Science and Technology Committee

Oral evidence: Zika virus, HC 808

Wednesday 10 February 2016

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Watch the meeting

Members present: Nicola Blackwood (Chair); Victoria Borwick; Chris Green; Dr Tania Mathias; Carol Monaghan; Matt Warman; Valerie Vaz

Questions 1-55

Witnesses: **Dr Alain Kohl,** MRC Programme Leader, University of Glasgow, **Professor Dilys Morgan,** Head, Gastrointestinal, Emerging and Zoonotic Infections Department, Public Health England, **Graeme Tunbridge,** Deputy Director, Emergency Preparedness, Resilience and Response, Department of Health, and **Professor Peter Horby,** Professor of Emerging Infectious Diseases & Global Health, Centre for Tropical Medicine and Global Health, University of Oxford, gave evidence.

Q1 Chair: Can I welcome the panel to this one-off session on the Zika virus, which in essence is a follow-up to our inquiry on science advice in emergencies and lessons learned from the Ebola crisis? Can I start by thanking you for coming at what I know is short notice? To start with a very simple question, given that there has been a lot of rumour in the press and it is quite a fast-moving situation, what do we know from a scientific standpoint about the Zika virus? Why is it such a major problem now given that there have been previous outbreaks? What do you think has caused WHO to declare a state of emergency? Perhaps we could start with you, Professor Horby.

> ***Professor Horby***: I thank everyone for inviting us to assist you in your deliberations. My colleagues will add to this. Zika has been around for quite a long time, since at least the 1940s, but it has become an issue only with its massive expansion since it spread into Polynesia in 2013 and then South America. It was a concern at a minor level. It was not until the birth defects arose and were recognised towards the end of last year that we saw this could be a novel public health threat. We had not anticipated serious birth defects related to a virus infection spread by mosquitos. That was the reason WHO announced the public health emergency. It was not the Zika virus itself but the complications in the babies.

Q2 Chair: There are already 1.5 million reported cases in Brazil with 4,000 cases of microcephaly. As I understand it, the cases of microcephaly being linked to the Zika virus are mainly in Brazil. The projections I am hearing are as many as 4 million cases with potentially 16,000 babies with microcephaly, but I have not seen any conclusive evidence that there is a

direct link. Has a clear scientific link been established yet, or is there a concern and this is a precautionary position being taken? Perhaps Dr Kohl might help us.

Dr Kohl: To add to what Professor Horby said earlier, one of the reasons we do not know much about Zika is that it has never been studied in the past. The ecological situation in sub-Saharan Africa is very different from South America. For example, in the Zika heartlands the mosquito, although called by pretty much the same name, has a different ecology and is genetically a bit different. In reality, we cannot say what Zika did in the past because we have never looked at it. What happens in Brazil may or may not be a novelty, so these studies need to be done.

With regard to the link to microcephaly, at the moment the evidence is circumstantial. The virus has been found in amniotic fluids, as far as I know, and also in miscarried foetuses. Whether that is a cause is very difficult to say. There are various possibilities about how microcephaly could arise. It could be viral; it could be genetic. The mechanisms are very poorly understood, so at the moment we have circumstantial evidence, which, although mounting, is not entirely conclusive.

Q3 Chair: Do you think those projections are reliable, or are they also based on circumstantial evidence at this stage? Perhaps Mr Tunbridge or Professor Morgan could assist.

Professor Morgan: With all estimates, they are very difficult to predict. The estimates are difficult because we do not know what proportion of births are affected by Zika or what defects are caused by it, if indeed they are. The evidence is coming most strongly from Brazil because it has the most cases. Even so, of the 400 confirmed cases of microcephaly it had, Zika was confirmed in only 17 infants. It is difficult to prove virologically that those infants' defects were caused by Zika, but 17 out of 400 is a proportion. You would have to extrapolate that number, not the total number of microcephaly cases because there are other infectious causes of microcephaly.

Q4 Chair: Stepping back from that, it seems to me that the most urgent priority, along with precautionary prevention of mosquito bites, must be scientific research better to understand causes of transmission. The first question is: what do we know about transmission? Secondly, what are we doing to understand it better?

Professor Morgan: I will deal with the first question about what we know about transmission. We know that the main vector is the Aedes aegypti mosquito. That is a very common mosquito found in high densities in urban areas, especially in South America. There is a second less efficient vector called Aedes albopictus. Those are the two vectors of Zika that we know of at present. Almost all the cases currently are mosquito-transmitted. A small number of cases occur between the mother and foetus, which has been shown by isolation of the virus in the foetuses, and two cases of sexual transmission have been reported.

Q5 Chair: Was there not also a case involving a blood transfusion?

Professor Morgan: There was a transfusion-associated case in French Polynesia. That is why we have put in place controls to inform and try to prevent sexual transmission, transmission by blood transfusion and other solid organ transmission.

Q6 Chair: It is fairly straightforward to understand what mosquito transmission means in terms of where those populations of mosquitos are, although I have a question about whether other Aedes mosquitos could possibly become vectors. What could possible sexual and blood transmission mean to other countries that do not have those mosquito populations? Has any research been done into that?

Professor Morgan: I do not know whether we need much research, because if we do not have the competent vectors in the UK, as we do not have currently, there is no risk to the UK population from mosquito-borne infection.

Q7 Chair: But what about sexual transmission?

Professor Morgan: In all the cases there have been only two reports of sexual transmission and three reports of the virus being found in semen, so there is the potential scenario of sexual transmission. That is why we issue guidance to members of the public and healthcare professions about the risks of sexual transmission. We were the first country in the world to do that. People thought we were being over-cautious at the time, but now others have followed in advising precautions in people returning from active transmission areas.

Q8 Chair: Dr Kohl, what research do you think we need to be doing? Do you share Professor Morgan's confidence that the measures in place are sufficient?

Dr Kohl: I largely agree. The risk to the UK public is extremely low. It is mainly a risk resulting from travel to affected countries, bringing viruses back here, and people who are infected travelling back.

As to research that should be done, clearly there needs to be an effort to develop vaccines for the virus. That is one of the research themes that needs to be pushed forward. There is a fair amount of experience in doing this as well, and I think that in the short as well as the long term that would be the best option to push forward.

Professor Horby: Evidence is what we need. We are giving public health advice. I agree with what has been said about the risks to the public in the UK. There is obviously some risk to UK citizens travelling and that is an issue with the upcoming games in South America, but there are so many uncertainties. You have probably realised that there are uncertainties about the association with birth defects and how much we can attribute to the Zika virus. What is the scale of risk of sexual transmission? It is probably very low, but we really do not know. For how long may semen be infectious? How long do we advise people who have come back from Rio not to have unprotected sex? How do we know the attack rate when we do not have good diagnostics? We have to develop vaccines so that we are ready if these risks prove to be substantial. There is a huge amount of stuff to be

done. Although the risk to the UK itself is very small, I think it can play a big role in pushing forward that science because we have a fantastic science base.

Q9 Chair: We are getting a lot of "we don't know" answers, which I understand because Zika has not previously been researched, but there has been a lot of coverage in the media that the Aedes mosquito can be found throughout southern Europe and Africa—everywhere in the world except the UK—and, therefore, basically, nobody should travel anywhere. It would be helpful to get an indication about risk levels in different areas. Various people, including journalists, will be watching this, and a clearer indication on that point would be helpful.

Professor Morgan: We are working very closely with the European Centre for Disease Prevention and Control, which regularly publishes an active Zika transmission list. They are countries reporting active transmission in the past nine months. If you look back at reports, many countries in Africa reported them several decades ago. We know it went through south-east Asia. We have been able to map it as it has moved from Africa going eastwards, ending up in South America. We know the entire route and we would expect occasional cases. So either we do not go anywhere, as you say, or we let the public and health professionals know where active transmission is at the moment. That is not precluding that there may be isolated cases coming back from the Cook Islands or areas that have had cases previously, but where is the greatest risk at the moment? Otherwise, we have to say, "Don't go anywhere." Therefore, at present there is an active list of countries where it is felt there is ongoing, sustained transmission.

Q10 Chair: Is there likely to be active transmission in southern European countries? This is a key question for people who are likely to take their summer holidays there.

Professor Morgan: We know that Aedes aegypti is present in southern European countries. It is in low numbers and tends to be in isolated pockets. There is a theoretical risk that it could be spread by local mosquitos, but, as we have seen with the small controlled dengue outbreaks and Chikungunya outbreaks within Europe, they are quickly responded to and stopped. They had the resources to be able to go in because they do not have the high population densities one sees in South America. It is not easy, but it is easier to be able to control outbreaks if they do occur in southern Europe.

Q11 Chair: I understand that a pre-SAGE meeting took place this week. We have not heard the outcome from that. It would be helpful to know what the conclusions were. Do you believe that SAGE should be convened at this point so that the Government will have the best possible scientific advice to trigger the kind of research that we need at this point—I agree with Professor Horby—to understand Zika better and ensure we are protecting not only the UK public but responding in a correct way? The UK has some of the best immunologists and virologists in the world. Professor Morgan, perhaps you can update us on where we are with SAGE.

Professor Morgan: Do you want to do the background to SAGE and I can deal with the findings?

Graeme Tunbridge: As to pre-SAGE, it met last week and was co-chaired by Mark Walport and Chris Whitty, who is the new Department of Health's chief scientific adviser. It brought together scientists with the relevant expertise to understand the evidence base and current science, but with a focus on the risks to the UK. Therefore, it was understanding how the message from Government should be appropriately framed.

In terms of convening a SAGE, Cobra has not been activated at this stage. SAGE provides advice to Cobra, so we are not yet in that space. While the risks to the UK remain extremely low, it is unlikely that Ministers will want to call Cobra, but obviously that is a decision for Ministers to take. We are showing by calling a pre-SAGE that the Department of Health and, indeed, the Government Office for Science are working very closely together at this early stage to pull together the right scientific advice. We have had one. I imagine there will be another pre-SAGE in the next couple of weeks to start to think about the more international research questions. In addition, this afternoon Sir Mark Walport is meeting all the research councils and other funders to look at what we are doing across the board to try to pull together a co-ordinated picture of the funding that we should be putting out.

Q12 Dr Mathias: Professor Horby and Dr Kohl, can you tell us how the virus is diagnosed and how specific and sensitive that test is, in your opinion?

Dr Kohl: At the moment, a variety of assays is being used in the field. They can be based on PCR. They are ELISA-type assays where antibodies are being used. PCR is a relatively sensitive method and a good method if the patients are viremic, which means they still have virus genetic material in the blood. ELISA is an indirect test of infection having taken place. One of the issues with current diagnostic methods such as ELISA is essentially specificity. The Zika virus is closely related to the yellow fever virus and dengue virus, all of which are present in Brazil but also parts of Africa, and that complicates the issue a little bit. There is a need for a number of studies or surveys that we may want to carry out in future to develop very specific type diagnostics. There is definitely a lot of room for improvement in this area.

Professor Horby: That is a great question, because what we need is underpinning science. There are lots of studies we can do to try to validate and see the scan of the association between Zika virus infection and congenital abnormalities, or even Guillain-Barré syndrome, but we cannot do those if we cannot diagnose the infection. As we have heard, the serology, which is probably one of the most important tools, is very difficult because of cross-reaction. One of the priorities has to be underpinning science that will allow the other evidence to be generated.

Q13 Dr Mathias: Are surveillance measures dependent on these diagnostic tests? Therefore, is there a problem with surveillance?

Professor Horby: Sero-epidemiology, which is looking at infection rates based on antibodies in the blood, is a critical tool for risk assessment—we saw that in influenza—because you can then look at the actual attack rate, given that a lot of the infections are sub-clinical or asymptomatic. What is the likelihood during the next season that there are enough susceptible people for continued transmission? For that you need two things.

Q14 Dr Mathias: Specificity.

Professor Horby: You need the reagents to do the assays and standardised sero-epidemiology protocols. An important issue, which we also saw in Ebola, is trying to standardise the scientific approach.

Dr Kohl: To give one example why in practical terms that would be important, if we cannot follow up mothers who have given birth to children with microcephaly and assess whether they have been exposed to the Zika virus, we will never be able properly to establish a link from that site. That is one of the many reasons it is important to develop such tools that need to be very reliable.

Q15 Dr Mathias: Would you say that the PCR test is the one that should be developed?

Dr Kohl: It depends entirely on the circumstances. A PCR test can be done if somebody presents in an acute viremic condition. If acute virogenetic material can be detected, a PCR test can work. If it is later and the virus has been cleared, for example, PCR is no longer useful.

Q16 Dr Mathias: Do you know what surveillance measures are already in place in Latin America and the Caribbean?

Professor Morgan: We are relying on what has been reported to WHO through the international health regulations. If a country has cases, it reports them through the IHR system to WHO, which then distributes that information.

Q17 Dr Mathias: You are saying it is case reporting rather than active surveillance.

Professor Morgan: It is case reporting. Active surveillance is difficult. What are you looking for? Are you looking for people with fever and rash? We have just seen Chikungunya go through the Caribbean and South America producing very similar symptoms, as does dengue, so we need a good serological test to be able to differentiate between various infections.

Q18 Dr Mathias: Therefore, there is not really surveillance scientifically.

Professor Morgan: There is little active surveillance. Obviously, much more is now happening in Brazil as the research community is being mustered to help the research in that country. There are lots of active researchers in Brazil who are being supported. We are learning more about the causes of microcephaly and following microcephaly, but there are so many. It is a question of making sense of the numbers they have and what particular aspect you look at.

Q19 Dr Mathias: Would I be correct in saying that Public Health England does not have surveillance data as case reports?

Professor Morgan: We would not have it for international countries, obviously, but we have very active horizon scanning and risk assessment work across government. We all talk to each other, so we know what is happening in the countries as they are reporting, and that influences the travel advice and public health advice we give through the travel industry, on our website and to healthcare professionals. We do horizon scanning and communicate through government the risks and where transmission is now occurring. That will feed into the activities we do.

Q20 Dr Mathias: We do not have the data we want at the moment.

Professor Morgan: We assume we have the tips of the icebergs.

Q21 Carol Monaghan: Could I ask about vaccine development? As I understand it, at the moment there is no vaccine. Lots of people are working on vaccines. Mr Tunbridge, what are the Government doing to fast-track vaccine development in a similar way to what was done during the Ebola outbreak?

Graeme Tunbridge: I will start and perhaps Alain can follow on given his interest in this area. The Government have already funded £400,000 to Dr Kohl and colleagues at the University of Glasgow through the Newton Fund on vaccine research. Furthermore, we are going to use the Ross Fund and the UK vaccines network within that fund, and there will be a call launched at the end of this month for more research on Zika with a particular focus on vaccines. We are in a very different place from Ebola. With Ebola we already had vaccines that had been tested in animals. Now we are way further back. Perhaps Alain could comment on the science part.

Dr Kohl: It is correct to say that with Ebola the science was much more advanced. In this case we have to start at the beginning. It requires basic studies of the virus that are very fundamental. Those have been in place for a number of similar viruses for quite some time. With Zika we are starting at zero. From previous experience, we have a number of good ideas of how we should approach this. We and colleagues have had discussions on this. As Graeme said, part of the money from the Newton Fund given to the University of Glasgow also deals with approaches to vaccine designs, and we have spoken to colleagues in other places on this. The UK vaccine research initiative is the one place that needs to take the lead in such a situation. This cannot be solved by one institute; it requires a number of groups and institutes to come together to work on it. A number of discussions are already happening. I think this could be spread out a bit further. From a purely scientific point of view, without wanting to bore people too much with details, a number of approaches can be taken to tackle a virus such as Zika.

Q22 Carol Monaghan: President Obama has just pledged $1.8 billion to tackle Zika. Is £400,000 going to be enough to make a significant contribution?

Professor Horby: Some scientists, not UK scientists but Brazilian and South American ones, are very frustrated. One of them, who contacted me recently, was fed up being asked by journalists when a vaccine would be ready, because he has been worried about this since September and still does not have any funding. His statement was, "What I tell them

is that it will cost less than a world cup stadium and may take even less time to finish." We are talking about reasonable-size investments, but, when you set it against such things as world cup stadiums, it is small. We are talking about a global public health problem, so significant investment is needed. Obama's $1.8 billion is a fantastic investment. We are seeing investment in UK science and what we can bring to the table, but I still think it could be quicker. We were first alerted to this problem at the end of last year. The MRC has called for £1 million now, but that is still several months down the track and we are approaching the new transmission season in South America. We need to have stuff in place now.

Q23 Carol Monaghan: Are there short-term solutions in place in possibly tackling the mosquitos themselves or information being given to people in the infected areas?

Professor Horby: There are certainly other public health measures like that, but on the research side what we need is faster turnover. There are existing systems in place. The UK is part of a consortium looking at dengue transmission in South America. That is set up and could immediately switch over to look at Zika, but it needs immediate bridging funds. We do not want to wait four to six months for that; it needs to be mobilised in four to six weeks.

Dr Kohl: The funding available at present will be very useful for taking the first steps, but to take a vaccine through various safety procedures—trials and so on—is a completely different dimension. That is where a different effort comes in. What we can develop in Glasgow and colleagues can develop elsewhere is usually something that is testable, but from there to having a vaccine that can be used in the field is still a long step.

As Professor Horby said, the mosquito transmission season, when we expect infections to occur again, will start in April in Brazil. That does not leave a lot of time. It is pretty inconceivable that we could have a vaccine in place by then, but, thinking ahead to the next year, that still does not leave a huge amount of time. Some of these efforts need to be mobilised very quickly to allow us to process any vaccines we develop to a clinical level in a reasonably fast manner.

Q24 Carol Monaghan: You are saying pretty much that we cannot get the vaccine in time for other infection this year. What should the people in Brazil be doing at the moment?

Dr Kohl: Brazil has had a long-standing history of mosquito-borne infections, be it dengue or yellow fever. Clearly, the first thing to do is to implement preventive measures, such as mosquito eradication campaigns and personal protection against mosquitos, but that is not so trivial. We are talking about a very large geographical area. The ecology is different depending on where you go. Social issues can also play into this—for example, how well an area is maintained. Are breeding sites being dealt with? Of course, transmission especially by aegypti mosquitos happens inside the house or locations where people are active. We know from studies in South America that, for example, the dengue virus in the Amazon is spread by people visiting one another's houses. Somebody who is unwell goes to visit a neighbour or friend and gets bitten by a local mosquito in that house or residence. That is how the virus is spread within communities. Taking that as an example, very

similar ideas need to be taken forward for Zika as well. Eradication is one thing, and personal protection is a very important issue too.

Professor Morgan: America is in a very different place from us. Albopictus mosquitos are present and established in almost all eastern European states, and Aedes aegypti are established in the southern states. They are in a very different place, in that they have the competent vectors and they are established there. They are very attuned to vector-borne disease having had the West Nile problem over the past 14 years. They have a long history of vector-borne disease. They have susceptible populations and the vectors, so they are becoming increasingly concerned.

Q25 Carol Monaghan: One issue that came up in the Ebola inquiry was the lack of co-ordination between all the different groups trying to develop vaccines. Have you seen a similar picture with Zika? Who is taking an overview to make sure that people are working in a more co-ordinated way?

Graeme Tunbridge: From the Government's perspective, we are acutely aware of that. I scribbled down "co-ordination" a couple of times in my notes, because early on we are having those conversations, particularly urging this on WHO. My understanding is that in the next couple of weeks it will be coming out with a written strategy that will try to bring a degree of co-ordination to where funding should go. Equally, we are working closely with the EU. There are likely to be funds coming through the EU and multilateral relations. We have very good relationships with the CDC in America, so we are trying to bring that to bear at an early stage.

Professor Horby: There are a couple of other non-governmental initiatives. There is the International Severe Acute Respiratory and Emerging Infection Consortium. That is a global consortium of clinical research networks hosted at Oxford University. That is supporting WHO with weekly teleconferences around the Zika virus, and it has been doing that since November. Part of that is to bring together researchers, try to define a research agenda and link up collaborators to work together. That is at a global scale. There is another initiative called GloPID-R—not an attractive acronym—which is a consortium of funders that has just been set up under the leadership of the European Commission. That is also looking at the research agenda and how research funders should support scientists to do the research quickly and in a co-ordinated way.

Dr Kohl: A number of efforts are taking place pretty much at grassroots level as well. Government, especially the UK vaccine initiative, needs to play a co-ordinating role in all of this. There are efforts within the virology community at grassroots level to try to co-ordinate this as well. A number of people are getting involved in this. I do not want to go into the details. To avoid a situation where there are too many things going on at the same time that duplicate each other, there are discussions between various senior virologists.

Q26 Chair: One particular issue that arose in our inquiry into Ebola was that there had been a delay in running the clinical trials and field-testing of Ebola vaccines because of concerns about ethics and differences of opinion. That led to concerns that there had not been effective testing because it had been so far down the line in the outbreak. In this case you would be

potentially testing the vaccine on pregnant women, which introduces a whole new ethical concern. This is down the line, but, if we are thinking about trying to save time and accelerate any kind of vaccine trials, do you think it would be sensible to think about that now and put in place protocols and processes?

Professor Horby: I was involved in some of the ethical dilemmas around Ebola. There are different ethical dilemmas here that go beyond the ones you mentioned. If we are doing surveillance studies to look at the Zika virus in pregnancy, what do we recommend to people in those studies who we find are Zika virus positive during pregnancy? What do we offer them? What is our duty of care? If we are looking at potential therapeutics that we might offer to pregnant women to prevent the foetus becoming infected, how do we trial those safely? The same goes for vaccines. The response based on the Ebola experience has been quicker. Yesterday, the Nuffield Council on Bioethics released a short statement about ethical considerations for pregnancy and the Zika virus. I know that the Global Forum on Bioethics in Research is also looking into this, so there is a process under way. There are no ethical solutions, but ethical discussions can happen earlier. The other part of that equation is to look at protocols that can be implemented and trying to standardise those. Groups have been putting up protocols and getting them peer reviewed so that we can try to standardise the scientific approach across those different groups.

Q27 Chair: So you think we are going to be ahead of it this time.

Professor Horby: It is difficult to predict that. The Zika virus has been a problem since 2013, but, if we bring forward the timeline and say it is only since November that we have thought of the issue with pregnancy, we are mobilising faster this time.

Q28 Chair: Given the stage of development of a vaccine, the Committee would not like us to get to the stage of field-testing a vaccine without a protocol being in place for how that will happen. The debate then has to take place. It would be better for that debate to happen now. Is that happening?

Professor Horby: It is starting much earlier; groups are already talking about the ethics and writing about it.

Q29 Chair: Which would be the lead organisation? Would it be WHO or the Council on Bioethics?

Professor Horby: WHO has the mandate to lead on global health issues, and it certainly has a convening and co-ordinating role, but, at the end of the day, it is up to the national authorities and their ethics committees to decide what kinds of studies they approve. Therefore, it ends up being a negotiation. The important thing happening now that did not happen in Ebola is a much earlier collaborative and co-ordinating approach.

Q30 Matt Warman: You have answered all the questions I was going to raise, but, essentially, to summarise what you have said, although we are ahead of where we were when it came to tackling Ebola, we still do not know whether there is a link between Zika and

microcephaly. We have not done a huge amount of research and still have an awful lot of questions to answer. With that in mind, obviously, the public are incredibly uncertain about what they should do and when they should take precautionary measures. We cannot just say, "Don't go anywhere." With that in mind, why is the advice of Public Health England, as I understand it, "Go and see your GP if you are worried"?

Professor Morgan: At the pre-SAGE meeting the evidence was discussed exhaustively and it was concluded that the evidence was sufficient for public health action. Indeed, that is what we have been doing since early on in this outbreak, from the start of the rash and fever that started back in March and April, to when it was diagnosed as Zika and the birth defects and their potential associations were reported. We have been issuing guidance and information at every stage. It is a very difficult public health message to give, because we are not really sure what the risk is but the consequences could be absolutely awful for that woman. It is always a very difficult message to give, so we have been cautious.

Q31 Matt Warman: But you have not given much advice to GPs in terms of what to say.

Professor Morgan: We have issued guidance to GPs. We have worked with the Royal College of Obstetrics and Gynaecology to produce guidance on what to do with women who have been travelling to these areas and have come back. That is one of the links on both our websites. The algorithm of how to deal with women when they come back is on the PHE website. We have been linking in with the medical professions—the Royal College of Nursing and many professional groups—on this issue, and a CAS went out to all medical staff.

Q32 Matt Warman: But ultimately it is about reassurance.

Professor Morgan: I do not think it is about reassurance. I do not think we are in a position to offer reassurance; I do not think that is our job.

Q33 Matt Warman: It is explaining how little we know in that sense.

Professor Morgan: We are explaining what we do know and how best people can be protected, reassuring them about the risk. There is no risk to the UK population; it is a risk to travellers. Of those travellers, your risk of acquiring Zika depends on where you are travelling. You are likely to get a very mild illness, if you notice anything at all, but, if you are pregnant, you may be at risk of an abnormal foetus, which is obviously devastating. We have been trying to communicate those risks as we have gone through the various stages and as the evidence has been accumulating. We have been working with the medical profession to keep it informed as well so that, when women do want to discuss it with their healthcare providers, they are in a better position to advise them. We also have very detailed questions and answers on NHS Choices, so women can also be very well informed before they go to their healthcare providers.

Q34 Matt Warman: For instance, if somebody went to Brazil in the past few months, came back and said to their doctor, "What's the risk?", the answer would still be, "We don't really

know." I am not sure how the public health advice in an individual consultation is going to help.

Professor Morgan: We are dealing with these cases all the time. It depends very much on where the woman has been and what she has done. Has she gone to an area of high transmission where lots of cases have been reported?

Q35 Matt Warman: But wherever she has been we still do not know what the risk is because we have not done the research.

Professor Morgan: We have not. If they are not reporting cases and have not reported cases, it is slightly more reassuring than if they have been to, say, Recife, which is a major affected area. There are gradations of risk we can give. I do not feel we should be worrying women too much when not every foetus will be affected. We do not know what the proportion is, but we know it is probably low, looking at the numbers. There are various reassurances we can give, but we should not give reassurances without the evidence. I agree there is a lack of evidence, but we are trying to do our best to interpret that for the public good.

Q36 Matt Warman: Is anything going on to track the number of people who are presenting to their GPs with worries about this?

Professor Morgan: There are various surveillance schemes ongoing. We are documenting women who want testing; we are looking at people who are reporting this to their obstetric services; we are currently working with various registry or surveillance systems, looking at abnormalities in pregnancy or adverse outcomes; and we are working with the congenital abnormality register. We are looking for cases in the UK. We are tracking women at least through Public Health England, because that is all centrally logged, with their worries, but we have to get this into proportion. The risk of Zika to the UK population is infinitesimally small compared with all the other things that we are currently facing and dealing with.

Q37 Chris Green: There is a variety of causes of microcephaly and Guillain-Barré syndrome. What evidence is there that the Zika virus actually causes these diseases or conditions?

Professor Horby: There have definitely been cases of foetuses with abnormalities where the virus has been detected in the amniotic fluid and in the child. There has also been evidence of transmission around the time of delivery, as opposed to earlier in the pregnancy. It is clear that the infection can be transmitted to the foetus and the baby. Whether there a causal association between that and microcephaly is less certain, although in some cases it looks like that is probably the case.

The real issue is: what is the scale of that association? We have seen all these microcephaly cases reported. Is that a reporting bias? Have people started looking much harder? There is an indication that that is the case. There is a whole range of other potential causes of microcephaly. Have all those been excluded? That is where we have a

problem. It looks likely that there is an association between Zika virus infection and abnormalities, but it is very hard to quantify that risk at the moment.

Q38 Chris Green: It is a statistical probability as much as anything else perhaps.

Professor Horby: I think most people would be prepared to say that there is a link between Zika virus infection in pregnancy and infection in foetuses and microcephaly. The real question is: what is the scale of that problem? That is critical information for advising travellers and pregnant women about what they should do, particularly about travel, but, if they do become infected, what they should do about the pregnancy. Should they be considering termination? These are real questions and dilemmas people will be facing. Until we can tell them that the risk is very small, small or moderate, it is very hard for them to make a decision.

Q39 Chris Green: There are other causes of or links to microcephaly. For example, there are reports in Latin America of women being urged before 22 weeks of pregnancy to take the Tdap vaccine for tetanus, diphtheria and acellular pertussis. There are reports that make a connection between that vaccine and microcephaly. Is that plausible? Is it realistic that there might be an association between that vaccine and microcephaly?

Professor Morgan: There is a lot of speculation at the moment as to what is causing this and that is one we have heard, but this vaccine is used very widely. Why would it be happening only in a very small part of the world, whereas the vaccine is used worldwide? It has a very good safety record. As to adverse events, it has not been reported anywhere else looking at the records. Everyone wants to explain it and we hear a lot of speculation about possible causes, but I do not think that is a realistic one looking at the safety records.

Q40 Chris Green: This is always one of the concerns with a new disease and virus emerging. There are all kinds of speculation about causes, associations, transmission and what action you take. It has been suggested that the rubella vaccine can help reduce the incidence of microcephaly in babies. Is there evidence to support that?

Professor Morgan: I do not think there is any evidence at all.

Professor Horby: Rubella infection in pregnancy can cause congenital rubella syndrome, which is one of the causes of microcephaly. With rubella vaccination you reduce the risk of rubella in pregnancy. It is a rational comment, but it will not prevent other causes of microcephaly.

Dr Kohl: These viruses are not related. They are related in the wider sense, but they belong to different virus families. It is pretty much inconceivable that a rubella vaccine would offer any protection, if you look at it from a vaccine angle, against the Zika virus, for example.

Q41 Victoria Borwick: To come back to what we are concerned about here, what is the risk of the Zika virus to the UK public? Inevitably, that is the question on everyone's lips.

Professor Morgan: I think the pre-SAGE concluded that it is "close to zero". Obviously, travellers are not in that group, but for the UK population it concluded that it is close to zero without the vector.

Q42 Victoria Borwick: Inevitably, people are concerned that individuals will be arriving and thus infecting them, so it is quite important to have an understanding and be able to explain it and communicate it clearly to people, because inevitably that causes a problem. What is your advice if people have been travelling and think they might have the Zika virus?

Professor Morgan: Currently, we are in a bit of a diagnostic difficulty, as we have explained, because we can diagnose only acute infection. We are issuing guidance that we are currently unable to test if they are over their symptoms and they have disappeared for two weeks. We have a problem with diagnosis. If it is a male, we are issuing guidance about condom use for 28 days after returning from the area. If they have compatible symptoms, or confirmed Zika, and their female partner is at risk of pregnancy, is trying to become pregnant or is pregnant, they should use a condom for six months. It is very cautious, but we feel it is the best advice we can provide at the moment.

Q43 Victoria Borwick: How many travel-associated cases have been diagnosed in the UK so far?

Professor Morgan: We have had seven cases, six associated with the current outbreak in South America, in the past three years.

Q44 Victoria Borwick: Just to make sure, it is six over the past three years.

Professor Morgan: Yes, but four of those are in 2016. It is true that we are seeing cases coming back. We have raised awareness so that people are more aware of the infection, and we are likely to see more cases. We saw exactly the same with Chikungunya when that went through the Caribbean and South America in 2013-14. Upwards of 300 cases of Chikungunya were diagnosed in the UK a year. Therefore, we can expect to see more Zika cases as people become aware of it and get tested for milder disease, and we are currently tracking those cases.

Q45 Victoria Borwick: Once they arrive, report to their GP and are diagnosed, what are we doing about other people with whom they might have come in contact?

Professor Morgan: We are concerned only with their sexual partners. We have so many cases at the moment and we give advice to those people individually. We do not have a situation like that which occurs in other countries. It is people who transport Zika to different countries, not the mosquitos. For example, in other European countries during the active mosquito transmission season, public health measures have to be taken around those people to make sure local mosquitos do not pick up the virus from infected persons and transmit it. Fortunately, we are not in that position here. We do not need to take public health action for the control of mosquitos around cases; we just advise about sexual transmission.

Q46 Victoria Borwick: There is inevitably interest about today's session and it is important that one is able to give people such reassurance as one can while presenting the facts in a clear way.

Professor Morgan: Yes.

Q47 Victoria Borwick: Are you issuing travel advice regarding Zika?

Professor Morgan: We are revising it at every stage.

Graeme Tunbridge: Travel advice is in place. As we have understood more about the spread of Zika and its effects, so the travel advice has been updated. The latest update was in the middle of January when, specifically, the advice to pregnant women was changed to consider avoiding travel.

Q48 Victoria Borwick: Consider avoiding travel.

Graeme Tunbridge: Yes, and they should discuss it with healthcare professionals if they are thinking of doing so.

Q49 Chair: Mention has been made of the Rio Olympics and the expectation of a certain amount of tourist travel. What plans are in place to ensure that British Olympians and various spectators will not be at unnecessary risk from the Zika virus?

Graeme Tunbridge: From the Government's perspective, largely through the Foreign and Commonwealth Office and the DCMS, they have been discussing this with both the British Olympic Association and British Paralympic Association so that they understand the travel advice and what it means for Olympians. The real concern is around pregnant women travelling, so the advice is focusing on that. Currently, the advice being given to athletes mirrors the public health advice that is going out to the broader population. Colleagues in the FCO who have liaised with colleagues in Brazil have been at pains to point out that it is not mosquito season when the Olympics are on, so the risk is that much lower. Equally, Brazil is doing an awful lot in terms of control measures, so they are managing the risk locally as well.

Q50 Chair: There was some controversy around the evidence base for the introduction of screening for travellers coming back from Sierra Leone during the Ebola outbreak. Are there any plans at the moment to introduce screening for travellers coming back who might be at risk of the Zika virus?

Professor Morgan: Ebola is a very, very different disease. I realise you have the report. We should not confuse the two. With Ebola there is person-to-person transmission. There is a very small risk of sexual transmission, but otherwise, apart from mother to child, there is no person-to-person transmission and no risk.

Q51 Chair: There are no plans for that. I am just checking.

Professor Morgan: There are no plans at present.

Q52 Chair: I know you have put in place the blood transmission measures for those receiving blood from the NHS. Are there any plans for screening health professionals? I know they already have to have screening for hepatitis C and so on.

Professor Morgan: I am not sure what benefit that would have, because they are not going to transmit it to their patients anyway. There would be no benefit in screening healthcare workers.

Q53 Chair: Are there any plans for NHS or PHE volunteering above and beyond the Newton Fund support, which has already been mentioned?

Professor Morgan: We are always able to respond to these requests, but they are normally from the Government. Brazil has a well-developed public health system and has expertise. There would be an issue about Portuguese speakers. We are always able to respond to WHO or country requests for assistance, but it has not happened in this case yet.

Q54 Chair: Professor Horby or Dr Kohl, is there any final message regarding research that you would like to give to Public Health England before we close the session, or any aspects of the response to this particular outbreak?

Professor Horby: Not directly to PHE because I think it understands the importance of research. Generally, as we have seen in the response to any emerging infection, the evidence base is always very weak at the start. All the public health and clinical care decisions can have big implications in terms of the costs and concerns of the public, so we always need a very strong evidence base as quickly as possible. The best evidence base comes from rigorous scientific methodology. Science needs to be embedded in the public health and clinical response, because in that way we will know what we are dealing with much quicker. I think small, marginal gains at the very start of an epidemic in the information we have can make big differences in the quality of information and the decision making. Very rapid and even modest investment in getting high quality scientific data at the early stage of an epidemic can have big pay-offs down the line.

Dr Kohl: I completely agree with that. I do not think I would have said it any better, so I will not add anything.

Q55 Chair: Professor Morgan, obviously pregnant women are at risk not just from Zika but also dengue, malaria and Chikungunya. What is your final advice to women who are considering travelling to these various countries? Would you like to send out a public health message?

Professor Morgan: There is advice out there. They should look at the NaTHNaC travel advice website, which has been updated as new information comes out of these countries. If they are concerned, they should take full precautions; and they should discuss with their

healthcare providers any anxieties. Everyone's risk appetite varies, so it is a decision for the woman to make. We have advised they consider postponing or delaying their visit, but it is an individual decision, in consultation with their healthcare provider, midwife or other healthcare professional. If they are going, scrupulous mosquito-avoidance activities should be undertaken to avoid exposure to mosquitos. I realise it is not always practical with many of the holidays people go on, but these mosquitos are day biters. We need to emphasise it is not a question of covering up at night, which is what we normally expect for malaria. We have to make those who are travelling aware of scrupulous mosquito repellent application, even during the day when these mosquitos are active.

Chair: Can I thank you all for the time you have taken today to come in at what I know was very short notice? The advice and information you have given us has been very helpful to our understanding, and we are grateful for that. That brings this session to a close.