HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: UK Science, Research and Technology Capability and Influence in Global Disease Outbreaks, HC 93

Wednesday 16 June 2021

Ordered by the House of Commons to be published on Wednesday 16 June 2021 .

Watch the meeting

Members present: Greg Clark (Chair); Aaron Bell; Dawn Butler; Mark Logan; Rebecca Long Bailey; Carol Monaghan; Graham Stringer.

Questions 2400 - 2497

Witnesses

I: Professor Wendy Barclay, Head of the Department of Infectious Disease, Imperial College London; Dr Susan Hopkins, Strategic Response Director, COVID-19, Public Health England; and Professor Sir Andrew Pollard, Professor of Paediatric Infection and Immunity at University of Oxford, and Director, Oxford Vaccine Group.

Written evidence from witnesses:

– [Add names of witnesses and hyperlink to submissions]

Examination of witnesses

Witnesses: Professor Barclay, Dr Hopkins and Professor Pollard.

Q2400 **Chair:** The Committee is now in session. The Science and Technology Committee continues its inquiry into the role of science in responding to the pandemic. We are interested today to hear about the impact of some of the new variants of Covid, their interaction with the vaccines that are available, and some questions about the implications for social distancing requirements and other restrictions that are intended to be extended now until 19 July.

I am delighted that we have three very expert witnesses to help us consider these questions today. They are Dr Susan Hopkins, who is the strategic response director for Covid-19 at Public Health England; Professor Wendy Barclay, who is a virologist and head of the Department of Infectious Disease at Imperial College London, and is a member of NERVTAG, the Government's New and Emerging Respiratory Virus Threats Advisory Group; and Professor Andrew Pollard, who is professor of paediatric infection and immunity at the University of Oxford, director of the Oxford Vaccine Group, and one of the leaders of the team who produced the Oxford-AstraZeneca vaccine, for which he was knighted in the birthday honours at the weekend to become Professor Sir Andrew Pollard.

Many congratulations, Sir Andrew. We are grateful, as the whole country and indeed the whole world is, for the extraordinary work that has proved so vital and productive. Everyone on the Committee, I know, agrees with me that it is an honour that is richly deserved for both you and your excellent team. Welcome and thank you.

Let us start with a look at some of the variants and the Delta variant that was first encountered in India. To understand a bit more about that, can I ask Professor Barclay to give us a guide to what we might expect from new variants of Covid? Am I right in understanding that new variants occur in very large numbers all of the time in all countries? Would you respond to that and fill us in about how we should think about variants?

Professor Barclay: You are quite right. SARS-CoV-2 is an RNA virus and it is replicating with unprecedented numbers around the world at the moment. It is, therefore, not surprising that we see variants occurring. It is widely spread and the variants emerge in different parts of the world independently.

What has been quite remarkable is that for many of the variants we see a degree of what is known as convergent evolution, where variants emerging in different places have either identical mutations in their genomes or have mutations that appear to confer the same properties to the virus. This is a virus, remember, that has come into humans relatively recently from an animal source, and, therefore, it is not very surprising that some of the variants are being selected for in the new

human host because they probably confer advantage to the virus in its replication or transmission in humans.

Public Health England risk-assesses the variants and tracks them very closely, as does the World Health Organisation. We rate variants depending on various pieces of evidence before us, including the genetic sequence but also including other pieces of information such as epidemiological characteristics or even laboratory work.

Variants fall into two groups at the moment: the variants under investigation and the variants of concern. When a genetic sequence is first noticed and something about it makes us feel that it is worthy of special attention, it becomes a variant under investigation, and then the number of those sequences, the location and the properties of the virus as they emerge are tracked.

If a virus, a variant, meets various criteria that suggest that the new virus would be more difficult to control using current measures, whether that be social distancing or any of the vaccines we have, or if it is showing any properties that would increase our concern about it—for example, increased severity—it might get upgraded to be called a variant of concern.

Currently, there are four variants of concern, and the World Health Organisation recently designated a new way of naming them after Greek alphabet letters. We currently have Alpha, Beta, Gamma and Delta. The UK saw the emergence of the Alpha variant back in December. It began to predominate and was indeed the predominant virus in the UK until relatively recently. We have seen incursions of Beta and Gamma into the UK—Beta more than Gamma—but Delta is now the predominant variant in the UK.

Q2401 **Chair:** Thank you. That is very clear and precise. I am very grateful for that. To probe that a little further, give me a flavour of the workload involved. You said that these variants arise all the time but only some of them give rise for concern. How many variants that exist appear in any given week or month and need to be filtered down into the ones for further investigation?

Professor Barclay: As well as the four variants of concern, there are WHO-designated variants of interest and PHE-designated variants under investigation, which do not necessarily completely correspond. I would estimate at the moment—I cannot remember the exact number—that people are looking at round about 20 or 25 different virus lineages that have hallmark genetic changes that designate them as a lineage of a variant. Those are picked up all over the world but also in the extremely strong and extremely intensive sequencing efforts that go on here in the UK.

Such variants are discussed and monitored at the Public Health England horizon scanning group as well as in several other places, and there is a

variant technical group in Public Health England that looks at them in more detail once they become variants that people need to study more intensively. There are several layers of triage, going all the way from the millions of sequences that appear on global databases, to grouping those using phylogenetics to understand their groupings and their sources, and working your way through looking at the mutations and the epidemiology to try to put them into groups and designate them as needing investigation or indeed of concern.

Q2402 **Chair:** In terms of the conditions that give rise to particularly dangerous variants, if I can put it that way, is there anything that we know about the conditions that might give rise to worrying variants, or is it essentially random? Could they happen anywhere at any place, any time, as it were, or are there things that we can control to minimise the dangerous threat?

Professor Barclay: One of the very interesting things about the variants of concern is that they have constellations of mutations in them. For example, the Alpha variant emerged with 23 mutations that hallmark it as Alpha that occur across the whole genome. That grouping of mutations, without necessarily having evidence of the virus evolving stepwise towards those, suggests that some of these variants are emerging after long-term replication in individuals who are unable to clear the virus, such as immunosuppressed people. In fact, there is a pre-print from the South African group quite recently where they have tracked the evolution of a virus in an HIV-infected individual in South Africa, and the properties, genetically speaking, are remarkably similar to the Beta variant that emerged in South Africa. Similarly, there are published papers describing replication in immunosuppressed individuals from around the world showing that mutations can occur and accumulate in that way. One place where we might expect them to happen is in individuals of that nature.

We also see that on top of the variants of concern you can get individual single-point mutations on top of those clusters. Those probably occur as the virus circulates in the population at large and are not necessarily being selected for in a special cohort of people. That is just the process of virus evolution where you get single or double mutations occurring every time the virus replicates, and if there is a slight advantage to the virus that is the one that will grow out.

It has been noted that variants of concern such as Beta and Gamma have emerged apparently from parts of the world that experienced fairly intensive infection rates in the first wave, probably round about the summer of 2020, so there is a feeling that the immunity of a population as it increases may drive selection of viruses with different properties.

Q2403 **Chair:** In terms of what you said about early evidence about whether immunosuppressed people might be more susceptible to developing new variants, does that have any public policy implications in the sense that we should be looking to focus particularly on immunosuppressed people, either to keep an eye on them or have greater restrictions there, or are

we too early into this study to be able to determine that?

Professor Barclay: The management of patients with long-term Covid infection is very difficult, both for the patient themselves whereby they can experience resurgence intermittently of the virus and get very sick, and potentially for the healthcare workers and even the public at large. I think that there is a need to look carefully at the management of patients who have long-term infections and are immunosuppressed. As we move forward and are able to use more treatments—such as, for example, some of the monoclonal antibody treatments where such patients are not terribly good at making their own immune response but might benefit from the passive therapy given by a therapeutic combination of monoclonals—that is worthy of consideration.

Q2404 **Chair:** Obviously, part of that is for these individuals' own protection.

Professor Barclay: Yes.

Q2405 **Chair:** However, if they are more likely to be host to a new variant, is there a broader public health interest or concern over and above their individual protection to concentrate on such people?

Professor Barclay: That is possible, but we do not have any evidence of a healthcare worker, for example, contracting their infection from such a patient. Sometimes, the patients themselves are sick for a very long time—you can see the virus accumulating mutations—but the viral levels are low in those people, and it is not obvious how the virus gets from them out into the wider community. The implication is that some of the variants have emerged in such conditions, but we do not have direct evidence that that has indeed happened.

Q2406 **Chair:** Finally from me, before I turn to my colleagues, is it possible to say or to reflect on whether over the course of time new variants of Covid or other coronaviruses tend to moderate in their impact and infectiousness or tend to become more malevolent and more aggressive? Is there a tendency that one would expect?

Professor Barclay: No, I think there is perhaps a fallacy around that as the virus adapts to humans it will get less severe, for example. I do not think that that is necessarily the case. The overarching pressure, if you like, on the virus is transmissibility. The thing it selects for most strongly is increased transmission. We have to consider whether the people who are transmitting are the people who are getting ill, and I would say probably not. Therefore, the two properties are separate and they do not necessarily get linked together. It is possible that as the virus becomes more transmissible it could cause more severe disease, or it could go the other way. At the moment, the virus is adapting to being fitter in the human host.

Q2407 **Chair:** That is very helpful. Before I turn to Carol Monaghan, do Sir Andrew or Dr Hopkins want to make any additional observations on the issues we have just talked about?

Professor Pollard: One additional comment is what we might expect to happen in the future. We know with these respiratory viruses that they do continue to throw up mutations. They will be doing that, as Wendy said, to allow them to continue to transmit. In an immune population, whether from natural infection or vaccination, to continue to transmit they have to escape immunity. One of the things that we are doing at the moment is looking in very granular detail at the variants emerging at the moment, because it is critical as we try to get high vaccine coverage and protect against hospitalisation.

As we go forward over the next few years, we are going to continue to see lots of variants emerge that will transmit between people. If we looked at the coronaviruses that all of us had as children, we would see those transmitting in populations. We know that happens with flu. If you look in that granular detail, it will look really worrying in the years ahead because we will still, I think, have this coronavirus transmitting, and I suspect my colleagues would agree with that.

The reason why we are looking at the moment is to understand its biology and to be in a good position to manage whether we need new vaccines to prevent hospitalisation. It is not the thing in the future. If we are able to build immunity in our populations that keep people out of hospital, we will reach a point where we stop looking in this granular detail at what is happening in the community. If we do, we will just focus on it to worry because it will escape from vaccines.

There is an issue here that we are talking about variants and their emergence. This will happen and it will continue to happen. In the end, we will have to come back to focusing on the really important public health issue, which is hospitalisation and death. As Wendy implied, if those are disconnected, if transmission is disconnected by vaccine immunity from the severe disease to a large extent, we will need to monitor the new variants if we need it for designing new vaccines and so on, but we are going to have to live with it being in our communities and transmitting. Hopefully, that makes sense.

Q2408 **Chair:** Thank you. We will go into some more detail on vaccines. To probe a little further on what you said, you said that the virus will escape vaccines, but we might look at the impact on hospitalisation and healthcare for reassurance. What you are saying is that, in escaping it, it will be a partial escape in a sense that it will infect people but not with the same consequences. Have I got that right?

Professor Pollard: What we have been waiting for over the last month with the Delta variant is to find out whether with two doses of the vaccine we have good protection against hospitalisation. The data that came out on Monday from Public Health England that show over 90% protection against hospitalisation are incredibly reassuring in that regard. That is the key bit that we have to look at with future variants. If that very high protection against hospitalisation continues despite spread in the community, the public health crisis is over. So far, up to Delta, we are in

a very good position as long as people are vaccinated. Of course, the WHO at the moment with its variants under investigation is up to Kappa. There are more Greek alphabet letters still to go through. Hopefully, we will still be in a good position when we get to Omega, but we have to keep monitoring it because we don't know yet. We have only got up to Delta.

Q2409 **Chair:** There is a dual significance to the robustness of the data on the Delta variant in terms of hospitalisation. One is for that variant itself, but, from what you just said, it is another test that has been passed, as it were, for variants in general that the risk of severe disease and hospitalisation seems to have passed. Am I right in inferring that, with every one that goes by, we can be confident in general over and above the particular variant?

Professor Pollard: We are still quite early in the pandemic. Remember, the vaccines were made from the original variant before Alpha. I do not know what we called that. Wendy, is it Alpha-minus or something? The one before Alpha that originated in Wuhan in China was used to make the vaccines, and the vaccines protect against that variant and they protect against Alpha. We have very good evidence here in the UK of very high levels of protection against hospitalisation, and now we can see that is the case with Delta.

We do need more time. We need to see what happens with future variants. So far, that is quite a reassuring position, but you have to have a highly immune population to make sure you are there. It is not enough to have lots of people unvaccinated.

Q2410 **Chair:** Thank you. We will come on to that in a bit more detail. Professor Barclay, do you have the answer to what is before Alpha?

Professor Barclay: Ground zero, I guess.

Q2411 **Chair:** Ground zero. I have heard it described as the "wild type". It does not have a particular letter. Dr Hopkins, do you have any particular addition to what your colleagues have said so far?

Dr Hopkins: I just want to highlight the point that we are living in a world of variants now. Everything we see is a variation of the original and, actually, everything we see that is going to live and not become extinct very rapidly is either going to have a transmissibility advantage or an immune-evading advantage. The challenge always is trying to understand which one of these will do something as it emerges. We start following and monitoring them when we get to about 30 cases that we can see in the genome sequencing, but that is not enough to give us real-life data on the impact of vaccines, on the impact on transmissibility.

When we call out a variant under investigation and, even before that, a variant under monitoring—we have about 25 under monitoring and eight under investigation at the moment—we are really looking to try to find those early signals. All of them have mutations that we are concerned

about, but mutation alone is not enough to predict, as Professor Pollard said, whether it will really impact on our journey through vaccines and impact on the public health risk of hospitalisation. That is the component that takes time in being able to deliver that science accurately and allows us to develop accurate risk assessments.

Q2412 **Chair:** You said that 30 is too small a number of cases to be able to draw firm conclusions from, and one can see that. Is there a threshold or rule of thumb that you have in mind for a number of cases to understand more substantially the threats that it might pose?

Dr Hopkins: What we need is a number of cases to understand the threat for hospitalisations. You need to have a number of cases hit hospitalisations, if you like. That requires people to have undergone follow-up for at least two weeks after the initial infection that has been identified so that you can monitor them in hospital and monitor their outcome. It takes three to four weeks to monitor the early outcome of mortality. With the doubling time for these variants, you would therefore expect that you will be able to start to make an assessment when you have thousands rather than tens or hundreds. Where we were able to start making an assessment on vaccine effectiveness, you need at least 100 cases in hospital. That is quite similar to the vaccine trials, actually, where you need a certain amount of events to have taken place to allow you to make that assessment.

Chair: At least 100 in hospitals and therefore thousands of cases. That is very helpful indeed.

Q2413 **Carol Monaghan:** As a former physics teacher, I am quite enjoying the focus on the Greek alphabet as it was always a bit of a challenge. Professor Barclay, the estimation is that the Delta variant has a dominance of about 91% at the moment. Is there any explanation for that?

Professor Barclay: Yes. In simple terms, it appears to be more transmissible. As for the genetic explanation, most of the information about this new virus is around the spike protein at the moment. That is the way that the virus latches on to cells and enters cells, and, therefore, it is the primary route in during the transmission events.

We know that there are some mutations in the spike of the Delta variant that helps it to enter cells more quickly. For example, it may be that a person gets infected more quickly and the virus gets on with replicating and wins the race between the virus and the host more successfully. You could put it another way. A person perhaps needs to be exposed to slightly lower doses of the virus in the environment for infection to initiate and take off.

In either case, there are genetic markers that we are now beginning to understand that suggest this virus is more transmissible. There may be further changes in other parts of the genome, because we actually know

very little about what all the other proteins of the virus are doing to modify, for example, the innate immune response of a person when they are very first exposed to the virus. It acts as a very strong barrier usually to getting infected, but viruses have cunning ways of stopping that from working properly, and those are also under extreme pressure during the early adaptation to a new host to hone in and get more efficient.

So it is probably down to a combination of these mutations because, as I said, there are constellations of mutation across the whole genome, but the ones that we understand the best are the ones in the spike protein.

Q2414 **Carol Monaghan:** Thank you, Professor Barclay. Could I turn to Dr Hopkins? We have heard about the increase of transmissibility with the Delta variant. What is your latest assessment of this figure?

Dr Hopkins: We have assessed this in a variety of ways. First of all, we have looked at the growth rate: how fast it is growing in comparison to the Alpha variant. The growth rate suggests that it has increased by 40% to 80%, using modelling techniques to estimate that.

We have also looked at in-household transmission studies. That gives us an assessment, when a case occurs in a house, of how many other cases happen in that household and we compare that to cases of the Alpha variant, the B.1.1.7, so that we can look at that. For the household study, we have an assessment that the odds of transmission are 66% greater for the Delta variant compared to the Alpha variant within a household.

We clearly also see that the secondary attack rate—how many people go on to infect another individual—is also about 30% to 40% greater. About 8% of individuals who have been identified as a contact of a case with Alpha go on to become a case, and about 12% of cases who have been identified as a contact of a case with Delta go on to become a case. All of the quite significant different components that we take in, along with the biological data and the mutations that we have identified, determine that this has much greater transmissibility than the Alpha variant.

Q2415 **Carol Monaghan:** This is pretty concerning, clearly. How confident are you of this assessment and do you need to be gathering further data to be entirely confident?

Dr Hopkins: We will continue to gather the data. We will review and look at all of the data as it comes in every day and do a formal analysis at least weekly depending on the number of new cases and the number of events that we see. What we have is quite wide confidence intervals—quite wide uncertainty around that. When I say 40% to 80%, and when I say 66%, that is between 30% and 100%. What we estimate is that, as we get more cases, we will be able to refine those estimates to get a narrower band of uncertainty around it.

We have reviewed this with our experts, both people like Wendy who sit on our technical group, and other virological and modelling experts, including with colleagues on SPI-M. We are seeing much greater

transmissibility than Alpha, which had greater transmissibility than the viruses that had gone before. Therefore, unmitigated, if we were in the real world where we had none of the measures that we are seeing right now, we would estimate that R was greater than 5 and maybe up to 7, compared to where we were right back at the beginning of this when we thought the R value was 2.5.

That is why we need people to have vaccinations because that is a clear mitigation measure. That is why we need people to take care and take caution, particularly in healthcare settings, in performing the IPC that has been recommended by the national IPC group.

Q2416 **Carol Monaghan:** You talk about large uncertainties. Even within that large window or broad spectrum, do you still see that as being far greater compared to, for example, the broad spectrum we might have seen with the Alpha variant?

Dr Hopkins: We are convinced scientifically—we have high confidence that this has much greater transmissibility. Our risk assessments started with low confidence, but we have moved that over the weeks to high confidence. It does not get any better than that, I am afraid.

Q2417 **Carol Monaghan:** Public Health England has said that this variant increases the risk of hospitalisation by two times and the increase of critical care intervention by 1.5 times compared to Alpha. What are the implications for us in terms of how we respond to this?

Dr Hopkins: We have two studies. Public Health England has performed a study looking at the data that has come through emergency care—individuals who have come through the emergency department—and Public Health Scotland has also done a similar study with the University of Edinburgh called EAVE II. Both of those studies show that this variant, after adjusting for age, sex, the time of the year and also by vaccination status, has more than twice the risk of hospitalisation compared to the Alpha variant. That means that for any one case that is unmitigated—not vaccinated—the risk of hospitalisation is greater.

However, I would say that we have had, again, quite positive news from the vaccination status showing that if you have had two doses of vaccination you have more than 90% reduction in the risk of hospitalisation. What we will see is a difference compared to what we saw in wave 1 and wave 2. I count wave 2 from September to March. For both of those, we did not have vaccination to mitigate the risk of hospitalisation. If we were in a situation now where we had no vaccination, we would be in a very difficult situation for hospitalisation. In a way, we have trade-offs. We have a large amount of our very seriously likely to be admitted to hospital groups—vaccination groups 1 to 9—who have already received two doses and therefore are mitigated. What we have to do is get the second doses into the next groups down who are the next groups that are at risk of hospitalisation.

Q2418 **Carol Monaghan:** Is there any evidence that complacency among those who have been vaccinated is allowing greater transmission and possibly further mutations?

Dr Hopkins: I have not seen any evidence of that. I think that people are still taking precautions. We have been very clear on the public health messages, saying, "Just because you are vaccinated, do not stop taking precautions." We do not have a transmission-risk-averted reduction yet for this. We are seeing a reduction in symptomatic disease after vaccination, particularly after two doses and less so after one. Our very strong public health message is that we need to continue to have some social distancing in place and some mitigations at least until we have high levels of vaccination throughout the population and we have low prevalence. Both of those things go hand in hand. That is what will reduce the risk of viral replication.

Q2419 **Carol Monaghan:** I think we are getting the message very clearly this morning that this variant is of great concern because of its transmissibility and because of the severity of symptoms. Which of those should we be most concerned about?

Dr Hopkins: Transmissibility is most concerning for me at the moment because it means that it can infect a lot of people and therefore it can find those people who are not doubly vaccinated or those people who, because of their underlying immune system response to the vaccine, will still have severe disease despite having two doses of vaccination. We have said over 90%, but it is not 100%. For me, the more transmissions there are and the more infections there are, the more it can find those people who are not protected.

Q2420 **Carol Monaghan:** Is there a danger that the more it transmits, the more opportunities there are for further mutations?

Dr Hopkins: Absolutely.

Carol Monaghan: Thank you. Thank you, Chair.

Q2421 **Chair:** Thank you very much, Carol. Just on what you said about a counterfactual, Dr Hopkins, you said that, had we not had the level of vaccination that we have, you think the Delta variant would be causing a much bigger impact on hospitalisations. We obviously have two mitigating factors at work now: one is the vaccination, and the other is the continuing social distancing—non-pharmaceutical interventions. In contemplating the impact, have you made an assessment of what the relative contribution to the level of problems that we would otherwise have comes from the vaccination versus the social distancing restrictions?

Dr Hopkins: The modellers from SPI-M have done quite a lot of work on this that bring a consensus model together. The papers that were released this week showed the difference between doing step 4 and not doing step 4. That is a measure of the mitigation by keeping social distancing and reductions in social mixing down to a lower level. It will

keep the R value down, probably in the order of 0.2 or 0.3. I take my expert advice from modellers to pick an exact number. There will be a range around that. That is a key factor in allowing us to have some time when the R value is not rising very quickly and rather rapidly. We know that each stage of the stepped process that we have gone through—each release—allows the R value to increase. We saw that between step 2 and step 3, even without the Delta variant having come in. We would have expected a 0.2 rise at least in the R value, and we would have hoped that that would have been mitigated by first doses of the vaccine. With the Delta variant, the mitigation of a single dose of the vaccine is less and therefore we need to have some measures of restrictions in place to allow us to vaccinate more people and get those two doses in.

Q2422 **Chair:** Thank you.

Professor Barclay, did NERVTAG consider what the relative impact of the vaccination rate that we have achieved versus the social distancing restrictions has been on suppressing the impact on hospital admissions of the Delta variant?

Professor Barclay: I do not believe we have specifically discussed that on NERVTAG. As Susan said, that really is something that we would expect SPI-M and the modelling colleagues to be weighing up. Certainly, there is an agreement in NERVTAG from a virus evolution point of view, for example, that keeping the numbers of infections as low as possible during this coming period is a very important thing to do to prevent, as was just mentioned, the concept that the virus might evolve further mutations. NERVTAG is agreed that keeping numbers low is very important and that the social distancing measures are clearly important contributors to that.

Q2423 **Chair:** But it is the case, is it not, that the decision was taken to prolong the current social distancing measures at least until 19 July, but not to add additional ones? That is obviously a political decision as to what steps to take, but scientifically and epidemiologically there is a calibration there that the current position should not really weigh excessively heavily. If we have a Delta variant that is causing problems and you are concerned that it should be suppressed, should you not determine the right level of restrictions to do that rather than simply note what is currently being applied?

Dr Hopkins: I think that is a Government decision. The modellers weighed up what we would be doing if you went backwards, what that would do to cases, what would you do if you stayed in step 3, and what would you do if you went to step 4. That was shared through SAGE to Government, who make the decision on what their plans are: further release or not release.

Chair: I see.

Dr Hopkins: The models have looked at all of that, and the models incorporate the vaccine effectiveness that we see, the transmission

dynamics that we see, and other factors related to the virus and also social mixing.

Q2424 **Chair:** I do understand it is a decision for Ministers.

Professor Barclay, in terms of the scientific advice that goes to Ministers, is it just a remarkable coincidence that the optimal package of social distancing measures are the ones that happen to be in place at the moment?

Professor Barclay: As Susan has said, we do not tell the Government what social distancing measures there should be. The advice that goes forward is that there is concern about a variant and that we can see it growing in these various figures, as has been described. It is then for policy makers to decide on the measures and ask SPI-M to model the effect of such measures. I do not think NERVTAG is really tasked in telling the Government what measures should be put in place.

Chair: Okay. Let me go to Dawn Butler.

Q2425 **Dawn Butler:** Thank you, Chair. Congratulations, Professor Pollard. Can I just thank all of you for coming to the Committee again and for your evidence, and explaining things in a way that everybody can understand? It is very much appreciated. Where is the Essex variant in the alphabet? What name has that been given?

Dr Hopkins: Is that what you mean by the original Kent variant? That was Alpha.

Professor Barclay: Alpha.

Q2426 **Dawn Butler:** How do the Alpha variant and the Delta variant differ?

Professor Barclay: From a genetic point of view, you can sequence them and you can see the difference. They have different constellations of mutations. Clearly, everything came from the original source spread around the world, but as it was geographically dispersed, like branches of a tree, the virus branched off into different but related lineages. Alpha and Delta are two different branches of the same tree that came from the same trunk.

Q2427 **Dawn Butler:** In regard to the Delta variant, a PHE study claims that two doses of Pfizer, as we talked about earlier, is 88% effective and two doses of Oxford-AstraZeneca is 60% effective against the Delta variant. What is the latest assessment around that, Dr Hopkins?

Dr Hopkins: What we see is that for dose one there is a reduction in the effectiveness for Delta compared to Alpha by about 17 percentage points and a reduction in the effectiveness of Delta compared to Alpha after the second dose by between five and 10 percentage points. It is really important that we look at the differences between Alpha and Delta for the same vaccine, because the vaccines take some time to mature and the responses take some time to mature. Both of them have quite similar

responses, but they have a different timeline. We know—and I am sure Professor Pollard will come in—that the AstraZeneca vaccine often takes a little bit longer to mature to its full response. When we looked at it initially, we saw that the vaccine effectiveness with AstraZeneca was lower after the second dose, but that has come up, and it is now closer to 70% vaccine effectiveness against symptomatic disease.

The most important thing is the vaccine effectiveness against hospitalisation. It is almost identical between the two—92% and 94%. The difference is so little that the confidence intervals overlap. That is the really important point that we are trying to achieve with vaccinations. Vaccinations were always there to prevent severe disease and hospitalisations. I do not know if Professor Pollard wants to comment on the immune response to AstraZeneca.

Professor Pollard: To re-emphasise, the virus is evolving away from immunity and we are seeing lower effectiveness against symptomatic infection. If we wind the clock forward a year or two from now, one would expect those numbers to get lower and lower. Unless the virus disappears from the planet, which I do not think is going to happen, it will have to be able to survive in vaccinated populations. If we focus on effectiveness against symptomatic disease in the future, we will go mad because those numbers will get lower and lower over time because that is the only way the virus survives.

The really important question is what effectiveness against hospitalisation looks like. As I said earlier, it is really encouraging so far. We are all hoping it will stay like that, but we do not know for certain, and that is why the excellent work that Public Health England does is absolutely critical to being able to monitor this going forward to help us make the plans as to whether further booster doses need to be used or we need new variant vaccines, and all those questions. So far, it looks very good.

Q2428 **Dawn Butler:** Dr Hopkins, you talked about Oxford-AstraZeneca taking longer, which reminds me that, initially, when they were doing the trials, there was a half dose, then a long period, and then a full dose, and that seemed to be quite effective. Has that just been abandoned, or are the results of that trial still being looked at? I know it was an initial mistake, but it was quite interesting output.

Dr Hopkins: I think Professor Pollard would be best placed to answer that considering he is part of the trial lead.

Professor Pollard: The different regimens that were used in the trials are a half dose followed by a full dose. If you use a three-month dose interval, it gives exactly the same level of protection as giving two full doses. It does not give you an additional advantage. Now that we have had a lot more time to evaluate the data, the programme that is used in the UK so far has been with the three-month dose interval. Whether it is a half dose first or a full dose, after the second dose you get exactly the

same level of protection. We will not suddenly be able to do some magic by changing the dosing schedules.

Q2429 **Dawn Butler:** As we ensure that we vaccinate the whole world and we are now distributing AstraZeneca vaccines, because we are now vaccinating people under 40 with Pfizer and Moderna, if it works and you get the full coverage with a half dose and then a full dose, it might be worth giving that information to other countries so that they can vaccinate more people.

Professor Pollard: It is certainly true that, if you give a half dose and then a full dose, after the second dose there is good protection. The problem that we have globally at the moment is a shortage of doses. We see much lower immune responses after the first dose if you use a half dose. If you give a half dose and then you are waiting for a very long time for your second dose, we just do not know how well protected people would be. I do not think we would recommend doing that at the moment. If you were in a situation where there was no disease around, it would be a good strategy because you could go a lot further, but, unfortunately, that is not the case anywhere in the world. So we need to stick with giving that first dose as a full dose, which gives strong immune responses—we saw with the original trials that that first dose gives very high levels of protection for at least three months and probably longer—and then get the second dose in as soon as we can.

Q2430 **Dawn Butler:** Thank you. Why are the current vaccines less effective? You kind of touched on this. What makes the current vaccines less effective against the Delta variant compared to the Alpha variant?

Professor Pollard: The mutations that the virus is adding in are ones that allow it to escape from these neutralising antibodies, which are important in protecting against symptomatic infection. The viruses that can survive, as Wendy said before, in a population that has either been infected or vaccinated are the viruses that can partially escape from those antibodies that we have been making to the vaccine or to infection—to the mutations in the virus.

Dawn Butler: I think Dr Hopkins wants to come in.

Dr Hopkins: To explain it in layman's term, when we think about mutations, we think about them in three dimensions. The mutations do not just add something that is in a line; they change the shape of the protein. That means the antibodies that are already produced just cannot bind as well and stick to it and therefore cause its impact. While we are talking about mutations, what we are also trying to understand is what that mutation does to the shape of the protein that is being produced. It is that shape that then means that the effective immune response is less. It is important that we think about these things in three dimensions rather than just the genome.

Q2431 **Dawn Butler:** In an earlier evidence session, we were told that the

mRNA vaccines will be easier to change if you are going to do the booster vaccines. Is it still the case that the mRNA vaccines will be easier to adapt to new variants?

Professor Pollard: From a biological point of view, there isn't any difference in the ability to adapt vaccines to new variants. I think the manufacturing side is a bit quicker for RNA vaccines. You can do it a matter of weeks quicker, but I do not think there is a fundamental difference technologically in adaptation whether it is an RNA vaccine or, in fact, any of the others, in the ability to use those for variants.

Chair: Did I spot that Professor Barclay wants to come in on that last point?

Professor Barclay: I was going to simply add to Susan's three-dimensional picture to let the Committee know that we measure in the laboratory the match between the neutralising antibodies and each variant as it emerges, and that is one of the earliest things we can do as our risk assessment.

Going back to an earlier question, as a new sequence emerges, provided we can get hold of isolates from the virus or synthesise a pretend virus, if you like, that has that sequence, we can perform laboratory tests to look at the match between the antibodies in people who have been vaccinated and each virus variant as it emerges.

What we see is that there is very little fall-off for the Alpha variant between the vaccine and the Alpha variant, but there is a drop-off for the match between antibodies in people's blood after vaccination and the Delta variant. It is not quite as big a drop-off as there is with the Beta variant, which was the one in South Africa, about which, before Delta, everyone was most concerned. None the less, the Delta sits somewhere between Alpha and Beta on that spectrum, and the laboratory assessment can guide us sometimes in when we understand what to expect in the field. As we get more experienced with this, we are beginning to be able to calibrate the relationship between vaccine effectiveness and the drop-off that we can measure in the laboratory, which helps us to know when to react with more concern.

Professor Pollard: Can I jump in there? There is a really important point to make here. What Wendy is describing is that link between neutralising antibody and vaccine effectiveness against symptomatic disease. That is an absolutely clear link that has been established. What we do not know is what you need to keep you out of hospital. There is good evidence that absence of neutralising antibody against a variant does not have a big impact on the ability of the immune response to keep you out of hospital. The neutralising antibody is critical for milder disease and transmission. We just do not know yet what you need to prevent severe disease. That is a major area of research.

Q2432 **Dawn Butler:** I know that previously the thinking was that it was not

worth testing people's antibodies. Is it worth testing people's antibodies, because there could be somebody who has a natural immunity to hospitalisation who might hold the key? Is it worth doing that yet on a mass scale?

Dr Hopkins: We are doing this within the SIREN study. We also have a very detailed immunological study called PITCH that we are doing with a number of immunological investigators, including colleagues from Oxford. What we do not have yet is a correlation between what the level of antibody is in your blood and what level of protection you have against asymptomatic, symptomatic or hospitalisation. Because the virus is changing and mutating, we will not be able to predict the future. It will take some more time. We need well-established cohorts so that we can look at what happens to individuals over time and we can do very detailed immunology to understand this. We have a number of different cohorts, but we have a process where if an individual comes into hospital we study that individual in more detail to try to understand what was different about their immune system compared to the general population. I do not think just doing a blood test right now will give us the answer, but I am very happy for others to come in and disagree.

Q2433 **Dawn Butler:** If you are only studying people who are in hospital, you will never find the person who may have caught the virus but not ended up in hospital.

Dr Hopkins: We are studying those people as well. We have the 45,000-healthcare worker cohort on whom we do PCR tests every two weeks.

Dawn Butler: Brilliant. Thank you all again for your evidence. It has been completely fascinating. Thank you, Chair.

Q2434 **Chair:** Thank you very much, Dawn.

Before I turn to Aaron Bell and Graham Stringer, I want to explore a bit further something that Sir Andrew said, which I think is particularly important for the future. Correct me if I am wrong, Sir Andrew. You were saying that the way that the virus is likely to develop through its new variants is that it is going to find a way to infect people mildly, but the evidence that we have and the expectations that we have are that we are likely to have protection from severe disease requiring hospitalisation. Have I understood that correctly?

Professor Pollard: That is where we are at the moment. As Susan Hopkins said, there is already some evidence of escape with this virus and also with the Beta variant from neutralising antibody, the Beta variant being particularly evil in that respect; and, yet, where there are studies that have looked at hospitalisation in, for example, South Africa, the vaccines are still giving very high levels of protection against hospitalisation. What we do not know is the future.

So far, it looks as if there is a distinction between needing these antibodies to prevent symptoms and mild infection, but we do not have

evidence so far that they are essential to prevent severe disease. Clearly, if you can prevent infection in the first place, you cannot get severe disease, so it is not the whole story. It still seems that it is possible to have high levels of protection against severe disease even without neutralising antibodies. We do not quite know what the virus will throw at us next, so we have to keep monitoring it. So far, up to Delta, it is quite reassuring.

Q2435 **Chair:** I think I remember you saying earlier that the expected course of the virus in order to be competitive would be to find a way to infect people. What we have seen and what has been notable about these variants of concern is that they have been associated with increased transmissibility, but, so far—as you point out, it is still early days—not with an increase in hospitalisation. Obviously, we have more time to pass and more studies to do, but that would be your a priori expected course of the development of the virus, would it?

Professor Pollard: I think we would all agree that you would expect the virus to find ways of escaping from immunity. Of course, one of the other things that happens in that context, as a virus that is not causing severe disease spreads, is that it is also boosting our immunity. Because it is the whole virus and not just the spike protein, it will give us much broader immunity, and it may eventually start to get to a point where the fire is quenched a bit more than just through the vaccine programme.

Chair: Absolutely.

Professor Pollard: That is why we really do not quite know what happens next because there are so many other things that are happening here. We have a virus escaping. We have infections building immunity. We have a vaccine programme. That is why this monitoring is so critical—to follow what is happening and be prepared to respond.

Q2436 **Chair:** Absolutely. That has very important implications for public understanding and public policy, does it not, because, so far, for the past 18 months, we have been terribly concerned about cases, about the level of infection, including asymptomatic infection across the country, and the possibility of vaccine escape has been cited and thought of as this great, almost existential threat? What you are saying is that we should, so far and a priori, expect there to be both vaccine escape and rising levels of infection or, certainly, continuing levels of infection. What the public and policy makers should be concentrating on then is the incidence of severe disease, including hospitalisation. Is my understanding of what you said correct?

Professor Pollard: From a vaccine person's perspective, that is absolutely the case. Wendy is the virologist. She should answer the question. The evolution of this virus has to mean escape from human immunity, otherwise the virus is eradicated, and I do not think any of us think that is going to happen.

Q2437 **Chair:** We should train our sights on hospitalisation rather than daily cases. Professor Barclay, do you want to add anything to that?

Professor Pollard: I think you have to focus on the hospitalisation, but daily cases are important at the moment because transmission is critical for planning what we do in the months ahead as we are trying to get the vaccine programme both here and elsewhere around the world up to the maximum that it can be, as that gives you the earliest possible warning signal of what might be happening to those who are unvaccinated at the moment. As Susan said, there is a time lag from new variants emerging to being able to get those critical pieces of information—the really important ones—that we need the answer to.

Q2438 **Chair:** I see. That is an important distinction. We may eventually be able to be relaxed about vaccine escape and infections because the protection is coming against severe illness from vaccination. We are clearly not at that 100% point yet, so we need to continue to worry about cases until the point that we get to whatever maximum level of vaccination that we can reasonably attain. That is the distinction, is it? Have I understood that correctly, Professor Pollard—our interest in cases should continue up to the point that we have vaccinated as many people as we can?

Professor Pollard: I think we will have to keep monitoring anyway because we are still so early in the pandemic. If it continues to be the case that we see vaccine escape and we see spread, but we do not see so much severe disease, at some point we are going to relax, but I do not think this is the moment to be relaxing.

Chair: Absolutely.

Professor Pollard: What we are talking about here is one view of what the future might look like from what we understand about viral evolution.

Chair: I understand. Professor Barclay and then Aaron Bell.

Professor Barclay: I think we are in uncharted territory here. I do not think there has ever been an example before where we have had a newly emerged virus and we have had a vaccine that we have used so widely. We are not really used to thinking about the way coronaviruses evolve. These are difficult questions. At the moment, we need to count cases very carefully because they give us early warning signals of new things happening, new clusters in different parts of the world or different parts of the country, which can be extremely important for understanding the evolution.

I also want to remind the Committee that, as Susan pointed out earlier, the vaccines are working extremely well against hospitalisation but not 100%. There is still a significant proportion of people who, unfortunately, will receive two doses but will not be protected even against hospitalisation. Therefore, the case numbers in the community relate to how many of those people will end up in hospital.

Q2439 **Chair:** That is understood. On our understanding of the evolution of coronaviruses, they have been with us, as you know better than anyone as the expert, for a long time. Why don't we know much about them? Obviously, Covid is new to us, but coronaviruses are not.

Professor Barclay: There are four different seasonal coronaviruses that cause common colds in adults every year. People probably catch one of those every five to seven years of their life, perhaps even more frequently. They have been less studied than some other viruses. Influenza, for example, has posed a very obvious pandemic threat in the last part of the 20th and first part of the 21st century, and there has been intense research. Until the 21st century, coronaviruses were considered to be rather mild viruses, and there was study of them but not very intensely. Of course, then we had SARS-CoV-1 and MERS emerge, and people became aware. I think it is fair to say that our expertise in coronaviruses in general as a family is much less. Certainly, in terms of monitoring their evolution and understanding the balance between immunity in the population and virus evolution, we do not have much experience of that at the moment.

Chair: Thank you very much. Aaron Bell and then Graham Stringer.

Q2440 **Aaron Bell:** Thank you, Chair. Thanks to all three of you for coming to our Committee again and congratulations again to Sir Andrew on his honour. If I could briefly follow up on what Greg just asked you, Professor Barclay, about coronaviruses, you have obviously studied the RNA of the coronavirus and all these variants. What is your personal opinion as to whether it is more likely that it came from animals directly or that it leaked from a laboratory in Wuhan? You can put a percentage estimate on that rather than a true-or-false question.

Professor Barclay: I will do what Susan did: I will say with high confidence that it came from an animal source. That is my answer: high confidence it came from an animal.

Q2441 **Aaron Bell:** Originally from an animal source, but is it possible that that was being studied in a lab for research and it could have then leaked from the lab?

Professor Barclay: I cannot exclude that possibility, but I would point out that we have instances of six other coronaviruses emerging into the human population where we do not think that is the case. On the probability, I would say it is much more likely knowing where viruses are and that there are live markets with animals mixed. For example, in the virus I am more familiar with—influenza—that is where you see zoonotic events happening very frequently. I would suggest that the opportunity for the virus to jump from an animal source into humans in the part of the world where we first saw this virus emerge is very high.

Q2442 **Aaron Bell:** Thank you, Professor Barclay. That is very helpful.

If I could turn to vaccine effectiveness and follow up on Dawn Butler's

earlier questions, am I correct in saying, Dr Hopkins, that the PHE analysis that was published yesterday showed 96% effectiveness for Pfizer after two doses and 92% for AstraZeneca? That is based on data that you have gathered.

Dr Hopkins: Vaccine effectiveness against hospitalisation is 92% and 96%. That is correct.

Q2443 **Aaron Bell:** The models that we seem to be relying on to justify the extension of restrictions, which was announced yesterday, do not appear to be using those sorts of numbers at all. In the Imperial model, their central vaccine effectiveness against severe disease for Pfizer is 89% and AstraZeneca 85%, and even their optimistic numbers are 90% and 87%. Ninety percent. to 96% is an absolutely huge advantage because, obviously, it is only 40% of the number of people going to hospital. Similarly, the model from the London School of Hygiene and Tropical Medicine used figures of 87% for Pfizer and 86% for Oxford-AstraZeneca. This is really important, because the number of deaths that the Imperial model forecast, if we had opened next Monday, was 59,000 additional deaths over the next year. Those mostly are, from the charts, deaths of people who have had both doses. If they have been using numbers that have been superseded by the PHE analysis, does that not alter the case for the continuation of restrictions?

Dr Hopkins: Can I first of all add that this is the first analysis? There are quite wide confidence intervals on that analysis. For example, for the Pfizer, it is 86% to 99%, within the bands of that modelling estimate. For AstraZeneca, it is 75% to 97%. That means that the true value is somewhere between those quite wide confidence intervals. We are quite reassured that it will be at the higher end. That is what our central estimates look like because both of the central estimates are above 90%, and quite reassuringly above that, but we will need more time to finesse it. I know that the modelling that was done had optimistic and pessimistic modelling, and they took a range of values that were the best data that they had at that point in time. They will, of course, continue to iterate them as we continue to iterate our vaccine effectiveness analysis. SPI-M will continue to update and use the data in their models to give best and worst-case scenarios.

Q2444 **Aaron Bell:** Thank you, Dr Hopkins. I understand there is huge uncertainty about so many variables here. We have a figure of 96% compared to a model where the optimistic scenario was 90%. We are now voting in the House of Commons this afternoon to extend these restrictions on the basis of those models. It is obviously very good news that we are at 96%. I understand the confidence intervals are wide. It is good news, but why are the numbers coming out so far ahead of even the optimistic scenarios that have been modelled, because that is informing the public debate and the decisions that have been taken?

Dr Hopkins: That was the best data that they had at the time those models were run. This data, as you know, was released this week. We

have been fast-tracking this analysis. I am sure that SPI-M modellers will look at these numbers very carefully as soon as they can, and I am sure they have already looked at them because they look at these things on a daily basis.

I would add that the hospitalisations in the north-west have risen by more than 60% and hospitalisations across the country are rising. When we look at those figures, and when we see the number of people coming into hospital who are unvaccinated—my latest figures are that 10% of people have had two doses and are in hospital, 18% have had one dose and arrived three weeks after their first dose in hospital, and the remainder are unvaccinated—we really need to get, first of all, second doses into people, and also first doses into as many people as possible, to reduce the risk of severe disease. We still have a large amount of our adult population who are unvaccinated and a large population who are at risk. I would say the at-risks are the over-40s, definitely, and even the over-30s because we are seeing those individuals coming to hospitals with comorbidities. There is a large component of those who have only had a single dose, and a single dose reduction, especially with AstraZeneca, in that 40 to 60-year-old age group is substantially lower than that.

Q2445 **Aaron Bell:** That is understood. The admissions are currently running, I think, at about 4% of lagged cases. Ten days after cases is roughly when you see the hospitalisation admissions. That is down from 8% in the autumn, which is obviously good news and shows that that link is weakening.

What data do you have about the severity of those admissions, the length of time people are staying in hospital and people who are staying overnight? Is that also weakening, suggesting that the cases that we are seeing in hospital are weaker than they were in the autumn?

Dr Hopkins: In the figures that we reviewed last week, there were 606 admissions through emergency departments. Many of those will still be in hospital. There is early data to suggest that the median length of stay may have reduced a small amount, but only a very small amount. When people need to come into hospital, by and large, they will need oxygen and monitoring and treatment for a number of days, and many of those treatments cannot be delivered in the community. If they are going to start on treatment, they will have to stay in hospital. For example, Remdesivir is one of the treatment options.

We will need some more time to determine the length of stay. We have a large cohort study, ISARIC4C/CO-CIN, that will allow us to look at that data weekly. We are seeing a younger population coming to hospital and we are seeing that the median length of stay is slightly less but not significantly less yet. More time is required for us to give fuller figures on that.

Q2446 **Aaron Bell:** You mentioned the number of unvaccinated people

presenting to hospital. Do we have a breakdown of what proportion of those are people who have chosen not to be vaccinated or have ignored the calls to be vaccinated, compared to the younger people who would not have had a chance to be vaccinated yet? Is that data available?

Dr Hopkins: We do not have that data for every hospital admission. What we know is that the population is younger, that we need to continue to convince people to take up the vaccine and that it is safe. Our job is continuing to be to roll out the vaccination; to get people to take it up; to ensure that we answer the questions about safety and the concerns that they have; and that we continue to have the excellent vaccine roll-out that we have done.

Some people are working and just find it difficult to make their appointments. Some people are concerned about vaccines and we need to overcome that vaccine hesitancy, but we have very high vaccine rates—over 95% in the over-70s. That is what we should be aiming for, for the rest of the population.

Q2447 **Aaron Bell:** I quite understand that there are challenges reaching everybody. Based on when we made the first doses available, I think everybody over 55 or so has had ample opportunity to have both jabs. You will understand that it is difficult for some Members to vote for things if it is being seen to protect people who have chosen not to be protected themselves, understanding the difficulties around that. Is it the case that the majority of cases you are seeing are people who could have and should have had the vaccine already, or is it more the younger people who have not had the chance? I know you do not necessarily have precise figures. If there is data around, I am sure the Committee will be grateful to see it. Anecdotally, is it older people who have not had the jab who are causing the most concern at the moment?

Dr Hopkins: The data that we have seen is that it has been driven by younger people who have not had two doses of vaccine yet rather than older people. If you would like accurate numbers, I will review what we can share with the Committee and see what the data will look like this week, which we will be reviewing tomorrow as a matter of routine.

Q2448 **Aaron Bell:** Thank you, Dr Hopkins. That is very helpful. Obviously, we are not actually rolling anything back. Is it your opinion that the delay will be sufficient, or is there a need to roll back anything else, given that the cases are clearly rising exponentially? From all the charts that are available publicly and the work that people like Oliver Johnson and John Burn-Murdoch are doing on Twitter, we can see that cases are rising exponentially, and the hope has to be that those links between hospitalisation and then hospitalisation to death are being severed because cases are rising exponentially. Is the delay, in your opinion, sufficient to control the situation we currently have?

Dr Hopkins: It is very early to say that. The modelling suggests that four weeks was the optimal delay because it allowed everyone over the

age of 18 to get an opportunity for their first vaccine and all of those over the age of 40 to have second vaccines. Therefore, that was the optimal delay within the modelling parameters. Clearly, that may change if they change the parameters in their models. That was reviewed and various durations were looked at. Clearly, we will suppress the virus more if there are more non-pharmaceutical interventions put in place. I think the challenge here is that suppressing the virus from where we are now will be quite challenging, and, as we can see already, the disconnect between cases in the community and hospitalisations is already starting. The clear challenge is to maintain life as much as possible as normal, getting to the point that we can, while protecting as many people as we can.

Q2449 **Aaron Bell:** Following on from that, we have heard 19 July described as a terminus date, depending on what happens with other variants coming in. From what you have just said, it would seem likely that we would need to continue with a certain number of NPIs after that date. Even if we open up all the businesses, we would still expect to see other NPIs being encouraged. Is that your understanding of what we will need to do on 19 July?

Dr Hopkins: I think there will be a certain amount of social responsibility that people will take, particularly for those who are elderly or immunocompromised, or at higher risk of infection. We will all need to make decisions for ourselves, particularly on wearing masks, using better ventilation and hand hygiene. Those are basic principles.

When we look back at how Asia did, considering their experience with SARS previously, and also the influenza viruses that have frequently been observed there, you could see the different behaviours that they have maintained for many years. We may find that some people—not all—will change their behaviours, particularly those who are more concerned about their health or the health of people they live with. It will be for Government to decide what rules and regulations will need to be in place and what legislation will need to continue after 19 July.

Q2450 **Aaron Bell:** From a personal responsibility point of view, that sounds quite encouraging. Obviously, yes, people's behaviour will continue to be different for at least the rest of this year, and perhaps for many years to come, on things like face coverings, but the mandate could probably safely lapse and we could leave it up to people's personal responsibility after 19 July, if I have understood what you have just said correctly. I know it is the Government's decision and not yours.

Dr Hopkins: This is a balance. Some countries like Sweden have done a lot through social responsibility. Other countries have legislated heavily. There is a middle road as we have vaccination heavily rolled out that is required, potentially, in some areas where there is higher risk to look at. One might consider, for example, transport. For those of us who pack ourselves into the tube regularly, we may feel more comfortable if everyone else was asked to wear a mask as well for those very close encounters for, potentially, periods longer than 15 minutes. In the more

general societal areas such as shops, I think it will come down to personal opinions and responsibilities rather than legislation for the longer term.

Q2451 **Aaron Bell:** Assuming we are continuing to deal with the Delta variant as our primary variant in the UK, is there a proportion of the population that we are looking to get to perhaps within these four weeks or more generally who need to be double vaccinated to allow for the safe relaxation of all the restrictions we currently have?

Dr Hopkins: I do not have an accurate number. I would like to see all the over-40s at least having been offered double vaccine and to have very high levels. Above 85% would be the minimum level I would like to see in the over-40s to really reduce the impact on them and the impact on the NHS. I would like to see everyone over the age of 18 offered a vaccine and be starting to reach in to the 30 to 40-year-olds for a second dose of vaccine. That will give us pretty good protection then against the severity of hospitalisation signals that we have seen so far.

Q2452 **Aaron Bell:** That is presumably why the Government have brought forward the second dose for the over-40s on an eight-week basis.

Dr Hopkins: Yes. When we were in wave 2, and when we had vaccines that we were starting to see, first of all, we were in national restrictions, so we had very little social mixing and the transmission potential was much lower than it is right now. Secondly, we could see the vaccine effectiveness against Alpha, B.1.1.7, for the vaccines that we were using, and we were quite reassured by what we were seeing in how we could manage the longer interval. What we need now is higher levels of antibodies and higher levels of neutralisation and responses, so that faster boost at eight weeks is critical at this moment in time.

Q2453 **Aaron Bell:** Just a final question to you and the other panellists if they would like to answer as well. I referred to the Imperial paper earlier with all the concerns that I have about the modelling and particularly the vaccine effectiveness numbers they are using. Even if we push back step 4 to 26 July, which was the date they modelled, rather than 19 July, it still has us peaking daily infections this year at around 300,000 per day. Is that a number that sounds realistic to the panel? Would that be the peak of the third wave?

Dr Hopkins: What we are seeing at the moment is about 7,000 to 8,000 infections per day. That is what we are detecting, but we know that that is less than half of what the true infections are in the community—and we have measured that in a number of ways. The estimate for current infections today is probably in the order of between 15,000 and 25,000 new infections a day. It does not take very many doublings to get to very large numbers. If you doubled that four times, you would be hitting those numbers. We know that in the January peak we were at least that high on some days.

What we hope we will not see—and I think we will not—because of the vaccine is the same numbers of hospitalisations. We will have a much greater amount of infection in the community without seeing the same impact of hospitalisations. The more infections we have, the more impact there will be. If we say 90% effectiveness, that means 10% could actually come into hospital. That means that we need to have some measures in place—both social responsibility measures and the measures that are in place right now—to try to hold that peak down so that we can get as much vaccine into the individuals to reduce symptomatic disease, reduce transmission and then, clearly, the severity and hospitalisation.

Q2454 **Aaron Bell:** Thank you very much, Dr Hopkins. That is an excellent series of answers. I will give Professor Barclay and Professor Pollard a chance to comment on that section and the peak of the third wave.

Professor Barclay: I think the numbers are reasonable bearing in mind where we are at the moment and the doubling time. In the REACT study, for example, a doubling time of 11 days has been reported at the moment, but we know that that can decrease. I think the numbers are reasonable.

The other thing of concern, which I think is appropriate here, is that the Delta variant, as we have said, is a fitter virus, and the viral loads that have been picked up in individuals who are infected are very high. Even though not everybody is getting sick enough to go into hospital, I think it is important to try to keep case numbers down in as practical a way as we can because we do not yet know the long-term consequences of people being infected with very high viral loads and of the virus replicating very strongly. The modelling suggests high case numbers if we do not do something, and, therefore, trying to do something reasonable to limit case numbers is appropriate.

Q2455 **Aaron Bell:** On that basis, you would support what the Government have done and you would urge Members of Parliament to vote for it this afternoon, I take it.

Professor Barclay: I do not think it is my role to do that here. I have expressed a personal opinion there, which perhaps I should not have done.

Q2456 **Aaron Bell:** Thank you, Professor Barclay. Do you have any comments on the last 10 minutes or so of evidence?

Professor Pollard: Just to reiterate one of the points that Dr Hopkins made, even if you have 90% protection with two doses of the vaccine, there is that 10%. What you do not want is that 10% to meet the virus all in the same month because that is a huge impact on the NHS. Having some restrictions in place that reduce the amount of transmission, even if it is only mitigated partly at the moment, is absolutely critical, not only to give more time to catch up with those who are unvaccinated but also in this period where we are peaking with the Delta variant, so that there is

some mitigation still to protect those individuals and to ensure that the NHS can cope if they become unwell.

Aaron Bell: The modelling would look quite different if we plugged in the actual PHE numbers into the models, but that still gives another doubling, I suppose, would be the argument against that. Everyone is nodding. I will not go to you individually. Thank you very much, Chair.

Q2457 **Chair:** Thank you, Aaron. I just want to pick up on some of the points that Aaron asked Dr Hopkins. You have very encouraging data—real-world data from people that you know have gone into hospital knowing whether they have been vaccinated—and yet the advice to Government about extending the lockdown restrictions has drawn on modelling evidence from Imperial College and the London School of Hygiene and Tropical Medicine. Happily, the real-world numbers that you have discovered are much better. You said that there is a confidence interval attached to the studies, but that applies to every study. That does not mean to say that you cannot compare them, does it? Presumably, there is a confidence interval attached to your numbers as there is to the Imperial and the London School of Hygiene and Tropical Medicine numbers, but it does not gainsay the fact that there has been a material increase in the confidence that we can have that hospitalisation is less. That is correct, is it not?

Dr Hopkins: If we took the lower confidence interval, which is basically the point within which the true value lies—we estimate the true value as a point estimate, but the true value lies somewhere within those confidence intervals—the lower confidence intervals are actually lower for AstraZeneca, which is by and large the vaccine that has been given to the majority of 40 to 60-year-olds, than in either the Imperial or London School papers.

It is important to note that they could have put a more pessimistic, worst-case scenario number in. What they have done is modelled the best estimate numbers they had at the time. What I am sure they will do is remodel it with the best estimate numbers that we have in this, but also with the lower confidence interval estimate, so that they can create a reasonable worst case or a pessimistic estimate as well. They have modelled a number of different scenarios. They have modelled it in a number of different ways for a variety of different areas. The consensus view from the SPI-M papers was that, no matter which way you looked at it, cases were going to rise, and that getting more vaccination into individuals over the next four weeks was the key parameter that would reduce the impact on our population, not just now but over the coming couple of months.

Q2458 **Chair:** In the past, we have been beset by uncertainties and difficulties with modelling evidence informing Government policy decisions, and, in evidence to this Committee, the chief medical officer, Chris Whitty, has always been consistent that he presents charts and uses real-world data rather than models. You are in possession of that real-world data. It has

just been published. Was that available to the Government this weekend when they were considering these decisions?

Dr Hopkins: Yes.

Q2459 **Chair:** Do you know when it was made available to the Government?

Dr Hopkins: I believe it was made available to the Government on Friday evening.

Q2460 **Chair:** Would it have been possible, surely, given that it is relatively new data but real-world data rather than modelled data, to say, "Actually, in the light of this data, we need a few more days to assess it before we decide what are going to be the right implications for public policy"?

Dr Hopkins: It is really important to come back to what I said earlier. The decisions that Government make are based not just on models but also on the real-world data. They reviewed all of the real-world data on a daily basis for the last two weeks. We have been looking at the rate of rise of cases and of hospitalisations, particularly in the north-west, which is at least seven to 10 days ahead of the rest of the country. What we are seeing there is that there is a more than 60% rise in cases and a 60% rise in hospitalisation.

The challenge we had is that, if you release even further than where we are now—coming back to what I said earlier, where there was an estimate that the R value would increase by a further release—you risk a rapid surge in cases and a rapid surge in hospitalisation when individuals have not yet received their second dose, particularly in that age group of 40 to 50; the vast majority of that age group have not received the second dose but will have been offered their second dose by 19 July. That is key. The Government made their decisions, but they had full access to the real-world data that we published in technical briefings and that we were reviewing on a daily basis from around the country, and the vaccine effectiveness and the models. All of that will have been considered.

Q2461 **Chair:** The impact on hospitalisations is clearly crucial, and, as my colleague, Aaron Bell, pointed out, these differences in the performance of the vaccine make a big difference in the number of people hospitalised for any given level of infection. You said that the modellers will now need to take into account this new real-world data and, I assume, re-present some forecasts. Do you expect that to be done within the next two weeks so that, as the Prime Minister promised, a reappraisal can be made and a change made if it is justified?

Dr Hopkins: SPI-M look at their models every week, so I have no doubt that they will be presenting models to SAGE within the next couple of weeks.

Q2462 **Chair:** You talked about hospital admissions. Do you know how many people are in-patients in hospital with Covid at the moment?

Dr Hopkins: The in-patients with Covid are more than 1,000 patients, and they have increased by about 30% in the last 10 days. I can get the exact numbers for you if you would like. We have seen rapid increases in the number of patients coming into hospital and also as in-patients over the last period. The most recent data available is that there were 1,136 people in hospital and 184 in-patients in the most recent day. After the most recent wave, not so long ago, the lowest number of patients coming in on a daily basis was 70, and hospital admissions were down to 850. There are increases on both the number of people coming in every day and the numbers of people in hospital. As the people come in, they will stay and hospitalise, and the numbers of those in hospital will start to rise quite rapidly.

Q2463 **Chair:** You said the number of people with Covid in hospital is just north of 1,000 at the moment.

Dr Hopkins: Yes. In the UK, it is 1,136.

Q2464 **Chair:** How many hospital beds are there in the UK?

Dr Hopkins: There are over 100,000 hospital beds in the UK.

Q2465 **Chair:** Around 1% of hospital beds are occupied with Covid patients.

Dr Hopkins: Correct.

Q2466 **Chair:** Is that a proportion that is compatible with the concern that the NHS will be overwhelmed by Covid patients?

Dr Hopkins: The NHS is well capable of looking after that amount of Covid patients, and even, I would say, many more than that, but I would leave that full response to the NHS. The issue is not about the amount of Covid patients now but the predictions of what is likely to happen over the next four weeks with the rise of cases, when we have seen a rise of more than 60% in cases being hospitalised in the north-west over the last two weeks. If we just looked at each day rather than being able to look at what are the predictions that would happen based on real-world data, the doubling can happen quite dramatically and quite rapidly. It does not take very long to go from 200 cases being admitted to hospital a day to 1,000 cases being admitted to hospital a day.

Q2467 **Chair:** Given what you know from the hospital admission real-world data that you have been talking about and the high degree of confidence that we can have that vaccines make an effect, and given that the decision was to move by four weeks the social distancing restrictions—the Prime Minister described 19 July as a terminus date—does that four-week extension make the difference from having 1% of NHS beds occupied by Covid patients to the possibility of it being overwhelmed? Is that four weeks necessary to prevent the NHS from being overwhelmed?

Dr Hopkins: I cannot give you an answer to the question of whether the NHS would be overwhelmed in four weeks. I would say that the four weeks is there to give the amount of people who have had two doses of

vaccine a better chance to have had two doses of vaccine and therefore to see vaccine effectiveness in the order that we are quoting in the paper from PHE. At the moment, a large number of the population have not had their two doses of vaccine and therefore are not effectively protected from requiring hospital admission if they get symptomatic infection.

Q2468 **Chair:** We understand that, but some of the charts that were presented were about the pressures on hospitals. Is it plausible to think that if we did not have this four-week extension we would have intolerable pressure on hospitals, given that only 1% of hospital beds in the NHS are occupied by Covid patients at the moment?

Dr Hopkins: It is, again, a decision for Government with the NHS to decide what is the pressure on hospitals that is reasonable or not reasonable. With the data we have, the NHS will be able to cope for the next four weeks. We know what the doubling time looks like. We know that, even if hospital admissions doubled every seven days and individuals in hospitals doubled every seven days, the NHS would be able to work. However, we also know that, when we have 10,000 to 15,000 individuals in hospital with Covid, it seriously starts to compromise their ability to deliver other care because of the infection control precautions that you need to have, because of the number of pathways that you need to have up and running, and because of the number of individuals who may receive ICU care.

ICU care is a real pinch point in the NHS, even with the massive expansions that have occurred over the last year. We do not yet know the impact from those admitted to hospital on ICU care. We know that we have had lots of advances over the last year—new drugs and more new drugs from trials announced today. None the less, we are also seeing rises in the number of individuals in ICU. It is ICU care that is in limited supply.

Q2469 **Chair:** Is it your view, as a director of Public Health England, that were it not for this four-week extension there would be a material risk to ICU care across the NHS?

Dr Hopkins: I did not say that. I do not believe in the next four weeks there will be a material impact on ICU care in the NHS.

Q2470 **Chair:** Either way, with the restrictions or without.

Dr Hopkins: With the restrictions or without. What I cannot say is what would happen beyond that if we did not get vaccinations in. The vaccinations are the key part in the next four weeks.

Chair: Thank you. I will turn to Graham Stringer.

Q2471 **Graham Stringer:** Thank you. I would like to look a little bit to the future. Professor Pollard, I think it is fair to say that when Professor Sarah Gilbert came and talked to us right at the start of this epidemic we thought she was being optimistic about the speed at which the vaccine

could be developed. We have all been amazed and pleased that the vaccine was developed so quickly.

In the future, what have we learnt so that vaccines can be developed even more quickly? When you go through the pinch points, it appears that the actual vaccine itself can be created quickly. Then there is testing. Then there is the production of the vaccine. Can any of those pinch points be dramatically improved?

Professor Pollard: First of all, let us hope that we do not have to do this again. I think that would be the best possible outcome.

If we look at the pinch points for speed that are perhaps within control, one of them is the speed of manufacturing for the trial. I do not mean for the roll-out. We had very limited capacity for manufacturing at the beginning of last year to start making vaccines for trials. That was the first component. That is changing already. There is investment in the new vaccine innovation centre in Oxfordshire. There will also be new opportunities with other manufacturing organisations to speed up that process.

The other is the scale of the trials. If you can launch larger-scale trials in more countries more quickly, you have a greater chance of catching a wave of disease in the pandemic, which gives you the cases earlier to get an answer quicker. Those two things would definitely make a difference.

The most worrying thing for me is that, if it had not been coronavirus, which we do know quite a lot about in terms of making vaccines, and it had been a virus that we do not know very much about, it would not just be the starting point with the genetic code; we might have to do a lot more work in the laboratory in animal studies to try to even decide how to make the vaccine. Fortunately, this time, we did not have to do that. We did not have that long delay that often will take years. We knew exactly what to do at the beginning, as did all the developers, and could get on with the manufacturing and the clinical trials really rapidly.

Investment over the years ahead in understanding more about other viruses and other potential pandemic threats so that we are prepared as we were with coronaviruses to go so quickly is perhaps the most important thing that we need to do in preparedness.

Q2472 **Graham Stringer:** In terms of the testing, it has been put to this Committee that to reduce that pinch point there should be a panel of volunteers selected, paid, infected and given placebos and the new vaccine. There are obviously ethical problems with that, but that would speed up the process of the development of a new vaccine, would it not?

Professor Pollard: I think it can speed up. Doing challenge studies with a virus that we have only just discovered is a very high-risk strategy initially. Once you understand more about it, as we do now—as I am sure you know, there are challenge studies going on today—and we know a lot about the virus, we know what the risk is in younger individuals, and we

know what the consequences are, people can be fully informed if they take part in those trials about what the risks are. In fact, we also have some treatments that can mitigate that risk.

If you are right at the beginning of discovering a new virus, that is a much more difficult equation to deal with until you have started to gather some of that evidence and you have some ideas about how you can mitigate risk in those challenge studies, which is why it is difficult to go very quickly.

Q2473 **Graham Stringer:** Just dealing with this epidemic and the different vaccines that have been developed by the Chinese, Australians, Pfizer, Oxford-AstraZeneca and others, would it be sensible now to focus on one or two of those vaccines as being more effective than others? Is there a meaningful choice to be made?

Professor Pollard: From a global perspective, the problem today is supply. We have now a total of only six vaccines out of about 300 that have been developed and authorised through the World Health Organisation. In terms of supply, somewhere around 2 billion doses have been manufactured, and we need another 11 billion if we are going to have any chance of controlling the severe disease in countries around the world.

I do not think having a focus on any one product makes any sense. One of the great successes has been having multiple products available, some of which have not worked. Some that both the UK and other countries had looked at initially have not so far come through. Some of the vaccines being developed by big pharma have not been successful. Having lots of options in the development process gives a chance that at least some are successful. As I said, six so far out of around 300 in development really tells us that you should not put all your eggs in one basket.

Q2474 **Graham Stringer:** Would it make sense to tweak any of the vaccines to respond better to the latest, more transmissible virus?

Professor Pollard: If the aim is to try to stop transmission and to stop symptomatic infection, I think there is no doubt that a tweaked vaccine would do that. The problem is that if we tweaked one now—for example, for the Delta variant—the Omega variant, the Epsilon variant or the Kappa variant might be the next one, and you would have to potentially be tweaking the vaccines very regularly. I just do not think that is going to be achievable during this period where there is so much transmission going on around the world, and new variants are going to be thrown up. If we get into a more stable situation in the future where there is one dominant variant each year, we might have an annual update, if indeed we need to do that.

I come back to the point before that, at this moment, we still have very high levels of protection against hospitalisation, even with the original

version of the vaccines. It is not yet clear whether we will need to have those new versions to prevent hospitalisation.

Q2475 **Graham Stringer:** At the moment, the race is on to get the second vaccination into as many arms as possible. Can you go through the case for a third vaccination, either a booster jab after 12 months or a third jab, to increase the efficacy of the vaccinations?

Professor Pollard: At this moment, we have absolutely no evidence that there is a need for a third dose, particularly when you consider that we have very high levels of protection against hospitalisation with two doses. The reason why you might look at a third dose is if that protection was waning, and, so far, we do not have evidence that that is the case; it is just too early to do that. From the clinical trials—

Q2476 **Graham Stringer:** So there is no evidence at the moment of a waning of the efficacy of the vaccines.

Professor Pollard: No.

Q2477 **Graham Stringer:** The antibodies are staying at similar levels, are they?

Professor Pollard: That is a different issue. You would expect to see the immune responses start to wane over time. We see with all of the vaccines that the levels of antibody will start to decrease over time. If you look at protection from the clinical trials—and there are data out about six months before un-blinding happened because of the national roll-out—there was no evidence of any waning of protection. The issue at the moment is that we do not know if or when we might need to boost because of waning protection.

The second question is this one about variants. If we had a new variant emerge that resulted in a loss of the effectiveness of the vaccines, you might need to boost in order to try to increase the effectiveness of the vaccines because of a variant. Those are the two things that we need to be monitoring. One is declines in effectiveness over time, against hospitalisation, and the other is new variants emerging that somehow break through the current levels of protection against hospitalisation.

Graham Stringer: Thank you very much.

Chair: Thank you very much. We will now go to Mark Logan.

Q2478 **Mark Logan:** Thank you, Chair. I would just like to put on record my thanks to all the witnesses for everything that you have been doing linked to public health in Bolton, where my constituency is based. I have a question around the experience in Bolton because, of course, we were very much at the epicentre of the Delta variant for a number of weeks, especially back in May time. What assessments have you made of the outbreak in Bolton? First, to Dr Hopkins.

Dr Hopkins: As I am sure you are well aware, as many are, we review the data on a daily basis with the regional directors of public health—in

Bolton that would be the north-west regional director—and very much with the local authority directors of public health as well. The actions taken locally and nationally are very much hand in glove. It is about engagement and a relationship to that.

What we saw in Bolton, because I think Bolton was first, and where we saw the Delta variant rapidly rise, very quickly, enlarging over the community in central Bolton, was different from what we have seen in many of the other areas where the Delta variant has taken hold. We have looked at and reviewed this and had some quite detailed modelling to go through it. There is no doubt an effect from being the first. There was a lot of community action developed through a feeling of community responsibility and community engagement, for people both to come out and test, and to get their vaccinations when offered. Both of those things were done at great speed in Bolton.

There was great action taken by the community health protection teams, from both the local authority and from Public Health England, to actively manage cases and outbreaks that were occurring. There was a lot of community engagement to get all contacts to come forward for testing. We really want people to do this more and more going forward, so that we can detect contacts early and start tracing their contacts in an effective manner.

Clearly, what we have seen in Bolton is a peak in ages of the younger age groups. The older age groups—the over-60s—had a very much lower rate of infection. None the less, despite all that, there was a rise in hospitalisations, and it is important to see that they felt they were beginning to come under some pressure.

Going back to the earlier point, almost 10% of their acute hospital beds were taken in the last week or so with Covid cases, which of course limits the care they can provide for other cases. Again, the population that was coming into hospital was predominantly an unvaccinated population. So, there were actions taken to test, vaccinate and improve social cohesion and action to mitigate the virus in their population.

Q2479 **Mark Logan:** Dr Hopkins, very early on in the outbreak—I think it was around the time of our local elections, so the first week of May, roughly—I was calling for a mass roll-out of vaccines in Bolton as well as surge testing. How effective do you think those measures have been up until now?

Dr Hopkins: In Bolton people took up the vaccine offer very effectively, and we saw vaccine rates rise. That is really important because it needs community engagement to do that, and that is what we saw happen, where vaccination and testing were happening at the same time. It is also important to recognise that vaccination is being pushed as fast as possible through NHS England. We have a limitation on supply, especially at Pfizer and Moderna, for the under-40s. There are about a million doses a week available, as far as I understand, in the country. It is about

getting to the groups and being able to vaccinate those people as actively as possible.

I think the key piece is for people to take it up when it is offered and to take the second dose when it is offered. Doing that within the operational roll-out that is being delivered by NHS England in a fantastic way, with all the volunteers, GPs, pharmacies and practitioners, will allow us to protect the population.

Q2480 **Mark Logan:** Professor Barclay or Professor Pollard, is there anything you would like to add to that?

Professor Barclay: No, but I just think it is a timely point to underscore the importance of the second dose. I am not sure if that has come out soundly enough. The wonderful percentage protection that negates hospitalisation requires that second dose. In areas where vaccine is being rolled out more intensely, you would not expect to see so much of an effect until you get that prime, and that boost, and then a certain number of days after that second dose.

Q2481 **Mark Logan:** Back to Dr Hopkins, do you still have a concern for potential hospitalisations in Bolton as being part of the north-west? I say that because there has been a tapering off, at least in the exponential rise, in hospital admissions in Bolton.

Dr Hopkins: Bolton has flattened its cases but they have not reduced dramatically. There was a reduction and now it is sort of flat and holding. I expect that is a picture we will see mirrored in hospitalisations. Continued ongoing admissions, even at lower amounts than we were seeing a couple of weeks ago, will put pressure on hospitals to deliver other care. I think the key point is that we will need to continue testing people, to find people early, to reduce the risk of transmission to other people, and vaccinate to mitigate this Delta variant that is surging across the communities now.

Q2482 **Mark Logan:** Lastly, what more could we be doing, either nationally or locally?

Dr Hopkins: My view is that it is really important to get the comms messages right. We need to have unified communications. When we pull in different directions, the community does not really know what to do. So we should be more unified in talking about the simple messages, which are about keeping social distancing as much as we can, mixing indoors with a maximum of six people or two households, keeping the windows open, and doing the two things that are additional to that. One is testing regularly, especially if you are going out to work regularly, so doing asymptomatic testing; and for young people, and particularly those who are socialising, doing a test before you go and socialise with your friends, indoors or outdoors, and, secondly, taking the vaccine when offered. That consistency of public health messaging is critical to ensure that we engage with all parts of our population, especially those who may not hear the messages clearly.

Mark Logan: Thank you very much.

Chair: Thank you, Mark. Just before I go to our final questioner, Rebecca Long Bailey, the Committee is fortunate to benefit from a multitude of north-western MPs as members of the Committee. I will go back to Graham Stringer, one of the Manchester MPs, to ask some questions about the region.

Q2483 **Graham Stringer:** I represent part of Salford, and Rebecca Long Bailey represents part of Salford as well. We are concerned that the supply of the Pfizer vaccine for the second vaccination is going down rather than up at the present time. It is reducing from 3,000 to 2,000. Can you give us an explanation for that, Dr Hopkins?

Dr Hopkins: I am not in charge of supplying roll-out, but I know that NHS England is rolling out the vaccination as fast as it has the supply, in as equitable a way as possible, to ensure that the maximum amount of individuals can get vaccinated, as rapidly as it can. I know that is done with equity and fairness to ensure that people are vaccinated across the country. I know where there are enhanced response areas any vaccine that can be released is being delivered in that area. It is important to recognise that, in bringing the second dose forward from 12 weeks to eight weeks, there needs to be some vaccine on reserve in case there are problems down the line. I know everyone is doing everything they can to release every bit of stock on a daily basis across the country.

Q2484 **Graham Stringer:** I know you are not directly in charge of the vaccination programme, but those figures for the stocks available for vaccine before they are released are not publicly available, are they? You do not know them, do you?

Dr Hopkins: I do not know them.

Q2485 **Graham Stringer:** Only those people doing the vaccination roll-out know them. I understand you are not responsible for it, but I do not find that answer satisfactory, in as much as we have just heard that the increase in second vaccinations for people in Bolton has had an immediate beneficial effect; I want to know why that is not being followed for Salford, Manchester and the other areas in the north-west where infection rates are very high at the present time.

Dr Hopkins: To clarify, I think there is a combination of measures in Bolton that helped turn it. Predominantly, testing is the immediate measure that breaks the chains of transmission. It is really important to have a powerful vaccination message that goes along with that. I would say that vaccination is critical for all parts of the country. I know that NHS England and the supply chain are doing everything they can to release it. I am afraid I would have to ask NHS England and supply chain colleagues to come back to you with details. I do not have those and I am afraid my responsibilities do not go that far.

Q2486 **Graham Stringer:** I would be grateful if that could be done as quickly as

possible. If it has worked in Bolton—those pop-up vaccination posts in Bolton have been successful; basically, if anybody wanted a vaccination in Bolton, they could get it—it seems to me that there should be a priority where the infection is at its highest at the present time. I find it completely unsatisfactory not to have the data available that justifies not doing that.

I have one final, slightly different question for Dr Hopkins. At the start of the epidemic, when the announced deaths were very low indeed, the statistics included whether or not the person had a comorbidity. We know certain factors—obesity and other diseases—make it less likely that people will survive. Why have those figures stopped being given in that form?

Dr Hopkins: Public Health England never released comorbidity data for it. The Office for National Statistics, which produced the deaths data and will have the comorbidities attached to it, may be able to release that. Public Health England has only released the number of deaths and not individual data on cases.

Graham Stringer: Thank you.

Chair: Thank you very much indeed, Graham. Another north-west MP, Rebecca Long Bailey.

Q2487 **Rebecca Long Bailey:** I just want to put on record my thanks to the panel of witnesses today, both for your work throughout the pandemic but also for answering our questions so well.

To add to the questions that Graham and Mark have already asked, as you know, I am a Salford MP, and Graham, myself and the other Salford MP, Barbara Keeley, have been repeatedly asking for the mass vaccination of all adults under 40 so that we can replicate the success that Mark has had in his constituency. I know you cannot answer any questions, Dr Hopkins, on vaccine supply, but could you tell us: what could Salford be facing in the next four weeks in absence of that mass vaccination plan for the under-40s?

Dr Hopkins: Can I just reiterate that vaccines take time to work? We do not think that what we saw in Bolton was driven by vaccines. We think vaccines are an important public health offer to go along with testing. As I have said already, NHS England, not Public Health England, deliver the supply according to the capacity that is available for the supply of vaccines. So I really cannot answer that.

On the second part, I think the most important things to do are to get the public health communications right, and to deliver testing to the community, so that we find cases and enable them to isolate, with the enhanced capacity for people to ask for funding to isolate, where necessary, from their local authorities.

The final bit is to have the public health message. We now know that everyone over the age of 23 can come forward for vaccination. That is there. Over the next couple of weeks there will be, increasingly, a capacity to offer everyone over the age of 18 vaccination. Those over the age of 23 are a large component of our population. It is critical that those people come forward for vaccination and ask for their appointment, which can be done easily online.

Q2488 **Rebecca Long Bailey:** Thank you, Dr Hopkins. Moving on to the issue of children and those under 18, press reports have circulated this morning suggesting that JCVI is going to be making a recommendation to Government against the mass roll-out of Covid vaccines to children until scientists obtain more data on the risks. I wanted to ask all of you what concerns you have on determining whether to vaccinate under-18s at this time, starting with Professor Pollard.

Professor Pollard: I am not part of those discussions, but the things that will be weighed up by JCVI in making those decisions are, first, the risk of severe disease in children, which I think we all know is extremely low. The second is the inflammatory condition called PIMS-TS—or MIS-C—which affects some children. Although it is a very rare condition, that is another issue it will be weighing up. There are also questions around long Covid. It certainly seems to be a collection of different syndromes, but that needs to be looked into. All of that evidence needs to be weighed up.

If we were talking about influenza, one of the key aspects would be transmission. Children are very important in the transmission of influenza. That is much less the case, from the evidence we have at the moment, for coronavirus. In particular, young children do not seem to be especially responsible for transmission. Teenagers are probably not very different from younger adults. The difficulty with transmission, as we have been discussing, is that, as the virus evolves away from human immunity in the months or years ahead, those vaccines given to prevent transmission will be less effective. All of that has to be weighed up to decide whether it is in the interests of children to be vaccinated. Is it in the interests of wider society for children to be vaccinated, and that may be less so in the future because of that change in the virus?

What are the risks? Are there any risks in giving vaccines to children? We know there are some side effects from the vaccines, and that is being investigated at the moment. For example, with the Pfizer vaccine, there are some very, very rare cases of heart inflammation that are being investigated, and we know about the AstraZeneca vaccine and the cases of blood clots that are being investigated. All of that needs to be put together in the decision making on moving forward with vaccinating children. I do not know where they are with those decisions. I am sure a statement will be made.

The only other thing to say is that an important part of the work they will be doing is looking to see if there are sub-populations of children who are

at greater risk and who might be prioritised. That might mean that there are some children who should be vaccinated sooner rather than later, and I am sure that, again, is part of what they are putting in the mix. We will have to wait for that assessment.

Rebecca Long Bailey: Thank you. The same question to Professor Barclay.

Professor Barclay: I have very little to add. With children, as with everybody, it is always the risk/benefit. As Professor Pollard has said, with children we do not really see them suffering severe disease at the moment. Certainly, in younger children, we do not have good evidence that they spread the virus particularly either, which is really different from, for example, influenza, where the evidence is very clearcut. I think it is right to wait for evidence before making a decision about a children's vaccine. We would be asking a lot of parents and children to enter into something where we do not have sufficient robust evidence yet, and there is no clear benefit to them, or to society, at the moment.

Rebecca Long Bailey: Thank you. The same question to Dr Hopkins.

Dr Hopkins: I would say likewise that you have to weigh up the risk and benefit. You have to look at the benefits of vaccinating children. The risk to their own health is small at the moment. Clearly, there is a risk of long Covid, particularly in teenage children, but we have yet to get a full assessment on that. I think the challenge we have is that the risks of vaccination have yet to be fully elucidated, particularly the potential risks of Pfizer and the evidence of heart conditions that is beginning to emerge from some countries that have vaccinated younger adults and teenagers, particularly after the second dose. We have some careful monitoring to do post second dose of vaccines in the next age group up before we make rapid decisions in the younger age groups.

Q2489 **Rebecca Long Bailey:** That is very helpful. In terms of where the scientific research is on this, we have already heard from Dr Hopkins and Professor Pollard about concerns with the Pfizer vaccine. I think it was the US Centers for Disease Control and Prevention that issued a statement recently, which stated—for the benefit of the people watching the Committee—that there were "higher…than expected" numbers of young men who experienced heart inflammation after their second dose of the mRNA Covid-19 shot from Pfizer-BioNTech and Moderna. More than half of the cases were between the ages of 12 and 24, but those age groups accounted for less than 9% of doses administered.

However, it is slightly confusing when you look at the UK coverage of this, because the Health Secretary told the House of Commons on 7 June that the MHRA has concluded that the jab is "safe and effective for children aged between 12 and 15 years old, with the benefits of vaccination clearly outweighing any risks."

I just wanted to ask you all a broad question about what you know so far about the key findings from Pfizer studies, what concerns you have, and

where you can see the studies going in the future, starting with Professor Barclay.

Professor Barclay: I am not expert in reviewing that kind of work. I am not a clinical trialist in any sense, so you probably know as much as I do in terms of those data, and I really think I should pass it to Andrew.

Rebecca Long Bailey: Thank you. Professor Pollard.

Professor Pollard: You made a comment about MHRA approval. Of course, what it is reviewing is the data from the clinical trials involving a few thousand children, which is fairly standard for reviewing the data. It is important to emphasise that what we are talking about here is an incredibly rare event. It is not until you start large-scale roll-out that you can begin to evaluate that. That is what is happening now through surveillance systems in the countries that are already giving large numbers of doses to younger adults and to teenagers. We are just at too early a stage to make too much comment about it, to know exactly what the rates are, and what the severity is. We just have a few reports at this stage. I think it is just too early to have an in-depth discussion about this issue and the extent to which it is an issue.

Rebecca Long Bailey: Dr Hopkins, is there anything that you would like to add?

Dr Hopkins: We have to learn from what has gone before. We have seen the studies that licensed the drugs showing safety and efficacy in the standards that we do. When we go into the real world, and we vaccinate very large numbers of the population, we will see some things that are different, which give us concerning signals. We saw that with AstraZeneca, and that is why we modified the age paradigms. It does not change the licensing. The licensing is still there in the same way as it always was. Because with vaccines we are always weighing up the risks and benefits, we have to look at it at a population level. We await with interest the data that will come from CDC. A bit like us with AstraZeneca, we had a lot of data, and we were able to show the world what that data looked like, along with some other European countries. Countries that have vaccinated younger populations—the US and Israel, for example—will tell us the data that they are able to show, and we will be able to use that in our risk assessments.

Q2490 **Rebecca Long Bailey:** My final question is a very broad one and it looks more at the global perspective. Earlier this month the head of the World Health Organisation urged that vaccine prioritisation be made in low and middle-income countries. In not comprehensively immunising older groups across the world as quickly as possible before children, certainly in the UK, is there a risk of further waves reaching the UK and more vaccine-resistant variants presenting? That question is first to Professor Barclay.

Professor Barclay: Yes, there is a risk that more variants will reach the UK. We are privileged here in the UK to be able to receive the vaccines

that we do. We are much luckier than people in some other parts of the world where the virus is circulating widely, replicating in huge numbers, and will continue to throw out variants, some of which will reach us, and, of course, affect millions, if not billions, of people in other parts of the world.

The people who are spreading the virus in different parts of the world will be different, too: the demographics, the behaviour. Each country in some ways is unique to itself in terms of the best vaccine policy. Even here in the UK there was some debate at the start as to who should receive the vaccine first. Was it better to vaccinate those who are at most risk, or those who are spreading the virus, because they mingle more and meet each other more?

These are complicated issues, but the big question that you are asking is: is it fair that we have all this vaccine here in the UK and we are not immediately sharing it with the world? I wish we had enough to share with everybody, and I think there is a balance here between what we must do for ourselves, and then sharing as much as we can.

Rebecca Long Bailey: Thank you. Professor Pollard?

Professor Pollard: We were discussing just now whether children should be vaccinated, but there is also a "when" question. If the decision was that they should be, there is still this—which I have talked about before—moral objection to vaccinating a population at extremely low risk of disease while we know in many parts of the world there are people who will die over the next three months because they have no access to vaccines.

I think that Dr Tedros at the World Health Organisation is absolutely correct that the priority, if we take a global perspective, has to be to save lives around the world, and to have doses made available as early as possible to those at greater risk. We know who they are. They are very clear in the UK data, and it is no different in any other country. It is older adults, those with other health conditions, and healthcare workers who are looking after them, who absolutely have to be prioritised.

Rebecca Long Bailey: Finally, Dr Hopkins, is there anything that you would like to add to that?

Dr Hopkins: I would agree with everything that has been said. The number of vaccines for people who are between 12 and 18 in this country is not enough to solve the problem of global vaccines. However, we will not be through this pandemic until the whole world has had an ability to get vaccinated. Realistically, that is two years away, I think. We have to be honest and open about that. Until we get some level of control over everything, we will continue to see variants emerge. We will continue to run behind as we try to understand this, and we will not get to the position of stability we have with routine epidemic/endemic/seasonal

influenza. We have some time to go and the world will need to be vaccinated before we get to a stable situation.

Rebecca Long Bailey: Thank you to all of the witnesses; that was very helpful.

Q2491 **Chair:** Thank you very much indeed. Finally perhaps on this, Professor Pollard, Kate Bingham, now Dame Bingham, said last October that vaccinating everyone in the country was not the plan, was not going to happen and should not be the plan; we just need to vaccinate everyone at risk. And she talked about 30 million people. Why did the plan change? Do you know?

Professor Pollard: I cannot answer that question from a UK perspective, but it is the case that the original aim of vaccination from a global perspective, led by the World Health Organisation, was to prevent death. As I have just outlined, we know which groups they were. We knew in October. The global health community's perspective was that you prioritise through COVAX those populations that are at greatest risk: those over-50, those with other health conditions and healthcare workers. That was the original COVAX distribution plan. Obviously, that would have put us in a very different place today if all the doses available had been used in that way. There is clearly a difficult domestic issue in countries that have access to vaccines, because they get the greatest benefit for their populations by widespread vaccination of the population. There is that tension between the global perspective and the domestic one.

Q2492 **Chair:** I have a couple of final questions for Dr Hopkins on things that engage a lot of public interest at the moment. One is the suggestion that social care workers and NHS workers should have compulsory vaccination. Could you perhaps set out briefly the rationale for that, as you see it?

Dr Hopkins: This is a Government decision. From a public health point of view, we have very high encouragement of vaccines across the population. We have not mandated vaccines ever before for health and social care, for school starts and children. There are pros and cons to any debate on mandatory vaccination. Of course, the pro is that you have vaccinated the carers for the most vulnerable in care homes. Therefore, that minimises the risk, as much as you can minimise it, to those individuals in that care home. The con is that people may vote with their feet and not want to have vaccine, and therefore not work in a care home, which could lead to staff supply issues in care homes. That has been clearly played out this morning on the radio.

We have had excellent vaccine uptake with this vaccine. Where people are hesitant, we need to work harder to make them understand why the vaccines work. We have seen populations that were very vaccine hesitant to start, but, as information came out, and as their friends, peers and networks got vaccinated, that was overcome. I have a strong belief in the

goodness of people and a belief that people really do want to do the right thing, but they can be nervous and cautious about new vaccines that have come in and been developed at pace.

We see that in healthcare in the vaccine component of hepatitis, where nearly everyone who wants to work in healthcare either gets vaccinated or looks at what they do. It is similar to what we will do in the care sector. I think, predominantly, care workers will get vaccinated, but some of them may be reluctant to get vaccinated early. I remain a little concerned that we will have shortages of care staff once the mandation has come in, but I am sure that the vast majority of care workers want to do the right thing and will get vaccinated to protect the elderly under their care.

Q2493 **Chair:** Obviously, it can have indirect public health consequences for the reasons that you say, if you do not have enough people qualified and working in care homes. Does Public Health England have a view as to the balance of advantage? Clearly, it is a difficult choice to make. Most people want everyone to be vaccinated, but have you made any studies of what is the best tactic to achieve that?

Dr Hopkins: Public Health England has always encouraged uptake of vaccine, through open information, communications and public health messaging. We have worked very hard across England and across the UK to have very high uptakes of vaccine. We have that across all of the childhood vaccines. We achieve ratings of vaccine acceptance in this country much higher than almost every other country in the world. I think we have done that because of openness and transparency about our information and feedback about uptake rates across very granular areas, not just for the Covid vaccine but across all the other vaccine data. I am a big believer in having open, honest conversations and using that to get vaccine uptake to the levels that we need to get it to.

I understand why the Government have made this decision because of the difficulties that care homes have had over the last year and a half. We will have to evaluate the outcomes of this to see if there are any challenges to care home delivery because of staff voting with their feet over the coming months. I do not know what the outcome will be. Our view has always been to have vaccines as a voluntary component, pushing knowledge and information to get uptake as high as we need it.

Chair: Professor Pollard was looking enthusiastic during the time you were speaking there. Is there anything you want to add to that? Is that your view as well?

Professor Pollard: I completely agree with Susan, as always. The only added bit of information is that compulsory vaccination for smallpox was introduced in 1853, because we had very low rates of vaccination. That resulted in an increase to about 80% of children being vaccinated, but there was a big backlash against that, and it dropped to extremely low levels over the subsequent years. We only managed to eradicate

smallpox and have a rise again in vaccination rates after we removed the law for compulsory vaccination.

Taking a long-term view, I completely agree that working with communities and making sure that people have the information, and access to vaccines, should be the priority.

Q2494 **Chair:** Thank you. It is very valuable to have a historical perspective as well.

Finally, just a particular question for Dr Hopkins. Obviously, the new regulations will be voted on by the House of Commons this afternoon. They involve some variation. For example, wedding celebrations and commemorative events for people who have died, wakes, and other events, are going to have their restrictions lifted. But over the next few weeks there are a lot of university students who are going to graduate and have graduation ceremonies planned. There are school leavers who have parties planned. They are not included. Why should they not be on the same basis as wedding parties and commemorations for people who have died in the last year or so?

Dr Hopkins: These are decisions for Government. From the public health point of view, social mixing, particularly in large groups, particularly indoors, has a risk of transmission. Weddings have a risk of transmission, but weddings have been decided by Government to be an important life event to be allowed to go ahead over the next four weeks, while there are still restrictions over others.

From the point of view of transmission, the more people who mix indoors, the more the likelihood of a super-spreader event. We are in a particular moment where we do not yet have sufficient individuals in the population with vaccination, particularly in that younger age group. You mentioned universities. We are starting to see outbreaks again in the university-age population as case rates rise. Particularly in that age group, large-group social mixing is likely to see onward transmission. Particularly if it is multigenerational social mixing, young people may transmit to their parents or grandparents. Consideration of all of this needs to happen.

I know that people who have been planning their weddings will be delighted to see this, but I note that the regulations being put forward by Government also say that social distancing should remain in place and that six people should be seated at a table. They are allowing the events but with some restrictions. I am sure they did that to ensure that the many people who have cancelled weddings over the last year and a half did not have to cancel again in the summer period. It is important to note that every event has the possibility of being an event where transmissions occur. I sincerely hope that they do not, but people need to recognise that. I hope that people will take precautions before they go by reducing their social mixing in the previous days and, ideally, doing a test before they attend.

Q2495 **Chair:** It is a relief for people going to wedding receptions and couples having their wedding ceremonies. Obviously, it is for Ministers to decide, but does Public Health England advise on these granular decisions, which may not be strategic but they have important consequences for a generation of students and school leavers, who will be saying goodbye to their classmates, their colleagues, forever in some cases? That ceremony can be important to them. I think they would hope that someone is thinking about the risk of those circumstances and is advising the Government. Does Public Health England do that?

Dr Hopkins: We consider the risk of the events and we consider the mitigations that can be put in place. It is the Government who decide what events will go forward and what events will not. For each of the events we would consider the mitigations that can be put in place to reduce the risk of those events, but Government make the decisions on what events are happening.

Q2496 **Chair:** Do you recall whether you did that for graduation ceremonies and school-leaving parties?

Dr Hopkins: We will have been asked what would be the mitigations for mixing in events. Government will have made the decision over what events are going to take place.

Q2497 **Chair:** Do you remember whether you advised them one way or the other—for or against?

Dr Hopkins: I personally was not asked about which events could go on or not, but I do not know whether other people in the organisation who were providing advice to the Cabinet Office task force, or to social distancing reviews, have been asked on specific events.

Chair: I am very grateful to you, Dr Hopkins, and to Professors Pollard and Barclay, for your compelling evidence. Today you were very generous with your time for the Committee, and you have informed us on previous occasions. These are very important matters. There is a great deal of public interest in this. It will be debated in the House of Commons this afternoon, so your evidence today is very timely. As all of my colleagues have said, we are very grateful for the work that you have contributed during the pandemic and, as is evident today, will be doing so for some time to come. That concludes this session of the Committee.