all those points. I would divide things into the known unknowns and the unknown unknowns. The known unknowns are things like Ebola, Marburg and a variety of others. As was said in the previous panel, we need to list those and the global community needs to work out countermeasures, which may be vaccines, but I want to be clear: vaccines do not work for everything. We do not have a good vaccine for HIV, malaria or TB. People have been trying for a long time. Let's not get hung up on the mechanism; let's start with the problem and work backwards.

Of equal importance is that at some point we will be hit by another unknown unknown where the disease comes out of nowhere, like HIV. The key thing is that what we know about it is that it will go down one of a relatively limited range of transmission routes. It will be faeco-oral, airborne or sexual; it will be vector-borne, broadly. We can think about countermeasures to those, which in a sense are non-specific to what the disease is and are much more about how we hit it at multiple points along its pathway, almost irrespective of what it is. That will get us a lot further forward in our response. We can then try to work specific countermeasures to the disease that comes up. We have not been terribly good at that, and we need to be a lot more systematic about it.

Dr Farrar: I absolutely agree with Chris that vaccines are not a magic bullet for everything, but to pick up what Rip said earlier, the GSK proposed the BPO support structure and I, along with Stanley Plotkin and Adel Mahmoud in the States, have proposed something similar that I hope will be complementary, which is a global vaccine development fund. Professor Hill and people on the academic side will do the research. Britain plays a critical leading world role in that, and the Jenner Centre and Adrian are in the lead on that, as is GSK. There is a problem in the middle, which is taking that academic work into the early phase development, where there is a gap—the valley of death. It is very difficult to get phase 1 and phase 2 clinical trial data, and I believe we need a global vaccine development fund that would bridge the academic sector and the industrial sector; otherwise, we are very vulnerable to unmet clinical needs where there is no commercial driver.

Professor Whitty: I do not want my comments to be understood as anti-vaccine; they are not at all. I chair the new UK vaccine network, and the reason it was put in place was that we perceived all those weaknesses, and we need to work out how the UK countries can get around them and try to address them.

Carol Monaghan: The valley of death has been mentioned a number of times in this Committee over a range of different subjects. We are hearing it again. It is very interesting.

Q94 Chair: Professor Whitty, given that the evidence we have received is that it is relatively simple to identify maybe the top 10 riskiest infectious diseases, and we have had the threat of emerging infectious diseases on our national risk register since 2008, can you explain why we have not had some protocol in place for responding to the top 10 diseases, and why there has not been at least a UK response plan in place?

Professor Whitty: I think that Ebola is the first time we have demonstrated—in a bad way—that one of the things we know can cause dangerous local epidemics could become generalised if it gets into the wrong place. That has been a wake-up call for lots of people. As one member of the first panel said, the reason we have Ebola vaccines is bio-defence concerns in the security sphere. The reason people were not concentrating on it was that we looked at Ebola and said, "Yes, this is a big problem, but we know how to deal with these small outbreaks. It is killing very few people. Let's put our resources into malaria, TB and HIV." I think that was a logical thing to do. What this has demonstrated is that some of those things can go beyond the point where they have been historically and start moving out, so that has led to a change in mindset. We need to respond to that and realise

that Ebola is not the only disease that could get into the wrong environment and then take off. We need to be mindful of that.

Q95 Graham Stringer: Dr Farrar, I am getting a very confused picture of the state of science in this area and our strengths and weaknesses. We have been told that the manufacturing side is almost non-existent, and you said that the academic side is very good both in quality and quantity. Overall, how would you assess our science base in this country for looking into this area?

Dr Farrar: In terms of vaccines or emerging infections?

Q96 Graham Stringer: Across the board. I suppose I am referring to infectious tropical diseases.

Dr Farrar: I may not be the best person to answer that question because it is my background, so, if it is a failure, it is my own failure. In vaccinology, it is absolutely true that the UK is world-leading in the academic sense—no doubt about that. There is the Jenner Centre in Oxford, but there are other centres, Imperial, Edinburgh, Liverpool and so on, where it is incredibly strong. The academic base for understanding immunology and the world of vaccines is as strong in the UK as it is anywhere in the world, and the UK should be very proud of that. GSK is one of the four major players in terms of industrial support for vaccinology. We are incredibly lucky to have GSK here. The problem lies between those two; it is the valley of death, where we do not have the capacity, which I believe is public health, and therefore I think there is a public responsibility. We can call it a market failure. In my view, that is a misnomer; it is a public health failure. This is where philanthropy and Government will have to work with industry and academia to fill the gap, because you cannot expect industry to do things for charitable purposes. That is a role for Government and for philanthropy like myself. The manufacturing issue is crucial, though, particularly around all the vaccines we need. Britain is very vulnerable to that, particularly if there is an emerging crisis in almost any infectious disease, including flu. Britain would not have the capacity to manufacture what it needed for its own purposes.

Professor Whitty: To add to the areas where we are strong, our tropical epidemiology and tropical public health is among the best in the world, if not the best, in many diseases. That is for historical reasons. The Liverpool and London schools of tropical medicine, Oxford, Imperial and various other places have real strengths in this area. The UK is looked to technically for a response, even if we are not responding in other ways, almost invariably. The danger is that people say, "Why are we doing this? Why aren't we concentrating just on domestic issues?" It is an area of huge strength, and what this demonstrates is that from time to time we really need it.

Q97 Graham Stringer: I am putting words into your mouth, because you did not actually say this, but you implied that we had become weaker in the World Health Organisation in terms of representation. Why has that happened when we have such a strong academic base?

Dr Farrar: That is a good question. There are other players and actors now. Perhaps 25 years ago someone like Professor Whitty would have gone to work in Geneva, maybe

even myself. Who knows? I would not particularly want to work there now, and that may be a reflection of where we have collectively allowed WHO to go. Twenty-five years ago the Gates Foundation did not exist in terms of global health; now it is a major place where world-leading figures who want to make a difference to global health go. Dare I say that even the Wellcome Trust might be somewhere you would go now if you wanted to make a difference to global health? Less and less is WHO seen as an attractive place to work, which is a great shame. Morale is low, they are getting kicked all the time and funding is being limited. Perhaps there has been a lack of leadership. We have to reverse that, because if we did not have a WHO we would have to invent it. It was established in the 1940s. I do not think it is fit for purpose today, but we absolutely need a global body that brings together the world health community and takes collective action. While it is easy to criticise them—I have been very vocal in that—we need a very strong WHO.

Professor Whitty: I would add a partially more positive spin. The relative decline of influence in the UK is because other countries have become technically much stronger, much more powerful and much richer, and that that is good, but leads to a problem.. For a long time multilateral organisations essentially were controlled by a small number of countries and others just took part. Now that they are genuinely multilateral, it makes it very difficult to get progress in every single one of them. WHO suffers from this, but so does almost every other multilateral organisation I can think of.

Q98 Graham Stringer: I think you have already touched on the answer to this question, but I will ask it specifically. At the start of the outbreak Ebola vaccines had not gone through phase 1 early clinical safety studies. Professor Whitty, you said that was a mistake. Why was the mistake made?

Professor Whitty: The mistake was made for the reasons I gave earlier. It was seen very much in the context of a disease that we thought we could control, and a series of decisions was made entirely on defence and security lines. We were not really seeing it as a public health issue. It is one of those things where, had I been making the decision 10 or even five years ago, I probably would have made the same decision if I had been in the room, so it was a mistake in retrospect. What it has taught us is that, if we have other vaccines which are through animal models and look pretty good but are not through phase 1 studies, let's not leave them there. If that is the situation you are in, when there is an epidemic, even if you go at a phenomenal rate—I take my hat off to everybody involved who tried to get the vaccines through—you will lose six months. If they are sitting there, through phase 1, you have some basic safety data and you can go straight into the clinical trials.

Q99 Graham Stringer: Is there anything you want to add about how we can avoid getting into a situation where there is critical unmet need for treatment and vaccines when the next emergency arises? What role should the pharmaceutical industry itself be playing in that?

Dr Farrar: I would reiterate what Chris has just said. Not taking things through to phase 1 was absolutely the fundamental error. If you had asked me two years ago, before this started, whether Ebola would be on that top list of 10, I would have put my hand up and said no; it would not have been on my list, and this is my own background, but now it would be. There is a list of diseases we know about, and there are some platforms we

could develop to respond to the unknown unknowns. Getting through phase 1 is critical. As we heard from Professor Lang earlier, we need to have protocols in place that allow you to go immediately—within days rather than months—into assessment. That can be put in place, and there can be global consensus that would allow it to happen, but we need to remember the timelines for that. We talk about therapeutics and vaccine trials that might take a couple of years in gestation. In the modern world with modern travel, we have to bring that down to days rather than even months if we want to intervene at the early phases of an epidemic.

Q100 Derek Thomas: We have established this afternoon that the World Health Organisation and the international community were slow to respond to Ebola. Do you think that was caused largely by insufficient disease surveillance, or is that too simplistic?

Dr Farrar: No. I think surveillance is critical to this. I have often said that you must combine surveillance with the capacity to respond. Surveillance on its own without the capacity, willingness and leadership that allow you to respond is not stamp-collecting but it is not far from it. Surveillance is the key, and the UK Government and ourselves, along with the Gates Foundation, are working towards setting up much better surveillance around the world with real-time sharing of data to allow these things to be picked up earlier, but you have to combine surveillance and response; you cannot stop at just describing things.

Professor Whitty: On this particular point, I would agree only partially. I completely agree that surveillance is critical, but I do not think that lack of surveillance had any part to play in why we were slow in this epidemic. We all knew about it; we were reading about it. MSF were there. We knew about it right from the beginning. It was a failure to act. Although I am totally with Jeremy on the importance of surveillance in many areas—for example, tracking drug resistance would be a very good one—let's not kid ourselves that that would have solved this problem. It would not.

Dr Farrar: I absolutely agree with that.

Q101 Derek Thomas: The Prime Minister has pledged to provide funds to establish a rapid reaction unit to act as disease detectives. Is that stamp-collecting?

Dr Farrar: I agree with it. I spent the last 20 years of my life living in Vietnam doing that sort of thing. We have a responsibility to do that. The idea is to establish a fund that would enhance local capacity. This can be about international response, but it will be the people working there day to day in the inter-epidemic period who will make the difference. That capacity has to be built where the challenges are at their greatest. The name has come to me—the Fleming Fund. What the Fleming Fund, the Wellcome Trust and Gates are doing is absolutely critical, but it has to be built in the countries that are most vulnerable, and there has to be willingness of the international community to add to that where necessary.

Q102 Chris Green: Dr Farrar, the Wellcome Trust raised concerns about the reason behind voluntary screening at airports and how it was communicated to the public. How could the communication have been improved?

Dr Farrar: One hopes that policies are made on the basis of strong evidence. I do not believe that in this case screening at airports would have made a difference. I also accept that policies need to take evidence into account but sometimes have to do things where there are other pressures. We saw this during SARS, where there was screening at airports, which I would argue had a greater impact than during Ebola. We also saw it during the pandemic of 2009. I do not think it was necessary during the Ebola outbreaks of 2014-15.

Q103 Chris Green: What do you think prompted the Government to reverse their policy and go against WHO advice?

Dr Farrar: I am not a politician, but sometimes there is a need for politicians to act and be seen to be acting. It was a public statement of how concerned the country was about the outbreak. I do not think that it was epidemiologically and scientifically justified, but I appreciate that there is scientific evidence that politicians then need to take into account when making those policy recommendations.

Q104 Chris Green: It was asserted at the time that it was based on expert advice. Sometimes a profusion of expert advice can cause confusion. How do we avoid this scenario happening again?

Dr Farrar: Just ask one expert.

Q105 Chair: Would that be you, Dr Farrar?

Dr Farrar: No, it would not be me. Airport infection control is not my strong area, but you are absolutely right. If you get 20 scientists in a room you will get a number of different opinions, and it is your job to try to filter those and make the right policy decisions. It comes back to having a standing group that is respected, is used to working together and comes to conclusions in a calmer, more rational way than in a response mode where you are pushing people together at the last minute.

Q106 Chris Green: So you know to which body to ask the question.

Dr Farrar: Yes.

Chair: That brings us to the end of our questions today. Thank you for all your answers, which have been very helpful. I think I am not wrong in saying that this has been the deadliest outbreak of its kind; over 11,000 people died. I think we can be quite proud of the UK's response in many ways. We averted over 56,000 cases with the response. I have a statistic here. In response to the October and November appeal for NHS volunteers, over 1,000 people came forward. We should recognise that bravery, because many people put their lives at risk. I know that each and every witness here today played their part. I would like to put on record the gratitude of all members of the Committee to you for the work you have done, and the work that I know you will keep doing, in trying to avert similar crises in future. I hope that some of the recommendations we make in our report will contribute a little as well. Thank you very much. That brings this session to an end.