HOUSE OF LORDS

Select Committee on Science and Technology

Corrected oral evidence: The science of Covid-19

Tuesday 15 September 2020

11 am

Watch the meeting

Members present: Lord Patel (The Chair); Baroness Blackwood of North Oxford; Lord Borwick; Lord Browne of Ladyton; Baroness Hilton of Eggardon; Lord Hollick; Lord Kakkar; Lord Mair; Baroness Manningham-Buller; Viscount Ridley; Baroness Rock; Baroness Sheehan, Baroness Walmsley; Lord Winston (co-opted); Baroness Young of Old Scone.

Evidence Session No. 18 Virtual Proceeding Questions 191 - 201

Witnesses

Professor Donal O'Donoghue, Registrar of the Royal College of Physicians, Consultant Renal Physician at Salford Royal Hospital, and Professor of Renal Medicine at the University of Manchester; **Professor Sebastian Brandner**, Professor of Neuropathology, Department of Neurodegenerative Disease, UCL Queen Square Institute of Neurology, Honorary Consultant Neuropathologist, University College London Hospitals NHS Foundation Trust, and Council member for London region, Royal College of Pathologists; **Professor Tom Solomon**, Chair of Neurology, and Director of the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool.

Examination of witnesses

Professor Donal O'Donoghue, Professor Sebastian Brandner and Professor Tom Solomon.

Q191 **The Chair:** Welcome to our witnesses for the next session. May I ask Professor O'Donoghue to go first?

Professor Donal O'Donoghue: Thank you very much for the invitation to join you today. I am a kidney doctor in Salford and the registrar at the Royal College of Physicians. I am chair of Kidney Care UK, the patient charity, and I chair the ISN advocacy group. I am the immediate past president of the Renal Association, and I was the national clinical director for Kidney Care UK from 2007 to 2013.

There are four points that I want to make. The first is that kidney disease is common and harmful and very much related to Covid, but it is silent. The second, where I will give you the most information, is about the impact of acute kidney injury or acute renal failure in Covid.

People with kidney disease are also affected by the delays to the restoration of normal services and the disruption of other services. There was a reduction of 85% or more in referrals for a period of three months, and disruption almost completely to transplantation for a period. It is good to see that is back up and running, but live donation, which carries additional risks for live donors and requires greater infection prevention control measures, is still slow to get started. These days half of all our donors are live donors. That is a major issue. A large part of the kidney disease population is shielding because of the high risks to them of Covid and the consequences of that as they play out. Obviously, that is similar for other patient groups.

Given the conversations just now, an important point is that people with kidney disease are often excluded from clinical trials. For many years, the vast body of research in cardiovascular studies excluded people with kidney disease. I think that is starting to improve, but I was disappointed to read last week that 45% of all intervention trials exclude people with kidney disease. There is no good reason for that. It is almost a question of ignorance.

Kidney disease affects around 15% of the adult population in the UK, according to the Health Survey for England. It is associated with age and with BAME groups; non-Europeans have very high rates of kidney disease, sometimes up to six times the rate in the Caucasian population. The global burden of disease is about 850 million people. By 2040, chronic kidney disease will be the fifth most common cause of years of life lost.

Acute kidney injury is often thought of as a condition where the kidney shuts down and repairs and recovers. That is what I was taught at medical school and I think it was still taught in that vein up to a few years ago. However, 16% of all people admitted for non-elective admissions in normal times develop acute kidney injury in hospital. That is about half a million people. We know that there is a similar number in

the community who do not get admitted to hospital. Twelve per cent of all people who develop acute kidney injury requiring dialysis end up on renal replacement therapy within the next five years. That is the background.

Kidney disease dwarfs other risk factors for severe outcomes, hospitalisation and death, apart from age. In all the various analyses, and the elegant work that Julia Hippisley-Cox is doing, that is the disease factor that comes out enormously; similarly with the MRC stratification study that was reported over the weekend. Apart from respiratory disease, it dwarfs other organ systems in impact.

There is some data from King's that is reflected in other published datasets. At King's, of around 1,000 patients, 58% had pre-existing kidney disease; 40% developed acute kidney injury, and the mortality in those was 42%. Studies from New York show 50% mortality in the acute kidney injury group versus 8% in those who do not get acute kidney injury. It is quite staggering.

In long Covid, what is the recovery? In the King's data, 36% of those who survived their acute kidney injury did not return to their previous level of kidney function. What will happen to those patients over time is a key research question and a key service delivery question.

The Chair: Thank you very much indeed.

Professor Sebastian Brandner: Good morning. I am professor of neuropathology at University College London and I am an honorary consultant neuropathologist at the National Hospital, which is part of University College London Hospitals. I am an elected member for the London region on the Council of the Royal College of Pathologists.

I would like to give you an overview of what happens in the central nervous system of patients who suffer from or die of Covid-19. The central nervous system, the brain and spinal cord, is involved in a proportion of patients with Covid-19. To give you an idea of the frequencies, I shall cite a study from New York University of over 3,200 Covid-19 patients who were all admitted to hospital. Of those, 450—14%—had brain imaging during their in-patient stay, and, of all the patients with imaging, 38 had some form of stroke in the brain, which is 1.2% of the 3,200 admitted to hospital. It is not a very large number. A fatal outcome was seen in approximately half of those admitted; one in 150 admitted to hospital had a fatal outcome related to CNS complications. Other studies that have looked at similar numbers and similar frequencies have reported 1.5% to 2.5% of strokes.

I would like to explain a bit more about what happens in the brain. First, as pathologists, in this context we have seen very few of those patient complications. Most of those with complications survived, fortunately. The disadvantage or downside is limited availability of post-mortem exams of the brain. During the entire Covid-19 outbreak, we had only just over a dozen, perhaps two dozen, post-mortems with available brains for full analysis. There is currently no published large post-mortem study with

more than one or two dozen brain autopsies. Those that have been published all show recurring findings in the central nervous system.

The complications that we found in Covid-19 all occur in the context of systemic disease. We have heard a lot about systemic diseases. The complications are acute ischemic stroke, which is lack of oxygen due to a perfusion problem in the brain; inflammation of the meninges of the brain and spinal cord—meningoencephalitis; and microbleeds, as well as a diffuse leukoencephalopathy, which is a disease of the brain white matter.

Let us start with the common ones. In the previous session, we heard a lot about the fact that disturbances of blood clotting in Covid-19 can cause varied amounts and sizes of blood clots to enter the brain circulation. A blood clot entering the brain circulation causes a stroke, an infarct. Depending on the size of the clot, it can be a very small infarct, a microinfarct that can be seen only under the microscope or on tissue exam, up to very large regional or global strokes, which are usually a cause of death. We have seen such strokes of small and very large sizes in the brain. They can be associated with haemorrhages—bleeds of varying sizes—which, again, are caused and aggravated by the systemic clotting problems that can be aggravated by certain treatments. In the previous session, we heard something about ECMO, which is done for oxygenation of the blood, but it can also aggravate clotting problems.

The other complications that cause disturbances of the brain are lung complications. All the respiratory problems in patients with Covid-19 can potentially cause a lack of oxygen in the circulation, including the brain. That is a condition called hypoxia. Hypoxia in the brain causes the death of nerve cells, often in a very diffuse distribution.

Another complication in Covid-19 is brain inflammation, which is thought generally to occur in the context of systemic disease. Brain inflammation is a common manifestation in multiorgan failure—kidney, liver, heart—all the things we heard about previously, regardless of the cause. Brain inflammation is not necessarily specific to Covid, but a term that has often been brought into this context is the cytokine storm, which is a massive and probably inappropriate activation of immune response.

We think that some of the unusual findings in strokes in the brain are related to such a cytokine storm. Among the brains that we examined, we found that some of the areas in the strokes showed very severe and unusual inflammation, so it is thought that that immune response can trigger some of the inflammation in those strokes. We have also seen some much milder inflammation in the meninges—the membranes covering the brain—and in the brain itself. That has always correlated well with the imaging findings.

What is currently not very well established is the role of the virus itself in causing direct effects. It was thought the virus might be entering the brain via blood vessels, or directly by docking on to receptors on the surface of the brain cells, but it is now thought that that probably has no major role and, instead, the CNS complications in the brain and spinal

cord and the meninges are secondary to systemic illness rather than direct viral brain invasion.

In conclusion, there is no single cause of brain involvement but a range of systemic conditions that cause brain complications. To sum it up, the most important complications of Covid in the brain are strokes, hypoxia and inflammation.

The Chair: Thank you very much indeed.

Professor Tom Solomon: I am the director of the National Institute for Health Research Health Protection Research Unit in Emerging and Zoonotic Infections. I am also professor of neurology at the University of Liverpool and the Walton Centre NHS Foundation Trust.

I head a large research team that has been working on emerging infections for many years, particularly those that impact on the brain. Our emerging infections research on Covid-19 started in mid-January, before it was even called Covid-19. We supported the setting up of the large ISARIC clinical characterisation protocol, which is the largest study in the world looking at hospitalised patients. It has studied more than 70,000 and has given us much important information on risk factors for particular patients and what their outcomes might be.

As we heard from earlier witnesses, we initially thought it was a respiratory disease, but it has become clear that it affects all parts of the body, including the brain, as we have just heard from Professor Brandner from a pathological viewpoint. I will provide more of a clinical perspective. In particular, I am going to talk about three aspects that have important long-term health implications and have important questions for this committee to think about.

First, Covid-19 causes neurological diseases such as stroke, as we have been hearing; also delirium, which is confusion in patients in hospital. One cause of that is encephalitis, which is inflammation of the brain. Sometimes that is directly due to the virus. More often, it seems that it is an indirect effect of the body's overall response to the infection.

Stroke is especially common. We have led some studies from Liverpool across the UK and global studies looking at comparative data, and it is clear that stroke is the most important neurological problem that we see. We need to think about how we can prevent patients with Covid-19 developing strokes, and, for those who have had a stroke, we need to make sure that they do not have subsequent strokes. That is often a risk factor after somebody has had one stroke.

The other important thing for all patients with any neurological complication of Covid 19 is rehabilitation of those who have had long-term illness. There is some fantastic work done by the NHS in conjunction with charities such as the Stroke Association and the Encephalitis Society, but more work is needed in that area. Rehabilitation will be a big issue. It already is. The Government announced some Seacole rehabilitation centres a few months ago, which will be specifically for Covid-19 patients, but in the last few days there has been uncertainty about how much

actual cash there will be to support capital build of new centres and refurbishment of centres. That is important and we need to keep an eye on it.

The second group of patients are those who have had Covid-19 infection that has caused mental illness, which can range from frank psychotic episodes in hospital to those who suffer from anxiety and depression after they recover. We have heard quite a bit today about long Covid; it includes not just physical problems such as breathlessness, but mental health problems—anxiety and depression—and potentially neurological problems, such as muscle pain and fatigue.

GPs are calling for patients to be assessed. They are now seeing lots of patients with those problems. It is the current epidemic in primary care. They are seeing lots of patients who are left with problems from Covid. They need to be able to refer them to get help and understanding of what is going on. For many years in Liverpool, we have had a combined neurological infectious disease clinical service that would look at such patients, but across the country there is not much service provision for those kinds of patient. In the UK, we have one neurologist for every 40,000 patients; across Europe, there is one neurologist for every 15,000 patients.

The third group is people who were not infected with Covid-19 at all but have still been seriously affected by the pandemic as regards mental ill-health. Again, it is probably an even bigger number than those who were actually infected with the virus. Mental health services, as we know, have had chronic underfunding. Potentially, there is now a chance to review the support that we give people with mental health problems, from children all the way through to the elderly.

The Chair: Thank you very much indeed. That was extremely helpful. We will start with my colleagues now. If we keep questions as brief as possible and answers to the point, we might get through a lot of the questions that no doubt we will have.

Q192 **Baroness Manningham-Buller:** Thank you to our witnesses. That was a very interesting session. I have a general question that has two parts. We have heard of a very wide range of symptoms in long-term Covid. How much of that is explicable by what we already understand of the disease? How much is still not very well understood and is where, for example, you might like to focus research if the resources were available? Where are the biggest gaps on which you would like some answers and where money could be focused if it was available?

Professor Tom Solomon: That is a good point. One thing that has characterised the UK compared with the rest of world is that the research response has been fantastic. We have had incredible support from the Government and other funders to do research. This is why we lead the world with programmes such as the ISARIC programme and PHOSP-COVID, which we heard about earlier—the treatment trials that are answering important questions about steroids. I have no doubt that our vaccine work will also be world leading.

There are some surprising gaps, and one of them, interestingly, is on neurological disease. We do not yet have any specific large, funded programmes in that area, although I must declare an interest: we are currently in the middle of an application. You asked which symptoms are explicable and which are not understood. With some of the neurological problems where we do not find that the virus is in the central nervous system, we need to find out how the infection triggered some of those problems. That is an area we still need to focus on.

Professor Donal O'Donoghue: People who have been shielding are a particular group, and the impact on those individuals is well worth studying. The majority of patients who get Covid have a range of comorbidities, as we have heard from a number of people today. Any research needs to be comprehensive as regards the populations it looks at, and not exclude people because they have a range of disease processes that make it more challenging to investigate issues of fatigue, psychological anxiety or depression. It is important that we do not exclude people from our research studies.

Professor Sebastian Brandner: From our perspective, it is important to understand how the disease affects the brain. To do that, we need material to study the effects on the brain. There have been amazing studies on clinical radiological correlation, which have provided fantastic insight into the disease pathogenesis and how the systemic effects of Covid-19 can affect the central nervous system. Very often, that is where it ends.

The gap that the pathological community sees is that there was a fantastic and enthusiastic response from pathologists, but very often not enough patients who died of Covid-19-related illnesses, with or without central nervous system involvement, have undergone autopsy, despite the availability of mortuaries. There was often reluctance on the part of NHS hospitals—understandably, because they had to divert resources to the treatment and management of those patients.

The 1918 pandemic, which had a remarkable lack of post-mortem material to study, has repeated itself. There are still opportunities, but it is important to address the issue and to facilitate that sort of research, particularly now when we are in a more balanced position, and resources have been readjusted and mortuaries are not overwhelmed with people who are dying from any type of complications. It is really important to understand the pathogenesis on the central nervous system.

Baroness Manningham-Buller: Thank you very much.

Q193 **Viscount Ridley:** I realise that Professor Brandner and Professor Solomon are neurologists and not psychologists, and we have already touched on fatigue, anxiety, depression and other mental health effects as a result of Covid-19. Can you speculate about whether those are direct effects of the disease, either through fatigue or direct physiological consequences, or whether they are mostly the indirect effects of lockdown? Are they confined to those who have been in hospital, or are we also seeing an effect in the community? When will we be able to say

whether there has been an impact on the suicide statistics?

Professor Tom Solomon: That is a really important but unanswered question. We do not know the extent to which the big mental health situation—perhaps epidemic is too dramatic a word, but we are certainly seeing a lot of mental illness—is directly related to the virus. The fact that we see quite a lot in people who clearly have not been infected by the virus perhaps indicates that a certain amount is because of the effects of the pandemic on people's normal activities: the effect of lockdown and not being able to interact with others, difficulties with exercise, et cetera. Some of it is that, but there is a critical question about whether the virus either directly in the body or indirectly, through causing things such as cytokine cascades and other aspects, is leading to some of the mental health issues. Those are the kinds of questions that we want to address.

Professor Sebastian Brandner: That was very well put. I cannot add anything. For the record, I am not a neurologist but a neuropathologist, which is even further distant from psychology.

The Chair: I was taught that pathologists always had the last word, and the answer.

Viscount Ridley: I apologise for calling Professor Brandner a neurologist and not a neuropathologist.

Q194 **Baroness Rock:** I have two questions. One is on mental health services. What data is being used to capture the mental health services provisions that are needed? Perhaps Professor Solomon could give a little more detail on that. Taking the data question a bit further, what barriers do you find in gathering reliable data on the wider effects of Covid?

Professor Tom Solomon: Again, I should preface my answer; I am not a psychiatrist or a psychologist, I am a neurologist. I do not want to duck the question, so I will give you the best answer I can.

Mental health services suffered even before the pandemic. It is no secret that mental health problems have increased in recent years and service provision has not. To capture data on what is needed, my understanding is that it would just be about looking at waiting lists, but part of the worry with that is that sometimes people are not even put on waiting lists. If people know there is no service, or that it will take more than a year to see someone, to some extent they will just not bother. They will either try to sort things out privately or not be able to get help at all, which is not a great situation. Donal O'Donoghue from a Royal College of Physicians' perspective may have a different view on the broader provision.

The Chair: Professor O'Donoghue, more widely.

Professor Donal O'Donoghue: Tom is right: provision in mental health is poor and patchy, with long delays and challenges, both in serious and enduring mental health and in lesser degrees of mental illness that can be quite catastrophic for people.

We have an opportunity to think about providing more holistic care than we have previously. We are mainly dealing, not just in a Covid world but in a 21st-century world, with people who have a number of conditions. Certainly in the kidney world, it is very unusual to see somebody who just has kidney disease, and if they just have kidney disease, a short time after that they will develop vascular disease and all the other complications, as we see in cancer. The burden of minor mental illness—anxiety and depression—is very high in those with long-term conditions and has a very big impact on the amount of resource utilisation and their clinical outcomes.

There is a real opportunity to work harder on parity of esteem. It has been on the cards for a long time, but we need to shift the needle on that. With the resource and capacity constraints that come from the situation we are in, and having to have infection prevention control measures in place, one of the things we can try to major on is more integrated approaches.

Thinking about the challenge of the follow-up for all the people who have had Covid, both in the community and in hospital, and the capacity constraints in primary and secondary care, we need to work hard at integrating the data and ensuring that there is a one-stop shop for most people, most of the time. Why can that not involve mental health issues as well, with signposting and so forth? That is quite a radical change from how we have siloed things in the past, but we need to do that. It is likely that, if we can, we will get a benefit, both through the population to study for research and in being able to implement the things that we know now that we are not doing, as well as finding new treatments for the affected populations.

We really have no idea about the long-term consequences for respiratory disease, kidney disease and the major organs affected. What is the outcome in end-stage renal failure or respiratory failure over the next five years? A considerably greater number of people could develop those end-stage organ disease conditions than we see in normal times.

The Chair: Thank you very much.

Q195 **Baroness Sheehan:** What evidence is there that neurological issues can occur in mild or asymptomatic cases? Which of the neurological effects of Covid-19 will have long-term health implications? Professor Solomon, you mentioned the importance of dedicated rehabilitation centres, given the multitude of organs that can be affected. Could each of you say a little more about whether capacity in the NHS is showing signs of preparedness to deal with patients suffering from longer-term Covid-19 effects and whether professionals from specialisms such as physio and occupational therapies and essential support staff are there?

Professor Tom Solomon: The first question was about mild or asymptomatic neurological disease. If somebody has brain disease but no symptoms, you will not know about it from anything that they report about how they feel or bits of their body that are not working; you pick it up from other types of research approach.

In the New York scanning project we heard about earlier from Professor Brandner, 3,000 patients had brain scans done. In just over 1% of them, there was evidence of a stroke on the scan. It was like a mini stroke. It was not something that caused them to have weakness in an arm or a leg, but when you did the brain scan you found that there was evidence of what we would term subclinical stroke. If you took 3,000 people off the street and did brain scans on them, you would find evidence of vascular disease and mini strokes, depending on the age of population, so you have to take such findings in context. Those are the kinds of approaches that will tell us that there has been damage without the patient being aware of it.

You asked about dedicated services. The Royal College of General Practitioners is calling for specialist clinics that will deal specifically with the consequences of Covid-19. As Professor O'Donoghue said, it might be an interesting approach. Traditionally, we think of clinics for neurological problems, respiratory problems or kidney problems. It is quite rare to have clinics that are combined. Our brain infections clinic combines infectious diseases and neurology, but to have a service that also combined respiratory disease and renal disease would require quite a shake-up. It is quite a novel way of thinking about it.

Finally, you asked about the capacity of physiotherapists, occupational therapists, et cetera. They are absolutely key to getting people back on their feet if they have had a stroke. Their service is hampered anyway, because currently everything that anyone does in the NHS has to be Covid secure. We have to make sure that patients do not have the virus and that everybody is protected. That is already like operating with one arm behind your back as regards capacity.

Increasingly, people are looking at innovative ways of doing things. I chaired one of the UK Research and Innovation committees that funded research across the country. We supported very innovative projects—for example, looking at how we can do physio and occupational therapy remotely, without needing to be with the patient all the time, and how much of it can be done with an iPad, Zoom, et cetera. This pandemic is obviously a terrible thing in many ways, but some of the things that may come out of it are new ways of working that may be helpful in the longer run.

Professor Donal O'Donoghue: I echo those comments. We need to think about new ways of doing things. The rehabilitation workforce shortage is so great.

The Chair: In relation to Baroness Sheehan's question and the answers that we have heard from you and Professor Solomon, have the Royal College of Physicians, which represents 27 different disciplines in medicine, and the Royal College of General Practitioners done any work and produced any papers to suggest what kind of care post-Covid people should have, and where and by whom?

Professor Donal O'Donoghue: We have produced some work on how we can work more closely together and support people with new ways of working. I can send the details through.

The Chair: That would be very good, if you do not mind sending it in. It might help to answer Baroness Sheehan's question, which was a good one.

Baroness Sheehan: I have a quick follow-up question for Professor Solomon, who has a specialism in emerging and zoonotic diseases. Has anything in the way Covid-19 has manifested itself surprised you?

Professor Tom Solomon: You could put the question the other way round: is there anything that has not surprised me? I work in emerging infections. We have known that a pandemic could happen at any time. On the back of my door is our business continuity plan. I have checked, and a pandemic was on it, but there is a big difference between theoretically knowing that something could happen and a pandemic on this scale actually happening. We have had flu pandemics. The last one was in 2008, but it proved to be a pretty mild, weedy virus that did not cause anything like the problems that SARS-CoV-2 is causing. This is a first for me, as it is for everybody living through it. There is almost a new surprise every day.

I wear two hats. One is the emerging infections hat, and one is the neurology hat. Early on, somebody in my team said that we should think about this respiratory virus causing neurological problems. I was so busy dealing with the problem that was definitely facing us that we were perhaps a little slower getting on to the neurology than we should have been. It is a question that you could spend an hour answering and two hours discussing, but I will stop there.

Q196 **Baroness Walmsley:** I have two questions. One is specifically for Professor O'Donoghue and the other is more general. Professor O'Donoghue, are the effects on the kidneys and liver because they have a lot of blood vessels in them, or is the virus attacking them directly? Are those effects treatable, or will we have to go for larger numbers of much more radical treatments such as dialysis, with much greater demand for transplantation? Are we prepared for that?

Professor Donal O'Donoghue: That is a great question. The kidney has receptors the virus would have affinity for. There is some work to suggest that the virus affects the kidney specifically, but most of the post-mortem studies indicate, and most opinion now is, that people are developing their kidney injury on the basis of the systemic disease that they get. Normally, maybe 20% of people who go on to intensive care units need to have a form of dialysis. During Covid, it was up to 40%, and 85% of people had some degree of kidney injury. No doubt that is happening in the community as well. It is probably happening to a lesser extent, but there is no doubt that it is happening.

From a kidney perspective, the unknown is how many of those individuals will go on to have more severe kidney disease as a consequence of

having that initial insult. From the data, it looks as though a third of people who survive will have some degree of kidney impairment. If even a small percentage of those go on to have progressive kidney injury, there are two or three imperatives.

The first is to do everything that we can to slow down the disease process. That is not rocket science, but it needs to be identified, treated and managed, with blood pressure control and so forth. The second is to plan for the increase, because there could easily be tens of thousands more people requiring dialysis and transplantation. In a normal year, we accept about 6,500 people on dialysis and transplant programmes, so you can see the order of magnitude. It needs to be modelled and then worked through.

Then there is the issue of including people with kidney disease in trials. We have the ludicrous situation that those people are excluded from trials, yet they are at the highest risk. They are excluded from trials because somebody has thought, "We don't know how to manage this drug if there is reduced kidney function". Hydroxychloroquine is a treatment for lupus nephritis, which is a kidney condition. People are excluded from trials of chloroquine because, "Oh, that would make it more complicated". As I said in the introduction, 45% of trials exclude people with kidney disease, yet they are a very high-risk population that we can learn so much from.

Baroness Walmsley: Given what all our witnesses have said this morning about the long-term effects of the virus, many of them among those who had mild symptoms, is the idea that we could encourage herd immunity by allowing a lot of less vulnerable people to get it a much more dangerous strategy than it at first appeared? Should we be messaging younger people, who are pretty confident that they will not get seriously ill, that they may have some very nasty long-term effects afterwards?

Professor Donal O'Donoghue: I will give a short answer. Yes. It would be foolish to go down that route, for all the things we now know about the consequences of having had Covid and how they may play out. Of course, we do not know what the consequences will be in younger people. We have a fairly good idea in children, but we all know of friends and relatives whom we think of as relatively young, and who are indeed relatively young, who are having serious problems. What the long-term consequences may be neurologically, cardiovascular-wise and renal-wise we do not know. One would be much better to go down a vaccination route, I think.

Baroness Walmsley: Does either of the other witnesses want to comment on that?

Professor Sebastian Brandner: I completely agree that we have no idea currently what the long-term effects might be. There are long-term viral effects that we cannot even predict now and that might come up in 10 or 20 years. Neurodegeneration has been a problem in previous

pandemics. The very famous 1918 pandemic caused Parkinsonism. There are long-term effects on the aggregation of neurodegenerative proteins.

Over the last 15 to 20 years, I have been involved in other studies, completely unrelated to Covid, where it turns out that pathogens—specifically, aggregated proteins—can be transmitted in a way that we had no idea about 20 or 30 years ago. Currently, that is not a problem because practices have changed. It could happen again with a completely new pathogen that is untested and only relatively preliminarily characterised. I agree that vaccination programmes are probably better than trying to rely on herd immunity, which may not even happen, because if the immunity ceases after a certain period we will start all over again.

The Chair: Lord Winston, I saw you nodding. Can we have your question?

Q197 **Lord Winston:** I am very concerned that we have completely missed one very important part of healthcare. That is not the fault of our witnesses, but perhaps our fault, in a way. It is women's health. In the United Kingdom there are some 700,000 births annually, and many more pregnancies than that.

One of the issues is the long-term effects on the foetus. During the pandemic, a large number of foetuses will have been in the time when there is development of organs, or organogenesis. We know that other viruses have an effect, certainly at the beginning of organogenesis. Can our witnesses give us any help on where we might find out about what follow-up is being done on those pregnancies? For example, is there any post-mortem material on the products of conception of women who have miscarried? What do we know about the brain in foetuses that have died during the pandemic? Perhaps we could start with Professor O'Donoghue.

Professor Donal O'Donoghue: I defer to Professor Solomon.

Lord Winston: I thought you might.

Professor Donal O'Donoghue: Let us go straight to Professor Solomon, rather than have me waste time.

The Chair: Professor Brandner might also know about the pathology. We will hear from Professor Solomon first.

Professor Tom Solomon: I can help a little bit. Our unit was heavily involved in the Zika global health emergency, which, as you know, had severe impacts on pregnancy and new-born children. The first thing to say is that there has been no great signal in this area. In other words, many pregnant women have been infected with the virus, but there is not a large number of obvious severe problems, as there was for Zika. We are not having hundreds of children born damaged.

We would not yet know whether there are more subtle problems, but there are studies looking at that. The committee that I chaired and

co-chaired has funded work in that area, so there are registries looking at children born during this time period, including some work led by a colleague of mine here at the University of Liverpool, Professor Louise Kenny, who has an interest in the area. Your committee may have overlooked it, but it has not been overlooked completely by the scientific community. We are looking at it.

The Chair: The reports that have been published do not suggest the same degree, or any degree, of vertical transmission at any stage.

Professor Tom Solomon: There are a few reports that suggest something, but there always are. If 300,000 people in the UK are known to be infected with a virus, there will always be a small signal, but I do not think there is a dramatic signal that suggests that it is a major issue at the moment.

Professor Sebastian Brandner: I have been very interested in finding post-mortem material of children. I have liaised with my colleague at Great Ormond Street Hospital, who is a paediatric neuropathologist. We agreed that a very small number of children have died. To my knowledge, no child has died of Covid-related complications, and there is very limited material available. I cannot really comment further on what might realistically be available for further studies.

Lord Winston: One of the issues that is not included in this half of the session is what happens with the care of women, who have their respiration and cardiac function in a very different position during late pregnancy. We cannot really ask you those questions, but it would perhaps be useful to consider that, although a large number of viruses do not kill the foetus, they may certainly result in abnormalities in the foetus that are not always described or noticed until later on. I know that I am not supposed to give an opinion here, but it would be helpful to hear from you, and perhaps from Professor O'Donoghue, whether you feel that this is an important area that we should make sure is being followed up in public health.

Professor Donal O'Donoghue: I think it is an important area. I can seek views from obstetric physicians, who would have more of a handle on that.

The Chair: There are two on the committee. Carry on, Professor O'Donoghue.

Professor Donal O'Donoghue: As I said, I do not have expertise in that area myself and I am not sighted on the detail, so I think it better that I send information through to the committee, rather than speculate.

The Chair: But the question Lord Winston was asking: you agree that whatever we say in our report should include a recommendation that part of the long-term data that is collected should relate to that?

Professor Donal O'Donoghue: Yes.

Lord Winston: Thank you very much. That covers my question.

Q198 **Baroness Young of Old Scone:** The questions that I was going to ask have pretty well been answered, but they raise another question. If we are predicting an as yet unsized uplift in long-term morbidity, ranging from fatigue right up to serious kidney and other damage, are you aware of anybody who is actually planning for dealing with that in the way that you described—in a multiple-morbidity integrated way that includes physical and mental health? Is the NHS planning to cope with that, or is it being dealt with piecemeal at local level?

Professor Donal O'Donoghue: It would be fair to say that people are just getting by, with the second wave perhaps starting, and trying to maintain the services that have been brought back and manage a workforce that has been fairly battered with things. It is not there.

Some very good research is being put in place, and we heard a little about that in the last session; but it has excluded some datasets. It is not linked to the renal registry. There is a great opportunity to link our datasets, which will tell us things we can model and plan for. That is something we very much should do.

The service model needs to be challenged. The only realistic way we can put in a service model to monitor and support people is by having one that is holistic, because otherwise we will have three or four people involved in each individual's care.

The Chair: Professor O'Donoghue, as an officer of a professional organisation, do you think that the professional organisations should get together to thrash out what kind of services we require for people who have been infected with Covid-19 and the problems they will suffer in the long term?

Professor Donal O'Donoghue: Yes.

The Chair: Might that happen soon?

Professor Donal O'Donoghue: I hope it will. We are working in that direction, but anything that can be done to support it would be helpful.

Q199 **Baroness Blackwood of North Oxford:** I want to follow up on Baroness Manningham-Buller's earlier question about research gaps. Do the witnesses know if there are any plans, or think there is any value in them, to compare the long-Covid cohort that is emerging with other post-viral and chronic fatigue syndrome cohorts? Are there datasets that are relevant? Would that be valuable in understanding how to go forward?

Professor Tom Solomon: That is a really interesting and useful comment. The long-Covid cohort is an emerging area. Some people feel very strongly that they do not want to be grouped with the idea that it is a post-viral fatigue syndrome or chronic fatigue syndrome. Comparing patients can always be helpful. Accordingly, it can help to guide services.

Q200 **Baroness Manningham-Buller:** Our witnesses might not be able to

answer this question, but I would like to follow up something that Lord Ridley asked. Do we have any data yet on suicides or in-hospital admissions for those who have not had the disease, as far as they know, but are deeply affected by it mentally?

Professor Tom Solomon: When looking at such data, particularly hospital admissions, it is difficult to understand quite what it means. Hospital admissions across the board were reduced at the start of the pandemic, so just looking at hospital admissions will not necessarily give you an answer.

There is quite a bit of data now showing that Covid-19 is associated with increased anxiety, depression, et cetera. I think there are some data on elevated suicide risk, but I am not completely sure about those. Lord Winston talked about gaps in the remit of this committee so far. I do not know whether you plan to have somebody with real expertise in mental health to talk to you.

The Chair: We have sessions on mental health next week.

Professor Tom Solomon: Good.

The Chair: Baroness Manningham-Buller, do you have any other questions?

Baroness Manningham-Buller: That was the main one. I was interested in the effect on people who did not have Covid. As you say, we will come to that next week.

Q201 **The Chair:** There are only two minutes left, so could I ask a very quick question and get a quick answer? It seems to me from the discussions that we have had that there are considerable gaps in research, particularly in the data collection that will be required for follow-up and research into follow-ups, and that there is a service gap for patients who have suffered from Covid-19 and survived but who will continue to suffer because of organ damage. Would that be a good summary?

Professor Donal O'Donoghue: It is a good summary, but it misses out the missed opportunity to link the datasets that we have and to address the IG issues that could allow that. We have great data, but some of it is still in silos. We have key issues with regard to the systemic follow-up of people.

Professor Sebastian Brandner: The final outcome for a small number of people with neurological complications is that they die of those conditions. It would be very useful to encourage everyone involved in the request and consent procedures for post-mortems to ensure that we get material to investigate. Without post-mortem material to investigate the effects of Covid-19 on the brain, it will be much more difficult to link definite post-mortem data with all the clinical data.

The Chair: Professor Solomon, do you have any comments?

Professor Tom Solomon: You summed it up very nicely. There are service gaps, but this presents an opportunity to think about how we might do service differently, in clinics where we have multiple inputs. We are not necessarily talking about six different consultants sitting together; I do not think that will ever happen. We are talking about using opportunities. If a patient comes because of a renal problem, that may be the opportunity to provide extra input on their breathing and how they are coping with that, whether they are coping with fatigue and stress, and whether there are other issues. It is about joining up services in that kind of way.

The Chair: Professor Brandner, Lord Kakkar asked the last group whether enough tissue material is collected from patients—most of whom, presumably, die—from different organs to enable us to do studies in the future, including for treatment development.

Professor Sebastian Brandner: There was indeed very significant effort on many sides, and there are some amazing tissue collections. Given the scale of the problem and the scale and variety of the disease, I think that more could be done to close the gaps, to enable us to capture the rarer events and to study them properly.

The Chair: Thank you all very much for helping us today. It has been a very interesting session, as they have all been. If you have any further material that you think might be of benefit to us, please feel free to send it. Professor O'Donoghue, you said that you will send in something that the Royal College of Physicians has produced.

Professor Donal O'Donoghue: Yes.

The Chair: Thank you very much.

Viscount Ridley: Is that an Olympic torch in Professor Solomon's background?

Professor Tom Solomon: It is. It is my Olympic torch. I ran through Liverpool city centre carrying the torch very proudly. Those are happy memories.

The Chair: I thought he was about to ask where your gold medal was.

Professor Tom Solomon: No such luck.

Viscount Ridley: Congratulations.

The Chair: It just shows that we are observant. Thank you all very much indeed.