HOUSE OF LORDS

Select Committee on Science and Technology

Corrected oral evidence: The science of Covid-19

Tuesday 15 September 2020

10 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. 17 Virtual Proceeding Questions 181 - 190

Witnesses

Dr Sonya Babu-Narayan, Consultant Cardiologist, Royal Brompton Hospital, Reader Imperial College London and Associate Medical Director, British Heart Foundation; **Professor Chris Brightling**, NIHR Senior Investigator and Clinical Professor in Respiratory Medicine, University of Leicester; **Professor Kamlesh Khunti**, Professor of Primary Care Diabetes and Vascular Medicine, University of Leicester and Leicester General Hospital.

Examination of witnesses

Dr Sonya Babu-Narayan, Professor Chris Brightling and Professor Kamlesh Khunti.

Q181 **The Chair:** Good morning all. Thank you for joining us today, and we particularly thank our witnesses for helping us with this important inquiry. We want to learn from you about the long-term consequences for people who have suffered from Covid. Are you happy to go in this order for your short presentation: Dr Sonya Babu-Narayan followed by Professor Chris Brightling and Professor Kamlesh Khunti? It is nice to see you, Kamlesh. I trained him once.

Dr Sonya Babu-Narayan: Thank you for the opportunity to give evidence to you today. Cardiovascular disease is at the centre of this Covid-19 pandemic, and I will outline three main reasons why that is the case.

First, people with cardiovascular conditions are at increased risk of Covid-19-related death. It is clear that heart and circulatory disease, and its risk factors—diabetes, hypertension and obesity—are key determinants of a risk of severe Covid-19 illness or of death. Diabetes more than doubles the risk of death from Covid-19. Repeated studies demonstrate that hypertension is linked to worse Covid-19 illness and outcomes. Morbid obesity doubles the risk of death, and being overweight with a BMI of 30 to 35 increases the risk of death by 27%.

Secondly, there are indirect effects of the pandemic that put people with cardiovascular conditions at increased risk. Some of that is illness behaviour. We have seen very clearly that fewer people sought emergency treatment for heart attack or stroke because of fear of coronavirus infection, or not wanting to be a burden on the NHS. For example, in March there was a 50% drop in emergency department attendances for myocardial ischemia, symptoms that could be linked to a heart attack. Similarly, during lockdown there was a 66% reduction in admissions for heart failure, which can be an urgent condition requiring treatment. In London, at the end of March and in April, there was a reduction of 38% in attendance at hospital for the most severe kind of heart attack, recognisable by its electrocardiogram in the ambulance and requiring paramedics to take the patient directly to the cardiac department for immediate procedure. Those reductions in heart attack attendance, stroke presentation and heart failure admission started at the time of the first cases of Covid-19 in the UK and before full lockdown, implying that the effects are behavioural and not a true change in prevalence.

The second type of indirect effect is the reduced availability of elective cardiovascular care. Waiting lists are indeed getting longer. As an example, waiting lists at the end of July showed that there were more than 180,000 people waiting for investigations or treatment in cardiology or cardiothoracic surgery. Investigations with diagnostic imaging are the gateway to appropriate treatment, and those services have fallen

markedly; for example, there was a 67% reduction in echocardiogram—ultrasound of the heart—availability in April and May this year.

You might ask whether that lack of health care has caused harm, or whether this is productivity and efficiency. We are seeing the tragic effect of Covid-19 in statistics related to deaths. While Covid-19 explains 80% of the excess mortality we saw during the peak of the pandemic, it does not explain it all, and it seems that some of the excess mortality was driven by patients with heart and circulatory conditions. In just one week at the peak of the pandemic, there were more than 700 excess deaths from heart and circulatory diseases, including around 300 from coronary heart disease and nearly 200 from stroke. Across the whole of the pandemic, there have been 3,600 excess deaths from heart and circulatory diseases. This raises concern that perceived or real barriers in access to care potentially caused avoidable harm, and that should not be repeated. The indirect effects need to be monitored and mitigated, and we need to restore and maintain vital heart services.

Thirdly, severe Covid-19 infection affects the circulation and the heart. Emerging evidence points to a direct impact of Covid-19 on the blood vessels and the heart. Severe Covid-19, of the type that admits you to hospital, causes clotting. This seems to be related to damage to the function of the endothelium, the inner layer lining of the blood vessels throughout the body, which appears to be the culprit.

If a clot occurs in the brain, it will result in stroke or other neurological deficit, and can affect younger people. If it is in a coronary artery supplying the heart, it results in a heart attack, because the blood supply to the heart muscle is blocked, potentially causing long-term damage. Clots in microvessels can cause lung and kidney damage. We have learned during the course of the pandemic that we need to thin the blood for severe Covid-19 illness to try to mitigate that.

In severe Covid-19, whole-body inflammation can affect the heart. This is demonstrated through measuring heart muscle damage markers in blood, which, when present, signify heart tissue injury and predict worse outcome, regardless of whether there is underlying heart disease before the Covid-19 illness. Myocarditis, stress cardiomyopathy and arrhythmia, as well as palpitations during recovery, have all also been described. In hospital, when we look with echocardiography at Covid-19 patients who have severe illness, there is a reduction in the heart-pumping function in some, including severe reduction in heart function. As a vital next step, we need to dissect the mechanisms of how and why the heart is affected, given that several mechanisms of heart injury are being described.

In summary, heart and circulatory patients are being dealt a double blow. They are at high risk of death from SARS-CoV-2 infection and Covid-19 illness, and of dying in excess of expected numbers from their heart and circulatory disease unrelated directly to Covid-19. The reduced availability of heart services that may additionally be needed to address heart care for patients with newly diagnosed heart disease post Covid-19 could result in significant morbidity and mortality, at risk of exceeding that due to Covid-19 directly. This would be a catastrophe given that cardiology

care has one of the strongest evidence bases and we know how to successfully treat those conditions. Health inequalities are being exacerbated, and cardiovascular disease is an important contributor to the deprivation gap.

The Chair: Thank you very much, Dr Babu-Narayan.

Professor Chris Brightling: Lord Patel and colleagues, thank you for inviting me to present today. I am a respiratory physician. I specialise in lung disease, and I lead Covid-19 acute and follow-up research in Leicester, particularly focused on lung disease, but beyond the lungs. I am also the science lead for our European professional society, the European Respiratory Society, which is leading the follow-up and impacts on people with premorbid lung disease.

Covid-19 is a respiratory infection and, although many of us were fearful of what was coming, having seen what was happening in Wuhan and in Italy, we were still surprised by the scale of the impact in the UK. It led to admission to hospital, in the early stages, of as high a percentage as 20% of people, with mortality figures in the region of 20% to 25% of admissions. It causes a severe pneumonia in those who are admitted, which you will be familiar with. In people who are not admitted, it is largely an upper respiratory infection, but for those admitted to hospital with respiratory failure it is almost entirely a consequence of a pneumonia, a lung infection.

There is a very broad inflammatory response. I agree completely with Dr Babu-Narayan that it is beyond the lungs; it affects the stickiness of the blood and leads to end-organ damage beyond the lungs. In the lungs themselves, there is scarring as well as pneumonia, and acute scarring can occur in approximately 30% of individuals at the time of the event.

As part of the national Covid follow-up study called PHOSP-COVID, which I lead, we started to look at the impacts longer term. We have some early clues from studies in Italy and China. They suggest that for people who have been hospitalised, even two to three months after discharge only between 10% and 15% have no persistent symptoms. Over 80% of people have symptoms, including fatigue, breathlessness and chronic pain. For the patients who are breathless, where it largely affects their lungs and cardiovascular system, it is over 45%.

We started looking at imaging. We are doing whole-body MRI scans. We are looking at the brain and all the organs. We now have pilot data from the first 50 patients, which shows end-organ damage in the kidneys, liver, lungs and heart, but less so in the brain. That affects over a third of individuals at the two-month point. We are getting a lot of clues that there are things happening across multiple organs from a disease that initially started as a respiratory infection.

We are starting to learn about treatments that can modify the effects. There are treatments that were given acutely, with which you will be familiar, such as the RECOVERY study with dexamethasone, and we will now be able to look at whether the benefits that were seen in the acute phase also modify the trajectory of recovery. To date, most of the

research has been focused on patients who were hospitalised and people who were discharged from hospital.

We are all familiar with friends and family who have had a Covid-19 infection in the community that did not lead to admission to hospital, and many of those people also have ongoing problems. There are plans for long-term follow-up studies of people who have had community infection. Some of them may also have had pneumonia and not ended up in hospital, but many may have had the broader inflammatory effects that may then affect many organs in the body. In the studies we are doing we are also trying to understand whether there are things we can change, not necessarily for the individuals affected, but for people who might be part of any future wave, where we can modify interventions acutely and modify interventions in the follow-up phase.

That is the direct response to Covid-19 itself, but, as has already been said by my colleague, there is also an indirect impact on people with premorbid conditions. We do not yet fully understand how Covid affects premorbid conditions. We certainly do not have a full understanding of the impact on services over the winter months. We are already familiar with how Covid has consumed our lives in many ways and has consumed healthcare resources away from routine care. That problem is likely to be compounded in the forthcoming winter. Other winter infections and other pressures on both the community and acute care will be even more problematic in any potential future waves over the winter.

I finish by summarising that of course, as a respiratory physician, I would highlight that this is a respiratory disease, and there is an impact on the lungs, but I am very mindful that there is a multiorgan impact that goes beyond typical medical responses and includes impacts on mental health, which we need to acknowledge and manage for those who have been affected by Covid-19, as well as all the collateral damage in the healthcare system and the economy that is consequent on Covid-19.

The Chair: Thank you very much.

Professor Kamlesh Khunti: Lord Patel, colleagues, thank you for giving us the invitation to present today. My remit is to talk about the disproportionate impact that Covid-19 has had on black and minority ethnic health populations. I and a colleague, Wasim Hanif, highlighted that for the first time, I think globally, on 4 April in a tweet, because we had seen a lot of patients coming into the intensive care unit. The ICNARC—the Intensive Care National Audit Research Centre—data came out the following week and showed that, overall, about 33% of people admitted to intensive care units were of non-white ethnicity, and we know that the overall population of the UK is about 14% non-white. The evidence shows that the largest inequalities affected are by age, sex and deprivation, and we know that more people from black and minority ethnic populations reside in deprived areas.

There are a number of studies. On average, blacks and south Asians have between 40% and 70% increased risk, after we adjust for other factors, of both hospitalisation and severe outcomes such as mortality. We and

others have looked at the literature and tried to explain the disproportionate impact on ethnic minorities by differential exposures and increased vulnerability. They can be categorised into structural, biological and behavioural reasons.

The structural inequalities are systematic disadvantages such as structural discrimination, which could be in social structures, housing, income, occupation, healthcare or education. On biological differences, we know from studies that have been done by us and many others—Dr Babu-Narayan also mentioned this—that cardiovascular disease, obesity, diabetes and hypertension are frequently reported comorbidities associated with adverse outcomes in Covid-19. We know that they are more highly prevalent in ethnic minority populations.

There are behavioural reasons. There is some data that there may be poor understanding of the need for social distancing, lower adherence to social distancing and a lack of understanding about social isolation when symptomatic or when a family member is symptomatic. There has been some evidence from a report that a lack of culturally appropriate and targeted public health messaging may have contributed to that.

There are additional plausible behavioural factors such as poor lifestyle. We know that physical activity is poor, and that is associated with severe Covid. We and many others have suggested potential actions for the short term, medium term and long term, mainly around the cultural tailoring of public health messaging, tailored test and trace and isolation strategies, priority testing of certain ethnic minority workers and specific recommendations for employers, religious festivals, religious schools, funerals, burials and weddings.

It is clear that a comprehensive multisectoral approach, supported by strong policy actions, is needed to tackle the multiple and complex structural, biological and behavioural reasons driving the disproportionate impact of Covid-19 on ethnic minority communities. Those recommendations are key to reducing the further health inequalities that we may see related to Covid-19.

The Chair: Thank you all three for your excellent presentations. I will ask my colleagues in turn to ask questions and, depending which specialty it is, feel free to pick it up. If any of the other witnesses want to join in, please do so.

Q182 **Baroness Blackwood of North Oxford:** I would like to try to understand the scale of the challenge that we may be facing with long Covid. I realise it is very early days for us to get a sense of that; nevertheless, it would be helpful to get your best understanding as witnesses who have been working in the field as to where we may be headed.

Professor Brightling, could I start with you, given the work that you have been doing? You gave us some very stark statistics on those who have come out of hospital and are still struggling with long-term health conditions. Are patients with mild or severe cases more likely to be

suffering, and what percentage of those who come out of hospital are likely to have ongoing symptoms?

Professor Chris Brightling: An important distinction is that the people who ended up in hospital had respiratory failure. That was the main reason for them going in. Sometimes it was also due to other social reasons and difficulty in maintaining them at home, but, largely, it was respiratory failure. Those people are more likely to be the ones who will also develop long-term consequences as regards lung damage and are probably more likely to have some of the more severe inflammatory consequences in other organs.

Notwithstanding that, people who had the disease in the community are likely to have some of the other long-term consequences such as fatigue, chronic pain, impacts on cognition or impacts on mental health, although they may be less likely to have conditions such as long-term breathlessness. One of the difficulties is how those changes affect the individual. If you can no longer perform at the level you did before, you may not be able to undertake your job or continue to study or look after members of your family. Relatively modest changes may have large impacts.

The other thing that we do not yet understand, and the thing I am most concerned about, is trajectories. The data I have been describing is very much the follow-up data from individuals who have been seen in hospital. We also have follow-up data based on apps such as the ZOE app, where people have been recording their symptoms. We do not know whether some of those conditions actually develop. There may be subgroups of people who become worse over time, and that would definitely be a concern for people in the community.

If there was early renal damage, for example, it might not be overt and could lead to long-term problems. The onset of new diabetes might have impacts on the heart that do not necessarily manifest themselves immediately as symptoms and might progress over time. There is the acute, the subacute over the next few months, and the longer-term trajectory that we do not know and will not know until we follow up people for a year and longer.

Baroness Blackwood of North Oxford: So far, have you or any of the other witnesses been able to establish whether those lingering long-Covid symptoms are driven by ongoing virus or are a factor, a side-effect, of the intense treatments people might have had through having a severe respiratory condition or other organ failure—intubation, ICU sedation, whatever it may be?

Professor Chris Brightling: It is slightly different depending on where you have had care. To answer your very first question on whether I think this is persistent virus, the answer will be no. There is no suggestion that people have a chronic viral illness. It seems to be very much a response from the host, from the patient.

The second question was about whether treatments have an impact. Especially if you have been in hospital, you may have been on a ventilator in intensive care, or even on what we call ECMO, and in both of those cases the treatment itself can cause damage to the airways and can lead to organ damage and affect many other systems.

Many of you, I am sure, have been in hospital at some time. Being in hospital itself leads to problems of deconditioning. It takes a long time to recover. There are also impacts from anxiety around acute illness episodes. All of those are really important. People in the community do not have the same treatment impacts, but they will still definitely have impacts. Many of us were concerned about our own health and that of our loved ones as regards who was going to catch Covid. There was huge and quite understandable fear, which is still there. That will lead to an enormous impact on people's mental health, at the same time as they will have physical impacts from the virus itself.

The Chair: I request that both questions and answers are short, please, or we will not get through them in time, although I know there is a wealth of information we can learn from. Baroness Blackwood, have you finished?

Baroness Blackwood of North Oxford: We can move on. I have taken your strictures on board, Lord Chair.

The Chair: I am sorry about that, both for our witnesses and for you.

Q183 **Lord Borwick:** I have a question for Dr Babu-Narayan. At the beginning of all this, way back when, we thought it was a respiratory disease, as Professor Brightling said, but it slowly became more complicated. One of the things that happened was that the Royal Brompton Hospital became a specialised Covid centre. Was it the right decision to make the hospital concentrate on one disease and to get rid of your paediatric cardiology and the other sections that the Brompton is so famous for?

Dr Sonya Babu-Narayan: I will answer that question as best I can. As you know, I also work as a cardiologist at the Royal Brompton Hospital; indeed, my subspecialty in cardiology is congenital heart disease, in particular people who have grown up with their congenital heart disease and are now adults.

There are two things. There was clearly a need to treat people with Covid-19 illness, including severe illness, and there was an aspect of care that hospitals such as the Brompton could deliver that other people might not have been in as easy a position to deliver well. For example, there was the kind of support—ECMO—that very sick people with Covid-19 illness require, which the Royal Brompton, St Thomas', Leicester and other regions in the UK are specialist in.

Having said that, going forward we need to consider very carefully cardiology patients who have subspecialty needs. For congenital heart disease, paediatric and adult, there are only 11 surgical centres in the UK that have the imaging-to-procedure expertise to see congenital heart

disease patients. Much of that specialty is a surveillance specialty. We do not necessarily wait until patients are sick with breathlessness; they do not really get chest pain, and we do not always wait for important arrhythmias. Some of the care is based on the imaging having shown change and showing that there is an optimal timing for a procedure or an intervention. Those patients have not been seen.

You asked specifically about paediatrics. Care has been delivered safely because hospitals have worked collaboratively with each other to make sure that all children and adults who need urgent care can get a place in hospital, but, as I alluded to in the broader picture, there is certainly now a need to protect and maintain core cardiovascular services including cardiac intensive care for children and adults. We cannot catch up. We are not even back to normal volume at the moment, and we will not be able to catch up with the backlog. That could be worse and more difficult to decide about for subspecialty conditions such as inherited cardiomyopathy, congenital heart disease and so on, where there are fewer places with the correct expertise for all patients. Does that answer your question sufficiently?

Lord Borwick: Very much so. Will the heart disease that is developing as part of the long-Covid syndrome be treated in the same way as other syndromes and other forms of heart disease, or is it a different form of heart failure?

Dr Sonya Babu-Narayan: That is an excellent question. We talked about one mechanism of heart disease; we have treatments for sticky blood and clotting affecting the vessels supplying the blood with oxygen—oxygenated blood, all the microvessels. We might not yet know exactly which patients should have an antiplatelet medicine at which point and which patients should have full anticoagulation, but generally we have learned during the pandemic that patients need blood thinning, and there are available treatments. We still need to learn how long people should continue the treatment when they go home from hospital, for example. Others may want to comment on that.

If we see heart dysfunction, where the heart does not pump as well, we have tried and tested medications for heart failure. In answer to your question, we broadly understand which drugs to use to support people through those complications, but there will be an increased burden of care if we diagnose more and more people with cardiac disease after their Covid-19 illness.

Lord Borwick: Thank you very much.

Q184 **Lord Browne of Ladyton:** I had two questions in mind, but in the interests of time I will ask one question and expand it slightly so that it engages all our witnesses. The question is initially directed to Professor Brightling, and it is an opportunity for him to expand a bit about the PHOSP-COVID study that he referred to in his opening remarks.

The study you lead, Professor, is a substantial undertaking and has attracted a significant proportion of the available funding. As far as I

understand it, you plan to study the experience of thousands—perhaps tens of thousands—of recovering Covid-19 patients over time. How do you plan to ensure that at that scale it will not become just a large bureaucratic exercise, but rather that the data collected will lead to improved clinical outcomes for recovering patients? How quickly do you think that can be achieved? To expand that slightly, will it specifically study and engage the issue of excess mortality, which was referred to by Dr Babu-Narayan in her opening remarks, and the disproportionate effect of Covid-19 on the BAME population, as referred to by Professor Khunti?

Professor Chris Brightling: I will try to answer as briefly as I can. PHOSP-COVID has funding of £8.5 million from UKRI. It will recruit 10,000 individuals, 4,000 of whom will have a detailed follow-up over a year requiring additional bioresource, and for 6,000 we will be looking at their clinical data. We are already looking at the interventions that were given during the acute stage to see whether they changed trajectory, so as to modify the use of interventions acutely for any future wave.

We have already embedded and repurposed other clinical trials. One of the very important topics that has come up is the stickiness of the blood and the risk of clots. We have a study funded by the NIHR HTA that we repurposed to link to PHOSP-COVID for early interventions in patients who have pulmonary emboli as a consequence of Covid-19. It is not just an ambition that we will be able to go beyond collecting data to making a change; it is something that we have already realised within the first few weeks of the study. I completely agree with Lord Browne that that is really important.

We have engaged very widely across the whole academic community. We have working groups in all the disease areas, including a very close relationship with the NIHR-BHF partnership for heart disease. We are linked to two of the flagship studies within that, one called C-MORE, looking at the whole-body MRI scanning that I have described, and the second called COVID-HEART. We will certainly be linking to others. Although I am a respiratory physician, something very important is that this is a disease that does not understand boundaries of organs; it affects the whole body.

On the BAME question, my friend and colleague Kamlesh Khunti and I are in the same institution. There is a working group looking across all the different disease areas to reflect on the impact of ethnicity. We are seeking additional funding from UKRI to bring together further work within PHOSP-COVID, but linking the ethnicity question, beyond PHOSP-COVID, to studies in the community and birth cohort studies. We are certainly very cognisant of it.

Professor Kamlesh Khunti: PHOSP-COVID will be one of the largest studies to be done prospectively. The largest study we have seen so far is from Italy with a couple of hundred patients. Another one has just come out on another couple of hundred patients. The longest follow-up is 60 days. Most of them are very short. This will be over a year, with a multi-ethnic population, which we have not seen in other studies described as yet.

Lord Browne of Ladyton: I invite Dr Babu-Narayan to make any comment that she wishes to in this context. I do not intend to ask a further supplementary question.

Dr Sonya Babu-Narayan: I am an associate medical director of the British Heart Foundation, which was mentioned in the context of PHOSP-COVID that Professor Brightling leads. He mentioned the substudy called COVID-HEART supported by the NIHR-BHF partnership. We still need to understand better the many mechanisms of heart dysfunction that are identified at the time of severe hospital Covid-19 illness. The study will elucidate that; more than 300 patients will be studied with MRI, with a six-month interval follow-up to see what resolves.

One of the fundamental questions concerns the medium or long-term effect. We may be able to identify effects acutely, and that may help our acute management, but we now need to understand what the medium or long-term effects might be for the future. It is a great example of how the cardiovascular community in the UK has been galvanised and has worked collaboratively with the core £8.5 million funding to make sure that all the questions that relate to all kinds of consequences of Covid-19 can be officially answered.

Q185 **Baroness Hilton of Eggardon:** I am interested in the long-term consequences of air pollution on people's symptoms. Is it possible to tease out air pollution from other factors such as social deprivation and the social consequences of living in large households? Professor Brightling might start on that one.

The Chair: The question is about the effect of air pollution on people who have had Covid infections.

Professor Chris Brightling: It is a great question. Reducing air pollution is clearly a good thing. Over 4 million deaths worldwide are attributed to air pollution, some 8% of deaths are due to particulates, and over 90% of the world's population are living in environments where pollution is above WHO-recommended levels.

We have linked with a network of environmental health centres. Anna Hansell, a colleague of mine in Leicester, leads a national centre, from which they are able to map pollution exposure on a postcode basis. We have permission on the basis of the ethics to be able to record pollution exposure. We can do that retrospectively as well as prospectively. On an individual level for all the 10,000 patients we follow up, we can look at pollution at the time of the acute infection, their burden of pollution exposure over time and how that impacts the trajectory of the disease. We are linking to control data from other studies. We will be able to unpick that. Clearly, we should be driving down pollution levels for a multitude of health and climate reasons, but I am sure that data will emerge to show an impact on Covid-19.

The Chair: Thank you very much.

Q186 **Lord Hollick:** There is widespread expectation of a significant rise in

Covid cases over the winter months, and Professor Brightling referred to that today, with complications of influenza and the like. You talked about changes that can be made. What changes can be made in the next three months that will help to deal with the expected surge in cases? Should pneumonia vaccination, for instance, be ramped up? Professor Khunti talked about messaging to ethnic communities. What steps do the witnesses think should be deployed to cope with the coming surge?

Professor Kamlesh Khunti: Currently, we can do the simple things. We need a really tight and robust "find, test, trace, isolate and support" programme. It is not working properly in all regions. We have learned a lot from our Leicester lockdown. As you know, we have not come out of the lockdown yet. The centralised scheme was not working and we have gone more localised. It has to be a locally driven system where we know the populations, where we know the key people, the faith groups, cultural people and businesspeople who can drive messaging in the right culturally appropriate format. It does not seem that we will get a vaccine this side of Christmas. All the evidence we have points to having a "find, test, trace, isolate and support" programme, with messaging going out in the most culturally appropriate manner.

Professor Chris Brightling: I agree that the public health impact will be the most important, ensuring that we have social distancing, that we wear masks and that we wash our hands. We now have a clear understanding of who the at-risk groups are, and we need to try to minimise the exposure of people who are at greatest risk and consider different strategies to try to ensure shielding.

We have improved hospital care. If you are admitted to hospital with Covid-19 now, your risk of death is reduced by about a third compared with admission in March. We have made great strides, and many of those will continue.

From a hospital perspective, where I work, we need a motivated workforce. One of the really challenging things is that people have been working flat out since the beginning of the pandemic and there has been no respite. There will be the usual winter pressures in hospital in addition to Covid-19. We need to think about how we maintain the normal services, keeping them away from the acute services, and protect individuals, to be able to deliver the acute service that will be required over the winter. It requires far more action than is currently being taken. That will be a really important additional way of beating Covid over the winter.

Dr Sonya Babu-Narayan: I mentioned at the beginning that we have clear data about the population risk of heart and circulatory disease being associated with severe Covid-19 illness and death. Those population data are not necessarily helpful to individuals at risk: how much heart disease, which heart disease, how severe the heart disease is, or how well controlled it is at the moment. We need to encourage and move towards more applicable individualised risk assessments. At the BHF, we are very supportive of the work in Oxford by Professor Julia Hippisley-Cox on exactly that.

Going forward, patients need clarity about which things they should not delay, so that the health service can protect them rather than them protecting the health service. They need to know which symptoms or changing symptoms are red flags meaning that they should seek medical advice and to call up if their care has been postponed. We need very clear messaging for that. The heart and circulatory patients I know about must not stay at home for fear of putting pressure on the NHS, because delaying their care may exacerbate pressures later down the line. They need confidence that the healthcare system is in a good place to treat them safely.

With regard to that, all around the country we need reliable and quick point-of-care Covid testing so that we can move through the non-Covid-19 patients, while at the same time hospitals are caring for Covid-19 patients. If we have a surge and a second wave, we need to ensure that there is medical advice and leadership on what is core medical care and what is the minimum medical care for each specialty, including cardiovascular.

Many patients, albeit not all, are gaining from the very abrupt transformation that we have seen in healthcare services. My clinic is on the telephone or via a virtual clinic. If there is good improvement in co-ordinating investigations to minimise the number of times you have to come to hospital as a patient, that is good for both patients and doctors, but not everything can be done remotely. I cannot do my MRI scans, cardiac CTs or echocardiograms remotely. Those are fundamental to managing the care of my patients, let alone doing procedures that save lives and prevent disability.

Elective care can very quickly become urgent. It is not only emergency care that we need to worry about. We need to protect cardiac critical care, paediatric and adult, and regional cardiologist services. That will avoid a build-up of care we just cannot catch up with and, most importantly for the population, prevent avoidable death and disability. I agree with the point made by Professor Brightling about the importance of somehow looking after and nurturing our workforce, who have been through a lot already.

I do not have the solution, but we need to do something about people who are minority ethnic in the UK. There is a cardiology example. Recently, on 10 September, NICOR published data, and it is very concerning to see that people whose ethnic background is non-white have had different care pathways and have had delayed care, and in a worse fashion than the disparity that exists normally. We need solutions for that. Those features are happening beyond correction for age, deprivation and cardiovascular disease, which we know is more common in certain ethnic minorities.

Lord Hollick: Is there sufficient capacity in the health service to make substantial progress in catching up with the elective surgeries that should be done, and would be better done now, rather than waiting until next year?

Dr Sonya Babu-Narayan: One of the limitations at the moment is social distancing. We have to deliver safe care, and patients have to be tested as Covid negative before they can be admitted for procedures. That is why I mentioned speeding that up. There have been creative ways of working. As a cardiologist, during the pandemic, I have seen Royal Brompton NHS patients at a private centre so that they do not get delayed. Going forward, we may have to see how creative we can be. Perhaps Covid-19, which many people now know how to treat, could be consolidated, so that some of the rest of the work can continue. As you can hear very clearly, I am very worried about excess deaths that could have been avoidable with tried and tested treatments; there are cardiology patients we know how to treat, and treat well, with good outcomes.

Q187 **Lord Kakkar:** I would like to turn back to the very impressive prospective research effort. It is clearly an important UKRI or NHIR investment. Beyond the one year of presumed follow-up at the moment, what arrangements will be made for the longer-term evaluation of those patients, so that we start to understand much more the natural history of the long-Covid phenomenon? In that regard, would there be merit in having—or is there the capacity to ensure—at least some kind of prospective registry of all patients who have suffered disease, so that at a time in the future, if there were the need to identify individuals and perform some kind of follow-up, those facilities might be in place?

Thirdly, has there been any capacity to collect biological material from patients during their hospital stay that would allow prospective evaluation of novel biomarkers or other molecular assessment that might allow better characterisation in future of patients who are at very high risk of long-term manifestations of this disease?

The Chair: Short answers please.

Professor Chris Brightling: The answer to question one is that we have ethical approval to follow people for up to 25 years, but funding for only one year. We can do that once we have sufficient resource if there is a continuing problem.

The answer to question two is that we will be linking up with a planned primary care community-based cohort that has not yet been funded but is being planned. We could also link up with some of the big data strategies that I know others are champions of. If we can link to longer-term registries, we absolutely will.

The answer to the third question is that in the ISARIC 4C observational follow-up there were approximately 2,000 individuals who had bioresource collections at the time of the acute episode. We are including as many of those people as we possibly can as part of PHOSP-COVID and will be collecting bioresource in up to 4,000 individuals. We are also closely linked to what is called UK-CIC, the national immunology consortium. We have a clear immunology stream where we will be looking at the persistence of immunity based on antibodies and memory

based on T and B cells, as well as looking at the inflammatory biomarkers associated with different disease trajectories. They are great questions and definitely things we have in mind.

Professor Kamlesh Khunti: I should have mentioned that I am privileged to chair the SAGE sub-committee on ethnic minorities and Covid. As part of that, we brought all the data science together and we have a data group. The UK definitely has the best data in the world. We are bringing together all the data, some of which Professor Brightling mentioned. Once we have the databases, we can look not just at 12 months but at the longer-term consequences. People will have had the disease at population level, and we can compare their key outcomes, especially the cardiovascular, the respiratory, the mental health, hospitalisation and mortality, with those of people who did not have the disease. It is quite an exciting longer term as well.

The Chair: Your question about tissue did not get an answer, Lord Kakkar, but perhaps in the next session when we have the pathologists you can ask them.

Q188 **Lord Mair:** May I ask the witnesses to say something about fatigue? Is the fatigue being reported by Covid sufferers some months after the outbreak more extreme than after other illnesses? Is it understood what lies behind the fatigue? Professor Brightling, could you answer that first? It seems to be associated with breathing difficulties, but is it connected or separate?

Professor Chris Brightling: There seem to be a multitude of reasons why people are getting fatigue post Covid. In some cases, it is deconditioning; they are unable to exercise so they are becoming weak and as part of that having fatigue. In some, it is more like the chronic fatigue syndrome that is seen post-virally in other conditions. In others, it is directly related to damage to end-organs, such as the lungs.

It comes in many different guises. We have a working group on chronic fatigue that includes those with a specialist interest in that particular area. We have a number of ways of trying to unpick it to try to understand the underlying mechanisms, because each will probably have a very different intervention, and that is where it will be very important.

Lord Mair: Do the other two witnesses have anything to add on the question of fatigue?

Dr Sonya Babu-Narayan: Nothing from me.

Professor Kamlesh Khunti: I do not think we will be able to clearly define what the causes of fatigue are, because it is, as Chris mentioned, a multisystem disorder, with multiple inflammation and multiple immunological comorbidities. About 50% have fatigue at 60 days. Health-related quality of life is also reduced, so mental health aspects could be impacting on fatigue as well. It is very difficult to disentangle the real cause of the fatigue. Chris and many others will be trying to disentangle the key reasons, but it will be very difficult.

The Chair: I have to let Baroness Young ask a question. As the one-time queen of Diabetes UK, I could not leave her out.

Q189 **Baroness Young of Old Scone:** My question is to both Professor Brightling and Professor Khunti. Moving away from the research that you have described, is a systematic approach to service level beginning to emerge either locally or across the NHS in order to routinise long-term follow-up and patient review? I know that Kamlesh is very keen on the NHS Health Check being used for patients from a black minority ethnic background at a much earlier age as a way of routinising follow-up and risk assessment, but should we be applying that to all post-Covid patients? Should there be a post-Covid system to make sure that people are not suffering in silence at home and getting worse in the way that was described earlier?

Professor Kamlesh Khunti: We do not know the natural history of this condition. We know it is a multisystem disease. We know that cardiovascular disease is affected. We know that it has insulin resistance so it has an impact on diabetes. We know there is an issue with chronic kidney disease. My good friend Professor O'Donoghue will be here later, and I am sure he will talk about that.

We do not have the history behind it, but we know that all those systems are affected, so it makes sense to follow people up. We have the NHS Health Check programme at the moment where people over the age of 40 are screened at five-year intervals. That lends itself to some form of longer-term surveillance in people who have been Covid positive, because we have already heard that there is a multisystem problem.

I chaired the NICE guidelines on the prevention of diabetes, and we know that screening people in ethnic minority populations from the ages of 25 to 39 is not just cost effective but cost saving as regards diabetes, pre diabetes and a prevention programme. We would recommend doing that for cardiovascular and kidney disease as well, because we have seen the inequalities that Covid has shown in minority ethnic health populations. Trying to screen people early and managing risk factors early may be somewhere to go, but we do not have the evidence for it. It is just one of the recommendations we are making.

Professor Chris Brightling: There definitely should be an integrated multidisciplinary healthcare approach to the consequences of Covid. As part of the research programme, essentially, we started there because we had to go through all the centres and try to understand what their clinical service looked like. It ranged from a multidisciplinary complex clinic through to people saying, "We have no post-Covid follow-up and we are relying on the primary care physician to refer people when they have significant pathology".

There is a very large spread of access to healthcare post Covid. There would definitely be value in improving it and having a more integrated national service. There are good examples where all the specialists have come together and we have certainly learned from each other. As an example, our clinic has diabetes experts as part of the follow-up clinic.

Baroness Young of Old Scone: Do you have any feelings about the NHS Health Check, or is it a busted flush?

Professor Kamlesh Khunti: The Health Check programme has worked to a certain extent. We have identified lots of people who are at risk of diabetes, and we have had thousands going through the prevention programme. We have seen from the data that we and others have published that it can lead to weight reduction. It is early days in knowing whether we can prevent outcomes. Covid has put a spanner in the works as regards seeing those patients. They are having it delivered remotely, but I am not sure how effective that is.

The Chair: That is an NHS England answer, Baroness Young.

Baroness Young of Old Scone: Absolutely, Chairman.

Q190 **The Chair:** There are only two minutes left, so let me ask a general question. Most of the treatments—you mentioned some, Professor Brightling—are related to patients who were admitted to hospital with Covid-19 infections; otherwise we just tell patients to stay at home and rest, and only go to hospital or call 111 if something happens. Have we got to a stage where we can suggest some treatment at the early phase of the disease once the test is positive?

Professor Chris Brightling: It is a great question, to which the very simple answer is that we do not have the data. The best treatment for reducing mortality, dexamethasone—corticosteroids—led to an adverse or worsening outcome in those with milder symptoms who were admitted, suggesting that if you took that treatment in the community it might lead to more harm than good. At the moment, we simply do not have the data.

The Chair: What about antivirals?

Professor Chris Brightling: The antiviral data is largely from in-patients. In the UK, that comes back in part to testing. The testing focus was very much on in-patients. At the peak, we had people in the community who obviously had Covid and symptoms of Covid, but we did not have clarity with testing, so the community-based studies have not been done in the same numbers and did not start as early as the in-patient studies.

Antivirals may be very valuable. There have been antiviral studies acutely with remdesivir, which is now available. There are other antiviral therapies, such as interferon beta, and in very small studies those have been very promising. Interferon beta will be tested further in the in-patient setting, and for remdesivir they are looking further into community bases. It will be dependent on treating early, which goes back to some of the earlier discussion around making sure that we have appropriate testing available early. If we had tests that could screen people before they became very symptomatic, that would be even better, but we are some way from that.

The Chair: Most of the patients you have seen who come to hospital

have pneumonia already.

Professor Chris Brightling: A number of the people are admitted between day seven and day 10, so absolutely there would have been a prodrome and we could have potentially changed the trajectory of their disease to prevent them coming into hospital. I am completely in agreement with the direction of the question, which is that we should be putting our focus on stopping the disease becoming severe rather than on efforts to treat people who are severely ill. That absolutely should be the case. There are certainly studies to try to do that, but they have not progressed as quickly as the studies in hospitals.

Professor Kamlesh Khunti: A study called the PRINCIPLE trial is the main one being conducted in primary care at the moment. Those are patients who are not experiencing severe symptoms. It is a randomised control trial run from Oxford looking at erythromycin and doxycycline against usual care. But it is early days. We do not have any results yet.

The Chair: Thank you very much. I am sorry to say that our time is up, because there is a lot more we could have asked you about. We are very grateful to all three of you for coming today to help us with our inquiry. Please stay on if you have time, as we are moving straightaway to the next session.