

Science and Technology Committee

Health and Social Care Committee

Oral evidence: Coronavirus: lessons learnt, HC 877

Wednesday 4 November 2020

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Members present:

Science and Technology Committee: Greg Clark (Chair); Aaron Bell; Dawn Butler; Chris Clarkson; Katherine Fletcher; Andrew Griffith; Darren Jones; Mark Logan; Carol Monaghan; Graham Stringer; Zarah Sultana.

Health and Social Care Committee: Jeremy Hunt; Paul Bristow; Rosie Cooper; Dr James Davies; Dr Luke Evans; Neale Hanvey; Barbara Keeley; Sarah Owen; Dean Russell; Laura Trott.

Questions 223 - 317

Witnesses

[I](#): Professor Peter Horby, Professor of Emerging Infectious Diseases and Global Health, University of Oxford.

[II](#): Professor Robin Shattock, Chair in Mucosal Infection and Immunity, Imperial College London; and Professor Andrew Pollard, Professor of Paediatric Infection and Immunity, University of Oxford.

[III](#): Professor Wei Shen Lim, Chair Covid-19 immunisation, Joint Committee on Vaccination and Immunisation; and Kate Bingham, Chair, UK Government Vaccine Taskforce.

Written evidence from witnesses:

- [Add names of witnesses and hyperlink to submissions]



Examination of Witness

Witness: Professor Horby.

Q223 **Chair:** Welcome to this joint session of the Science and Technology Committee and the Health and Social Care Select Committee. Our inquiry into the lessons learnt from our handling of the pandemic continues.

This morning, we have three sets of witnesses. We will hear, first, about the development of potential and actual treatments for Covid. Then we will hear from two of the representatives of the leading candidates for a vaccine against Covid. Finally, we will hear from the chair of the Government's Vaccine Taskforce and the chair of the Joint Committee on Vaccine and Immunisation.

To discuss the treatments and therapeutics that are being developed, I am very pleased to welcome Peter Horby, who is Professor of Emerging Infectious Diseases and Global Health at the University of Oxford. Welcome, Professor Horby.

Perhaps I could start with a general question. Would you update the Committee and tell us the following? In a world in which we did not have vaccines—I hope we will come to a discussion about that—do you expect treatments to make a material contribution to helping us live with the virus? If so, what are the principal ones and what are their effects?

Professor Horby: It is important to think about different stages of the disease. Drugs, as opposed to vaccines, have a role in three different areas. One is prophylaxis; it is possible to give treatments to people before they have been exposed that prevent them from getting disease. That may well be a strategy that can help those who are particularly vulnerable. As we know, the risk of severe disease and death increases exponentially with age. It may be that there are treatments that can be used in the very vulnerable that prevent them from getting disease. That is prophylaxis. [*Inaudible.*] —those who are at high risk of developing complications. That would be out-patient treatment of people who have mild symptoms but are at risk of progressing to severe disease.

The third area is the treatment of patients who are hospitalised. Across those three categories, drugs could have material impacts on the morbidity and mortality related to Covid-19. They are not likely to have any impact on transmission risk, because you need to cover a very large proportion of the population, but they may have a material impact on the health system and the number of deaths.

Q224 **Chair:** Thank you. Can you summarise for us the leading treatments that are able to make a contribution, either now or in the foreseeable future?

Professor Horby: Two drugs have been shown to have an effect. The only one shown to have an effect on mortality rates is dexamethasone. It is a steroid. It is probably true that steroids as a class of drugs have a benefit in hospitalised patients who have lung disease. We have shown in the RECOVERY trial of patients who required oxygen or invasive mechanical



ventilation that we reduced the risk of death by about a fifth in patients on oxygen and by about a third in patients in ICU. That was a surprisingly big effect. That drug is now part of treatment recommendations internationally. It is part of recommended treatment guidance.

The second drug is remdesivir, which has received conditional approval in the US and Europe, and is an intravenous treatment, unlike steroids. It is much more expensive. It has not shown a benefit on mortality, but it has shown a benefit in reduced hospital stays. An international trial, led by the United States, showed a reduction of about four days in duration of hospitalisation.

The WHO Solidarity trial has just reported its study of remdesivir. It was about five times as large as the US trial and did not show a difference in hospitalisation. About five trials of remdesivir have been published. Overall, if you put together all the trials, there may be a marginal benefit in the risk of death being reduced, but it is also compatible with no effect on death.

Those are the two drugs that have been shown to have an effect. Other treatments are being evaluated. The most promising are the antibody-based treatments. There is convalescent plasma, which is taking plasma from recovered patients that contains a mixture of antibodies against SARS-Cov-2 and giving it to patients and improving their chances of survival. The jury is out on that, but we are studying it. Then there are monoclonal antibodies, which are artificial antibodies selected to be very potent against the virus. There is some emerging evidence that they may be beneficial in early treatment. What makes them attractive is that they have a long half-life, as we call it; they last a long time in the body. You could give one treatment, either as prophylaxis or for people who have early disease but are high risk, and it may provide protection for several months. It is important that we study those aggressively because they hold a lot of promise.

Q225 **Chair:** When do you expect to have enough evidence from the trials to deploy at scale?

Professor Horby: In RECOVERY, the UK-based trial, we are currently running the largest convalescent plasma trial; we have about 1,500 patients versus 1,500 patients not on treatment. We are aiming for 2,000 versus 2,000. We could have a result on convalescent plasma in the next six to eight weeks. That will be very important. That resource is there. Obviously, we need to scale up the collection of convalescent plasma, but if it works it is a scalable treatment. It is attractive because it would also be available internationally; countries could create their own pool of treatment.

The monoclonal antibodies have come much later into the trial because they took a while to be developed as investigational drugs and to go through the phase 1 safety data. We have introduced them in the UK, but



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we currently have only about 150 patients versus 150 patients, so we are in the early stages of that trial.

Chair: Thank you very much.

Q226 **Jeremy Hunt:** Good morning, Professor Horby. Thank you for joining us. I have a slightly technical question about the regulatory approval process for new treatments, which could be very relevant to both monoclonal antibodies and convalescent plasmas. Normally, the process involves approval on the basis of both safety and efficacy. In the middle of a pandemic, would there be benefit in allowing companies to put their products on the mass market as soon as safety had been approved but when you were still trying to establish efficacy, on the basis that people are dying of this disease every day and, therefore, it may save lives to speed up the process?

Professor Horby: That is the wrong approach. I feel that very strongly. I have been involved in a lot of epidemics. We often see the argument, "These things might work. We're in the middle of a crisis, so we should roll them out on the basis that they are probably okay and they may save lives." What we have actually seen is that that delays understanding how the drugs work, and whether they are safe and effective.

If there is widespread use of the drugs, it impairs the ability to run trials, because patients say, "I can get it outside the trial so I'll have it outside the trial." You then have numerous biases as to who and who does not get the treatment, which it is impossible to unpick later. You end up, several months down the line, with tens of thousands of patients using a drug with no idea if it works. There are fantastic examples of that. We saw it in the 2009 pandemic; 40,000 people were treated off-label, by which I mean drugs that were not registered and proven for treatment. They were given to patients hospitalised with flu. We came out of that pandemic with no new evidence and no new drugs.

In the US, they have given convalescent plasma to tens of thousands of patients outside the trial, and we still do not know whether it works. If they had put those patients into a trial, we would have a definitive answer by now. You have to make sure that it is done in a trial. It is the only way.

Q227 **Jeremy Hunt:** Thank you. I have a question about long Covid and whether there are any drugs being developed or research happening. The King's College study says that 30,000 people have pretty horrific symptoms, even after three months. What is the situation with respect to drugs that might help those people?

Professor Horby: Long Covid is a really important issue. It is clear that Covid is a multi-system disease, both acutely and chronically, and that a substantial proportion of patients who have had the disease require long-term care and follow-up. We do not really understand the nature of it. Some reviews suggest that there is a cluster of syndromes rather than a single syndrome. We need research to understand who is at risk of chronic



symptoms, what are the different clusters and the organ systems involved and how we can mitigate that.

There may be treatments that we can give during the acute illness that reduce the risk of getting the chronic symptoms, which would be the best thing to do. For people who get chronic symptoms, managing those is through both rehabilitation and treatment. At the moment, we do not know. Research is really important. There are a number of initiatives internationally. In the UK, the post-hospitalisation Covid study, PHOSP-COVID, run by Chris Brightling, is planning to enrol 10,000 patients and follow them up and intensively investigate some of them to see what is causing chronic symptoms.

Q228 Jeremy Hunt: Is it your view that that research is adequately funded at the moment?

Professor Horby: I believe so. That large cohort of 10,000 patients is linked to some of the trials. We are linking the data from the RECOVERY trial to that cohort, so that we can see whether the treatments given in our study affect the risk of long-term complications. That cohort is extremely important. Patient engagement is also important and getting the patient groups involved—*[Inaudible.]*

Chair: We lost the end of your answer, Professor Horby.

Professor Horby: The long-term follow-up and engagement with patient groups is happening, and I believe it is adequately funded.

Q229 Graham Stringer: From the first reports of this disease coming out of China to the first death attributed to it in this country, on 5 March, did we prepare quickly enough and appropriately enough to deal with the disease? Using the benefit of hindsight, what could and should we have done?

Professor Horby: That is a broad question. If I stick to therapeutics, not just in the UK but globally, we have been poor in investing in the development of platforms for developing new treatments and, as you will probably hear later, new vaccines for emerging infections. Quite a lot of work is done at the basic level, but you need to bring that right through, so that you have treatments that are ready to give to patients at the start of an epidemic. A good example is monoclonal antibodies.

The platforms are there, but it was not until September that we had them ready to give to patients. You cannot develop monoclonal antibodies before the new infection rises, but you could accelerate them. They could have been ready by August as opposed to September. We could have had UK-based products as opposed to the product we are using, which is from a US company. You could do much more to develop classes of drugs right through, and do the safety data and the pharmacology, so that you know what doses to use, and you know the safety profile, so that you are ready to go straight to patients when an epidemic hits us.

Q230 Graham Stringer: Would it have helped earlier to have recognised loss of



taste and smell as symptomatic of the disease? Would that have made any difference to the progress of the disease?

Professor Horby: I don't think so. That was an unexpected symptom. Early on, in China, it was clearly predominantly a respiratory disease with fever, cough and shortness of breath. It took some while for the symptom of loss of taste and smell to become apparent. It adds something to the sensitivity and specificity of the case definition, but it is not always a very early symptom. It adds something, but not a huge amount, to detecting early cases. What is more important is the ability to diagnose cases with laboratory tests quickly and at scale. As we have seen, the development of the test and trace system has been a huge effort. Obviously, it still needs work, but it is one of the most critical components.

Q231 **Chris Clarkson:** Professor, I want to drill down on new medicines and treatments. The UK seems to have been leading the way in getting randomised control trials up and running. What have the main challenges been?

Professor Horby: We have been very successful. It is probably true to say that the UK has, of any country, been the most successful in running clinical trials for treatment of Covid-19. We have been successful because of the NHS and the National Institute for Health Research. It has been critical that we had that infrastructure in place across the whole NHS so that we could open the study across hospitals in the UK and recruit at pace. At the moment, we are recruiting about 150 patients per day to the RECOVERY trial, which is more than many trials are recruiting in total. We are, by far, the biggest trial in the world. It is mostly a story of success.

At the same time, the system is very stretched. We are recruiting only about 10% of all patients admitted to hospital. It is important to understand that we are talking about getting an answer on convalescent plasma in six to eight weeks, but, if we doubled recruitment, we would get an answer in half the time. That is true for the monoclonal antibodies and all the drugs that we are studying. We have 10% of patients enrolled. That means 90% are not enrolled. We need to understand why we cannot increase that number.

If we look across hospitals in the NHS, some of them are doing very well. Some of them are recruiting 35% of all patients to the trial, which is fantastic. There will be patients who are not eligible and patients who decline to be involved. I think we should be aiming at that kind of number. At the other end of the scale, we have hospitals that recruited many hundreds of patients in the second wave but have recruited less than 1% of patients. Some hospitals have recruited between 200 and 300 patients but have recruited none to the RECOVERY trial.

There is scope for improvement, and we need to understand how to do that. A lot of it comes down to resourcing research staff, empowering non-research staff to get involved in research and, to some extent, performance management of some trusts, where I cannot see a reason why you would



not be able to recruit any patients out of 300 recruited in the second wave. This is a national effort to find treatments. If we want to find treatments, like dexamethasone, before Christmas, if we can get 10% recruitment up to 30%, we will find answers much quicker.

Q232 Chris Clarkson: It is fair to say that it has been a learning experience. How much has your current approach been informed by previous outbreaks? What would you say are the known unknowns that you still need to solidify in order to improve your approach?

Professor Horby: We have learnt a lot from previous outbreaks. I have been involved in trials and outbreaks for some time. We learnt that the most important parameter is speed. You have to get the trials up and running extremely quickly, because you get a very quick increase in cases and you have to capture the cases and enrol them. You have to do it at scale because the outbreak moves around geographically. You cannot just have all your hospitals in the trial in one place. You have to have them scattered across the country so that you can capture the epidemiology as it moves around the country.

You have to keep it simple because hospital staff are under extreme pressure. You need a trial that can be embedded in care and can be part of routine care. When you are talking to patients about them needing stockings and heparin to stop them getting blood clots, and about getting oxygen, you should also say, "There are experimental drugs. Would you like to be in a trial to contribute to this?" It needs to be in routine care. We have learnt those lessons and put them into practice in this outbreak, which is why we have been so successful in the UK.

We have been a bit less successful out of hospital. The trial that I co-lead is in hospitalised patients, but there are also the prophylaxis trials that I talked about, giving preventive treatments. There is real scope for that. A good example is care homes, where people are very vulnerable and there are very high death rates. The monoclonal antibodies would be a great drug to try in prophylaxis. One injection might provide cover for several months. That is a group that may or may not respond well to vaccines because of an ageing immune system. We have not yet got those trials off the ground. The out-patient trials—the primary care trials—have been slower to get going. In the hospital system, we've cracked it, apart from increasing recruitment numbers. In primary care and prophylaxis trials, there is still work to be done.

Q233 Chris Clarkson: From a research perspective, we are doing Covid all the time at the moment. What has the impact been on research in other areas, and what are the wider implications in the longer term?

Professor Horby: You are right. In the second wave, we have seen an attempt to return to normal practice. The NIHR research network, which we are utilising for Covid trials, also has a whole bunch of other trials, in cancer, cardiovascular disease and renal disease. Those cannot be neglected. We must find a solution—*[Inaudible]*



Chair: Professor, we lost your sound briefly again.

Professor Horby: We need to find a sustainable solution to running the Covid trials alongside the other research that needs to be done. We now have the vaccine trials, so there is increasing pressure. While there are groups and people like me saying that we need to increase recruitment to the Covid trials in hospitals, NHS staff are also being asked to increase recruitment to vaccine trials, to go back to routine research in cancer and so on. They are under pressure. We need to talk with the teams on the ground to find out what can be done to deliver all of this much-needed research.

Q234 **Chair:** On the recruitment to trials point, the RECOVERY trial programme is one of the best, if not the best, in the world. We have the NHS, which is a unique asset. The level of recruitment you describe is disappointingly low and, as you recognise, we should increase it. What can we do? Who is in charge of it? Who can drive better recruitment, which would be good for, I assume, individual patients and patients as a collective?

Professor Horby: There are two key groups, NHS Executive and the NIHR. We have to be very careful not to browbeat people on the ground. We are relying on research nurses, nurses and clinicians, who are under extreme pressure, for routine care, routine research and Covid research. We need to talk to them and work with the NIHR infrastructure and NHS Executive on how we can support them to recruit patients.

We could probably do with more marketing of the trials. It is important that patients and their relatives are aware of the availability of the trials and their importance. When a patient asks, "Why should I be in this trial?" the answer can be, "You're receiving dexamethasone. The reason you're getting that is that patients before you were in a trial, so you can make a contribution for future patients by being in the trial." We have been having discussions with NIHR and NHS Executive about how we can identify ways to support better recruitment.

Q235 **Chair:** For the reasons you gave, you don't want to put extra pressure on the people who are caring for patients. Therefore, the approach may be to simplify and to standardise, so that it is a matter of routine rather than individual persuasion. Do you think there is scope for that approach— for making it a routine consent?

Professor Horby: Yes. We have tried to make the RECOVERY trial part of routine care. We said that it does not have to be done by research teams, which are limited in their numbers and their working hours. It is something that should and can be done by the care staff, the nurses and doctors on the wards. We specifically designed it so that it can be done like that. It is important that it works so that it can be embedded as part of the care package.

There is a lesson for research in the NHS going forward. If we can do a trial of 15,000 patients in Covid over a few months, perhaps that can be done for other diseases in the future, and we can make our clinical evidence



base much stronger by making research part of routine care, as opposed to a specialist activity for those down the corridor in the research room.

Q236 **Chair:** Would that apply to primary care and care homes, as you have suggested?

Professor Horby: For primary care, yes. Care homes are a different kettle of fish. The training and turnover of staff there makes it a bit more challenging.

Q237 **Dr Davies:** Thank you, Professor Horby, for your time this morning. There is, understandably, huge public interest in drug treatment for Covid. I and I am sure many of my colleagues are frequently contacted by constituents who say, "What about vitamin D? What about ivermectin?" That was raised with me this week. Can you outline how, in the RECOVERY trial, you identify drug candidates to go forward for evaluation?

Professor Horby: Yes. It has gone through some evolution. Originally, a Government/DHSC committee called NERVTAG—the new and emerging respiratory virus threats advisory group—looked at the very first tranche of drugs that were available and made a recommendation about which of them went into the RECOVERY trial.

Then we went through a phase when many of us were bombarded with emails and letters from people recommending a whole range of treatments, hundreds of them, which we could not keep up with, because we could not look at all of them in a rigorous way, screen them and decide what would come into the next trial. What has been useful is the third phase, which was the COVID-19 Therapeutics Advisory Panel, a panel set up by the Department of Health, to look at all the options that have been put forward. It has a number of sub-groups.

There are three broad categories of drugs: the antiviral drugs; the immunomodulators, which are the anti-inflammatory drugs; and the anticlotting drugs. Sub-committees have been set up to look at all of those. They have done a fantastic job. They have been very rigorous. They produce multi-page reports on every drug and systematically look at the evidence base for it. They then recommend that it is not prioritised or that it is shelved for now, pending new data coming out, or it is recommended for going to trial. That has been very useful for us. This week, in RECOVERY we have just added aspirin to the trial because clotting seems to be a big problem. Aspirin is a widely available and cheap drug, which, if it were to work, would be a huge boost. That came out of the CTAP process of looking at all the options and saying, "This is the one we think should go forward." That is functioning very well, and we are very happy with it.

Q238 **Dr Davies:** Are there any emerging developments internationally that RECOVERY is not looking at that you think we should keep our eye on?

Professor Horby: We are watching carefully. There are many thousands of trials, so it is a bit difficult to keep track. Most of them are small and



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unlikely to give definitive answers, so we are keeping our eyes on the bigger trials.

In terms of antivirals, I am afraid that the field is rather disappointing. As we saw, remdesivir, which was one of the front leaders, probably has an effect on the duration of hospital stays but perhaps not on mortality. The monoclonals are exciting. There is emerging data of efficacy in out-patients, preventing hospitalisation and reducing duration of stay. They are promising. Two of the big companies, Eli Lilly and Regeneron, have temporarily suspended their trials in hospitalised patients. Eli Lilly stopped theirs for lack of effectiveness, and Regeneron paused theirs due to potential safety concerns. That is a bit disappointing. We need more data to know if that is something to worry about. There are not many patients in those trials, so it remains to be seen whether they will be effective in hospitalised patients.

We are keeping an eye on convalescent plasma. Again, I think the answer will come from RECOVERY. Otherwise, I don't think there is anything we are missing. As I said, we have just added aspirin. Anticlotting drugs were an area where we had a gap. Hopefully, we have filled that.

Q239 **Dr Davies:** How effective do you think the NHS has been at adopting best-practice management of Covid patients?

Professor Horby: Good question. Although it is early days, it would appear that the case fatality in hospitalised patients has come down quite a lot. At the moment, it looks as though the case fatality rate is about 15% in hospitalised patients, having come down from about 30% in wave 1. There is really a big difference—*[Inaudible]*—wave 2, so we have to be a bit cautious because it may creep up a bit—

Q240 **Chair:** Professor Horby, we lost you for a brief second when I think you were giving us a crucial figure. Would you go back to that?

Professor Horby: The case fatality rate in hospitalised patients appeared to be about 30% in wave 1. It now appears to be about 15%, about half, which is fantastic news. We have to be a bit cautious because the age profile is not the same at the moment. As more older people come in, I think it will creep up.

It indicates that the NHS is getting better at treating Covid patients. There are a number of areas where improvement has happened: the use of respiratory support, the use of oxygen, and non-invasive ventilation—face masks with positive pressure—and hoods, intubation and invasive mechanical ventilation. Clinicians are getting better at managing that part of the disease, and that is improving survival.

We are seeing better use of anticoagulants, such as heparin and other anticoagulants, to prevent clotting. One would anticipate that the introduction of dexamethasone has also had an impact. As I said earlier, it would probably reduce the case fatality rates. I would like to see data on the proportion of patients who ought to get dexamethasone who are



getting it. We are trying to capture that through various systems, but we do not yet have an answer.

Q241 **Barbara Keeley:** Professor Horby, what exactly needs to be done to get the trials on monoclonal antibodies off the ground in care homes? We all understand that the care sector is not like the NHS, and it is more difficult to get trials off the ground. You mentioned the need to market the different types of trials. Is anything happening? Is work going on with the care sector?

Professor Horby: There is. Prophylaxis has been identified as an area that was lacking, so there have been efforts to change that, and a call has been put out for research groups to run a trial in care homes. It has been recognised as a problem. I believe funding has been identified, and a call has been put out to research groups to put themselves forward to run such trials in care homes.

We need to secure supplies of the drug. Discussions will need to be had with the companies to make sure that we can secure supplies of the drug for those trials. Once we have the right research group and we have access to the drugs, we can market that. Care homes ought to find it a very interesting proposition; a one-off injection that may provide protection for several months during the winter to care home residents will be attractive. That is why it is an important trial to do.

Q242 **Barbara Keeley:** What is the timescale? You said it is at the stage that a call has gone out. When could something happen?

Professor Horby: I honestly do not know the answer to that, but we need to put the accelerator on it. As you know, we are still in the midst of the second wave and we are coming into the winter season. We have seen that infections in younger age groups leak through into older age groups and into care homes. Although measures have been put in place to try to protect care homes, inevitably, there will be some leakage and there will be care home outbreaks. We need to be able to test the efficacy of the drugs during those outbreaks. There should be a great deal of urgency to get these trials up and running in the next few weeks, if possible.

Q243 **Barbara Keeley:** You say there should be, but is there?

Professor Horby: I cannot answer that question. I don't know. I know it is perceived as an important issue.

Q244 **Chair:** Who is responsible for driving it, Professor Horby? If we wanted to take it up, who should we take it up with?

Professor Horby: Probably with the DHSC, because they have commissioned a group to look at prophylaxis. I believe the NIHR put out the call. I anticipate that they are treating it with great urgency. If you wanted to check that, it would probably be best through the DHSC.

Q245 **Dr Evans:** Thank you very much, Professor. In the spirit of lessons learnt, I am keen to canter over the path of physiology that we heard about in the



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Health Select Committee. An airborne virus in droplets comes in through the mucosa, hits the ACE-2 receptors, people become unwell and then, after seven days, for some reason there is a cytokine storm and people end up in ARDS—acute respiratory distress syndrome. Is that still the way it is understood at the moment?

Professor Horby: Yes, pretty much. You asked a very professional question.

Dr Evans: I am a GP by background, so I should declare that.

Professor Horby: There are still some questions. A dichotomy has been proposed of a viral replication stage early on that then transitions into an inflammatory stage. I don't know whether cytokine storm is quite the right phrase, but there is certainly an inflammatory stage. There is still a question as to what extent there is viral replication ongoing in the inflammatory phase. There may be a tendency to say that antivirals will only work early and anti-inflammatories will work late.

My feeling is that, even in severer patients, you see data that viral loads are higher and more prolonged in patients with more severe disease. The inflammation may well be driven by continued viral replication, particularly in the lower respiratory tract, because a lot of the data we have is from swabs in the upper respiratory tract. In hospitalised patients, we should not neglect the virus. We should be looking at immunomodulators and antithrombotics as well as antivirals.

Q246 **Dr Evans:** That is important. The Committee heard that we were not able to identify who was likely to go into ARDS. That was the hardest part of seeing who is going to recover well and who is going to be in the 10% who need hospital. Is there any understanding from your work in research or therapeutics that can target that, to identify those people and prevent them from ever getting to hospital in the first place?

Professor Horby: There are, potentially, three ways of doing that. One is through the broad risk groups. Age is clearly the biggest, but there are people with comorbidities who are not so old who also end up in hospital, and there are people who do not have comorbidities who end up in hospital.

You have to go beyond the crude risk factors of age and comorbidities and look at biomarkers, which is another way to do it. You can detect signals in the blood either through chemicals or in the way the DNA is being transcribed; it is called transcriptome analysis. You can get early signals in those who are progressing towards severe disease or are likely to progress to severe disease. I don't think we have those yet, but there are studies looking at them.

Q247 **Dr Evans:** We are not in a position to have that on a nationwide basis. You picked up on the risk factors. We know now from studies that age, obesity and diabetes are really important. Are any therapeutics being targeted specifically at those risk factors, or again are we too far out and do not have enough data yet?



Professor Horby: We are too far out. Things like obesity and diabetes are markers of processes. We need to understand the underlying process and why some people with obesity or diabetes become severely ill. Biological studies look at the biomarkers; they also look at the host genome. There have been some NICE studies. The national genomics study identified particular genes associated with viral innate immune responses that would suggest that there may be certain people who have less well-functioning parts of their immune system that you could identify through genomic studies. They might be at risk of severe disease, which you could target. In the future we may be able to identify people through either biomarkers or genomics, but we are not there yet.

Q248 **Dr Evans:** We know from the data that is coming out that BAME frontline professionals were affected more. A systematic review in *The Lancet* that pulled all of the studies together said that it is still inconclusive, but it seems broadly to be biologically related around ACE-2 receptors, with risk factors and then health inequalities behind it. Do you have any thoughts about the therapeutics of targeting specifically, for example, blood pressure? Obviously, we have a different set for Afro-Caribbean. We use different blood pressure medication. Based on that, does targeting therapeutics for ethnicity depend on efficacy being looked at, or, again, are we too far away from having the data to support that?

Professor Horby: That is a very interesting proposition. As you highlighted well, the BAME risk group is multifactorial in socioeconomic exposure through work settings and potential biological risk factors as well. The more we can look into the biological risk factors, the more we can look at personalised medicine where we target certain risk groups. As you said, the renin-angiotensin system, the ACE receptor, is another therapeutic area that CTAP is looking at. We need more biological evidence that targeting that part of the system will have an effect on the development of disease. We need to do more studies.

Q249 **Dr Evans:** Is work being looked at in both of those areas?

Professor Horby: CTAP is looking at the emerging evidence around the renin-angiotensin system. I am not particularly aware of work ongoing. We would want to see animal models of that system and whether, if you intervene in the system of animal models, it has an effect on virus replication and disease. I do not know what is going on in that area.

Q250 **Dr Evans:** You mentioned therapeutics. When people have long Covid or have had it, is there any form of long-term therapeutic, a bit like we have statins to use for blood pressure? Do you see there being a medication as a secondary prevention in the future, as we would use aspirin or clopidogrel in patients, to try to prevent anyone ever being reinfected, supposedly, if we do not have an immunity in vaccine?

Professor Horby: Do you mean secondary prevention for long Covid?

Q251 **Dr Evans:** Yes, or a Covid reinfection if immunity is not proven. You could get reinfected. If we don't have a vaccine and we have to live with it, do



you foresee a therapeutic position where someone will be taking something to prevent it once they have an infection?

Chair: Briefly, if you would, Professor Horby.

Professor Horby: It is a possibility. We saw for influenza that neuraminidase inhibitors are much more effective in prophylaxis than they are in the treatment of severe disease. It is conceivable that you could get a drug that could be a successful prophylactic, but we are a long way off that yet.

Q252 **Chair:** Professor Horby, the Science and Technology Committee took evidence from practitioners in some east Asian countries who told us that their practice was to bring people with relatively mild symptoms into hospital settings so that they could help them and prevent their symptoms from becoming severe. The practice in the NHS has been for people to wait until they were quite sick before they went into hospital. Have you learnt anything from the experience of the pandemic in other countries? As we go into this new wave, will we be changing that practice?

Professor Horby: In general, it is a fair principle that early treatment is better if you have an effective intervention. Dexamethasone is for the inflammatory stage, for late disease. We are still searching for an intervention in early disease. Remdesivir is an antiviral, but it is not easy to use. It is an intravenous infusion and it is quite expensive. We still need an easy-to-use and relatively affordable early intervention. If you had that, it would certainly be an area to target. It could be done on an out-patient basis through primary care, but first things first: we need to find a medicine that is effective at that stage of disease.

Q253 **Chair:** What about the provision of oxygen? Alison Pittard of the Faculty of Intensive Care Medicine said that the experience is that oxygen therapy, short of intubation, has shown itself to be more effective than was first thought at the beginning of the pandemic, and requires people to be there earlier than if they need to go into an ITU.

Professor Horby: We are still learning a lot about appropriate interventions. Things have improved in the use of oxygen and ventilation, but there are still knowledge gaps. There are some trials ongoing. There is one called RECOVERY-Respiratory Support that is looking at different oxygen interventions and at which is optimal. We are improving. Studies are ongoing. Hopefully, that improvement will continue.

Chair: Thank you. Professor Horby, we are very grateful for your evidence this morning and for your very important work on behalf of us all in advancing those therapies.

Examination of witnesses

Witnesses: Professor Shattock and Professor Pollard.

Q254 **Chair:** We now turn to our second panel of witnesses. I am delighted to welcome two people who are leading work on two of the potential vaccines



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being developed against Covid. Andrew Pollard is the Professor of Paediatric Infection and Immunity at the University of Oxford. Professor Pollard is the chief trial investigator for the Oxford vaccine trial. Professor Robin Shattock, who is the Chair in Mucosal Infection and Immunity at Imperial College, London, is the principal investigator for Imperial's Covid-19 prospective vaccine.

Perhaps I could start with a question to Professor Pollard. When do you think your vaccine will be available for deployment?

Professor Pollard: The first step is to reach the point where we can do an analysis and find out whether the vaccine works. Our job is to conduct rigorous clinical trials and reach a point where we can do that analysis. I am optimistic that we could reach that point before the end of this year.

Your question, though, was about deployment. Two steps have to happen after that. First, all the data needs to be put together and presented to the regulators both here and in other countries around the world. The regulators then have to review it all. We absolutely need that to happen, so that there is very careful scrutiny of everything that has been done in the clinical trials, to look at their integrity and the quality of the data and verify that the results are correct. The policy decision about who should get it, and the provision and deployment, would happen after that.

The answer is that with our bit we are getting closer, but we are not there yet. Then there are those other steps that have to follow.

Q255 **Chair:** A degree of optimism was expressed by the chief scientific adviser and the chief medical officer about vaccines coming to our aid. In terms of your central expectation, which I understand is subject to different obstacles, do you expect them to be available and to start to be deployed and distributed before Christmas?

Professor Pollard: It is very difficult to answer that question. First of all, we have to do the analyses to find out whether they work. If they do, there are other steps that have to be gone through. The timelines for those are not entirely clear to me at the moment. There is a small chance of that being possible, but I don't know.

Of course, our trials are among the many going on around the world, a number of which may well report before the end of the year. Those steps will need to happen for multiple different products. I hope that we have lots of successes with the different platform technologies that are being used, not just for the UK but for the world, because to have a supply of vaccines for 7 billion people, potentially, needs a lot of success for all the different developers.

Q256 **Chair:** We all share that view. What do you believe should be the level of efficiency of a vaccine—yours and others—to justify its approval and deployment in the middle of a pandemic such as we have?



Professor Pollard: That is probably a question for those who will be involved in the policy decision, but walking through how you get to that point might be helpful. The FDA—the regulator in the US—has set the bar that vaccines have to be at least 50% effective. That does not mean that in the US they want the vaccines to be only 50% effective, but they recognise that if you can reach 50% it has a huge impact on the pandemic. We would halve the number of deaths or hospitalisations here in the UK for the NHS. That is a dramatic change from where we are today. They have set the bar at that level.

To be able to test 50% scientifically is a lot harder. You need a lot more cases to occur in the trials to rigorously be able to ensure that you have at least 50%. To reach that threshold, if it is only 50% effective, will take longer. We all hope that the vaccines will be more effective than that, which means that we will have an answer sooner. The actual level of efficacy is unknown at the moment. No one has unblinded their trials and looked at the data so far.

To take that argument further, if vaccines only prevented 40% of the cases, would that be useful to the NHS? Those are the sorts of decisions that, potentially, policymakers may need to think through in the months ahead, depending on where vaccines land. We all hope that, if indeed the rigorous trials show that they work, we have much higher efficacy than that, but we need to think about how we would handle vaccines that were less effective.

Q257 **Chair:** Indeed. It is in the days and weeks ahead, perhaps more than the months ahead. It is useful to know what the FDA said. There are, are there not, vaccines against other diseases—influenza, for example—that are licensed at a lower rate of efficiency?

Professor Pollard: Yes. Influenza is the difficult one. In a good year, you can get quite high efficacy of influenza vaccines, but there are lots of reasons why, in some years, because the vaccine does not match terribly well to the virus that arrives that season, the protection is a lot lower. Influenza is slightly difficult because of that variability. Most of the vaccines we use routinely in the NHS have much higher efficacy, certainly over 70% and often over 80% or 90%.

Q258 **Chair:** Thank you. Perhaps I can put the same question on the timeline to Professor Shattock.

Professor Shattock: Our timelines are slightly longer than with the Oxford vaccine because we are developing a completely new technology that has never been in clinical trials before, so it has taken us longer to get to the stage of being able to move into efficacy trials. With the right level of support, we could deliver an efficacy signal midway through next year, with regulatory approval following closely after that. It is important to recognise that right now we do not know which of any of these vaccines will work and what success will look like, whether success at preventing disease or success at preventing transmission. Those different outcomes will have very different impacts on how the vaccines are used.



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One of the advantages of the technology that we are developing is that it can be used for repeated boosting immunisation, either to boost existing vaccines or to boost itself. If immunity wanes, we would be well positioned, with this technology, to provide boosting strategies for the UK.

Q259 Jeremy Hunt: Thank you very much. I would like to understand what the likelihood is of your vaccine being something that you would give to the whole population, or whether there are chunks of the population that you would not be likely to want to give it to—for example, children. Some people say that with a vaccine that is developed in a hurry, as both of these rightly are, you do not know about long-term neurological effects. With children, you might say, “If they are not going to suffer badly if they get Covid, they shouldn’t get the vaccine.” What is your view of the likelihood of giving it to everyone?

Professor Pollard: To deal with your point about the hurry, there has been due urgency to try to accelerate all the development that is going on and the clinical trials, but that does not mean that things have been done in any way less stringently than normal. We follow the same regulatory processes, the same stringency and the same quality control of the vaccines that you would expect in normal times.

What has been incredibly successful in the development work here and in other countries is that many of the normal obstacles to speed have not been there—for example, funding. We had a bit of a problem at the beginning working out the funding strategies, but since we started the Government have been very clear that funding should not be an obstacle to moving ahead. With normal vaccine development, you do your first trial and you may wait another year for funding to become available so that you can do the next trial. That has not been a hold-up at all. From the regulatory process side and so on, we have not had any of those delays.

Another thing from the in-a-hurry perspective is that for most drugs or vaccines relatively small numbers of people are normally recruited into clinical trials before licensure. For vaccines in Europe, somewhere between 3,000 and 5,000 would be studied in clinical trials as a standard before licensure. Just in our trials of the Oxford vaccine, there are already 23,000 people enrolled. With the partnership at AstraZeneca, that will rise to 50,000 over the next month or two. These are much larger trials.

We will have a lot more information about the safety of these vaccines than we normally would, and—

Q260 Jeremy Hunt: Are you likely to recommend that they are given to children? That is what I am trying to get to. Sorry, I need to get to that point.

Professor Pollard: I was distracted by the suggestion that there is something unsafe about the process.

Jeremy Hunt: Doing it in a hurry was meant as a compliment. It was not meant in any other way.



Professor Pollard: As to which segments of the population should be vaccinated, it comes back to the comment that Robin made. It depends a bit on the characteristics of the vaccine. Clearly, if you have a vaccine that prevents severe disease and death, the first thing is to target and to use it for those at highest risk, who are older adults and those with other health conditions.

If you have a vaccine that prevents transmission, there could be much broader benefits for the wider population to use it.

Q261 **Jeremy Hunt:** Does your vaccine prevent transmission?

Professor Pollard: We don't know. We are doing trials to address those questions. It is not something to speculate on at the moment. We have to understand in humans exactly what the vaccine characteristics are. Can it prevent acquisition of the virus? Can it prevent symptomatic disease, hospitalisation and so on? That has to be conducted through trials.

Q262 **Jeremy Hunt:** You said that it might, potentially, be approved by Christmas. Is it likely to be a vaccine that is recommended for use by children? Can I ask you that question?

Professor Pollard: I did not say that it would be approved by Christmas. I said that I hope we will have some results by the end of the year.

As far as giving the vaccine to children is concerned, the first step is that clinical trials have to happen in a childhood population, and those trials are being planned. At the moment, we do not have any data about the immune response or safety in children. That has to be done through the normal scientific process. I anticipate that it will happen towards the end of this year or during the early part of next year. That is the first step.

Deploying vaccines in children will be a policy decision based on the understanding of the characteristics of the vaccine, whether it can prevent transmission and disease, and whether there are groups of children, from the epidemiology, who are at particular risk of severe disease who might be targeted. Then there are questions about whether broader use among children could have a wider benefit both for children and for society as a whole. All of that has to be looked at from a policy perspective, from independent scientific advice.

Q263 **Jeremy Hunt:** Professor Shattock?

Professor Shattock: The answer is very similar. We will be looking at doing trials in de-escalating age, assuming that we have the funds to do it. I do not think it will be immediately rolled out in young children. There is the risk-benefit issue, beyond those who may have underlying conditions that may make them more susceptible to Covid-19. Most young children will not suffer seriously from Covid-19. In many ways, the equation between tolerability of vaccine and side-effects versus the benefits are quite different in that age group where, by and large, if it was a vaccine



that prevented transmission, they would be taking it to protect vulnerable populations, rather than getting an immediate direct benefit themselves.

Q264 **Chair:** Thank you. On this point, there are two broad approaches, are there not? One is to vaccinate those who are most vulnerable, and the other is to vaccinate those who are most robust, because by protecting them, you protect the more vulnerable people. In other words, do you target, first of all, the elderly and those with pre-existing medical conditions, or children? For your particular vaccines, do you have a view as to which of those approaches should pertain?

Professor Shattock: Again, the fact that we don't know whether the vaccines will block transmission or prevent disease is a critical determinant in how they will be used. If they are very effective in blocking disease but do not have an impact on transmission, the argument is totally for vaccinating vulnerable populations, because that is where it will have the most immediate benefit. That should also be the most effective prioritisation strategy.

Until we get information about whether any of the vaccines block transmission, the question as to whether they should be rolled out widely in the UK population remains unanswered. That will be balanced by the level of efficacy against transmission and the level of vaccination at a population-wide level that would be required to prevent ongoing transmission. We do not have data to make those equations right now.

Q265 **Chair:** Professor Pollard, do you have a view as to how your vaccine should be deployed first?

Professor Pollard: As I said, that will be a policy decision. Initially, when you have relatively constrained supply, which I am sure there will be for many of the vaccines, the first groups to be targeted, in my view, will be those at risk of disease, such as healthcare workers, or at risk of severe disease, in particular older adults and those with other health conditions. I completely agree with Robin that children are relatively unaffected by the virus. For their own protection, the priority should not be children but should be others in the population.

Chair: Thank you. That is very clear.

Q266 **Dean Russell:** I have a few practical questions to both of the witnesses. I will go through them all together, if that is okay. I am interested to know whether the vaccine is planned to work on people who have already had Covid. A large number of the population will have had Covid during the past eight or nine months. Will it be used for them?

My second question relates to previous questions around the order of roll-out. It also relates to a comment that has been made about what the vaccines will actually do. Could they prevent transmission and so on? Do you see there being a chance that there will be multiple vaccines, with one reducing transmission and another preventing somebody from getting the symptoms? Do you see a position where we might get to a point where we



have an annual vaccine or do you see it as a one-off?

I am also very keen to understand the trials. One of the big issues that has been reported is the impact on the BAME community. How is that going in terms of trials? Does it have more or less of an impact? How is that working.

Finally, I have a very practical question. Am I correct in assuming that any vaccine that comes out will be an injection, or will it be delivered through a different approach from the work that has been done so far?

Chair: Three questions. Perhaps we could start with Professor Shattock.

Professor Shattock: The first question related to whether the vaccines would be used for those who have already had Covid-19. The answer is that yes, there is evidence that they would boost, potentially, those who may have a variety of levels of immune response to Covid-19. That is already incorporated in our current trials, and I suspect in the Oxford trials as well.

The question about transmission versus infection is one that we will not know until we get the data.

Q267 **Dean Russell:** Do you see a point where, if one vaccine could work for transmission, and a different trial, perhaps from another country, works on another level, there could ever be a case where there were two vaccines that people would have to take?

Professor Shattock: It is more likely that we will see different waves of introduction of vaccines. It is unlikely that a vaccine that blocks transmission will not also prevent severe disease. It is certainly possible that the first vaccines may reach the bar of preventing severe disease but may not necessarily block transmission. Those may be introduced first, because they will be first past the post, but, as we see later vaccines that may be more potent, they may be replaced.

It is quite likely that we will have a number of vaccines introduced. They will need to be monitored carefully because we will not know how long they will provide immunity. We certainly need a strategy for re-boosting, most likely the re-boosting of vulnerable populations where immunity may potentially wane faster. Those considerations need to be taken into account. The approach that we are developing is particularly suitable for re-boosting campaigns because you get no immunity against the vaccine itself, which is something that occurs with some of the viral vectors delivered to vaccines.

You asked about BAME effects. We are certainly looking at that in our trials. We would still like to encourage more people from those groups to come forward for clinical testing because it is an important consideration, but so far we have not seen any evidence of increased side-effects or less potent immune responses in those groups.

Q268 **Chair:** The same questions to Professor Pollard.



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Professor Pollard: The first question was about people who had previously had Covid, those who are positive already at the baseline. One of the requirements for regulators around the world is that that group of people is included in the clinical trials. The reason is that, when we get to the point of roll-out, we know that there will be some people in the population who do not know that they have had the disease. We need to know, first of all, whether or not they need a boost, and whether there are any safety concerns for people who have been previously infected getting the vaccines. In our trials, we have included zero-positive people, people who have previously had infection. We will be able to answer that question.

The second question was whether we will have different types of vaccines that do different things. First of all, we do not have the data so I don't know that yet. That is something we will have to find out in time. Secondly, when you look at the different trials that are going on around the world, I am not sure that all of them will address the question you are asking. We may have quite good clarity about whether the vaccine prevents symptomatic disease, because that is the primary end point, the primary analysis, that is undertaken in all the trials.

The transmission question is much harder to get to. One way you could do it is by looking at the households of people who are vaccinated to see if fewer people in the household get the disease. The other would be to look at individuals to see whether they get infected when they have been vaccinated, even if they have no symptoms. That is what we are doing in our trials in the UK. There has been a pretty amazing effort with the Government and the NHS. We are taking swabs from 10,000 people in the trials every week during the course of follow-up, to find out whether people have asymptomatic infection. If those who are vaccinated do not get asymptomatic infection, it makes it very likely that the vaccine could be transmission blocking. That is something we will know in time, but it is going to take a while to begin to resolve. One word of caution is that I am not sure that we will have the transmission question from all the trials that are going on around the world.

You asked whether we need annual vaccines. Of course, we do not know the answer. The main reason you would need an annual vaccine is that the immunity you get from the first two doses does not last and you become susceptible to reinfection. That is possible. The only situation we have to fall back on is the coronaviruses that all of us normally get as children. This is a family of viruses that are very common. We all get those viruses as children. Unfortunately, we do not get perfect immunity when we get those infections as children. Through our adult life, every few years we will get a cold caused by coronavirus. We do not get severely ill with it. We get a mild infection. That tells you something about immunity from natural infection over time not being complete. It does not give you complete protection.

We do not know whether vaccines are going to be like that or whether they will give complete protection that lasts for years. The only way we will know



the answer to that is by time passing. The first vaccines are only six months in, so we cannot tell whether we will still be protected a year from now. We do not even know yet whether the vaccines are protective in the first six months.

The other reason why we might need annual vaccination is that it is like influenza, where the virus changes each year. Perhaps if you have many people vaccinated, the virus will have to mutate in order to survive, so the vaccine will no longer be able to protect against it. That is what influenza does to some extent. That would be another reason why we might need a revised vaccine in future years. At the moment, we do not know the answer to that question. So far, we have not seen changes in the virus that seem likely to have that impact, but there are a lot of immune people in populations at the moment to drive the virus to do that.

You asked about the BAME population included in the trials that we are undertaking here in the UK. That will be part of the analysis that we do later on. One of the really important strategies in our vaccine development programme was to ensure that we were inclusive of the UK population and that there was generalisability around the world. Our trials are set up such that we have 10,000 people vaccinated in Latin America and 2,000 in Africa, and, through our partnerships, we have people being vaccinated in Asia as well. We have a large database of information gathered from different ethnic and geographic settings around the world, as well as trying to address those issues here and in the UK.

Lastly, you asked whether it was all injection. The answer is that almost all the vaccines being developed are looking only at injections. It is possible that there could be some vaccines later on that use a different route of immunisation, like the nasal flu vaccine that is used at the moment. None of those is at an advanced stage of development. We cannot answer as to whether that is possible, certainly not in the near future.

Q269 Katherine Fletcher: As so often in my life, Mr Dean Russell has already landed very much on the question I wanted to ask, so I am going to go slightly off piste.

Ultimately, what is this about? It is about people having confidence that they can go and hug their granny without giving her something that might put her life at serious risk. I would love to hear from those in the field where you think that bar is in terms of success. We would all love to take one injection that gives us 100% confidence that we cannot put anyone at harm and we ourselves are not going to come to harm. Is that possible in the future? We are not going to get there right now. For different populations, different ethnicities and different communities in the UK, what does success look like?

Professor Pollard: We, first, have to have the results of the trials that tell us the level of efficacy of the vaccines. Let's say that the answer is 70%, to pick a figure. That means that 30% of the people vaccinated are not protected. If only 70% of the population agree to be vaccinated, of



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whichever group you are talking about—older adults or those with health conditions—you end up with only about 50% of the people you want to protect being protected.

It makes a huge difference to impacts on the health system, the economy and so on, but it does not mean that the pandemic ends on the first day that you have a vaccine available. We will still have some ongoing transmission and a need for treatments for those who become unwell. The vaccines could have an enormous impact from where we are today, but it is unlikely that they will immediately end all the measures that we have in place and the need for development of the treatments that Peter Horby talked about earlier.

Q270 **Katherine Fletcher:** May I push you? What does success look like? When I get stopped outside Tesco, what is good? We know we are not going to get to great, but what's good?

Professor Pollard: Good is having vaccines that have significant efficacy. Whether that is 50%, 60%, 70%, 80% or whatever the figure is, it is an enormous achievement. It means, from a health system point of view, that there are fewer people with Covid going into hospital, so people who develop cancer can have their operations or their chemotherapy. It is a complete game changer and a success if we meet those efficacy end points. Unfortunately, it does not mean that we can all go back to normal immediately, because it takes time to roll out vaccines, not everyone will take them and people will still get the virus because it is too good at transmitting.

Q271 **Katherine Fletcher:** Thank you. Professor Shattock?

Professor Shattock: I have nothing to add. Professor Pollard has given an excellent answer to your question.

Q272 **Katherine Fletcher:** In layman's terms, we are going to eat the elephant of Covid a spoonful at a time. There is no silver bullet when it comes to vaccines or vaccine production.

Professor Shattock: That is right. It is unrealistic to expect that the UK will wake up and hear that there is a vaccine that is successful and life will get back to normal immediately. We are likely to be living with the consequences of this virus for many years to come, even though vaccines will make life much, much better and reduce, hopefully, fatalities and serious illness significantly.

Katherine Fletcher: May I say that for a virus that we had not heard about last December it is a testimony to the scientific community, both in the UK and around the world, that we are even having this conversation in a great level of detail? Let me extend my personal thanks.

Chair: The Committee shares that sentiment.

Q273 **Sarah Owen:** Professor Pollard, the success of any vaccine is reliant on take-up, as we have just discussed, and distribution. Every year, we have



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the flu vaccine, and the winter flu season is upon us. We struggle to reach the 75% of people who need it and are vaccinated. Obviously, this is going to be a much bigger programme. How do you see it being distributed effectively?

Professor Pollard: I am not party to the discussions about that. It is for the Department of Health and the NHS.

Q274 **Sarah Owen:** Who would you see administering it?

Professor Pollard: I am aware that there is a huge amount of planning going on to think about how it might actually be resourced and delivered. We have seen news reports that have demonstrated that in the NHS a lot of planning is going on to try to work out how distribution should happen. Of course, it will depend a bit on how the vaccine is targeted, which again will be a policy decision from the Department of Health at the time a vaccine is available. The answer is that I do not know. Other people are the experts.

Chair: There will be a chance to put those questions to the next panel. Is that okay, Sarah?

Q275 **Sarah Owen:** That's fine. It depends on what type of vaccine we are looking at. Are we looking at one of the vaccines that needs to be frozen, or are we looking at a vaccine that could be much more simply distributed?

Professor Pollard: That is an important question. From a UK infrastructure point of view, it is more difficult if they have to be frozen, but not impossible. In other parts of the world, frozen vaccines are much more difficult to manage. The vaccine being developed here, from Oxford in partnership with AstraZeneca, is at fridge temperatures. It could be deployed through the normal distribution system for vaccines. Some of the other vaccines will require freezing, but I do not see that as a show-stopper. It will need some logistics, but it is not a show-stopper.

Q276 **Dr Evans:** Professor Pollard, in the summer, Russia announced that it had a vaccine and was rolling something out. Could you pass comment on the efficacy of that and what has happened, because it has gone very quiet from a UK perspective? I wonder what the scientific evidence in the world is about that.

Professor Pollard: I do not have any insight into efficacy data because none has been published. The Russian vaccine is, in many ways, rather similar to the one we are developing and the one that Johnson & Johnson is developing and one of the Chinese developers, in that it is a viral vector vaccine. They have published some early data showing good immune responses for their vaccine. It is what you would expect when you compare other viral vector vaccines. There is nothing surprising about what we have seen so far. In the public domain, it is immune response data. We have not seen any published efficacy data. Like everyone else, they need time to accumulate sufficient cases in trials to be able to measure the extent to which the vaccine prevents disease. It may be that they have not quite reached the point of giving an efficacy estimate.



Q277 Neale Hanvey: A lot of the discussion has been about the general population. I want to focus on a very small but vulnerable group: the cohort of patients with blood cancer diagnoses. Given that the pathology of many of those diseases and the effect of the associated therapies has a significant impact on risk, immunity, coagulopathies and various other challenging issues, I would be interested to know what conversations have taken place within the haemato-oncology specialisms to help understand whether those types of patients are suitable candidates at any stage.

What immunotherapies could be deployed to support them? If they are not suitable candidates, would it follow that the next best thing would be to ensure that the staff treating and caring for such patients and their families should be urgent candidates for vaccination, when we are in that position?

Professor Shattock: We are still at the stage of testing the vaccine in healthy volunteers, and we need to get more safety data before we go to such at-risk groups. Your question is very much a clinical one, so I will defer the answer to Professor Pollard, who has more experience in that area.

Professor Pollard: There are two components. The first is that if you have a condition that means your immune system does not work—for example, some people with blood cancers on chemotherapy are not able to make immune responses—vaccines will not work. That will be true for all vaccines, whether they are Covid or otherwise. If, however, we are talking about people who have recovered or are recovering from various types of cancers, and their immune systems are now working, there is no reason to think that, if they are suitable for other vaccines, Covid vaccines would not work. It depends a little bit on the context. There are expert bodies in this country that represent either through charities or expert medical groups the different segments of the population with health conditions. They will give specific advice, once we know more about the available vaccines.

The second point was about family members and healthcare workers. This goes back a bit to the previous question. If the vaccines prevent transmission, vaccinating those in a cocoon around vulnerable individuals could be extremely important in protecting them from Covid, if indeed they cannot be protected themselves with vaccines. If, however, the vaccines do not prevent transmission, the main purpose of vaccinating family members and other healthcare workers who are looking after them will be to defend those individuals from the disease so that they can continue to look after their relatives.

As was indicated, there is a role for vaccines, but for the individuals with those diseases, the earlier discussion about treatments is probably much more relevant. For example, are there monoclonal antibodies that could be given to those individuals immediately after exposure to ensure that they do not develop the disease, or, if they develop disease, you treat them very early?

Q278 Dr Davies: Professor Pollard, my understanding is that the risk of Covid-



19 mutating regularly is relatively low, certainly compared with influenza, for instance. What is your assessment as to the likelihood that we will need vaccines that change each year, or at various intervals in the future?

Professor Pollard: The coronavirus is an RNA virus, which is the same as influenza. RNA viruses make mistakes all the time when they copy their genetic code, so the chance of the virus changing is quite high. The chance of it changing in the particular component of the virus that binds to the ACE-2 receptor to cause infection is relatively lower. In order to be able to bind to the receptor, the shape of the spike protein, which is the protein on the virus that binds, cannot change; otherwise, it will not be able to invade our cells through the ACE-2 receptor. It is not impossible. As the virus has changed over the past nine months, we have not seen major changes so far in the bit that binds to the ACE-2 receptor to make it no longer preventable through the vaccines in development.

The uncertainty comes from the fact that at the moment the virus is not under any pressure to make changes in that bit of its genome, because we do not have immune human populations; at the moment, it is still transmitting very happily across the world. If it has to change that bit of its genome, it may be less fit and transmit less well, or not be able to cause infection so readily. It remains a possibility that it could change, and that may be a problem for vaccines and will require redesign. At the moment, we have not seen that, but we have not really put it under pressure.

Q279 **Chair:** Professor Pollard, if we have a vaccine that perhaps has not had the approval of the American authorities, the FDA, and the European authorities, the EMA, but our regulatory authority, the MHRA, approves it, do you think we should be able to proceed?

Professor Pollard: All the regulators around the world are very rigorous; they use very similar approaches to regulation and review. I would not imagine either that developers can submit for approval in all regulatory authorities at the same time or that all regulatory authorities will take the same time for approvals. It is likely that we will have some regulatory approvals happening before others. I do not see that as a problem. I would expect it to happen just because of the scale of interest around the world in vaccines for prevention. Regulators are talking to each other and looking at alignment to try to make it as smooth a process as possible. It will be down to them. They have to do it independently and rigorously. We provide them with the data, but we do not get involved in the decision making.

Chair: That is very clear. Professor Pollard and Professor Shattock, thank you for your evidence today. Most of all, thank you for the extraordinary work that you and your teams have been doing on behalf of the whole world over a relatively short period of months. It is of crucial importance. We are very grateful for that work and for your evidence today.

Examination of witnesses

Witnesses: Professor Lim and Kate Bingham.



Q280 **Chair:** We move to our final panel of witnesses. I am pleased to welcome Professor Wei Shen Lim, a consultant respiratory physician at Nottingham University Hospitals Trust and chair of the Joint Committee on Vaccination and Immunisation in respect of its Covid-19-related work. I am also very pleased to welcome Kate Bingham, chair of the UK Government Vaccine Taskforce. Kate Bingham, you were appointed chair of the vaccines taskforce on 16 May. Can you tell the Committees and those watching the purpose of the taskforce and what it has achieved since your appointment?

Kate Bingham: The vaccine taskforce was asked to ensure that the UK has access to clinically safe and effective vaccines as soon as possible and in so doing placed the UK at the forefront of vaccine research and development. It is important that we ensure equitable access to vaccines worldwide—one of our key goals—and that the UK is well prepared for future pandemics. Those were the three tasks we were given.

I was in front of this Committee four months ago and have been in post for about six months. I think we have made huge progress. The UK now has access to six different vaccines across four different formats, because we do not know which, if any, of these different types of vaccines will work. We have secured 350 million doses, vastly in excess of what we need, because we are expecting vaccines to fail. As we have just heard from Professor Pollard, we could be weeks away from the first interim data review of the Oxford vaccine. In the same timeframe, we should be looking at the interim data for the BioNTech Pfizer vaccine. They are the two vaccines that have the possibility of being ready before the end of the year.

Q281 **Chair:** Which are those two?

Kate Bingham: The Oxford AZ is one vaccine; the Pfizer BioNTech is the other one. They are very different vaccines, but they are both in a position where we should be able to look at the interim data this year, or at least the first set of interim data.

There has been discussion this morning about neutralising antibodies, which are critical to have prophylactic protection for people who are immunocompromised or cannot receive vaccines. We have secured rights to AstraZeneca's cocktail of antibodies, as it is called. To ensure that the vaccines are ready as soon as they are approved, we are manufacturing now. We have vaccines already in place, so that as soon as we have approval from the MHRA we will be able to start to deploy them, or hand them to Health to deploy. We have done that because we have been able to accelerate the development of the clinical trials, not in terms of safety but in how we get the trials enrolled.

For the very first time, a national citizen registry has been created on the NHS website. As of this morning, 305,000 people have registered their interest in getting involved in clinical trials. To all those people, I would like to say thank you. That is a phenomenal resource that is being used as we speak for enrolment in clinical trials, including prophylactic clinical trials with the AZ antibody.



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We have put in place standardised immune assays, so that we can compare vaccines head to head. We have created, a world first, a human challenge model for Covid vaccines. Subject to final ethics approvals—all sorts of things have to work—we should be in a position to start evaluating new vaccines in a much more streamlined, rapid way next year, which will accelerate the development of the next wave of vaccines.

The other aspect of the role that the taskforce has been asked to deliver is related to manufacturing. To give you a quick tour around the UK, starting in Scotland, we have expanded the manufacturing plant of a Scottish company called Valneva in Livingston. We have funded the Centre for Process Innovation in Darlington to help develop GMP manufacturing capability for mRNA vaccines. We have significantly expanded and started to build the Vaccines Manufacturing and Innovation Centre at Harwell. We have bought a vaccine manufacturing site in Braintree, which is managed by the Cell and Gene Therapy Catapult.

We have just issued a request for proposals for bulk antibody manufacture in the UK—we have no such capability in the UK—and we have been working very closely with contract development organisations around the UK, without whom we could not be in this very fortunate position. That includes Cobra in Keele, Oxford BioMedica and Wockhardt in Wrexham to do the fill and finish. I think we have done a pretty neat job getting manufacturing capability in the UK fit for purpose. Three of the six vaccines we have secured for the UK are being manufactured in the UK.

The last and probably most important aspect is the global role we have played in shaping COVAX, which is the global facility for buying and distributing vaccines. The UK has given a pledge of half a billion pounds. That has not only encouraged others to participate but will really make it a phenomenally important and essential facility to ensure that everybody who is vulnerable to the disease is vaccinated, not just the countries that are best able to pay for it. Overall, I think we have done pretty well.

Q282 Chair: This is a lessons learnt review by the two Committees. You have noted some of the successes and achievements. If I can put it this way, what have you succeeded on in spite of? What are the obstacles you have had to overcome, so that we can learn how not to impose them in the future?

Kate Bingham: As you all know, generally Government is not a quick-running organisation and speedy decision making is not necessarily something that Governments should normally be doing, but in this case they have worked incredibly well. I have been given the space to build the team and the team has been incredibly effective. I am proud to be working with my team members. We have also been given a ring-fenced budget, controlled by Ministers. The vaccine taskforce makes recommendations for ministerial approval and then we have very quick decision making. Speed is a very important lasting legacy for how we can do this again in the future.



The other side that has been a challenge for us is that we need stronger scientific expertise and industrial experience in the Government. We do not have enough scientists. We do not have enough people from STEM or industrial backgrounds. Those are the skills I have brought into the immediate team, but, more broadly, it would be helpful if we had more scientists in Government.

Q283 Chair: When you say in Government, are you talking about the Department of Health, the Department of Business, No. 10 and the Cabinet Office?

Kate Bingham: I am talking about all of it. All those Departments are groups with whom we have worked very closely. Our investment committee, for example, includes the Secretaries of State for BEIS, Health, Cabinet Office and Treasury. It would be great if all those Departments could be much better populated with scientists and industrial experts.

Q284 Graham Stringer: That was quite a tour de force. You have answered some of the questions I intended to ask. The first was about whether or not a vaccine was being manufactured now. You have told us that it is. At what capacity is it being manufactured in this country? Perhaps you could answer that first, before I come to a question about why Braintree.

Kate Bingham: Typically, we have bought vaccines in units of 60 million doses. Wei Shen can talk a little bit about the JCVI advice on the target populations. We have been working on a population of about 30 million vulnerable people. To take Valneva in Scotland, we have acquired 60 million doses, but we have funded the expansion of the plant such that it will have the capacity to manufacture 200 million doses next year. Where we have the ability to control and influence how manufacturing is done and the scale at which it is done, we have done so at scales in excess of what the UK needs, to reinforce our commitment to global and equitable access to vaccines and their distribution.

Q285 Graham Stringer: Can you be specific? Today, 4 November, how many doses of the Oxford vaccine have been manufactured?

Kate Bingham: I know the answer. The dose numbers are not being disclosed. There are two stages of manufacturing, which is why I am being a little hesitant. You have to make the bulk drug substance itself. In Oxford's case, you have to make the adenovector vaccine. Once you have made the drug substance, you have to put it into vials. We have not yet put it into vials because, as soon as you do that, you start the clock for its shelf life and how quickly you have to use the vaccine. We are all ready to do that, but we have not done it yet.

Once we are reasonably sure, and that will be soon, that we will be in a position to look at the interim data, with the expectation that we may be able to start rolling out, we will vial the doses and hand them over to Health for deployment. It will be a ramp-up. Scale-up in manufacturing normally takes years, as we talked about. We are doing things at speed; people have used the word "unprecedented". This really is unprecedented speed,



and trying to scale up at speed is very challenging. We will be starting with low numbers of doses, by which I mean millions but not tens of millions, and that will then ramp up, so that we end up with the 100 million doses that we have secured from AZ in the first half of next year.

Q286 Graham Stringer: I am slightly less reassured by the second part of your answer than the first. How many of the vaccines on order have to be stored at very low temperatures? Some vaccines have to be stored at the temperature of solid carbon dioxide, which is very cold indeed. How many of those have been ordered?

Kate Bingham: So far, we have ordered those only from Pfizer BioNTech. What you are referring to are the mRNA vaccines, which are in a similar class to the vaccine Robin Shattock is developing. His is a self-amplifying RNA vaccine. These are very small pieces of very unstable genetic material, hence the need to keep them at such low temperatures. They may be relatively straightforward to manufacture initially, but the cost of deployment and the complexity of deployment is very high. I have written about it extensively. We have to find better vaccine formats, so that we are not dependent on such low temperatures and complex cold chains and can build something better. The work we are doing with CPI in Darlington is to try to find different solutions to stabilising what are potentially incredibly potent and valuable vaccines.

Q287 Graham Stringer: Were you involved in the decision to invest in vaccine manufacture at Braintree? If you were, why Braintree? One of the aspects of this virus is that it appears to have a greater impact in the north of England, and the Government have a policy of trying to level up the country. Why invest in a manufacturing capacity in Essex?

Kate Bingham: Because it was a veterinary vaccine manufacturing plant already and was the quickest way we could ramp up GMP production of vaccines in a flexible way. We looked at everything: de novo sites, brownfield sites and all the different alternatives. The requirement and request from the Prime Minister was to do so as soon as possible. It is a good site. We are very keen to ensure that we have manufacturing capability around the UK, but that vaccine plant happened to be in Braintree and that was the one we prioritised.

We have a request for proposals for bulk antibody manufacturing, and there is an opportunity to create a state-of-the-art antibody plant in the UK. That process has only just started, and there will be huge interest in the different options for us to build that plant. That would provide an opportunity for the levelling-up you mention.

Q288 Chair: Graham asked about how many doses had been manufactured. The day after your appointment, the Government announced that they had signed an agreement with Oxford University and AstraZeneca to make up to 30 million doses available by September for the UK. Has that been accomplished?



Kate Bingham: No. Those 30 million doses assumed a linear yield on scale-up. When you manufacture these vaccines, you start at test tube level, scale up sequentially and ultimately get to the 1,000 or 2,000-litre scale. The projections, made in good faith at the time, to get to 30 million doses in September assumed that absolutely everything would work and that there would be no hiccups at all in going from microlitre scales to 1,000 or 2,000-litre scales.

It has not gone linearly, and that is not through lack of care and attention, availability of equipment or anything like that. It is just that it normally takes a very long time. The answer is no, but it is now at the 1,000-litre scale, and that is working. I am quite sure that we have the process, but we are growing live cells and it is not a straightforward activity. The skills in the UK in advanced manufacturing are world-class. It is challenging.

Q289 **Chair:** To update that figure, it was thought appropriate in May to make an assessment of what we would have available on the stocks, as it were, in September, for the purpose of reassuring people that as soon as a vaccine was licensed and approved it could be deployed at scale. As of now or, if you want to forecast, perhaps six weeks ahead, how many doses of the Oxford AZ vaccine will be available in the UK?

Kate Bingham: As of now, we have low numbers of million doses in bulk drug substance, not vialled, and the third batch of 1,000-litre manufacturing is now under way. That should probably get us up to about 4 million doses at the end of the year.

Q290 **Chair:** Four million by the end of the year.

Kate Bingham: Yes. It then increases. Having got to that scale, you can then run it quickly, but the challenge is to get to the 1,000-litre scale.

Q291 **Chair:** The point of the communication of the 30 million was to convey the idea that we were getting ahead of the curve and anticipating the need for a mass vaccination programme as soon as a vaccine was approved. That was done in advance of many of the trials we have been hearing about, but if there is a prospect of having low numbers of millions, it will not be available for mass deployment the moment that, as we hope, we get approval, will it?

Kate Bingham: There are various things. We have to look at the data; it has to go through the regulators and then it has to start to be deployed. The earliest possible time to look at the data will be late November to December. Then it still has to go through the regulatory period, so my expectation is that we will have more vaccine than we will be able to deploy because that will take some time. Vaccinating millions of adults in this pandemic will be a heroic achievement. It has not been done at this scale before. I do not think that vaccine supply will be the greatest limiting factor.

Q292 **Chair:** No one does that. When do you hope to see the first deployment of vaccines to the public?



Kate Bingham: Deployment is a Health-led activity. If I put on my rose-tinted specs, I would hope to see positive interim data from both Oxford and Pfizer BioNTech in early December. If we get that, there is a possibility of deployment by year end. If not, we will have to continue running the studies, as Andy described earlier, until we get efficacy data that is acceptable to the regulators, and then you can start deploying early next year.

Q293 **Chair:** Let's take the rose-tinted view that we might have it available for deployment by the year end. By the year end, how many doses of vaccine will we have in stock?

Kate Bingham: We will have low single-digit doses for Oxford and up to 10 million doses of the Pfizer BioNTech.

Chair: By that date? At the end of the year. Thank you.

Q294 **Jeremy Hunt:** Thank you very much for joining us, Ms Bingham. We have been hearing from some very eminent scientists at Oxford and Imperial this morning. They naturally use quite cautious language, but I think the public want a stronger sense of the likelihood of a vaccine riding to the rescue and getting us out of a hole during the course of the next year. As you look ahead, could you tell us, in very layman's terms, what you think the chances are in percentage terms that we will get a vaccine at some stage in the next year that will wipe out coronavirus?

Kate Bingham: To wipe out coronavirus, very slim; to get a vaccine that has an effect on both reducing illness and mortality, very high. If you look at the data that has been generated so far by multiple different vaccines and companies, it is pretty good. What we can see is pretty compelling immunogenicity data from the two-dose vaccination regimes coming from whole inactivated viral vaccines, adeno vaccines, mRNA vaccines and protein adjuvant vaccines, all of which the UK has access to.

What we do not know is to what extent the immune response we have seen correlates to protection against disease. Do I expect that those vaccines, even if they do not protect 100% against infection, are likely to reduce the severity of illness and the levels of death? I am not a clinician, but my view is that we will see a vaccine that will reduce illness and death.

Q295 **Jeremy Hunt:** Putting it again very much in layman's language, what do you think the chances are that by next Easter in the UK we will have a vaccine and will be able to give it to everyone who is most vulnerable from catching Covid?

Kate Bingham: The deployment and vaccination process itself is handled by Health, not me. We have two more vaccines coming through in the first half of next year, the Janssen Ad26 vaccine and the Novavax adjuvanted protein vaccine, and we will have the AstraZeneca neutralising antibody vaccines all in the first part of next year, some of those closer to Easter. That, together with the Pfizer BioNTech and AstraZeneca Oxford vaccines, gives me a fair degree of confidence.



Q296 **Jeremy Hunt:** More than 50% confidence?

Kate Bingham: It would be, but I am a naturally optimistic person.

Q297 **Jeremy Hunt:** You have more than 50% confidence that by the early summer we will have a vaccine that we can give to all vulnerable people. I appreciate that you are being optimistic, but I want to get a sense of what you believe, with the caveat that you are a natural optimist. You think that we could be in a situation by Easter or early summer where all the vulnerable people in the country have had a vaccine that will have some impact on reducing the dangers of coronavirus.

Kate Bingham: That is my view: 50%.

Q298 **Taiwo Owatemi:** My questions are about distribution and the administration of vaccination. We know that the UK pharmaceutical supply chain could be more robust. What challenges do we currently expect in the supply chain? How resilient is it for the distribution of the Covid-19 vaccine?

My other question is about administering vaccination. We have heard that there will be changes to the way vaccines are administered. Could you let us know what regulatory changes there are? Have they been put in place? How balanced are these changes with regard to safety? We know that there is an NHS staffing shortage. Do you think the NHS has the capacity readily to deliver a mass vaccination programme, if it was ready? What is the estimated number of staff needed to reach that capacity? How do you plan to increase that capacity?

Kate Bingham: That is a lot of questions. I am afraid I am not the right person to ask about detailed deployment. My job finishes at the point at which we have the vaccines ready, regulated and available for use. Then I hand over to the Department of Health, which is responsible for all the deployment activities. Our team supports the Department of Health because this is a massive challenge, with two-dose regimes, and with flu as well, because they cannot be co-administered.

We are asking vulnerable people to undertake two different vaccination visits, which again has never been done at this scale before. We are not able to tell them precisely when a vaccine might come and what the nature of the vaccine is in terms of the data. We do not know the effects of the vaccines on different groups, and whether or not they work in elderly cohorts. Do they work better in younger people with underlying disease, or do they work better in black, Asian and minority ethnic communities? We do not know that.

The information we give Health is very ambiguous: "These are the different scenarios that you need to expect." What I have seen, sitting on the sidelines, is that there is a massive effort. It looks as if it is being beautifully run and it is, but don't be under any illusions. It is very complicated, especially when you add the cold chain requirements. These are multi-dose vials. The BioNTech RNA vaccine has a short shelf life. The complexity of



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administration is phenomenal. I think you need to ask the Department of Health to answer that specific question.

Q299 **Chair:** Perhaps Professor Lim might comment on Taiwo's questions.

Professor Lim: Unfortunately, I too am not the right person to explain to you the details of the deployment. I have seen some of what has been planned, and, as Kate Bingham said, it looks highly comprehensive and very professional, but if you want details you need to ask the Department of Health and NHS England about the exact deployment schemes.

Q300 **Taiwo Owatemi:** Is no one involved with regard to supply chain management for the vaccine?

Professor Lim: I think you misunderstand. Neither I nor Kate, if I may speak on her behalf for a moment, is involved in managing this, but that does not mean there is nobody involved in managing it. There is a huge team we are aware of that is managing it and, as far as I can see, doing a fantastic job in what is a very difficult project, but we are not the right people to answer on the detail you are asking about.

Kate Bingham: I can say that we have 150 million vial stoppers and over-seals and have the supply chains in place for future vials. We have gone from saying, in the case of revaccinations, "How many future vials do we need?" to, "Do we have enough tubular glass to make the vials?", and even, "Do we have enough borosilicate sand to be able to make the tubular glass?" Therefore, as far as getting to the point of having vaccines to deploy, the supply chain is under control.

Q301 **Sarah Owen:** Kate, I was going to ask about the roll-out of vaccines, but you have already said that is not your department. I was then going to ask about the supply chains and possibly the roll-out of vaccines for Covid-19. Will the end of the transition period with the EU affect that in any way, whether the supply chain or the roll-out? Even if there is a deal between the UK and the EU, how might it affect vaccine roll-out or the supply chain in Great Britain and Northern Ireland?

Kate Bingham: Caveated by all the factors that are not me, we have put all the Brexit plans in place. For deployment, there is a separate schedule for deploying vaccines to Northern Ireland. On the logistics of shipping vaccine, for example the Pfizer BioNTech vaccine, which is coming from Belgium, there is a separate supply chain that goes directly to Northern Ireland, and a separate supply chain to England with distribution to Wales and Scotland.

It has been planned. It is certainly an additional complexity, as if this wasn't complex enough, but I think it is under control. To be sure that we have vaccine onshore in time, we are even using air freight in some cases. It is more expensive, but we have the additional certainty that we know the vaccine is not caught up in blockages anywhere.

Q302 **Dean Russell:** My questions were also about roll-out, but I have one big



question connected to that, on which, hopefully, you can help. I have heard conversations recently to do with concerns about taking the vaccine. I do not mean extreme anti-vaxxers—a very dangerous movement—but where the general public have said, “This has gone through very quickly. I’ve got to inject something into myself that we’re unsure of.” Could you give me reassurance on two parts? The first is whether it will be safe and, the second is whether at this point there have been discussions about a sophisticated and strong communications strategy to reassure the public that, should they be able to take a vaccine, it will be okay for them.

Kate Bingham: Great questions. Will it be safe? Andy talked a little bit about that earlier. The safety testing and safety standards being imposed in these vaccine trials are no different from any new therapy or vaccines that are developed. There has been no diminution of standards, no shortcuts or anything. Are we using gold-plated and well-trusted safety monitoring? Yes, we are. We also benefit in the UK because everybody has an NHS number, so we can do realtime pharmacovigilance, which is how people who have received the vaccine are performing, and monitor the long-term safety of the studies.

As an aside, I have joined a vaccine study. If I thought there were concerns about safety, I would not have done so. I have done so and can be quite clear that, in the treatment I have been getting, care with safety is absolutely paramount. That is your first question.

On the second question about comms, there are two aspects. From the vaccine taskforce perspective, our broad strategy for public education is to tell people how the vaccines work, what progress we have made and what strategies we are using to tackle some of the issues, because our goal is to establish the UK as a global leader in vaccine R&D and encourage international communication. Ultimately, this will be a great industry for the UK economy.

In our strategy to communicate and collaborate, I have talked to all sorts of groups, whether women’s groups, civil society groups, like Global Justice Now, industry, clinical and manufacturing groups, as well as international groups like the World Bank and Gates. I have given more than 100 interviews and have written in *Nature* and *The Lancet*. We now have nine podcasts on Spotify and Amazon where we tackle some of the specific issues about safety. How do we get different communities into clinical trials? How are we manufacturing it? What role is the UK playing in the international community?

There is narrow communications activity from the vaccine taskforce, but the broader vaccine communications will be led by the Department of Health as part of its broader vaccination and deployment campaigns and communications. That will address vaccine hesitance. A lot of vaccine hesitance is not to dismiss people’s concerns. They are right to be concerned. It is a complicated, fast-moving field, and we need to address the concerns and allow people to have conversations with their doctors,



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civic leaders or whoever is trusted to give them advice and the discussions that would be helpful. We need to be open to it.

Dean Russell: I have a couple of related questions. First, I am pretty confident that I asked a question a few months ago in one of our Health and Social Care Select Committee sittings where I heard about tests of a combined vaccine with flu. I heard a comment earlier that seemed to indicate that that is not the case. I would be keen to know whether there is any movement on a combined vaccine.

Secondly, related to that, how have tests been done with regard to people who are taking other types of drugs? We do not live in a Covid-only world. People take lots of other things. I am keen to get reassurance on that.

Thirdly, you mentioned tracking symptoms once the vaccine is out there. I am conscious that the NHS track and trace app has performed very well, and, I believe, had the fastest download of any app ever on App Store. Have there been any discussions on using an app to enable people who have had a vaccine to track their side-effects, if there are any, or their symptoms immediately after they take it? Many people report not feeling too great for a few days after having the flu vaccine. If you could cover those points, I would appreciate it.

Kate Bingham: There are a lot of questions. Small arms of clinical studies are being done on co-administering with flu, but the bulk of the main phase 3 studies is currently not being done with flu. The initial label is not expected to allow for co-administration with flu, albeit that it is under investigation now. Ultimately, from a vaccine taskforce perspective, I would like to see a single shot, ideally a pill or something that does not involve a needle, which could combine a flu and Covid antigen and then stimulates immunity twice. At the moment, the initial label the regulators are likely to give will not allow for co-administration with flu. By this time next year, I am sure that the answer will be that it will be, but not yet.

On co-administration with other drugs, yes, because the point of the trials is to include a diverse group of people in clinical trials, so that we can be sure the vaccines can work in all people who are most vulnerable. We have pushed very hard to enrich for black, Asian and minority ethnic communities in our vaccine trials because they are at specific risk from Covid infection. We are also enriching for the elderly and people with underlying serious diseases. All of those, especially the people with underlying serious diseases, will be taking medicines. We want to be sure that the vaccines are safe in those groups and that they are effective. That is in hand. We need to wait for the data to see whether or not the vaccines actually work, but that is being investigated.

Tracking is an issue for the Department of Health. The MHRA is an agency within the Department of Health, and how it uses the different tools is up to it. I do not know whether or not track and trace feeds into electronic medical records, but ultimately that is what we want. We need to be able to get to a position, using the latest AI tools, where we can identify how



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vaccines are performing in the wild, as we call it, to be sure they are doing what we expect them to do and that they are safe.

Professor Lim: The UK is a world leader in surveillance of vaccine efficacy and safety. We have done that for flu vaccines in children and shown that it creates indirect protection in adults. That is a first in the world. We have shown that there are replacement serotypes when you give the pneumococcal vaccine, and that is a first in the world. We have very good systems for surveillance.

Surveillance covers three areas. One is safety, which is ongoing. There is a passive and active surveillance system. The second looks at vaccine effectiveness. The clinical trials will give us some information, as described by Andy Pollard and others earlier, but they will not give us all the information we need. We need more information on sub-groups of patients and particular outcomes, such as hospitalisation or mortality. Those things will come from good surveillance systems, which are already in place for flu, for example, and will be adapted for Covid as well.

The third area is vaccine coverage. We need to know where the vaccine goes, who is having the vaccine and how we can adjust vaccine coverage accordingly. That is already in place. Quite apart from whether or not there is going to be an app, there are already in the UK all of those embedded systems, which are world-class, and I think we will get lots of good information from them.

Q303 **Barbara Keeley:** Kate Bingham, you mentioned earlier the cocktail of antibodies. We heard from Professor Horby how important it might be for people in care homes in giving them some protection, for a number of months at least. I understand that requires action by the Department of Health and Social Care. If steps were taken to get trials off the ground, how ready are we to get that out in terms of supply, and how many vulnerable people could be protected? We have hundreds of thousands of people in care homes, so how many could we protect?

Kate Bingham: We are just starting those studies. AstraZeneca's cocktail is particularly good for prophylaxis because the antibodies have been engineered to have a much longer half-life than a naturally occurring antibody. We are expecting and hoping that they will give at least six months' protection.

AstraZeneca has filed its CTA already. I think we are due to hear about approvals today or imminently. It is running two different prophylactic studies. One targets people who are at high risk of exposure. Those are people in hospitals, prisons, transport or any public-facing role where they are at high risk. AZ has a second study planned and due to start shortly. It is called a storm-chaser study, where somebody in a care home or meat-packing factory tests positive and you vaccinate all the people around them.



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We have those two prophylactic studies under way. We hope to get efficacy and safety data that those prophylactic antibodies work probably by the end of the first quarter of next year. At that point, we will have prophylactic antibody cocktail doses negotiated and completed. I cannot give you numbers yet because we are still negotiating on that, but the goal is to ensure that all immunosuppressed people, and people who are either unable to respond to a vaccine or need immediate protection, such as healthcare workers or the military, are protected at once, because two-dose vaccines typically take about six weeks to mount a full immune response.

We hope to have sufficient vaccine to cover all immunosuppressed people, whether they are going through solid organ transplants, bone marrow transplants or very severe cancer chemotherapy where their immunity is eliminated. Neale Hanvey talked about blood cancers. Those are the people we want to protect. My role is to ensure that we have vaccines for everybody, not just people who can respond to vaccines. Although this is a short-term prophylaxis, not a vaccine per se, currently it is the only way of treating those people.

Q304 **Barbara Keeley:** You say you cannot provide the numbers yet and it is being negotiated, but would it be at a scale where we could protect all the people in care homes?

Kate Bingham: Not necessarily care homes; at the moment, we do not know that people in care homes cannot receive vaccines.

Q305 **Barbara Keeley:** Vulnerable people who need it.

Kate Bingham: Maybe I will let Wei Shen talk about that. The focus is absolutely on having sufficient vaccine to treat all those who are immunocompromised and unable to receive vaccines. If it turns out, for example, that in the over-80s we cannot get a sufficient immune response, we will need to broaden the scope of how many doses we need. One of the reasons why we issued a request for proposals to build a bulk antibody manufacturing plant in the UK is that we recognise that it is an ongoing need.

Q306 **Dawn Butler:** Kate, you talked about the complexity of the administration of the injection. First, are you concerned about the impact of the virus because of the complexity associated with it? Secondly, what is your communications strategy for different languages, including BSL? We know that people who have learning difficulties have a higher death rate as a result of the virus.

Kate Bingham: I do not understand the first question about the complexity of administration and what impacts it has on the virus. I do not know what that means.

Q307 **Dawn Butler:** You talked about requiring people to attend three times, once for a flu virus and then twice for the coronavirus injections. There is one and then in seven days another one. It is the complexity of requiring



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somebody to attend three times. If they do not attend three times, what effect would it have on the effectiveness of the vaccine?

Kate Bingham: It won't be as effective. Like all these things, if you do not take the full course, it will not be as effective as if you do. It does not mean that it will not have any effect, but it will not be as effective. That is part of the trial. Oxford has done that. They looked at the immune response and immunogenicity after one dose and then again after two doses. While there was a good response after one dose, there was a very profound effect after two doses. If you do not complete the course, that is a problem. We need to make sure that that happens.

I think that information about Covid and vaccines is translated into nine different languages. We have been working specifically with different ethnic groups around the UK. Often, they do not look at mainstream UK media; they do not necessarily listen to the BBC, so we are making sure that we communicate in media channels that are suitable for all communities in the UK. We need to make sure that everybody has access to these vaccines, not just people who are pushy and at the front of the queue. Wei Shen, do you want to comment on the communications?

Professor Lim: There is a strong communications strategy, which I think we will see more and more of in the coming weeks. Timing is important. Part of the communications strategy is to try to tackle the inequalities that we know exist in our society. We have seen inequalities in many ways. Tackling the inequalities will require vaccine deployment to be implemented in a way that is flexible and appropriate for the patient or person groups where inequalities exist. All of that has been taken into account.

Q308 **Dawn Butler:** On British sign language, are we working with all the key organisations?

Professor Lim: I do not know that in specific detail, but I hope Public Health England has that in hand as well.

Kate Bingham: We have instructions in Braille and instructions for people with learning difficulties—from PHE, I think. I do not know about BSL.

Chair: Perhaps you will come back to us on that or ask your colleagues to do so.

Q309 **Katherine Fletcher:** Professor Lim, as a Nottingham University graduate, I'm giving a little shout-out on their marvellousness.

This has been a fascinating session. I would like to step back slightly from the immediate crisis response to the pandemic and refer back to some of your opening remarks, Kate, about the investment that is going into both manufacturing capability and UK science. Will there be a positive legacy from the effort by the UK vaccine taskforce, or is it something that has got lost in the heat of battle at the moment?



Kate Bingham: I would be incredibly disappointed if there was not a very positive legacy. The UK is absolutely punching above its weight and performing in an incredibly strong way in the global community, and not just because we have been able to assemble manufacturing capabilities in the UK very quickly without, I might add, a strong and dedicated vaccine manufacturing capacity in the UK to begin with. The speed at which we have been able to put things in place and the flexibility we will have in future capability for vaccines is important. We will have whole inactivated viral capability, so the next time we have a nasty pandemic virus, assuming it can be grown, which is not 100% certain but reasonably likely, we will be able to generate very quickly whole inactivated viral vaccines for a future virus. That is squarely in our sights for pandemic preparedness.

We will have capability for adeno vaccines. We are making those now, but we will have that capability in the future. VMIC, which is the Harwell site, will have flexible surge capacity to make 70 million doses within six months of a pandemic. We have radically expanded that. It was 3 million doses, and we have taken it up to 70 million. We have to be better prepared for future pandemics and it has to be at population scale, in case that is how JCVI and the Department of Health decide that we need to vaccinate. We have the Braintree site and we have done all the work on the mRNA vaccines.

I am pretty happy that we will come out with a big legacy. We have already invested in skills and training, and we hope that will help to create jobs. They should be around the UK and not concentrated in the south-east. The cell and gene therapy sector is predicting 6,000 jobs by 2024, mostly in manufacturing and bio-processing. It is an important legacy not just to show that we are organised, and that we can do things quickly and make decisions, but that we can be broad and agnostic in the scope of different vaccines that we are able and willing to look at.

The other key legacy is in the role we have played internationally. This is not a pandemic that affects just the UK. The virus does not respect national borders. We have to make sure that everybody around the world who is vulnerable has access to the vaccine. The UK has played an absolutely central role in ensuring that that has happened. As a permanent legacy, I would like to see a permanent global facility. Nine months in, COVAX is still in the early stages of getting its vaccines organised, whereas it should be at the front edge. That is what we need to ensure happens for the next time.

Q310 **Katherine Fletcher:** Professor Lim, these are dark days. There is a very important vote in the House today. Could I ask you to look forward, especially from an educational institution? I observe that lots of people who are solving this problem are not the classic Professor Brainiac, white-coated, grey-haired cartoon professors. Is that something you see? Do you think there is a legacy for encouraging diversity in STEM, be that women or people from different backgrounds? I would love to hear your reflection on that.



Professor Lim: It has been challenging for academics as well as clinicians. I am a clinician and an academic. The academic community has put its weight behind understanding Covid, and we have come a huge distance. The UK has contributed enormously to that understanding. That by its nature will have pulled a lot of other people into science.

This is an anecdote. My two sons are at university. They are both in science, and they tell me that their friends and colleagues are encouraged and inspired by the fact that science has made a big impact on the pandemic and how we manage it. That on its own will be enormously encouraging for all people, whatever their background, to join science and make a difference in society. That will have a positive impact.

Kate Bingham: As part of the interviews I have given, I have had reach-outs from schools asking whether or not I would be willing to talk to them about what we have been doing at the vaccine taskforce as an example of how you can use science to change the world. I am excited about that, especially about bringing women into science.

Katherine Fletcher: The rise of the nerds.

Q311 **Chair:** It is very important. Let me ask a question that I think is on the minds of some people, having read some reports in the press. In terms of communication, you gave a presentation on the leading vaccines to a group of investors. Was that presentation approved by the Government?

Kate Bingham: Yes, it was. All communications that I do on behalf of the vaccine taskforce I seek approval for, both to do the event itself and on the materials that are shared at whatever the event is.

Q312 **Chair:** Who gives that approval?

Kate Bingham: BEIS. There is a BEIS process. I ask for it and then I am told yes or no.

Q313 **Chair:** In the presentation you gave, did you disclose anything that was proprietary and not available in the public domain?

Kate Bingham: No. There have been a lot of nonsense reports and, I am afraid, inaccurate and irresponsible reports suggesting that I did. What I described was the landscape of vaccines. There are over 250 vaccines, with about 50 in the clinic already. I think of it as a bit like a race—the Grand National. There are lots of hurdles and runners, and lots will not get to the end of the race, and it is all being done very quickly.

What I described in that particular presentation was, "This is the overall landscape. These are the six vaccines that we have chosen for the UK, but we are also monitoring other vaccines that are relevant to the UK vaccines we have selected." For example, GSK Sanofi is one of the vaccines that we have selected for our portfolio. The key aspect of that vaccine, which is an adjuvanted protein, is GSK's adjuvant. That adjuvant has worked very well in Shingrix, showing strong immunogenicity in the elderly, so it is an



important aspect for this pandemic. There are two other vaccines also using the GSK adjuvant, Clover and Medicago. Those two companies are highlighted as being ones we are monitoring because we hope to learn something about what they are doing with the vaccine, which might be efficacy in different clinical cohorts, or it might be a safety signal. Those are the ones we watch.

We also look at the other mRNA vaccines. We have selected the Pfizer BioNTech vaccine, but there are other vaccines like Moderna, CureVac and the vaccine from Imperial. Those are also vaccines that we continue to review, because they relate, and we may learn things that will be relevant for the vaccines we have chosen for the UK.

Finally, a key thing that really matters is that we cannot have vaccines that are all delivered by needles, and require cold chains and healthcare professionals. We need vaccine formats that are easier to deploy. I have written and talked about this; in fact, I talked about it at a previous Select Committee. We need new types of vaccines. Other vaccines that we are monitoring, which I discussed at that presentation, among other places, are some of the oral vaccines like Vaxart and Symvivo, which could potentially get away from the need for cold chain and needles, and could be scaled up quickly.

It is important that people understand that. It demonstrates that we are doing what we are supposed to be doing, which is making a selection of what we think are the most promising, but also monitoring the landscape. There was nothing commercially sensitive or confidential. There was an error on slides, because there were footers that suggested they were confidential. I am afraid that was my fault. I was working too fast. There was nothing confidential, and those footers should not have been there.

Q314 Chair: On 4 October, you said that people keep talking about the time to vaccinate the whole population, but that was misguided. You said it was going to be an adult-only vaccine for people over 50, focusing on health workers, care home workers and the vulnerable. Is that still your view?

Kate Bingham: The bit I was challenging, which did not get reported quite like that, was that all adults would be vaccinated before Easter. That was my question. My personal view is that that is not likely, because it may not be necessary for all adults. We heard from the other professors that there will need to be evidence that it makes sense to do that.

Wei Shen can talk about who should be receiving vaccines. As far as children are concerned, we heard from Robin and Andy that at the moment there aren't big phase 3 studies being done in paediatrics and children. The initial vaccinations are not likely to be labelled for paediatrics and children until sufficient tests have been done on those cohorts to prove that they are safe and effective, but I might hand that question to Wei Shen because he knows much more than I do.

Q315 Chair: Professor Lim, the Secretary of State, in response to what was said,



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stated that it was a decision for Ministers but on advice from the Joint Committee on Vaccination and Immunisation, of which you chair the Covid aspect. Are you clear? Have you determined who, if the approvals are given, is going to get the vaccine first?

Professor Lim: We have so far determined that there should be a first phase that will be directed at vulnerable people. As you mentioned earlier, Chair, there are two ways of using a vaccine. One is to target vulnerable people, and the other is to target people who are involved in transmission. They are mainly younger people who have more social contacts and are more mobile.

In the first phase, we would target vulnerable people because that is where we think the vaccine will have most impact. What JCVI has not decided yet is how to prioritise the rest of the population because, as you have heard, we need to know whether the vaccine works to prevent transmission before we can make such decisions. No upper limit has been decided as to how much of the population is to be vaccinated at this point. We have only determined who should be vaccinated first—the vulnerable.

Q316 **Chair:** But is it your assessment that for the period from now until Easter a majority of the population will not be able to be vaccinated, even if the approvals are given?

Professor Lim: Will not be able to be vaccinated? That is a question about availability.

Chair: Correct.

Professor Lim: Is that what you mean?

Q317 **Chair:** You are prioritising who should get it, but is the prioritisation based on the assessment that most of the population will not be able to get it by Easter because it is not available in manufactured quantities?

Professor Lim: Our prioritisation is not based on availability of vaccine or the ability to deploy the vaccine; we base our prioritisation on scientific principles as to who would benefit most. That is the usual way that JCVI makes a decision. We will make a decision based on scientific priorities for the greatest public health benefit. How those recommendations are translated into implementation—buying enough vaccine or getting enough people to deploy the vaccine—is taken on by others.

Chair: I understand.

I am very grateful to Professor Lim and Kate Bingham for giving their time this morning. As has been evident from the questions, the work that you do is of absolutely crucial importance, alongside the scientists we heard from earlier. We all hope that there will be a vaccine that is effective and safe, and able to be deployed. Your work in making sure that it is available to be deployed at scale across the country in your different respects is vital. We are very grateful for that work and the work of your colleagues. It is now time to draw this session of the joint Committee to a conclusion.