HOUSE OF COMMONS

Science and Technology Committee

Oral evidence: UK Science, Research and Technology Capability and Influence in Global Disease Outbreaks, HC 136

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Watch the meeting

Members present: Greg Clark (Chair); Aaron Bell; Dawn Butler; Chris Clarkson; Katherine Fletcher; Andrew Griffith; Mark Logan; Rebecca Long Bailey; Carol Monaghan; Graham Stringer.

Questions 2272 to 2399

Witnesses

I: Professor John Aston, Harding Professor of Statistics in Public Life, University of Cambridge; and Professor Sir Munir Pirmohamed, Chair, Commission on Human Medicines.

II: Professor Anthony Harnden, Deputy Chair, Joint Committee on Vaccinations and Immunisation; and Dr Mary Ramsay, Head of Immunisation, Public Health England.

III: Dr Ruth Payne, NIHR Academic Clinical Lecturer and Honorary Specialist Registrar in Infectious Diseases and Microbiology, University of Sheffield; and Professor Christopher Dye, Professor of Epidemiology, University of Oxford.

IIII: Professor Ran Balicer, Clalit Research Institute and Professor of Public Health, Ben-Gurion University.

Examination of witnesses

Witnesses: Professor Aston and Professor Sir Munir Pirmohamed.

Q2272 **Chair:** The Committee is now in session. The Science and Technology Committee continues taking evidence on Covid and the response to the pandemic. Today, we are considering the latest information and research on vaccines, including their effectiveness in protecting against Covid and transmission, and the question of reported associations with blood clotting among some people. Then we will turn to the question of vaccine certification or Covid-status certificates.

To begin our session this morning, I am very pleased to welcome our first panel of witnesses. Professor Sir Munir Pirmohamed is chair of the Commission on Human Medicines, which is the body that advises Ministers on the safety, efficacy and quality of medicinal products. Sir Munir is professor of medicine at the University of Liverpool. We are pleased to welcome Professor John Aston, who is Harding professor of statistics in public life at the University of Cambridge and, until recently, was the chief scientific adviser at the Home Office. In that capacity, he has participated in SAGE during the pandemic.

Welcome to both of you. We have lots of questions, so I would be grateful if answers could be as crisp as possible, please.

To start, Sir Munir, will you give us the latest assessment of the Commission on Human Medicines on the link between the AZ vaccine and blood clots among some patients?

Professor Sir Munir Pirmohamed: Thank you for the question and thank you for inviting me to give evidence.

The latest data, which was published by the MHRA last Thursday, highlights that 168 cases have been linked with the AstraZeneca vaccine. The number of cases has been increasing since they were first reported. We feel that evidence is firming up of a possible link but we do not have true causality determined yet. The jab is given in the deltoid, where an immune reaction seems to occur, but how that jab actually leads to the immune reaction we do not know. The true causal association has not been determined, but the evidence is firming up of an association.

Q2273 **Chair:** That is very helpful. On the scientific backdrop to that, is there any reason why the adenoviral vector vaccines, of which the AZ vaccine is one, should behave differently than the MRNA vaccines, of which the Pfizer is one of the best-known examples?

Professor Sir Munir Pirmohamed: There are many hypotheses out there at the moment as to why this may be occurring. One of the hypotheses is that this is related to the adenoviral vector. You will have heard of the association with the Johnson & Johnson vaccine, which also has a human adenovirus. The Oxford AZ vaccine has a chimp adenovirus vector. It is a hypothesis at the moment, but the proof is lacking that it is truly adenoviral related.

We know also that clots occur with Covid itself. The rate of thrombosis and the low platelets occurring with Covid are much higher than we have seen with vaccines. There is still a possibility that they may be related to the actual spike protein itself. Further work needs to be undertaken to understand what the mechanism is, but you are quite right in saying that the numbers of reports with the Pfizer vaccine have been very low compared to the AstraZeneca vaccine. The mechanism of the adenoviral vector together with the spike protein and how that leads to the reaction needs further mechanistic scientific work.

Q2274 **Chair:** Thank you; that is very clear. My colleagues will follow up with some other questions on that.

That leads me to an introductory question to Professor Aston. Professor Aston, your centre produced some very helpful comparative statistics presented at the press conference that the MRHA, JCVI and Public Health England fronted comparing the risk of the potential harms from Covid, in terms of ICU admissions, as Sir Munir implied, for different age groups against what we know so far about any risk for four age groups from the vaccine.

Three different scenarios were painted for risk of exposure: low exposure, medium exposure and high exposure. Where are we in those scenarios? How does that map on to the current experience of Covid in the country?

Professor Aston: Again, thank you for inviting me. You are exactly right in the sense that it is very important that we consider the risks on both sides: the harms associated with Covid and catching Covid, and the harms associated with the blood clots that come from the virus now.

The reason we produced the three different scenarios was exactly to address the question of how different exposure will affect this. If you think about it, very obviously, to be at risk of getting high harm ICU events, it was very important for us when we produced these graphics that we compared like with like. So we chose ICU admissions as the harm from Covid, because we felt that that was a relatively balanced risk, against the harm of a blood clot, which is of course a serious event as well. It is obvious that to have an ICU admission you have to catch Covid in the first place. Therefore, we looked at the three different exposure rates.

Apparently, the exposure, according to ONS in the latest values, is about 1.3 per 10,000 new incidents of Covid per day. That is their latest figures. That is, roughly, similar to our low estimate. We had a low estimate of 2 per 100,000 as our low value for the incidence rate in that picture. The medium incidence rate was 6 per 10,000, and the high incidence rate was 20 per 10,000. The high incidence rate was equivalent to something around the peak of the most recent wave of the virus, and the 6 was somewhere in the middle. We are currently around that low value.

At the time of the press conference, the value for the current incidence at that point in time was a little bit above 2, hence the reason why we chose 2 as the low value at that point as we were coming out and restrictions were changing.

Q2275 **Chair:** It is currently 1.3, which is below the low exposure scenario of 2 by quite a considerable percentage. It is nearly half the stat. Presumably, it has lagged, I would imagine, because you are obviously analysing data that was collected in recent weeks. Given that the trajectory is falling, we would probably be some way below that low exposure risk, happily. Would that require a change in the assessment of the administration of the vaccines as a conclusion of that?

Professor Aston: I looked at what the effect would be if we chose a value of 1.3, the current value, and that would not materially change any of the conclusions from the slides that we saw. The numbers would obviously change but the conclusions themselves did not change. If things went considerably lower, you would have to re-evaluate the benefits on the benefits side of the slide. It is important to realise that that 1.3 or 2 is the average exposure across the entirety of the country.

Another way of thinking about those exposure levels is not simply just about how high the country is but also about individual circumstances. Some people will, by the nature of their jobs or other things, be exposed to higher incidence rates. If you are in a job where you have lots of contact, that may potentially have a higher exposure rate. People who have very little contact with people, will, by definition, have a much lower exposure rate. Therefore, we should not think of it simply as the exposure rate in the country, because that is one way of thinking about it, but you should also think about it in terms of other factors that could affect the exposure rate. That is why high, medium and low are still relevant even now when the exposure is falling.

Q2276 **Chair:** Is the implication of that, rather than take broadly the approach that the advice is by age group, that it should be more about the circumstances of people's lives?

Professor Aston: The main thing is that we cannot break down the clot risk by anything at the moment other than age group. To have a sensible comparator, if you want to think about the comparators and the clot risk, at the moment it is only able to be stratified by age. Therefore, we need to have a very good understanding of the age.

However, as we know, Covid affects different populations in different ways. It will be the benefits side that changes. I understand that the harms from clot risk at the moment can only be stratified by age. Therefore, it is probably only a fair comparison if you do it on an age basis in that way.

Q2277 **Chair:** One final question from me before I turn to Rebecca Long Bailey. Given that we are below the low exposure risk—unless you correct me,

given that the level is falling—and that we are likely to be lower still in the future, would it be right and appropriate to have a new category of modelling, perhaps a super-low exposure risk, so that we can see this very useful information for what is likely to be the relevant level of exposure risk that we are experiencing now and are likely to experience?

Professor Aston: It would certainly be helpful as things change. We need to be slightly careful because, as you said, things are lagged. Also, restrictions are changing. I would not want to guarantee that incidence rates are going to come down much lower. We will have to see what happens over the timeframe. It would be useful, and we are very happy to generate figures with lower exposure rates if that is useful for people.

Q2278 **Chair:** Were you asked to perform this analysis or did you volunteer it? How did it happen?

Professor Aston: We were asked to come up with a way of explaining the analysis. We were the ones who chose which exposure rates to do, which at the time we prepared the slides seemed like a sensible set of rates.

Q2279 **Chair:** To meet what you said you would be willing to do, do you need to be asked or can you get on with it yourselves?

Professor Aston: We can certainly get on with producing that. We will talk to MHRA about the best way for us to produce that.

Chair: Thank you very much. Let me turn to Rebecca Long Bailey.

Q2280 **Rebecca Long Bailey:** Thank you both for coming to the Committee today. On the issue of the AstraZeneca vaccine, from the data we have seen so far, of the 79 cases, 51 were female and 28 were male. Of those who sadly died, out of the 79 cases there were 19—13 being female and six being male. Do you think that the data so far suggests that women are more at risk from a blood clot? I ask that question, first, of Sir Munir.

Professor Sir Munir Pirmohamed: Thank you for your question. There are two things to consider. The first is the way the vaccine was deployed, particularly in healthcare workers and social care workers. The majority of the workforce in those areas is female, so they had higher exposure rates. When you start relating to the exposure rate in different populations, you find that the case incidence rate in male and female is very similar. From our data in the UK, it does not look as if the females are at a higher risk of this adverse event compared to males.

Q2281 **Rebecca Long Bailey:** Thank you. Professor Aston, what are your thoughts on this?

Professor Aston: I would absolutely agree with Sir Munir. It very much depends on the number of people who are vaccinated, the number of females versus the number of males, and the expected number of cases you would see in females and males. Particularly, if we are thinking about the low age groups where that was predominantly driven by people who

were working in healthcare and so on, and because there are a higher number relative of females to males working in that area, it is not unexpected that we would then see that proportion coming out in terms of cases, even if there was no male/female difference in the actual underlying case incidence rate.

Q2282 **Rebecca Long Bailey:** In terms of blood clot cases linked to the AstraZeneca vaccine, are you able to confirm at this stage who had a relevant pre-existing medical condition and whether there is a link between blood clots and pre-existing conditions? Perhaps Sir Munir could answer that question first.

Professor Sir Munir Pirmohamed: I have read the data very carefully. Every week I now chair a committee that is looking at all the cases coming through, which is really important, and building up that database. Overall, last Thursday, 168 cases were reported. We are seeing an extremely rare reaction. From the 168 cases, we have been looking at whether there are any particular predisposing factors, including age, gender, whether they have any background illnesses, whether they are on any particular drugs and so on.

So far, in terms of previous diseases, whether they have a previous history of thrombosis and so on is not seen as a risk factor for this particular adverse event. The only risk factor that we are finding is age in that there is a slightly higher risk in the younger age group compared to the older age group. That is the only risk factor that we are finding at the moment.

Q2283 **Rebecca Long Bailey:** Professor Aston, would you agree that there is no real direct link between blood clots and pre-existing medical conditions?

Professor Aston: We don't have the data on pre-existing medical conditions that would allow us to answer that, so I would not be able to give you an opinion from a statistical point of view.

Q2284 **Rebecca Long Bailey:** I have one final brief question to Sir Munir. I note that the full review does not appear to be in the public domain. Would you be able to undertake for it to be published as soon as practicable?

Professor Sir Munir Pirmohamed: The minutes from the expert working group and from the CHM are commercially confidential. Those are not shared. However, website minutes are shared from the Commission on Human Medicines in terms of the deliberations of the committee, and those will be published as soon as possible.

Q2285 **Chair:** Before I go to Aaron Bell, on that point, the minutes are one thing, but the statistical analysis to allow the scientific community globally to validate the calculations is a standard and very important feature of scientific endeavour, is it not? Is there any reason why that is not being provided, and can you say when it will be?

Professor Sir Munir Pirmohamed: The MHRA publishes a report every Thursday on all the adverse events that have been reported to the MHRA, including these events with clotting and lower platelets. The MHRA is looking at the data behind that on the age-stratified risk and so on, and is considering publishing that as part of its future assessment report as it goes through.

Q2286 **Chair:** You would accept, I am sure, for something as important as the response to the pandemic, the more eyes and brains that are able to look at the evidence, the better. Would you agree that it is urgent that that should be available for global scientific scrutiny?

Professor Sir Munir Pirmohamed: I would absolutely agree that we need openness and transparency for all data to be published. As a scientist, as a clinician researcher, I publish all my data. I would agree that data on all aspects should be published.

Chair: Thank you very much.

Q2287 **Aaron Bell:** I thank both witnesses for their time. I will follow up, first, with Professor Aston on what you were asking him, Chair. First, Professor, thank you so much for those infographics; I found them extremely helpful in communicating with my own constituents as to what was going on when the AstraZeneca story broke.

You said yourself that exposure risk is personal. It is obviously personal to the individual's circumstances and also personal to where they are in the country because the level does not apply across the whole country.

It strikes me, bearing in mind the levels we are at already, that there must be some individuals in that 30 to 39-year-old age group whom we are about to start inviting to have vaccines, given the current rates, given their own personal circumstances if they don't socialise much or they are being very careful at the moment, regardless of their pre-existing conditions, for whom the potential harms due to the vaccine must be pretty close to the potential harms due to Covid.

Given your understanding of the precautionary principle, should we not be a bit more flexible about individual circumstances in that 30 to 39-year-old group, given the present situation in the UK?

Professor Aston: Let me answer it from a statistical point of view. You are absolutely right that there will be a large range within any of the age groups of people with different individual risks. The infographic was not designed to try to be an individualised idea. It is not a number that I would apply to any one person in any of those age groups. It is trying to visualise what the levels are on average across those populations and trying to give it in a way that people can understand. If you have 100,000 people of this particular age, this is the number of people you would expect.

The other thing to consider, which we should be very clear about when we talk about these infographics, is what is not on the infographics. We

were very careful to make sure that we were making a fair and balanced comparison. So we had ICU risks—the risk of catching Covid, becoming hospitalised and ending up in ICU on one side—and the blood clot risk on the other side.

The risks from Covid and the benefits from the vaccine are not simply related to ICU. People might also want to consider the reduction in risk of becoming hospitalised or the reduction in risk of getting long Covid. We were very keen not to try to add things in where we did not have good, solid quantitative evidence so we could put these numbers together.

While we wanted, absolutely, to be able to allow people to make that comparison on the serious risks on both sides, I would be very reluctant for people to think that they were the only risks that they were preventing by having a vaccination. The AstraZeneca vaccine has been demonstrated to be effective against those risks as well as simply the risk of ICU admission. We would want to be very clear about doing that for any age group in the infographic.

Q2288 **Aaron Bell:** Let me ask both of you about the international comparison. You implied in your reply to the Chair earlier that if there was a third wave the advice could change. Conversely, if it continues to die away, the advice could change again, because it is based on the statistics. A number of other countries, which currently have much higher rates of Covid, such as many of our continental European partners, have limited it to much higher age groups. It strikes me from the stats that they are just wrong. Is that your assessment? I appreciate you do not want to be too critical of other regulators or other countries, but it strikes me that they have just got it wrong. What is your assessment?

Professor Aston: I will start and then hand over to Sir Munir to get his view on that. I was very pleased that, at the end of last week, the European Medicines Agency, the European equivalent of the MHRA, decided to reproduce our infographics with their data. They, broadly, show exactly the same thing, although they did have slightly different incidence rates.

In actual fact, their incidence rates were a lot lower than ours simply because they took a complete pan-European approach. As you can imagine, if the epidemic is high in one country, it may not be high in another. That then pulls down the overall incidence rates across Europe. But they still came to the same conclusions as MHRA did in terms of the fact that AstraZeneca had very little risk across all age groups.

In actual fact, while different European Governments may be taking different approaches, the European Medicines Agency are taking the same risk-benefit approach now and being very open and transparent in the way they are doing it, using the same kind of infographics that we have used at the MHRA.

Q2289 **Aaron Bell:** Sir Munir, could you comment on that as well? In the same

way as I said to Professor Aston, I appreciate you do not want to say that the European countries are getting it wrong. The EMA do seem to be in line. If we are getting it right and they are doing something very different, are they not getting it wrong?

Professor Sir Munir Pirmohamed: The first thing to say is that there is regulatory alignment across the world between the MHRA and the European Medicines Agency in looking at benefits and risks, but also with the WHO in looking at benefits and risks. If you look at what the FDA did with regard to the Johnson & Johnson vaccine—the AstraZeneca vaccine is not licensed at the moment in the US—they came out with the same conclusion. They did not have an age cut-off at all. That is exactly what the MHRA and the EMA have said. The risk benefit is positive in being highly beneficial.

With regard to decisions that have been made locally at different country levels, it depends on local immunisation policies and immunisation committees. It depends on the underlying background rate but also on the availability of alternative vaccines. That is a critical issue to think about. It is important that people take that into account, and the local committees in different countries are taking that into account in coming up with their own age cut-offs, which is exactly what has happened here with what the JCVI has done.

Aaron Bell: Thank you. That is very diplomatic.

Q2290 **Chris Clarkson:** Thank you to both of the witnesses for coming today. Did the Commission on Human Medicines and the Winton Centre for Risk and Evidence Communication consider the impacts of Covid-19 vaccination on the wider protection of other groups, or was the individual risk the main factor considered?

Professor Sir Munir Pirmohamed: As part of any assessment of any medicine, including the vaccine, we have to consider the individual benefit risk and the public health benefit risk as well. We consider both as part of the assessment of any medicines. The three attributes that we look at are equality, efficacy and safety. We would look at that at both individual and public health levels. Obviously, in our determination and the changes that we have made to the product information, or the advice we give to the HMRA on changes to the product information, those aspects were all looked at.

Professor Aston: I completely agree that that is a very important point. In actual fact, in our own infographic it was designed to explain decision making—either at the level of the JCVI about why they decided to change their advice, or around an individual's decision making about what sort of factors an individual would take into account. However, we have been very clear in all the information we have put out how we computed those risks, that these are individual risks and not risks of you passing it on to somebody else. That is absolutely something that should be borne in mind by people.

The biggest difficulty for us was that, while there is growing evidence that vaccination prevents transmission, it is very hard to quantify. Therefore, it would be very hard to quantify that risk in the same way as we did in the infographic, between harms and benefits, in a way to say, "This is the kind of benefit you bring to others," when it is a lot easier to think about the harms and benefits for an individual or an individual as part of a larger cohort of the population.

Q2291 **Chair:** On that point, Sir Munir and Professor, you will be aware that, this morning, today's news is that the evidence is firming up to say that there is an impact on transmission. That is not included in your infographic in the comparisons. Would I be right in thinking that for the country as a whole this understates the benefits of vaccination in that it is just about the individual's prospect of being admitted to ICU, not someone who has been infected by someone who might be injected with this vaccine?

Professor Aston: Absolutely. The harms and benefits were absolutely clearly laid out for a particular cohort and how many people would be affected in that cohort simply from the harms and benefits of instantaneous incidents of Covid and the risk from the blood clot. It does not take into account any changes in transmission risk that you would gain from, potentially, the bigger thing of transferring between different age groups. As we know, with the risk of Covid going up in higher age groups, that is another factor that people of different ages would want to take into account.

Chair: Thank you very much.

Q2292 **Mark Logan:** Good morning, Sir Munir and Professor Aston. I have a question. According to the data, what are the key risk factors that may lead to a higher chance of developing blood clots?

Professor Sir Munir Pirmohamed: Is that developing blood clots generally or developing blood clots in relation to the vaccine, just to clarify?

Mark Logan: In relation to the vaccine.

Professor Sir Munir Pirmohamed: We have looked at all the data that has come through from the 168 cases in trying to identify particular risk factors, such as looking at the background and looking at the underlying medical illnesses, where there are underlying thrombotic conditions. So far, we have not found any specific risk factors apart from the fact that it seems to be more prevalent in the younger age groups and gets less prevalent as you get older.

Q2293 **Mark Logan:** Professor Aston, do you have anything to add to that?

Professor Aston: The only factor we put into the model that we had was age, but it turned out that that was significant in the model so there was an effect of age on the change in risk factor.

Q2294 **Mark Logan:** That makes the second part of my question a bit

redundant. At this point you are not able, really, to say if there is anything that can mitigate against the risk because it just looks like it is age, essentially, at this point in time.

Professor Sir Munir Pirmohamed: Absolutely, at the moment. I think it is important to stress that this is extremely rare—only 168 cases, given that millions and millions of doses of the vaccine have been given. If you go back to when the pandemic started with Covid-19 itself this time last year, we needed tens of thousands of people to be infected, thousands of people to be hospitalised and hundreds of people to have, unfortunately, died from Covid-19, before we were able to define what the risk factors were for Covid-19 itself.

To have the granularity of data to define what the risk factors are for a disease process—let's call this clotting in a thrombocytopenia disease process—you would need much larger numbers, and we are only working with 168. To define what the risk factors are with such a small number is probably not a good thing to do at the moment. That is why in the product information the CHM did not advise MHRA to put in specific risk factors, because we just do not have the precision of estimates to say that something is a risk factor at the moment.

Q2295 **Mark Logan:** Just on that, Sir Munir, in aggregate, if we worked across countries and brought together all the data, would that still be a negligible amount of data and thus not be helpful in finding that cause?

Professor Sir Munir Pirmohamed: Yes. Obviously, communication is going on between the different regulatory agencies. Joint work goes on between the MHRA and the European Medicines Agency in sharing information. When you put all that data together, together with the manufacturer as well, AstraZeneca, the total numbers are still small. Again, we really cannot estimate exactly what the risk factors are with those small numbers.

Professor Aston: To add to that, you are talking about 168 clots that have been found in the UK in about 21 million vaccinations. You are looking at about 142 cases of clots found in the EU on 18 million vaccinations of AstraZeneca. We are talking very, very small numbers and you are having very, very large populations being vaccinated. It is really hard to find additional causes unless something is clear. The age factor happens to be something you can see. We should also remember that the risk is about one in 100,000. It is a very, very small risk, even at the 20 to 29 levels.

Chair: Thank you.

Q2296 **Dawn Butler:** Thank you very much, Sir Munir and Professor Aston, for coming in today. Sir Munir, you talked about how very rare this blood clotting is. It is a lot rarer than for other medications, such as the contraceptive pill. Although there are different types of blood clotting, how helpful is it to compare the contraceptive pill or flying blood clots to that of getting a blood clot through the vaccination?

Professor Sir Munir Pirmohamed: A lot has been written about this, hasn't it, as to the different levels of risk within different medications that you may be exposed to—crossing the road or being hit by a bolt of lightning and so on? It is probably best that we actually relate this to the vaccine itself and give accurate estimates of what the risk is with the vaccine rather than do comparative estimates with other events that you may come into contact with or other medications you may take.

Professor Aston has done some work on this, and it may be better that he answers that question in terms of the importance of actually focusing on the vaccine itself and then giving accurate figures of what the risk benefits are with the vaccine itself.

Professor Aston: Thank you. We have looked at some work on this. This case, in particular, is a good example of where there is a decision to be made. One of the ways that people in the Winton Centre have thought about this is that you want to say something like, if, on the one hand, I did this and if, on the other hand, I did that; and the two things you are comparing have some kind of merit in their comparison.

For example, the reason why we took ICU risk was because we wanted to say, on the one hand, if you take the vaccine, you may end up with a serious effect of the vaccine from a blood clot. On the other hand, if you don't take the vaccine, you may end up with a serious effect of Covid and end up in ICU. Then you can look at the numbers of people in the 100,000 who would end up in that situation.

We have also done some work looking at the effect of presenting information to people about vaccines and understanding what that does to their understanding of the risk. We found that if you present factual and balanced information in that way, where you present both the benefits and the harms, it does not cause people to get more hesitant. People understand that vaccines have risks and benefits, so knowing about the risks of vaccines does not change that. But, importantly, those who are already vaccine hesitant receive the information better if you give it in a balanced way.

Some work by John Kerr in the Winton Centre has shown that people who receive balanced information have less negative emotion towards it than people who believe they are trying to be persuaded by information. We were very keen to try to make sure our infographics were simply a balanced display of the information saying, "These are your harms from doing something. These are your benefits from doing something."

Q2297 **Dawn Butler:** I agree. Thank you very much. In different countries—Professor Aston touched on this earlier—they have different modelling and different databases. They are all very different and none of them match up. Is there any like-for-like modelling in regard to the different vaccinations? We know, for instance, that there are rare cases of blood clotting with the Pfizer vaccination, but the modelling is done differently. Is there any like-for-like modelling with all vaccinations?

Professor Aston: I do not know of any like-for-like modelling for specific risk effects. The risk effect of the Pfizer vaccine of blood clots is very low. There have been very few cases seen as a result of that. That would be very difficult to build models for. It is useful to see that the EMA, for example, have built their own independent set of models for the AstraZeneca vaccine, which then show remarkable coherence with the models that we have produced in the UK.

I am confident that the analysis done by the EMA and ourselves does bear each other out in that way, but it depends on what you would call a serious side effect or even a mild side effect. We know that people who have the vaccination can get mild side effects, but at what point do we need to include all of those in a fair comparison between vaccines, which is quite a difficult thing to do?

Q2298 **Dawn Butler:** Are you confident of all the modelling in all the countries? I say this because Sputnik are saying that they have no side effects, yet they use the same technology, in layman's terms, as Oxford AstraZeneca and Johnson & Johnson. Are you confident of all modelling in all the countries?

Professor Aston: It would be very hard to know exactly what has been done in many other countries. I am confident in the modelling that we have done on the data from the UK. That would be the best way to put that.

Q2299 **Dawn Butler:** Very tactful. Sir Munir, are you confident in the modelling in other countries?

Professor Sir Munir Pirmohamed: To come back to the point of Sputnik, Johnson & Johnson and AstraZeneca, although they are all adenoviral vectors, they are all different as well. It is important to understand that. Just because you have an adenoviral vector does not mean that you may get it with one but not the other, and vice versa. We need to do more work on that.

Based on the modelling, I am confident in what I have seen from what we have done in the UK and what the European Medicines Agency has done, but I have not seen any specific data at the moment with regard to Sputnik as to how it is being used and how many people have been vaccinated.

In order to come to any conclusion with regard to Sputnik—hopefully, more data will be coming through as it is more widely used—with regard to the FDA and what modelling they did with the Johnson & Johnson vaccine, that was very similar to what has been done in the UK and the European Medicines Agency, with similar conclusions again.

Q2300 **Dawn Butler:** This is my last question to you both. Looking ahead, if we were to remove profit from vaccinations, what would that look like? How would that present itself in how we develop vaccines and how we deliver vaccines around the world? Can I start with Sir Munir?

Professor Sir Munir Pirmohamed: We are in a global pandemic. As the Director General of the WHO has said, nobody is safe until everybody is safe. I think everybody needs to get a vaccine throughout the world. Clearly, the ability of some developing countries to afford vaccines is limited. Therefore, it is important that vaccines are provided at cost price. This is a personal opinion.

The CHM does not consider cost at all. The CHM only considers three aspects: quality, effectiveness and safety. This is a personal opinion. We need vaccines for the rest of the world at an affordable price. Obviously, the AstraZeneca model was very much related to that to provide vaccines at a very cost-effective price for the whole of the global community.

Q2301 **Dawn Butler:** Professor Aston, if we were to remove the money?

Professor Aston: That would not be a statistical question that I would be able to answer. I would absolutely bow to Sir Munir's opinion on that.

Dawn Butler: Thank you both very much.

Q2302 **Chair:** I have a statistical question that you might be in a position to answer, Professor Aston. The infographic has been very helpful, as everyone has said. You have just said to Dawn Butler that presenting it in terms of an actual choice that people make is a good way of communicating it. The choice that is presented is whether to have a vaccine or not in terms of admission to ICU or the side effects, but that is not the real choice, is it? The point is that there is a variety of vaccines. Is not the right comparator to have another vaccine or to have the AZ vaccine?

Professor Aston: That is a really good question. That becomes then a question of how you would operationalise this. We were very much trying to help explain how the decision of the JCVI and others related to the data of the AstraZeneca vaccine. In almost every case, apart from the low incidence case for 20 to 29-year-olds—and even there it is a relative equipoise—there are still benefits to having the AZ vaccine over the harms that would come from it.

As you say, other vaccines are available. If the choice was that the other vaccines were available and it was equally easy to do, then they would absolutely want to take that into account, but I do not know whether that is a valid argument to make or not, because that is an operational decision, and you would want to take that into account when you present that. Simply, I wanted to present in the infographic what the risks and benefits were of the AstraZeneca vaccine for those who were being offered the AstraZeneca vaccine.

Q2303 **Graham Stringer:** Professor Sir Munir Pirmohamed, at the end of last week I received a letter that, at first, I thought was phony—but apparently it is not phony: it is from Professor Luc Montagnier, the French Nobel prize winner. In it, he claims that the messenger RNA vaccines have a risk of incorporation of the RNA into the human genome,

transcribing it into DNA. First, I wondered if you had seen that point of view put forward and, secondly, whether you would give it any credibility.

Professor Sir Munir Pirmohamed: Thank you for that question. I have been involved in assessing the vaccines as they were being developed and through the rolling reviews that the MHRA undertook. As you know, we were the first country in the world to authorise the use of the Pfizer vaccine, which is an mRNA vaccine. We now have the Moderna vaccine, which is also an mRNA vaccine.

Through that process, I have been able to evaluate all the data that was produced in terms of the pre-clinical data, the laboratory data, but also the quality data as well as the safety data from the clinical trials, and the biological plausibility of how the vaccines work and what we know about how the mRNA vaccine works. From that, there is absolutely no evidence, as far as I know, of the vaccine mRNA being incorporated into human genomic DNA as such. There are a lot of these stories floating about, particularly in social media, but there is absolutely no truth in that from the data that I have seen—and I have been exposed to an awful lot of data in relation to the development of these vaccines.

Q2304 **Graham Stringer:** Were you aware that Professor Montagnier had that point of view?

Professor Sir Munir Pirmohamed: I was not. I have not seen anything from him in the scientific literature.

Q2305 **Graham Stringer:** When you say there is no evidence, do you mean that there is no empirical basis for that or that there is not even a theoretical basis for the incorporation of RNA into the human genome?

Professor Sir Munir Pirmohamed: Both really. There is no theoretical basis. Also, from the data that I have seen, I have not seen any evidence that that happens.

Q2306 **Graham Stringer:** That is very helpful. Thank you. Do you think you could expand on the answer to the Chair's first questions on the apparent case that the AstraZeneca and Johnson & Johnson vaccines, which were adenoviral vaccines, were causing more clots?

Professor Sir Munir Pirmohamed: We have epidemiological data with small numbers of cases. With Johnson & Johnson in the United States, there have been 15 cases. Last Thursday, we reported 168 cases in the UK with AstraZeneca. Again, those are very small numbers compared with the millions of doses that have been given. Again, the adverse effects are very rare.

What we do not know is exactly how this is occurring. We have data from the work of the haematology community that some people seem to have an immune response and they produce a particular antibody that seems to be activate platelets, and the platelets then are causes of thrombosis. Platelets are critical for preventing bleeding, but platelets can also lead to

clot formation as well. What we do not know is what links the vaccine to the activation of the immune system that leads to activation of the platelets. That scientific work is ongoing at the moment by lots of different groups throughout the country, and in Europe as well, to assess that.

When we can identify the mechanisms, it will be possible to think about how we can develop mitigation strategies to prevent that, if we can actually show a true mechanistic link between the adenoviral vaccine and the occurrence of this particular adverse event. As I said, I do not know at the moment whether it is truly just related to the adenoviral vaccine or whether it is related to the spike protein antigen, which is present in all the vaccines, but somehow an interaction goes on that increases the risk associated with the AZ vaccine.

It is really important that we do that mechanistic scientific work to be able to understand what is going on so that we can develop better mitigation strategies, not only for what is going on at the moment with the Covid pandemic, but we need to be aware and prepared for future pandemics as well.

The more we learn with this at the moment will help us to develop better vaccines in the future. Not only do we need to have the epidemiological work we are undertaking but also to undertake some mechanistic laboratory scientific work to better understand this so that we can improve things for the future, to maximise benefits and reduce risk associated with the future vaccines as well, given that we will need a booster vaccine in the autumn but we need to prepare for future pandemics as well.

Q2307 **Graham Stringer:** That is really helpful. We heard from the statistics about the side effects, fatal in some cases, albeit in very small numbers, but is there any evidence or theoretical basis that there might be some other side effects of even smaller numbers that are yet to appear and to be observed?

Professor Sir Munir Pirmohamed: We are undertaking the biggest vaccination campaign in history. When you undertake that kind of big vaccination campaign, when you are vaccinating millions and millions of people, you are going to pick up very rare adverse side effects. This is one such case. Others may come up that are even rarer than this. One cannot exclude the possibility. When we look at other medicines, when we have identified these rare adverse effects, there has been an underlying genetic factor that predisposes individuals to those kinds of adverse effects. Some work is going on at the moment to identify whether there are any genetic risk factors.

If you look at other populations of the world, for example, India, where the situation is absolutely horrendous at the moment, I think 100 million doses of the AstraZeneca vaccine have been given, but the total number of cases reported so far of this clot at the moment is only two. It may

have increased since the last time I looked at that data. It may suggest that there may be other factors, such as genetic risk factors, that we need to look at as part of the work that is going on at the moment.

Q2308 **Graham Stringer:** My final question to you, Sir Munir, is this. I also have one question for Professor Aston. The roll-out of the vaccine programme in this country has been very effective both administratively and in the effectiveness of the vaccine. As to further development of vaccines, is there anything we can learn from the less effective Chinese vaccines? Sometimes in science you learn things because things do not work as well as things that are effective. Is there anything we can learn from the Chinese vaccines?

Professor Sir Munir Pirmohamed: We can learn from everything that goes on in the pandemic at the moment. That has been shown in how quickly science has responded to the different situations that have occurred over the last year. Certainly, we need to learn from the vaccines deployed in this country but from the vaccines deployed in other countries as well. Collecting data is going to be critical.

Having open access to that data, as the Chair said, so that independent scientific investigators can access that data and analyse that data is going to be critical to understand further the effectiveness and safety of all the different vaccines in the different circumstances. We need to be able to put that into context. I have not seen the raw data for the vaccines produced in China, so I cannot comment on exactly how it is being deployed and what the adverse event and effectiveness profiles have been, because it has not been published in the peer-reviewed scientific literature either. Having open access to data available is critical for us to learn from both the successes as well as the failures of what we employ within this pandemic.

Q2309 **Graham Stringer:** Professor Aston, Professor Whitty has told this Committee in the past that at some stage the Government will have to make a decision that the risk and the level of infection from Covid is so relatively low that it has become endemic and we will have to live with it. With the successful roll-out of the vaccine, can you extrapolate and tell us when we are likely to reach a level of infection that is comparable, say, to an average flu season?

Professor Aston: We have not done that work, although I am pretty sure that that work will be being done by a number of groups who are looking at epidemic modelling across the country.

As you well know, the rate of vaccination and the number of people vaccinated is a factor when calculating the R value, for example. There is some early evidence—this is not peer reviewed yet—from some economists of the effect of a number of roll-outs of vaccinations across the world.

If we look at a panel of about 120 countries, which I believe they looked at, as to what the effect of vaccination was in the relaxing of social distancing and the number of infections, they found across the world that there was an association between the levels of vaccination and the actual social distancing that people did through mobility data and the levels of infection. We are starting to see the effects of vaccinations worldwide, although we need a lot more data to understand what that is going to do. It is something that can be incorporated into the models, but I do not think we are quite there yet to be able to say what the level will be.

Q2310 **Chair:** Professor Aston, is there any reason looking forward to expect a third wave, as it is sometimes called, of infection in this country?

Professor Aston: A number of people have said that it is something that could happen. It is not something that we could guarantee will not happen. It will depend on the way the virus spreads, the level of restrictions in place, the number of vaccinations and how that comes about. They are all related together. It is very difficult at this point in time to say one way or the other.

Q2311 **Chair:** Clearly, there are all sorts of things that could happen in the future that we do not know about, but there is no particular reason to expect it, in your view.

Professor Aston: I do not think I have the data available to really give a definitive answer as to whether you would expect to see one or not. It will very much depend on what we see happens in the next few weeks as restrictions change again.

We are going through a process. Assuming things follow those processes, I think people will take their time, and if the numbers of vaccinations continue at their present rate that will have a distinct effect on the R number. Again, it is very difficult to make predictions. One of the things we have seen in the pandemic is that it is very difficult to come up with what will definitively happen.

Q2312 **Chair:** You have the statistics, and we have had a releasing from the measures over the past few weeks. Have you seen anything from that that would indicate, as we release restrictions, that we experience another wave?

Professor Aston: I would not say that. The ONS numbers are stabilising. They are not dropping at the same rates, so that is something we would want to watch. I could not say that I have seen anything to suggest that things are rising quickly in any way, shape or form. There is certainly no evidence of that.

Q2313 **Chair:** Is there any evidence that they are rising at all?

Professor Aston: No. There is evidence that they are stabilising. The ONS numbers have been coming down, but I am not sure that the

numbers of cases are dropping as rapidly as they were. I would not want to go any further than that.

Chair: Thank you.

Q2314 **Carol Monaghan:** Sir Munir, are you able to tell us anything about how the MHRA will consider issues such as those relating to the Johnson & Johnson vaccine in the US before approving a vaccine?

Professor Sir Munir Pirmohamed: The Johnson & Johnson vaccine has been licensed, as you know, by the European Medicines Agency. As per the agreement through the Brexit deal, the MHRA can undertake approval of that through a reliance procedure, basically relying on exactly what the EMA have said, but taking into account any new safety issues that arise and any new safety data that has been presented.

The MHRA will be looking at that and will be coming to the Commission on Human Medicines to look at the data based on quality, effectiveness and the new safety data with the 15 cases that have been reported in the United States, and it will take that into account before deciding exactly what to do in terms of the product information and authorisation of the vaccine.

Q2315 **Carol Monaghan:** When we are looking at new vaccines coming online, you are looking at the experience of other countries that are already using these vaccines.

Professor Sir Munir Pirmohamed: Of course. We are dealing with a global pandemic so you look at data that is available from everywhere. The manufacturing authorisation holders are legally obliged to provide all the data that they have, irrespective of where it arose in the world.

Carol Monaghan: Thank you.

Q2316 **Chair:** Finally, Sir Munir, talking about the side effects again and looking at the experience of Johnson & Johnson and other vaccines, we know from the clinical trials of the AstraZeneca vaccine that some people accidentally were given a lower, smaller dose during the clinical trials. We know from the write-up of that research that they had fewer side effects. Has your commission looked at the impact of dosage on the incidence of clots?

Professor Sir Munir Pirmohamed: When we reviewed the dossier on the AstraZeneca vaccine, clearly, we looked at the low dose vaccine that was given to some patients, but the total number was small in terms of both effectiveness and safety. You are quite right that the reactogenic events, which are pain and swelling at the injection site, muscle pains and so on, were lower with the lower dose compared with the standard dose being used.

With regard to the efficacy, we found from the data that it was related to the extended interval. The higher efficacy of the lower dose was related to the fact that it was given at 12-week or longer dose intervals

compared to the standard dose vaccine. Hence, that is why, when we authorised the AstraZeneca vaccine, we said it should be done between the four to 12-week interval. Now, data is accumulating showing that the longer the dose interval between the first and second dose the better effectiveness you have.

With regard to the safety and relating to the current issue of clotting and thrombocytopenia, some people have suggested that we should reduce the dose, but this is all supposition and hypothesis. Just because you get a lower rate of reactogenicity with the lower dose, which is a predictable type of reaction you get where the vaccine is injected, does not necessarily extrapolate to the fact that that will lead to a lower rate of thrombocytopenia and clotting events. Further work, as I said, needs to be undertaken to understand the mechanisms, which will allow us to fully understand whether it is a dose-related issue and whether future vaccines need to be modified in terms of the total dose administered to individuals.

Q2317 **Chair:** Professor Greinacher in a current learned science journal has said that part of the problem might be the dosage. Is that actively under consideration? Will there be an outcome of that in time to inform policy decisions?

Professor Sir Munir Pirmohamed: Yes. I have read the paper. He said that, and various other people have also referred to the dose. As a pharmacologist, I firmly believe in a dose-response curve—that effectiveness varies with dose as well as safety. It is a really important aspect to look at, and further work is being undertaken to understand the dose response relationship in both the efficacy and safety with that vaccine.

Chair: Thank you very much to both witnesses for your evidence this morning. It is very important for us to be able to understand the current science behind policy decisions, just as it is for fellow scientists to scrutinise your work. You have done us a great service in that. It is worth reflecting on the policy choices that we have here, which—I think I am right in saying—are not based on any new adverse findings of the propensity for clotting. Some of the difficult policy judgments come from the happy circumstance of the prevalence of Covid dropping to such a level that, even set against the low incidence, there are questions for policymakers. That is the context of the questions in our inquiry today. We are very grateful to you for your help this morning but also for the work you are doing on the pandemic and have been doing for the past year. Thank you.

Examination of witnesses

Witnesses: Professor Harnden and Dr Ramsay.

Q2318 **Chair:** We now turn to our second panel of witnesses. I am very pleased to welcome Dr Mary Ramsay back to the Committee. Dr Ramsay is the

head of immunisation at Public Health England. I also welcome back Professor Anthony Harnden, who is deputy chair of the Joint Committee on Vaccination and Immunisation, the JCVI, and is professor of primary care at the University of Oxford. Thank you very much indeed.

Perhaps I could start with Dr Ramsay. We have had some encouraging news this morning reported that the impact of the vaccines on transmission of Covid seems to be positive and significant; this was an area in which there was some uncertainty as to what it would be like. Would you summarise the findings of the research that Public Health England are responsible for?

Dr Ramsay: Yes. This research, basically, linked information from cases of Covid with the household that they lived in and was able to show that if the index case in a household—the first case in a household—had been vaccinated, then their household members were less likely to catch infection than if the index case had not been vaccinated. That reduction was of the order of 40% to 50%, so quite a significant reduction.

To clarify, that is on top of the fact that the vaccinated individuals themselves were less likely to become a case in the first place. That is an additional benefit on top of the benefit we have already seen in the actual reduction in cases in people who have been vaccinated. It is very good news. Obviously, it is only after one dose, and it may be more after another dose. It is a relatively short-term observation at the moment because it is based on just the 12 or so weeks that we have been using the vaccine.

Q2319 **Chair:** Thank you. So far we have been looking at the effect on the individual, but this means that now we can say with some degree of confidence that the approval of the vaccines and the benefits of the vaccines are having an impact on society and the country generally.

Dr Ramsay: Yes, although the fact that the vaccine prevented people getting cases in the first place—or the individual—is already reducing transmission, because if you are not a case you cannot transmit, obviously.

Q2320 **Chair:** Thank you. Professor Harnden, I don't know whether you heard the discussion we had in the previous session, in which we have some knowledge of the very low level of risk of some vaccines—the AZ and the Johnson & Johnson vaccines—in terms of clotting. Because of the fall in the level of prevalence of Covid across the country, that is informing policy choices as to what is the right advice for people looking to be vaccinated. It has been suggested that the under-40s might be included in advice to consider an alternative. Can you say what the latest thinking in the JCVI is on that?

Professor Harnden: We are looking at this group very carefully. As you know, we have given advice that the under-30s should be given the choice of an alternative vaccine when it is available.

The first key thing about all of this is understanding what the true incidence rates are of this very unusual side effect; that is still an evolving situation. The second key thing is trying to understand, when restrictions are released, what public behaviour will be and what will be the background incidence rates—that is to say, will the incidence of Covid go up when restrictions are released?

Then we need to look very carefully at the risk and benefit to the individual, but also the risk and benefit to society, particularly now we have information, as Dr Ramsay said, about transmission and how vaccines prevent transmission and, therefore, protect other people who may be unvaccinated or unfortunate in not responding to the vaccine as the majority of people do.

There are still vulnerable people in society. If we see infection rates rise, potentially, there is a public health imperative to carry on with the vaccine programme. This is against a background, of course, of supply and availability of the vaccines. We are given information, although it is commercially confidential, about how much vaccine we have and what we can offer people.

For instance, if we make a decision for the under-40s, that will delay the immunisation programme. Therefore, it may push infection rates up. From a public health perspective, we may end up getting many more deaths and hospitalisations because of that. It is a really difficult issue to work through. We are trying our best on the JCVI to try to get a really good understanding of the incidence rates in the various age groups.

As I say, that information is still evolving as it comes through to the MHRA. Of course, like any new condition, when you find it and look for it, you find many more cases. What then happens is you find the past cases, and then the new incidence cases become apparent. So the number of cases, I would expect, of this side effect settle down once the figures reach certain points. Then we will see what the true incidence is.

We have a difficult problem in that the vaccine programme is so successful at the moment that we are rolling down the age groups so quickly that we are going to get to those under-40-year-olds within the next couple of weeks. In some parts of the country, for instance in Northern Ireland, they are already starting to immunise. We are very aware of this at the JCVI, but these are not easy decisions at all to make.

Q2321 **Chair:** Thank you. Just before I turn to Rebecca Long Bailey and Katherine Fletcher, given the information on which Dr Ramsay has just commented on the impact on transmission, we heard in the previous session that the comparisons made at the time of the original decision were based on individuals' experiences as to whether they were themselves more likely to be admitted to an ICU. Presumably, the knowledge that transmission is being suppressed by the vaccine will be considered by the JCVI when it comes to advice pertaining to the under-40s. Professor Harnden, is that the case? Will that be part of your

assessment?

Professor Harnden: I am sorry. Was that question directed at me or Dr Ramsay? I was not sure.

Q2322 **Chair:** It was. I am sorry not to be clear, Professor Harnden. There is obviously the effect on individuals, and there is the effect on society in the country as a whole. Will the JCVI be considering both of those together in its next set of advice?

Professor Harnden: Yes; of course we will look at this. We are quite dependent on the modellers providing this information for us. These are things that will be factored into the modelling in trying to predict the number of cases that will occur. Of course, there are so many uncertainties in public behaviour. As we unlock, what the public will do in their behaviour is uncertain.

If we continue with the messaging that we carry on being cautious, even though we unlock slowly in terms of social distancing, mask wearing and so on, we may keep infection rates down. Therefore, the number of infections we get will be less and the risk-benefit of these vaccines changes. There are a lot of uncertainties. It depends so much on what parameters you put into these models as to what answers you get out of them, but transmission will certainly be one of those parameters.

Q2323 **Chair:** When does the JCVI expect to make a decision on its next advice for the under-40s?

Professor Harnden: We are actually meeting twice a week at the moment. Almost all the discussions have been about this, so we will be meeting tomorrow and making a decision about whether we leave that decision to the following week or whether we take it this week. These are things, as we are speaking, that we are discussing on a twice-weekly basis.

Chair: Thank you very much, indeed.

Q2324 **Rebecca Long Bailey:** Thank you both for speaking to the Committee today. It is very helpful. Just to elaborate on some of the comments that you have both already made, as you know, within a lot of our communities there is certainly a feeling that we are returning to normal and people can start to go about their everyday activities.

Just so we can be clear to the public, could you explain the risk on the efficacy of the vaccine roll-out on virus suppression of the further easing of restrictions, particular amidst a backdrop of partial vaccination of the population? I ask that question, first, of Dr Ramsay.

Dr Ramsay: Clearly, the main reason that numbers have come down since January has been because of the restrictions. On top of that, we have seen the additional benefit of vaccination. Obviously, it has affected different age groups differently. This is where it is very difficult with this balance, particularly when we are looking at safety as well.

As Professor Harnden said, it is very important that we have as many people vaccinated before we release all those restrictions. At the moment we are trying to balance it very carefully. As more people get vaccinated, we are releasing gradually. We are observing, as you know, what happens. That is allowing us to carry on. It does depend on what the future holds, how people behave and how the vaccine works. We have better and better data every day on that. So far, people have mainly only had one dose. There is a proportion now growing very quickly with the two doses, which should help a lot.

Obviously, a proportion of the population is not vaccinated, even in the very elderly. It is a very small proportion but there are some people. There are younger people who are still yet to be vaccinated, and children who, at the moment, cannot be vaccinated. Those transmission characteristics are very important.

It is quite difficult to measure transmission. You measure it at an individual level, but actually it works at a population level. Very subtle differences can make quite different features. It may be that we begin to see more transmission in certain pockets, as we did with the epidemic last year, where there will be some areas, because of social factors, vaccination uptake and so on, where there is still a risk of transmission. It would be very hard to say, confidently, that by X we can stop doing Y. It really is a question of keeping observing and monitoring so that we can get that balance right.

As we have discussed several times already, there is a risk that we get a resurgence as we release restrictions. Hopefully, that will mainly lead to mild disease in younger people, but there will still be the risk that those people can, potentially, pass it on to older individuals, who are, for whatever reason, either unable to respond to vaccines or unvaccinated, or, maybe, if the vaccine even begins to lose protection over time. Those are all the factors that we are having to raise. As Professor Harnden said, it is a very difficult balance.

Q2325 **Rebecca Long Bailey:** Thank you. Professor Harnden, the same question to you.

Professor Harnden: I do not think I have much more to say than Mary has already outlined, other than we only have to look at other parts of the world to see how we can be lulled into a false sense of security. The vaccines are doing a huge amount of good and a lot of the heavy lifting, but the lockdown easing is so important as well.

Broadly speaking, for instance, one dose of these vaccines is about 65% protective against disease. Okay, they are much more protective against hospitalisations and deaths, which is what the programme is. With 65% protection against disease, even if some of those do not transmit, you are still going to get a proportion of those who are vaccinated with one dose who will transmit infection to others.

If we all go completely wild, as I have been saying on the media, and just ignore everything that we have learnt during the past year in terms of social restrictions, there will be another wave, and that wave will be much larger.

We need to celebrate our success with vaccines. They are tremendously effective and the data is hugely encouraging, but we also need to be cautious because we do not want to see what is happening in other parts of Europe and the world happening in the UK.

There are a lot of uncertainties. One thing for us is the seasons, because this is going to happen in the summer. Of course, we know there is seasonality to any respiratory-transmitted virus. That is one positive bit of news. Hopefully, people will be outdoors more, but I cannot help emphasising that we must all stay cautious and on our guard.

Q2326 **Rebecca Long Bailey:** I have one final question. The Medicines and Healthcare products Regulatory Agency raised concerns about lateral flow tests and the false reassurance that they might provide to those who receive a negative result. This question is for both of you. If you think that this is skewing data on vaccine efficacy in suppressing the virus, are you concerned about the evidence base for the use of lateral flow tests as a test to enable Covid certification or entry to large events, to Dr Ramsay first?

Dr Ramsay: In relation to the data, we think our data at the moment is still very valid because people are getting a PCR if they have a positive lateral flow test. We need to keep an eye on that because that will change the balance of testing and the pattern of testing. Our data on the effectiveness of the vaccine is observational data. It is not trial data. We cannot control it that carefully. We have to adjust for all these factors. Those are the kinds of things we will be looking at when we do any analysis.

In relation to how we let people carry on doing things, or start to do things that they have not been doing, every single element is a risk. Vaccine is reducing that risk. A lateral flow negative is reducing that risk. A PCR negative is reducing that risk. They all work in different ways. Also, the nature of the event is important, whether people are wearing masks, whether they are distanced, and so on. It definitely can be part of that package.

Obviously, each of those risks needs to be carefully assessed and balanced for each of the events we are talking about, alongside what is going on in context in the population, such as how much disease is around. Obviously, if there is much less disease around, the risk of missing a case through a lateral flow device is much lower. Those are the factors we have to consider. Nothing is risk free, but we can get the risk as low as possible by using all the tools that are available to us.

Q2327 **Rebecca Long Bailey:** Professor Harnden, the same question to you. Do

you think the false reassurances of lateral flow tests are skewing data? Are you concerned that they might be used as an evidence base for large events or Covid certification?

Professor Harnden: I do not think they are skewing data in terms of the vaccine because we are looking at lots of different studies on their effectiveness and so on. If you have a positive lateral flow test, it is quite helpful in the sense that you know you need to have a PCR, you may well have the infection, and you may be infectious to other people. The problem is that a negative lateral flow test does not mean to say, necessarily, that you do not have the infection.

It goes back to my previous comments that everybody has to be cautious. Just because you have been vaccinated and just because you have a negative lateral flow test does not mean you are invincible. These tests are not perfect. The sensitivity of a lateral flow test is not perfect. Of course, as the prevalence of the infection goes down in the population, the predictive value of all these tests alters, and that becomes problematic as well. They are helpful as part of an arsenal of test, investigations, vaccines and everything else, but they should not be taken in isolation.

Rebecca Long Bailey: Thank you both. That is really helpful.

Q2328 **Chair:** Thank you, Rebecca. Professor Harnden, you talked in one of your answers to Rebecca about the prospect of a wave that would be a larger wave than before. What is the basis for expecting the possibility of a larger wave than we have experienced in this country?

Professor Harnden: Sorry, I meant to say a large wave, not a larger wave. The London School, Warwick and Imperial have all done models on this, which have been presented to SAGE, of different heights of a potential third wave. Some of those models show a larger wave than others. That is what I was saying. I was not saying it would be larger than the second wave; I was saying that some of the models show a larger wave than others.

Q2329 **Chair:** Thank you. Dr Ramsay, in terms of unlocking and behaviour in releasing restrictions, we have some evidence of that because we have released restrictions over recent weeks. Has that given you any concern that it will lead to a rise in infections?

Dr Ramsay: So far—Professor Aston mentioned this in the earlier session, didn't he?—the data is reassuring. It seems to be stabilising and not continuing to go down. Obviously, there are lots of different data sources.

One of the things we have found with this virus in general is that it is not equal across the country. We know last year that we had pockets of transmission in certain parts of the country. There is always the risk that those pockets of transmission, whether it is due to social factors, housing, behaviour, vaccination or lack of vaccination, could potentially

all coalesce and you could have, potentially, pockets where there are quite worrying rates of transmission.

The real importance is that we continue to monitor this on a very careful basis, and we continue to look at local level. We work with our directors of public health, who are all based in local authorities and know their population. They can look at the rates and decide what they think is going on in those patches.

It is a mistake just to assume that everyone is the same and every area is the same. Uptake has been incredibly high, but there are some pockets where it is a little bit lower. We know London, for example, is lagging behind on that.

Q2330 **Chair:** Clearly, one should not assume it, but you have had the benefit of studying the data over recent weeks during which time we have had substantial unlocking with, for example, every school in the country having gone back and people able to meet beyond their households. Have you seen anywhere any evidence of behaviour leading to a rise in infections?

Dr Ramsay: Not specifically due to behaviour, no. We did see an increase in rates in secondary school children when the schools went back, but that was because they were not mixing at all beforehand, and we were also testing them more exhaustively with all the lateral flow devices and so on. I think we expect to see an increase in rates.

The question is whether that increase in rates is translating into increases in more worrying things like hospitalisations and deaths. That is what we have not seen. They are still continuing to go down at very sharp rates, a very sharp decline, because the vaccine is adding that protection to the vulnerable population.

We have relatively recently opened up with shops and outside venues, and, as Professor Harnden says, people are mixing outdoors at the moment. We do not have any evidence of any serious concerns about the behaviour at the moment.

Q2331 **Chair:** This Committee has considered in the past Public Heath England's studies of other countries' practice overseas. We may be an island, but, in scientific terms, we are not. We are very well connected. I know you have good links with the US authorities, for example. I am sure you would agree that the Food and Drug Administration, the FDA, and the Centers for Disease Control and Prevention, the CDC, have a very high reputation internationally. Would you concur with that?

Dr Ramsay: Yes. We can learn from everyone, as Sir Munir said earlier. The data itself may be very difficult to compare. You need to interpret that in the context of the population.

Chair: Absolutely.

Dr Ramsay: The health service set-up and the access to testing—all those things—affect how the different data sources may compare. We work very closely across the international sectors.

On the vaccination, we have had more contact, for example, with Canada and Israel and other countries than the States because we were a little bit ahead. The Canadians have done a similar thing to us on their scheduling. We are in regular contact with all those other agencies as well as with the WHO. We are on various international groups that allow us to learn from the experience of other countries.

Q2332 **Chair:** We will discuss Israel in some detail where a lot of the restrictions have been released in response to the level of vaccination. Specifically on the US, where the CDC is very rigorous and very highly regarded, it has said that fully vaccinated people can have restrictions lifted on them; they can visit other fully vaccinated people indoors without wearing masks and without staying six feet apart. They have stated that it is based on the latest science. Why should the science be different in America than it is here?

Dr Ramsay: The Americans have taken a very different approach to delivering the vaccination programme. Right from the start they kept their accelerated schedule—the schedule where the vaccines were given closely together. Most of the people who have been vaccinated have had two doses, whereas here we chose to separate them, and we are just beginning to ramp up. It is going very well, and we now have 12 million people who have had two doses.

Our policy for the programme was always about preventing deaths and preventing hospitalisations. That was the focus and why we gave one dose to more people in order to reduce that as quickly as possible, which is what the data suggests has happened, but we were not focusing on transmission. They are able to be less cautious than us perhaps because of the fact that more people have had two doses, which one would expect to give even better protection against transmission. Our data is now coming through showing that even one dose is very good, so I think we can begin to look at those factors, and we are looking at those factors.

The other thing is that we have a slightly different cultural perspective in this country in that we tend to do everything together. We are trying to say that this is about the population as a whole rather than the individuals— those privileged individuals who have had two doses being somehow able to do things that other people can’t.

Again, the advice in this country is very much about all going together. I think that makes sense. We are a very densely populated country. It may well be that we are able to start giving specific advice to individuals, but I think the approach has been to do everything for the population largely as a whole rather than picking out individuals in terms of their particular characteristics. There are some people who may not respond as well to

the vaccine for medical reasons, and we do not really know exactly who those are at the moment.

Q2333 **Chair:** That is fascinating. The CDC's advice was about those fully vaccinated, in other words those who had had the two doses, which could equally apply here. There are increasing numbers of people who have had two doses. It would be open to us to follow the approach of the United States where the regulator has said that it is based on the latest science. You are telling the Committee that we could do that, but the choice here has been to delay that for sociological reasons of doing things together rather than—

Dr Ramsay: I have maybe misled you slightly. That is not necessarily my decision. Obviously, as PHE, our role is to generate the evidence, to put the work together and to develop guidance—and we are working on guidance. I think the United States says it has to be at least two or three weeks after your second dose before you can release those restrictions. We are only really just reaching that now. We started vaccinating second doses towards the end of April. It is very early.

The road map and the policy decision that has been taken by Government, not by PHE, is about doing everything as a whole so that people can release restrictions as a whole across the population. That is just a slightly different approach, I think, to potentially giving individual risk advice in relation to individuals who have had particular characteristics.

Q2334 **Chair:** Is it the Ministers who have decided to delay the lifting of restrictions until things can be done as a whole?

Dr Ramsay: No. What I am saying is that the road map is talking about how we lift restrictions at a population level. That is the focus that we are currently doing. It may be that within the future road map we are able to pick out individuals, but that is the direction of travel. We will all be able to release certain things as time goes on. The next level will be to allow people to meet indoors. It will not necessarily depend only on having been vaccinated.

Q2335 **Chair:** I am interested in the boundary of what are public health decisions and what are political and social decisions, because the CDC, in taking that advice that it was scientifically safe for people who had been vaccinated twice not to have to wear masks when meeting other similarly vaccinated people, concluded that the benefits of avoiding disruptions such as unnecessary quarantine and social isolation may outweigh any potential residual risks there. Given that this is based on science, is that available to us? Could we follow the scientific advice that the CDC has followed?

Dr Ramsay: I think we could, and we will be looking at it once we have reached the same context that they are reaching. That is where we are a little bit behind because we were delivering the single dose to more people—that was our focus initially—to prevent deaths and

hospitalisations, as I have said before. We are now reaching the stage where there is a bigger cohort of people who have had two doses, and we will be looking at the individual advice that we give to people. In relation to the overall policy, which is a Government decision, that is about trying to get the whole of society to be able to behave more normally as time goes on. That is what the road map is all about.

Within that, there may be variations. As you know, shielding has stopped. There are those sorts of particular decisions. There have been some decisions given to individual groups, but, as I said, the overall focus has been about how we can get society back to normal rather than how individuals themselves might behave differently.

We will get data very soon on two doses. The United States has used predominantly mRNA vaccines. We have some people who have had Pfizer and some people who have had AZ. There will be differences in the science as well that we will have to have before we make those choices.

Q2336 **Chair:** Are you suggesting that, because we have used more of the adenoviral technology for vaccines, we should be less able to release restrictions than the US because they have used mRNA? That is not consistent with the advice that we have heard.

Dr Ramsay: No. What I am saying is that the data from mRNA may not be directly comparable with the data from AstraZeneca. We know that the AstraZeneca vaccines are very good at producing antibody—they work in a different immunological way. We know they have very good protection against severe disease. But we do need to have some data to support for both vaccines. At the moment, I think all the two-dose data we have in this country and from the States is with the mRNA vaccines.

Q2337 **Katherine Fletcher:** Dr Ramsay and Professor Harnden, your time is appreciated when you are working so hard in other ways, so thanks for popping in. If I could offer you a cup of tea I would, but, as you have so articulately put it, we need to maintain these social distancing restrictions to help as part of the battle.

A lot of people would be really quite interested in what we have already achieved. The British public are working very hard to keep what are very challenging restrictions on their lives and liberties, never mind the economy.

I will start with Professor Harnden to give Dr Ramsay a brief break from chatting. Can we start to quantify the effect that the vaccine programme has already had? I accept it will be a range, but do you have a number of the deaths prevented by the current vaccination programme?

Professor Harnden: I think Public Heath England have published this recently, have they not? There are 10,400 estimated deaths that were prevented because of the vaccinations. The majority of those deaths prevented were in the elderly groups. You need also to remember that that was looking back. Actually, these vaccines will also prevent deaths

moving forward. The total impact of the vaccine programme will not be known until the pandemic eventually subsides, but it will be many-fold greater than that number, I am sure.

Q2338 **Katherine Fletcher:** Would we be getting to the kind of numbers that fill Old Trafford at 70-odd thousand?

Professor Harnden: In terms of deaths prevented? I would imagine so. I will defer to Mary Ramsay on that because she does these calculuses. I think it will be that sort of number.

Q2339 **Katherine Fletcher:** That is a remarkable figure. Dr Ramsay, we know that it is not just tragic that we have lost friends and loved ones, but it is also the deleterious effect of significant hospitalisation stays and even the sub-ICU level long Covid effects. Can you quantify for the British public how many people have been prevented from having those adverse reactions through the vaccination programme?

Professor Harnden: We have not done a formal quantification of that. We could look at that. One of the difficulties with looking at the data is that obviously a lot of the effect on the reduction in numbers is about the lockdown. What we have managed to do is estimate the additional benefit of preventing deaths in the people who have been vaccinated. What we have looked at is only the direct effects. The way that vaccines work most effectively is by their indirect effects in reducing the overall risk. Obviously, if lockdown had not reduced the numbers, if we had not gone into lockdown, we would have continued to see more cases, and therefore the benefit of vaccines would have been higher.

It comes back to this issue that, as we release restrictions, if people behave in a way that had there not been a vaccination programme there would have been more transmission, then the preventive deaths from the vaccination programme are obviously much more profound and much larger, and they will accumulate. They will easily get beyond your Old Trafford example, I am sure. If we were to stay in lockdown forever, that would not have happened. But we are not expecting to. That is the whole point of the programme.

Q2340 **Katherine Fletcher:** What I am trying to get to is that you are rightly doing this at a population level—the epidemiology of it and those big levers and big choices. As Rebecca Long Bailey and others mentioned earlier, we have a bunch of people whom we want to desperately encourage to take the vaccine but to not see that as, "Woohoo, I can go and swing from the chandeliers," metaphorically. A lot of that is about understanding your personal effect.

I am in cohort 6. I was vaccinated a few weeks ago. I have had a single dose. I am incredibly grateful for the amazing work that has got us to that point. What effect has that on my likelihood of transmitting the disease to unvaccinated people? Do we have any figure on that at the moment?

Dr Ramsay: It depends a bit on your individual situation. I am not going to try to make it individual. It reduced your chance of getting infected with Covid by about 60% to 70%. By definition, if you can't get infected, you can't spread. The new data today suggests that, even if you were to be in the 30% to 40% who were still able to get infected, you would probably be less likely to spread it because your overall level of virus is still suppressed a little bit and you are not shedding virus as much.

Katherine Fletcher: Lower viral load.

Dr Ramsay: It is an additive effect. It is very profound. We expect, obviously, the second dose to improve that protection, but there also may be some decline over time.

Q2341 **Katherine Fletcher:** I do want to try to quantify it a bit. Once you have had a second dose, you are probably 85% to 90% good for not transmitting, but the messages you are giving us today are that you still have a one in 10 chance of being able to transmit.

Dr Ramsay: Yes. It depends again on your situation, your context, your risk of exposure, the nature of your job, the nature of your family contacts, and whether or not you choose to be more cautious. We want people to continue to be sensible. If you are in contact with very vulnerable people, you do that a lot and you are having very close contact, you will continue, I am assuming, to take precautions. For example, if you work in healthcare, you will continue to use PPE to prevent infecting others even if you are fully vaccinated. We are not expecting people to stop following all of those restrictions. It is about understanding that nothing is risk free. Obviously, we have massively reduced the risk by vaccinating people both of getting disease and passing on disease, but we don't want people to go in completely the other direction and make it worse.

Q2342 **Katherine Fletcher:** There are these statements that, come the end of the year, the actions of the British public and the amazing vaccine roll-out will have saved tens of thousands, if not more, lives. Everybody has an individual role to play in getting that from a 100% risk to a 10% risk of transmission, because when you add up all those ninety per cents across the population that is a figure that protects us all, including the most vulnerable in society.

Dr Ramsay: Yes, I think that is a fair prediction.

Q2343 **Katherine Fletcher:** That is cool. Professor Harnden, do you want to add anything?

Professor Harnden: What is amazing is how successful these vaccines are really. As Dr Ramsay said, one dose gives 65% protection approximately, but 50% greater on top of that in both transmission and hospitalisation and death. Two doses give 90% protection, and possibly much higher than that in terms of the prevention of hospitalisation and deaths. These vaccines are incredibly good, but this virus is very agile

and will try every way it can to transmit. That is why we need to be very careful because we just need to keep on top of the virus. Of course, we have not even got on to talking about variants.

Katherine Fletcher: That is a very good point. The way I have tried to explain it to the British public in terms of variants is that we are so good at smashing the original version that we are giving all of these multimillion virus particles that are out in the population the biggest kick up the bum to try to find the one way to get through it, aren't we? We are putting an enormous selection pressure on the whole viral genome by our actions. It is worth the British public remembering that, isn't it? Brilliant. Thank you, Chair.

Q2344 **Chris Clarkson:** Thank you to both the witnesses for taking time out today. I want to turn to this idea of a booster shot, which is something the Health Secretary has promised everybody. Are we talking here about guarding against waning immunity, which Dr Ramsay mentioned earlier, or are we talking about defending against some of these new scary variants that Katherine has just been talking about?

Professor Harnden: Both is the answer. We really need to know what the duration of protection is both from natural infection and from vaccination. We do not know that yet because we are in the early days. It is looking like it is long. It is looking very good, but we do not know what the duration of protection is. Also, we do not know quite how these vaccines are going to behave against new variants.

It may be that the vaccines give you such a good protection against the major circulating variant at the moment that they will give you cross-protection. We have a little bit of evidence from some of the trial data in South Africa that the Novavax and Johnson & Johnson vaccines are not quite as good against the South African variant, but we know that they may be much more protective against hospitalisations and deaths. We do need to know that information.

When we come on to thinking about the booster, we need to think about three things. We need to think about who we are going to give it to, what we are going to give them and when we are going to give it to them.

"Who?" becomes an interesting question. We know from other vaccines that immunity rates drop in older populations slightly more quickly than they do in younger populations. We know that older populations are more susceptible to severe Covid. Therefore, do we restrict a booster campaign in the autumn and winter to those first four priority groups—the older population? That is the "Who?" question.

The "What?" question is: which vaccine do we use? There are studies going on about mixed vaccines, because every adult by then will have been offered a vaccine and will have either Moderna, Pfizer or AstraZeneca. Therefore, can we boost with an alternative vaccine? There

are studies going on about this at the moment looking at alternative vaccines.

Which variant of the virus do we need to tailor against? We do not know that at the moment. We know that the major variant in the UK at the moment is the so-called Kent variant, which the vaccines are very protective against. We know that there are small pockets of the South African variant and small pockets of the Brazilian, but they do not seem to be as transmissible. Dr Ramsay can talk about that more. Whether we have a significant problem with the variant in the country at the time we do the booster will be a key question.

The "When?" question is a little bit about when we get the data, but it is also when we have the vaccine availability in terms of supplies.

There are a number of questions that will be addressed on the JCVI over the next number of weeks and months to try to plan for this, but there are still a lot of uncertainties at the moment in that data.

Q2345 **Chris Clarkson:** Dr Ramsay?

Dr Ramsay: I do not have much to add really. As Professor Harnden said, if we had known the vaccines were going to be as good as they were when we talked about this a year ago, I think we would all have been incredibly pleased. We are pleased, obviously. Actually, they are very high levels of protection. In fact, waning may not be happening as quickly as we might have predicted.

When we were modelling it on the flu, we were talking about a vaccine that generally has much lower protection levels, and there you do need to have it every year. The issue is probably more going to come down to variants and the protection against variants as to when we do this rather than the expectation that we are going to see a rapid decline in protection. That is something that we really need to keep a close eye on.

We are just beginning to vaccinate the second doses now, as I said. We hope, we think and we assume—and we will be able to show, I hope—that those will extend protection for several months, if not potentially years. It will be a difficult balance in deciding the best time to boost, because there is no point boosting if you are already protected. It is a waste of money, supply and all those other things. Those are the difficult decisions. If a new variant comes in, there is a different vaccine and our current vaccine is not working, that will be the biggest pressure to boost.

Q2346 **Chris Clarkson:** I can see rather aptly that you have a flu immunisation poster behind you. Is it fair to say that this will basically be like the new flu jab almost? Risk categories will need to get it maybe once a year in order to defend against where the prevalent version is, but not everyone will need one of these.

Dr Ramsay: I think that is most likely, partly because the vaccine is incredibly effective, as I am saying, and there are groups of the

population at particular risk. As Professor Harnden was saying, probably the more elderly and people with underlying conditions are where we are going to be more cautious about boosting more often, perhaps not as often as flu, but certainly in a similar model in picking out people who are at highest risk to receive more regular boosting.

Professor Harnden: It is also important to state one other point. There are studies going on in Oxford at the moment about combining Covid vaccines with flu vaccines. It may be an option that we can combine both the flu vaccine with a booster for the Covid vaccine.

Q2347 **Carol Monaghan:** Professor Harnden, you have just said that the virus is agile and will find any way to transmit. We are hearing from different people that children and adolescents might be the route that the virus transmission takes. We had evidence from Kawsar Talaat, an infectious disease physician at the Johns Hopkins Bloomberg School of Public Health. He said, "Covid transmission is now hottest in younger people. The virus will find ways to survive and spread unless we close off pathways."

Clearly, there are ethical considerations when we look at the vaccination of children and younger people. What is the current scientific understanding on whether they should be vaccinated?

Professor Harnden: That is a really interesting question. Children are important. There are 12 million children under the age of 16 in the UK, and, globally, a quarter of the global population is children under the age of 15. It is clearly a key issue.

At the moment, there are no vaccines approved for under-16s in the UK, although there are trials for the Pfizer going on at the moment in younger groups. The AstraZeneca one, as you have probably realised, has been postponed because of the safety signal, although they are still collecting data on that trial.

The difficulty with this issue is that you are absolutely right that it may well be that certainly older children are transmitters of the virus, although the data on that is still a little unclear. Children have relatively low mortality and morbidity from Covid. A small section of children, maybe those with underlying illnesses and some random ones, get very desperately ill, and a proportion of older children, it has been increasingly recognised, get long Covid. They are not without morbidity, but it is much lower than the rest of the population.

Given that information, you would then be immunising children not for their own direct benefit but for the indirect benefit of others in society. That becomes a really complicated ethical question. We would have to be absolutely sure about both the safety and the efficacy of those vaccines to be able to do that.

Of course, we immunise children from influenza, partly for their own direct benefit but a lot for the indirect benefit of transmission, with a very

successful nasal influenza vaccine. It may be that in the future, as vaccines are developed for Covid, an easier delivery mechanism such as a nasal vaccine becomes possible, or even an oral vaccine, and that it is shown to be very safe and very effective. That might be a very good method for immunising children.

Going back to the key question of what you are immunising them for, whether it is for direct benefit or indirect benefit, if it is predominantly for indirect benefit, safety, efficacy and ethical issues become paramount.

Q2348 **Carol Monaghan:** Is it likely that over the next 12 months we will be having a serious discussion about vaccination of children?

Professor Harnden: Absolutely. Because of the safety issue and the question about boosters, it has not involved a lot of JCVI discussions at the moment, but it will do in the future. Of that I am absolutely sure.

Q2349 **Carol Monaghan:** Dr Ramsay, you look like you want to contribute.

Dr Ramsay: I am just agreeing very much. We are going to be actively discussing this. It will depend on how the pandemic evolves and what we see. At the moment, as Professor Harnden says, secondary schoolchildren seem to be relatively commonly infected but less commonly affected by the infection. Those are the points we will need to see. As more of the adult population is vaccinated, we are naturally going to see relatively more infections in younger people. So it will be the next thing to discuss.

Q2350 **Carol Monaghan:** Thank you. Professor Harnden, with the recent change in policy with regards to pregnant women, could you tell us a little bit about the reasoning behind that? We are now advising that pregnant women do get a vaccine.

Professor Harnden: No. We are recommending that pregnant women are offered a vaccine when they fall into a category that is eligible for the vaccination. That is not the same as saying all pregnant women.

Q2351 **Carol Monaghan:** Sorry, apologies. The previous advice was that pregnant women did not get the vaccine.

Professor Harnden: No. The advice has always been that the risks and the benefits for an individual pregnant woman needed to be discussed before they received a vaccine when they were eligible. The change of advice that we have made is that, because they have been vaccinating a lot of pregnant women in the United States, they have a huge amount of experience of the Moderna and the Pfizer vaccines. So we have issued advice for preference for pregnant women when they are offered the vaccine, and their clinician thinks the risks and the benefits are such, that they should have the choice of an alternative vaccine to the AstraZeneca vaccine. That is the key bit of change of advice.

That is based on the fact that we do not have as much evidence of the AstraZeneca vaccine in pregnant women as we now have with the alternative vaccines. Given that none of the trials initially did any safety

studies on pregnant women, we now have a realtime safety trial that has gone on in the States, and therefore we are able to offer pregnant women an alternative vaccine.

Q2352 **Carol Monaghan:** Thanks. We have minutes from the JCVI meeting on 22 December that concluded there was insufficient evidence to recommend the routine use of Covid vaccines during pregnancy. That would suggest that they would not have been offered it at that point.

Professor Harnden: That is absolutely correct. There was very limited evidence from the trials—well, there was no evidence—of the safety or efficacy of the vaccines in pregnant women. There is no theoretical reason why they should be harmful or why they should not be used. Therefore, we said on the JCVI right from the start that this was a risk/benefit discussion with the individual clinicians.

We were not recommending a policy of all pregnant women or even pregnant women in the risk groups having the vaccines. For instance, you may have a pregnant lady working as a nurse in the ITU and having potentially a lot of exposure, and maybe in those circumstances the risks were such that the benefits of the vaccine outweighed the small but theoretical risk of harm. It was a clear steer from the JCVI that pregnant women could still be vaccinated but only after a discussion about risks and benefits at that stage. The difference now is that we have a lot of experience from the States. We have recommended that, when they have the vaccine and still have the same risk/benefit discussion, it is an alternative vaccine that has been used in the States.

Q2353 **Carol Monaghan:** Thank you for that. You have helped clarify that, which is really useful, but I think there is probably a false understanding among the public that pregnant women were not being recommended to have the vaccine. As a result, are we seeing vaccine hesitancy among pregnant women now, and how are we dealing with that?

Professor Harnden: Perhaps Dr Ramsay can answer the hesitancy question. Certainly, what I will say is that we now have quite a good culture of vaccinating in pregnancy in this country, particularly with the very successful whooping cough immunisations that we have offered pregnant women, and of course the influenza immunisation. The culture of accepting vaccines in pregnancy is pretty good in this country. That is driven often by health professionals giving very clear advice to pregnant women, whether they be midwives, GPs or obstetricians. It is good.

Inevitably, with any new vaccines such as these Covid vaccines, there will be hesitancy. That is to be expected. I do not think there is any more hesitancy than with other groups. Perhaps Dr Ramsay could comment on that.

Chair: Very briefly if you would, Dr Ramsay.

Dr Ramsay: We do not have any particular evidence. Clearly, the change that we are now moving into younger people means that more pregnant

women will be eligible. We will be advising people to make that decision themselves. I have not as yet heard anything particular about hesitancy in that group.

Carol Monaghan: Thank you.

Q2354 **Aaron Bell:** Thank you, both, for your time and your evidence today. I congratulate the JCVI on the preprint I saw the other day, which seemed to confirm that your decision, which was brave at the time, to go to 12 weeks was entirely the right one. You have both been relatively cautious about where we are at present. The risks of variants and immune escape that my colleague, Katherine Fletcher, was talking about are real.

What do you make of the ONS data out today that suggests that over seven in 10 adults have antibodies to Covid in their system, and more like 85% in the groups most at risk from Covid? With a continuing process of vaccination, how close are we to herd immunity, Professor Harnden? Notwithstanding the risks of other variants, how close are we to herd immunity against the main variant we have at the moment—the Kent one?

Professor Harnden: It is an epidemiological question rather than a vaccine question. Herd immunity depends on the R number. The R number is the number of people that an individual with an infection would transmit to on average. It just depends on that. For instance, if you have an R number of 3—the individual transmits to three other susceptible individuals—you would need to vaccinate at least three out of four of the population to stop transmission.

You are right, Aaron, in saying that the higher the levels of immunity within the population the less susceptibles there are, and you are getting much more towards herd immunity. I do not think we are there yet. Clearly, the vaccination programme and higher levels of natural infection will get us pretty close to it. Mary is an epidemiologist, so maybe you should ask her.

Q2355 **Aaron Bell:** I will ask Mary the same question. To follow on from what Professor Harnden just said, notwithstanding the risks of variants, are we not quite close to that point now? That is not to say that everybody should go nuts. Everyone needs to deal with their own circumstances. If they have a lot of contacts or if they have relatives who are still at risk, people need to judge that. Are we not getting quite close to a point where we can put that down to personal responsibility in the same way we do with flu?

Dr Ramsay: I think the ONS data will be probably in the adult population. You have to remember that there are however many million under-18s or under-16s who have not been vaccinated and will not be vaccinated for some time. That obviously will feed into the R. That is how it works for flu, for example, which is why children are more likely to transmit flu as they are more likely to be susceptible because they have

not yet seen the infection. We may not be at that level overall if you included children in that R calculation.

Before the recent variant was recognised, we were talking about 70% immunity to be sort of the level at which one would expect to be able to keep the R below 1 in normal behaviour. You can get away with less if people are contacting each other less. It is a combination of both things. Clearly, as the adult population are more fully vaccinated and we move down to those younger age groups, we will be getting there.

I think the younger age groups are the ones who we know have had higher infection rates because they mix more often, they are out at work, and so on. I do not think we are yet at the level where we are saying that, if we went completely back to normal, R would be below 1.

Q2356 **Aaron Bell:** No, I can see that is not the case. On the other hand, all the lockdowns and all the restrictions were sold to us to protect the NHS and, indeed, save lives. The effect on serious illness and death is so strong that essentially a higher rate among the young, yes, will have some knock-on consequences, but it is not as consequential if R goes above 1 when it is mostly among people who are not at serious risk from Covid, is it?

Dr Ramsay: That is right. That is the point about releasing things bit by bit because, if we begin to see more infections but the connection between the number of infections and the number of deaths and hospitalisations stays separate, that will be very reassuring. It will tell us that we can allow a little bit of circulation in younger people—maybe children, maybe young adults—and still not see the serious consequences of people going into hospital, blocking up the hospitals and causing all the other effects.

Yes, you are absolutely right. That is the whole purpose of the programme. It is just about making sure that we are where we are before we make a change, because once we have opened up it is very difficult to go back, as you know.

Q2357 **Aaron Bell:** I realise that. There seems to be a lot of high precaution about where we go after 21 June and what other things people want to keep in place.

On that note, what steps are Public Heath England taking to prepare for the booster campaign that my colleague, Chris Clarkson, mentioned earlier? What support is needed, if any, to speed up decision making ahead of that? Obviously, the MHRA may need to do their thing with any reformulation of the jab. What support might you need? What preparations are you making, and will it be rolled out alongside the flu jab?

Dr Ramsay: The NHS is the main body that delivers a programme. I think they have already started planning on the grounds that there may be a programme alongside flu, or it may be a programme later. All the

experience they have had of running the Covid vaccination programme has given them a lot of infrastructure that they could potentially use in a revaccination programme. PHE's job is more supporting on the technical and clinical side on the advice and guidance. We support JCVI decision making in saying who we think should be revaccinated. There is a separate piece of work that the VTF are leading on in making sure that we have the vaccine and which vaccine.

All those things are under way. There is still a lot of uncertainty about whether a variant vaccine will be needed; if so, which variant; whether we can mix vaccines; and whether we can give vaccines alongside flu. All these things are under active study now. We have to watch this space a bit. It would be really nice to tell you now that, in September, this many people are going to get vaccinated, but that would be a mistake.

Q2358 **Aaron Bell:** Professor Harnden, on what Dr Ramsay just said, on the mixing of vaccines, how close are we to having a decision about whether we will be mixing vaccines as a matter of policy for everybody?

Professor Harnden: I would not have thought we are going to get the readouts to the immunogenicity studies of the mixed vaccines until early autumn. We are a little way off that.

I agree with you, Aaron. As a GP who vaccinates, we need to know this information and whether we are going to be doing an autumn booster campaign or not. They are such important decisions, and it will be very difficult to make them, I suspect, in time for the autumn booster in September.

Aaron Bell: We need the right data behind it. Thank you very much.

Chair: That brings to an end this panel. We are very grateful for the evidence this morning of our two witnesses. We are very grateful for the continuing hard work that you do, as Aaron just made mention of. Some very important and not obvious decisions are in front of both organisations, including the decision to space out the doses in the way that was done, and that has obviously provided a lot more protection to the citizens of this country. We are very grateful not just for the work that you do but for the weight of the decisions that you take. Thank you to both of you.

Examination of witnesses

Witnesses: Dr Payne and Professor Dye.

Chair: We will now move to our third panel of witnesses. We are going to consider questions of vaccine and Covid certification. To help us think about those issues, I am delighted to welcome Professor Christopher Dye, who is the professor of epidemiology at the University of Oxford and previously director of strategy at the World Health Organisation, and Dr Ruth Payne of the University of Sheffield, who is one of the authors of a Covid-19 report by the British Society for Immunology. Thank you very

much indeed to both of you.

I will go straight to my colleague, Dawn Butler, for the first question.

Q2359 **Dawn Butler:** Thank you very much, witnesses, for coming in today. I want to start with something that Professor Susan Michie said. She said, "The words 'passport' and 'certificate' are ill advised because they suggest a degree of certainty that we will never have however accurate the antibody tests are." She went on to say, "One should not be talking about immunity. We can however talk about antibody level and the risk of getting reinfected or the degree of protection." Do you both agree with that, starting with Dr Ruth Payne?

Dr Payne: Thanks for the question and thanks for the invitation. Yes, they are very difficult concepts to get your head round as to what those types of certificates might mean, whether we are talking about immunity certification or a vaccine certification. The difference is that one looks directly at whether you have those antibody levels and the other is a proxy for immunity in that you have received a vaccination.

We know that although the vaccines are really effective—and we have heard a lot of data on that this morning already as well as previously—they are not 100% effective, and they never will be. There are always going to be parts of the population who do not respond as well to vaccination or who for many reasons do not want to receive the vaccination. Introducing a passport runs the risk of discriminating between those aspects. That is one of our big concerns.

The other thing to say is that, from an immunological point of view, having a clear correlative protection that we can measure and that translates to something meaningful is something we are lacking at the moment as something that is easily measurable. We know that neutralising antibody, for example, in many of the studies has been shown to correlate with protection, but that is not something that can be easily measured throughout laboratories across the country. I do not think there is anyone who is anticipating currently doing an antibody titre of everyone who is vaccinated or has had infection in the country.

Q2360 **Dawn Butler:** That is a big area, is it not? As you say, a vaccination is assuming antibodies by proxy. Thank you very much.

Professor Dye, do you agree with that statement?

Professor Dye: Thanks very much for the question. I broadly agree with what Ruth has said. There are two key elements to your question. One is the language that we use to have this conversation about passports, certificates and so on. The important aspect of that is that we do not use language that discussants immediately become hostile to.

Passports have been antigenic, if I can put it that way, in many conversations. They have been a barrier to having a conversation around the second important part of your question, which is about the facts. The

first point is that I think we need to discuss this in neutral language. The terms "passport" and "certificate" have been difficult. A word like "pass" is more neutral. We should try to have the conversation in neutral terms.

The second part of your question is the facts that lie behind this language, which is what we really need to get to. With regard to the performance of vaccines, we know, and you have heard extensively in the previous session, that vaccines are very good but not perfect in carrying out the two functions that we really want—that is to protect individuals and then to protect others who might be infected by those individuals, in other words, to stop transmission. We now know that vaccines are not perfect but rather good at doing both of those things.

The question with regard to certification or use of passes is: do vaccines now give us greater freedoms than we would otherwise lose through the disadvantage of discrimination, which is the word that some people have used? "Discrimination" is a loaded word in its own terms. The question about using passes is whether we now have the option to explore those greater freedoms that vaccination gives us and that there is not too much of a downside in terms of discrimination—let us use that word as others have used it.

Q2361 **Dawn Butler:** Thank you so much. Dr Payne, freedoms seem to be restricted if we have these vaccine passports for people over 30 and not under 30 because they have not had the vaccines yet. I know that you sit on SAGE. Have there been any discussions about the discriminatory element to those people under 30 when making further decisions?

Dr Payne: I should correct you and say I do not sit on SAGE.

Dawn Butler: Apologies.

Dr Payne: So I do not know what the discussions have been relating to that. Certainly, there are a lot of discussions going on, and there is plenty in the literature, for example, by wide-ranging discussions from ethicists and clinicians, and plenty to be found in the media too about concerns that are going to be faced either one way or the other. There are lots of people who are very keen to have a pass in order to open up freedoms, completely understandably.

I think everyone is fairly fed up with lockdown and the restricted living that we have been in. But, equally, there are others with serious concerns about what that might mean and what it means for their rights and their freedoms of choice.

Professor Dye: May I add to that?

Dawn Butler: Yes, of course.

Professor Dye: What is important in the way we use terminology here is that, if we refer to a pass, we are embracing not just vaccination as a

way of issuing a pass, but other alternatives as well. As you rightly point out, younger people have not had the chance to be vaccinated yet.

If in a particular circumstance, and we can discuss whatever those circumstances might be, you provide alternatives—and two are frequently discussed at the moment: a negative PCR test or a negative rapid antigen test, or a previous evidence of infection—we would not necessarily insist on vaccination as being the criterion. What would be insisted on, should passes be used, is one of those possibilities being satisfied. That, therefore, would allow a pass to be open to people of any age in principle.

Q2362 **Dawn Butler:** Great; thanks. In that vision, Professor Dye, would that include tests for antibodies to be included as part of that pass?

Professor Dye: In my view—and Ruth may want to comment on this—the test for antibodies is the weakest element of the options that have been proposed. The three options are vaccination, negative PCR test and negative rapid antigen test. Evidence of antibody is a weak link, I think, because antibody per se does not guarantee immunity.

Ruth spoke a little earlier about correlates of protection. I think there is still a great deal of debate in the immunological and medical world about what the presence of antibody signifies. It does not necessarily signify complete protection. We know, for example, that people can be reinfected either from a natural infection or reinfected even having been vaccinated, more rarely. Testing for antibody is the weak link in a pass or a passport process at the moment.

Q2363 **Dawn Butler:** Does anything guarantee immunity?

Dr Payne: No.

Professor Dye: I am not an immunologist, but my broad understanding of immunology as a background to what I do in epidemiology is that the immune response to coronavirus infection is very broad-based. It is not only about antibody. It is about T-cell or white blood cell responses—T-cell responses as well. Not everybody responds to infection in the same way.

There is a broad range of immunological responses. That broad range of responses is what adds up to protection, not simply antibody alone. If we are measuring solely antibody, that will not be a strong enough indicator of protection, and, therefore, I think there is general agreement in the immunological world that we do not yet have a good enough correlate, as it is called, of protection.

Q2364 **Dawn Butler:** Dr Payne, does anything guarantee immunity?

Dr Payne: Nothing is 100% and no test is 100% effective. One of the issues with the antibody test is that at the moment there are huge numbers of different types of antibody tests being used. You cannot

compare across studies or across countries even in terms of what antibody levels or results mean. There is a difference between what we call qualitative antibody tests, where you basically get a positive or negative, and a quantitative test, where you might get a titre. I know that there is work ongoing to see whether we can use that antibody titre quantitative readout as a proxy for a response to either infection or vaccination, but it will not be perfect.

There are people that we know following natural infection who do not have a detectable antibody response. It does not mean that they do not have protection. Although you have serum antibodies, which we measure in the blood, what we are trying to induce by vaccination and what happens by natural infection is creating these cells called memory cells, which are then what react rapidly when you are re-exposed to the same infection. That is why you tend to see a higher response in antibodies after a second vaccination because you are already primed; your body has those memory B-cells to make a rapid antibody response.

We know from some of the studies even in healthcare workers that, those with very low or even undetectable antibody levels after natural infection, after a single dose of vaccine have very high antibody levels. They have memory B-cells there. They have immunity, but we would not have detected it on an antibody test. I agree that nothing is perfect.

Having said that, the same goes for the PCR tests and the lateral flow tests. They are not perfect tests. There are always going to be results that are wrong for one reason or another. The reliability of those tests varies depending on many things, such as how they are taken, the kits that are used, and what the background rate of infection is in the population. Those can all vary the reliability of the data that comes out of those. There is not a perfect way to measure anything. We have to go with what the best option is for the most people.

Q2365 **Dawn Butler:** I agree. I have a couple more questions, Chair. What do you think the best option is, Dr Payne?

Chair: Very briefly, because we have a few more questions to get through.

Dr Payne: I agree with Professor Dye that there needs to be a combination of approaches and that there is not a one size fits all. We need to have options for those different parts of the population—those who have been offered vaccination versus those who have not, and those who have had infection versus those who have not.

Q2366 **Dawn Butler:** Big Brother Watch has reported today that Michael Gove will make an announcement later today on the introduction of domestic Covid-status certificates. What do you think about that, Professor Dye?

Professor Dye: The use of passes or certificates has been discussed both internationally and nationally or domestically. Different countries have taken different views about that. Broadly speaking, my reading of

public opinion not just in the UK but around Europe, for example, is that people are more ready to accept passes and passport certificates for international travel, but less ready to accept them, under some circumstances, for domestic use.

I think the debate about domestic use will come down to balancing the advantages and disadvantages. It is also going to be a question of who gets to choose—whether it is the Government that make a decision or whether it is, for example, individual businesses that get to make a decision.

It is difficult—impossible, actually—to say that under all circumstances or no circumstances passes should be used domestically. I think we need to consider each of the sets of circumstances under which they might be used. We could go through the examples, but there are going to be a range of examples where people will readily agree that they should be used—for example, large congregations of people, or live events such as sporting events. There will be other circumstances where they clearly should not be used. That is a certification process that prevents people from gaining access to the essentials of their lives—for example, food shopping in supermarkets. That clearly is not appropriate. But live sporting events clearly is much more appropriate. We could discuss the advantage of other examples.

Q2367 **Dawn Butler:** That is a good point. Dr Payne, before you answer, it is also rumoured that under-30s will be asked to take two tests, and if those tests come back negative they can apply for a freedom pass to go about their business the next day. In that answer of the possible announcements that are going to be made today, it would be great to get your expert opinion.

Dr Payne: Other countries are trialling out this type of approach as an alternative to having immunity certification either from previous infection or from vaccination where you are allowed a 48-hour pass because of two negative tests. How well that will work and how it will be instigated or monitored is beyond me. It is certainly not something that I have been involved in discussions about.

Dawn Butler: Thank you both very much. It was very informative.

Q2368 **Aaron Bell:** Thank you both very much for your evidence today. I think a number of Members of Parliament are still reserving judgment on vaccine passports, so what you say today will, I am sure, be read and listened to by all of those.

On that note, do you see vaccine passports as a short-term measure to speeding life back to normal, or is it something that you could envisage being in place in one form or another for a number of years, given the global pandemic will presumably take quite a number of years to blow out, if it ever blows out?

Professor Dye: I think vaccine passports, certificates or passes, or whatever you like to call them, will be a very helpful short-term measure. I think they are going to be in place for the long term as well, for one reason on the latter part. Covid is not going to go away. It will be endemic around the world. It will keep resurfacing.

Just as we have had yellow fever passports for years and years—let us call them that; that is what they are, and they have been used for other infectious diseases as well—I think we are going to have Covid passports too. I think they are here for the long term. We are finding our way forward on these both internationally and domestically. The system will settle down nationally and internationally into a long-term form of certification and protection.

Q2369 **Aaron Bell:** Dr Payne?

Dr Payne: I agree. I think it is really important to work internationally on this, particularly for something that is considered to be longer term. Once something is introduced and it has been used for several years, it is very unlikely that it will be retracted.

I know that, currently, the WHO on its last position statement has not encouraged the use of passports yet. It is still waiting on further details about the reduction of transmission and the impact there might be on equity, particularly for moving around the world, in countries where they do not have as ready access to vaccination as we do, for example. We are very fortunate in that almost 20% of our entire population is vaccinated compared to 3% of the world population. We are not on an equal footing. I think that has to be borne in mind.

Q2370 **Aaron Bell:** Going back to Professor Dye because he brought up yellow fever, could the existing infrastructure around the schemes for yellow fever be applied to an international Covid passport? What might need to be changed or adapted? Is that a working model basically for how international Covid certificates could work?

Professor Dye: I think it is a working model in principle, but the implementation of it has to be greatly updated. Yellow fever certificates, which have been around for decades and went hand in hand with other certificates like plague, typhoid and other things in the past, were pre-digital, if you like. We now are clearly operating in the digital age. We are very likely by preference going to be using apps, cell phones and related technologies. That is not necessarily to exclude paper-based certification systems, because they will be required in some places for some people, but I think it is going to be a digital drive forward on this.

The background principles of certification are there. There is a precedent for doing this, but the way in which it is implemented will have to be greatly updated for the times that we now live in.

Q2371 **Aaron Bell:** Thank you. Looking at the domestic situation, I have to say I am worried by the idea that we might be living with domestic passports

for any prolonged period of time. What could the UK learn from other countries' approaches to domestic Covid-19-status certification? In particular, the United States has said it will not use it. However, the CDC guidance has suggested that fully vaccinated people can meet without masks or social distancing. That is an alternative approach. It requires some personal responsibility once you know your vaccine status changes. What can we learn on the domestic passport front from international comparisons? We have Professor Balicer from Israel joining us shortly.

Professor Dye: I think you are going to hear a number of interesting things about Israel later. Let me just make a couple of remarks before Ruth does.

Regarding the United States, we are getting very mixed messages at the moment. The statement from federal Government, from the White House and so on, is that passports will not be used, and yet CDC guidance—and you can read it on their website—specifies things that people who have been vaccinated can do.

In the last 24 hours, there was a discussion about vaccinated people no longer having to wear masks. Essentially, that is moving towards or carries the implication of using a certification process. I think there are mixed messages coming out of the US at the moment. Some people might find that confusing. I hope such mixed messages will not emerge in the UK because I think that will be confusing.

The other thing I think you will hear more about with regard to Israel—and this is really important—is that there is a good deal of testing and experimentation that needs to be carried out with regard to the way in which passports or certificates are used. We are going to learn a lot about what is acceptable, a lot about the way in which they are implemented, and a lot about whether they really are successful in preventing infection of individuals or stopping transmission to other individuals. I think we have to embrace the uncertainty and be prepared to carry out those tests and trials in the way that they have done very usefully in Israel, which has helped them test the boundaries of what is publicly acceptable and what is effective with regards to public health.

There is lot to be learnt from Israel but also other countries in Europe. Denmark is rolling out certificates. I am speaking to you from France where I live. France has begun to do it and will increasingly do it. We have to roll these things out. We have to put in place the appropriate monitoring and evaluation systems so that we can really see what works rather than asking people in advance hypothetically what they think about a passport system of which they have no prior experience.

Q2372 **Aaron Bell:** Before I turn to Dr Payne, could I go back to that US example you expanded on? If we move to no formal restrictions after 21 June, but we are still talking about social distancing and masks, and we then make that a matter of personal responsibility, is that not more analogous to the US situation?

Professor Dye: The implication of what is being said by the CDC in the United States is that, for people who have been vaccinated, they then can do the following. In other words, doing the following like not wearing masks, not social distancing or congregating in large numbers is conditional on having been vaccinated. That could be left down to personal choice or there could be circumstances under which some sort of certification procedure is needed to check that that is so.

Q2373 **Aaron Bell:** It could be made into advice rather than law is what I am suggesting.

Professor Dye: Yes, and I think that is one of the things that will really need to be put to the test. Can people be trusted, if I can put it like that, to behave in a way that is consistent with their own personal safety and the safety of the public at large, or is a stronger regulatory framework required?

I think, as I alluded to earlier, there is not going to be one simple answer to this domestically because the consequences of failure will be different under different circumstances. If you have an outbreak among young children in school—as we very well know, children are much less susceptible—the consequences of that might be rather less serious than, for example, the consequences, as we know, of an outbreak in care homes inhabited by elderly and vulnerable people. In the latter set of circumstances, you would want greater strictures and greater guarantees that the health of those people will be protected. I would not leave it up to individuals to make their own decisions. I would be very strongly inclined to regulate that very firmly because the costs of failure are too great.

Q2374 **Aaron Bell:** Thank you, Professor. I want to ask the same to Dr Payne about any domestic lessons from international comparisons above and beyond what Professor Dye has already expounded upon.

Dr Payne: I do not have much to add on the use of passes except for this. There has been a lot of talk about the yellow fever certificate as an example of international requirement, but there are other examples where specific vaccination requirements are put in place for specific events.

I am thinking in particular of the Hajj and the introduction of meningococcal certification of vaccination as a requirement of entry into the Kingdom of Saudi Arabia. That is because there were several large outbreaks of meningococcal disease—it is a vaccine-preventable disease—and around 2 million pilgrims attend that in a normal year. There are other examples to look at internationally about specific situations in which vaccination passport certificates or measures are taken in order to mitigate risk in certain circumstances. That is obviously a huge number of people and a measured risk, but a much lower risk in number of cases than Covid would be, for example.

Aaron Bell: Thank you. That is a very interesting example.

Chair: Finally to Graham Stringer.

Q2375 **Graham Stringer:** Professor Dye, for the last 50 years, every flu season people have died and the death figures have been between 5,000 and 85,000. As we get closer in this country to herd immunity as more people are immunised or get some sort of immunity because they have had the disease, is there really a difference between flu, for which we have never required an internal passport or a certificate, and Covid? What would be the case, if we got to a very low level of infection but it is endemic, for any kind of internal certification?

Professor Dye: First of all, with regard to influenza, I think the up to 85,000 deaths a year should not be regarded as generally acceptable in the first instance. Many of those deaths could be prevented if we had higher coverage of flu vaccinations.

One of the first things we should do is be reminded that we should attempt to increase the coverage of flu vaccination among people who are vulnerable rather than simply accepting that as tolerable.

Q2376 **Graham Stringer:** My point really is that, although that has happened and there have been different levels of effectiveness of the campaigns to get people immunised against flu, we have never required a certificate to show that you have had that injection.

Professor Dye: Yes. That goes to the second part of what I wanted to say, which is that Covid-19 is a far more serious illness on a per capita basis than is influenza. As is widely now known, the risk of death and serious illness is substantially lower for influenza than it is for Covid.

The complications from Covid—I am thinking about long Covid, but not only that—are also serious. Covid is a much more serious illness. We are more concerned with regard to Covid not about personal protection but also about transmission to others.

In the context of influenza, as you heard earlier this morning, there is concern about using vaccination to prevent transmission, for example, among children in schools. Primarily, it is fair to say—Ruth will comment on this—that the influenza vaccination is largely used to protect among older people the health of those people rather than stopping transmission, and, therefore, there is less need for certification.

Q2377 **Graham Stringer:** Thank you. Dr Payne, what are the technical issues about producing a Covid-status certificate? Would it be easy to do? Is it difficult?

Dr Payne: As to the available technology, I believe that many groups are already working on it and it is being researched at an international as well as a local level. I think the key concerns that have been raised about it are obviously how much data will be available through that in terms of

medical and sensitive data, who will have access to it, and how secure it will be.

I think all those things are legitimate concerns that will need to be addressed. That goes back to what Professor Dye was saying about public involvement in the discussions and in the roll-out in what is acceptable and how these things are developed going forwards in order for them to be successful, because they have to be acceptable if they are going to work.

Q2378 **Graham Stringer:** Thanks. Do you think any system could take account of both new variants—a change in how dangerous the virus was—and booster vaccinations? Do you think you could have technology that would be flexible enough to deal with both sides of that equation?

Dr Payne: I think that is the great advantage to digital technology over the old paper-based system on top of the higher risks of fraud and so on that have been mentioned. If it is linked to vaccination records in terms of booster vaccinations, that could obviously be updated.

As to variants of concern, we are in very early days in regard to the real-world effectiveness of vaccines against those. We have laboratory data about how well antibodies produced by vaccinated individuals respond to those different viruses, but we do not have a large outbreak, thankfully, of other variants certainly within the UK. Other research is going on across the world to look at those and will emerge. I think we are too early to read too much into that as to what impact that will have on a pass, for example.

Q2379 **Graham Stringer:** One factor that would affect the effectiveness of having a Covid-status certification would be public resistance to it for civil rights reasons and access to personal information. What do you think would be the best way of measuring public resistance to the introduction of a Covid certification scheme?

Dr Payne: I think we need to involve the public in those discussions and do the studies in order to see how acceptable they are, what the concerns are, and what measures can be taken to try to produce the information that the public needs in order to reassure them that they are not a risk of huge data leak or their medical records being available to their employer, potentially.

Other examples are being given of where they might be used in going to sporting events. We have to think about what data is going to be available through them and who is going to have access to them. That has to be really clear to people for those to be acceptable.

Professor Dye: Very briefly to add on that, I think it is important to evaluate public opinion and the way it changes through time. We have seen already very profound changes in the United States, for example, through willingness to be vaccinated. Right at the start of this pandemic when vaccines became available, vaccine hesitancy was very high. It has

now fallen to substantially lower levels as people have seen the effect of vaccines, the safety of vaccines, and the threat of the pandemic. Public opinion will need to be monitored and tracked over time.

Q2380 **Chair:** Thank you very much indeed. Just to finish on that point, Professor Dye, obviously other countries are facing the same questions that we are asking today. In your estimation, do you think public opinion might change if it were the case that, for example, the EU is about to adopt a digital green certificate that other countries have? Perhaps if we have all the advantages of being ahead of the world in terms of vaccination but then lose out because we are not able to unlock ourselves when other countries do, do you think that might be a force that might have an impact on public opinion, if that is not too leading a question?

Professor Dye: Yes, absolutely. I think what lies behind all these issues that we are discussing here is how people see the pros and cons of vaccination. There are advantages and there are disadvantages to a certification process, and people will be constantly evaluating those in their minds.

With regard to the international point that we raised right at the start, clearly the UK cannot make decisions in isolation here. What is on everybody's minds at the moment is where they are going to go on holiday this summer. The certification or the pass system that is generated clearly has to be an international one. The UK will develop its own opinions and its own views, but it will have to take notice of what is being decided internationally if this certification system is going to work.

Q2381 **Chair:** Thank you very much indeed. Finally, Dr Payne, do you have anything on that? Do you think international experience will inform what will be regarded as needed or tolerable in this country?

Dr Payne: I think it is really important to work internationally. I think the other aspect to think of and the other aspect where international collaboration and leadership is needed is that there are huge numbers of vaccines available globally that do not all work in the same way. They do not all have the same efficacy. They do not all have the same data available internationally in order to judge and compare them.

The other aspect to consider is that what one country might accept as okay for their vaccines certificate may not be what another will because they may base it on the vaccines they have used in their roll-out programmes. That is where it is important to have an international overview of this, where all the vaccines that are available and are being used internationally can be assessed and looked at in terms of this.

Chair: Thank you very much indeed, both of you, for your evidence today. As Dawn Butler said, these are matters that we expect to come before Parliament one way or another, possibly even imminently, so it is incredibly helpful to be able to pick your brains on this matter and benefit from your learning and experience. We are very grateful for your time

with us this morning.

Examination of witness

Witness: Professor Balicer.

Chair: We now come to our final panel—a panel of one. We are delighted to have Professor Ran Balicer, the chairman of Israel's National Experts Advisory Team on the pandemic response. I guess we might say it is the equivalent of SAGE in in this country.

We are very interested, as I think you may have caught from viewing the previous session, Professor Balicer, in the experience of Israel, obviously with a very strong record in terms of vaccination, which has been accompanied by some measures on vaccination certification or other terminology, which varies. We have some questions on this. I will go straight to my colleague, Mark Logan, for the first question.

Q2382 **Mark Logan:** Professor Balicer, thank you very much for making the time this afternoon. For the layman or laywoman out there, what is the purpose of the green pass, and how is it used?

Professor Balicer: Thank you. It is a pleasure and a privilege to be speaking to you all today. The key aim of the green pass in Israel is to provide, for those people who are interested in participating in activities within high-risk settings, and especially high-risk indoor settings, an opportunity for safe participation in such an event, because, as we all know, even if you get vaccinated or if you are recovered, you are not fully immune and you are not 100% able to withstand a potential infection, a symptomatic infection and severe infection. There is residual risk. Especially for some of the people within the highest risk groups, when they go out and participate in a such an event that takes place in an indoor setting, there is a residual meaningful risk that needs to be tackled.

The green pass rules allow these people to go into a restaurant or a concert hall to participate in some of these high-risk activities with the lowest risk possible for them of contracting Covid-19 and suffering from its consequences.

Additionally, it helps us make certain that mass dissemination events within these potential areas will not occur in practice. In a disease that tends to be transmitted not only by a gradual person-to-person infection but in some events a higher number of people are infected in a single event, they usually happen in those high-risk indoor settings, and they are thus controlled through this measure.

Q2383 **Mark Logan:** Professor Balicer, what have been the major challenges so far with implementing the green pass system?

Professor Balicer: There are different types of challenges, some of which are technical: trying to get an app that is easy to use and allows

fairly simple non-digitally literate populations to take part in; to create an alternative, which is a QR code that you can print for yourself for people who do not have smartphones—not everybody has smartphones; to provide businesses with the means of actually being able to ascertain that the person coming in is indeed who he claims to be and that it is his green pass; and to help promote adherence to the rules associated with the green pass, because if businesses do not adhere to the basic rules this is, of course, meaningless.

Mark Logan: Thank you very much, Professor Balicer.

Q2384 **Katherine Fletcher:** Professor Balicer, I am very grateful for your time. Thanks very much for coming to speak to us.

It is an idea that is not without controversy. The idea of giving papers to somebody is something that lots of people instinctively resile from. Could you give us a bit of insight into the scientific considerations that were made to justify the imposition of this, because it is an erosion of liberty in some respect?

Professor Balicer: The situation that we were in was a little different from where the UK is right now. We were, at the time that all of this was deliberated on, exiting our fierce lockdown that was several weeks long and had only partial impact. We had witnessed a tremendous wave of infection and severe morbidity caused mainly by a dramatic increase in the B.1.1.7 Kent strain that was pretty horrendous in its impact on the third wave that we have seen. It was very difficult to contain it even with a full lockdown, which is something we had not seen before that specific wave.

At that point in time, because we had vaccinated a good proportion of the population—over 40% of the population—we knew that the vaccination rate was very high. We took a leap of faith and opened the lockdown, and started the gradual process of opening up the economy despite what were at the time very high rates of ongoing infection. In this, graduality and safety measures were key to make sure that we did not overstep and we did not have a resurgence.

In a setting where the key variant is a highly infective and more problematic variant, you do not want to see resurgence as you go one step too far. So we had to have a gradual process.

One option was to postpone all of the high-risk settings to later on. There is no need to open, for instance, indoor eating where you do not have any masks and to bring 70 or 80-year-old people into a closed room all cramped up together. We will just postpone it. In all of our previous reopenings, we always postponed these high-risk settings to the latest stages, and in many instances we did not even get there, because, by the time it was time, the next wave was already coming in.

The economy really needed revival at that point, and we needed to find a compromise that would allow us to open the economy quick enough but

to do it in a safe manner that would not jeopardise the achievements both in public health and in the economic opening. This was deemed to be a proper, balanced approach, which said on the one hand there is infringement of some of the basic things that we want to preserve but, on the other hand, the measures are done in the most appropriate way to reduce to the minimum the burden that it creates, on the one hand, and allows public safety and public health to be maintained while opening those businesses.

Basically, it was hailed by everyone. When you compare it with the other option of postponing opening the restaurants, all these activities and concert halls for four more weeks, anybody would opt in to this. If we were in a different position where all of these were already open and we had to put it as an additional restriction, I guess it would have received a different traction and we would have had a different type of negotiation with the public and decision makers on that.

Q2385 **Katherine Fletcher:** Understood. Do you know what impact it has had? Has it succeeded in its aim of allowing a selective reopening of the economy without spiking case rates and hospitalisations, and, tragically, deaths?

Professor Balicer: Tremendously so. As we look at the outcomes, by now we have seen a hundredfold reduction in overall daily cases. We have gone from 10,000 cases per day to less than 100 cases per day.

Q2386 **Katherine Fletcher:** Do you attribute that directly to the green pass system?

Professor Balicer: It is impossible to attribute every specific proportion of the achievement to the specific measures. How much could you attribute to the direct protection of the vaccines? How much can you attribute to the indirect protection of those vaccinated and those who are unvaccinated, and what is called an indirect protective effect? How much of it comes from maintaining social distancing? How much from masks indoors? How much from masks outdoors that are now not even employed any more? How much from the green passes? How much from what we call the purple permits, which means the basic rules of conduct when you open a setting and you have to maintain social distancing and basic hygiene rules? It is a composition of all of these at once, and it is practically impossible and scientifically impossible to tease them out.

Q2387 **Katherine Fletcher:** I accept that, but you can understand why I am asking the question while we are going through our own considerations. Have you learnt anything? Is there anything you would do differently that you would say to us? Are there any changes you are going to make to your system now that you have it up and running?

Professor Balicer: First, let me just say in reply to your previous question that I can say on a positive note that we have not seen an outbreak in any of these settings where the green passes have been employed. Even when we have had quite a significant amount of daily

infections—not at this point in time when it is much more non-existent—we did not see something that was considered to be a complete breach of what safety the green passes should have afforded. It seemed to have done the trick in protecting people in those settings.

As to the question of what we would have done differently, we are trying to improve as we go. As the numbers are continuously decreasing, we introduced into the green pass zones additional easement of restrictions. For instance, starting today, children who have had a negative test in the last three days will now be allowed to enter the green pass zones despite the fact that they officially do not have a green pass because they are neither vaccinated nor recovered. This is something that perhaps would have been an excessive risk to have done a month ago when community dissemination was very widespread, but it is acceptable today when the a priori risk of these children being infected is smaller. This is all a balancing that you need to do judiciously and change over time as the change of the settings takes place.

Q2388 **Katherine Fletcher:** You are talking about giving the ability for the businesses to police those green pass zones. Is that how the system is set up? It is the businesses that are checking people in and it is the businesses that are allowed to effectively say, "Your name's not down. You're not coming in."

Professor Balicer: Indeed. This is part of the permit of the business. They have to adhere to it, otherwise they might have some questions to answer from the local authorities. It is not that we are sending inspection teams to do the checking. It is the responsibility of the business of who comes in, and it should be in their interests to allow the people who come in, trusting them to keep them safe that they are actually doing this, in the same way that they need to make sure that they do not serve food that is not used in a hygienic way or in any other means that are supposed to maintain public health in their establishment.

Katherine Fletcher: Understood. Thank you very much for your time.

Q2389 **Andrew Griffith:** Thank you, Professor. Is there a sunset clause? Could you give us your view as to at what point the green pass is deactivated?

Professor Balicer: We had a meeting of our advisory committee last evening and we discussed for three hours or so whether and when we will have a sunset clause on that. The overwhelming opinion was that at this point we could not have a sunset clause. We think that this will be probably one of the last things to survive in the overall recommendations that we have, because it is the most strongly ingrained in public health basic sense that you take the highest risk of all settings and you keep them last in order to keep them safe. From everything we know about this illness, it tends to be dramatically disseminated through mass dissemination events.

There is the K coefficient that determines whether a disease is slowly propagated one by one or through mass dissemination events. This disease tends to be high disseminable in those mass dissemination events. When you control the settings that are probably harbouring many of these multiple transmissions and you control them, you keep the highest level of safety. Above and beyond that, I think that it allows a higher percentage segment of the population to participate in activities that otherwise they would not have done because they would be fearful to do them in indoor settings. By keeping that and allowing them to participate, it is helpful for everybody involved. At this point, we did not find—

Q2390 **Andrew Griffith:** We heard clearly from previous witnesses as well that we were going to live with this for a significant period of time. Is it fair, therefore, to assume that once introduced this will have a degree of permanence? Why not then, having introduced it, go forward and attach other medical requirements to it? We heard from a previous witness their concern about the fact that there were unnecessary deaths from influenza. Surely, there would be an equally strong case to mandate an influenza vaccine. My final point is at what point does one know one has gone too far?

Professor Balicer: That is a very fair question to ask. I do not think there is a permanence to it. Opinions will change as some of the things that now have a lot of question marks will have exclamation marks at some point scientifically and otherwise. We are still living in a mist in terms of our ability to answer key questions. How effective is the vaccine in stopping transmission? We have some preliminary evidence, but we do not know for sure. How much residual infection happens by kids through kids? What is the meaning of that in the ability of different currently existing variants of concerns and others that will emerge in being able to transmit, and how likely will this scenario be?

As more and more answers to these questions become scientifically clear, we will be able to take more difficult decisions and maybe relax additional things that we are doing right now. It is not permanent. On the question, "If you are doing it for this pathogen, why not for others, because they have a detriment to public health as well?", I would say that it amounts to the question of how detrimental the impact of the mistake will be.

By looking at some of the countries that are now suffering dearly, we understand that there are several settings in which things can go wrong—different variants can be one—and this gives you some kind of safety. When the variant is introduced it will be problematic. It will have a limited rate of dissemination. That is the first point to your question.

The other point is that the residual risk that remains for those unvaccinated people and those at risk still remains larger than it is for influenza. For influenza, you can vaccinate in order to reduce your risk dramatically. If you choose not to, that is a different point.

Q2391 **Aaron Bell:** Thank you, Professor Balicer. You said earlier that the green pass scheme had been widely welcomed. I appreciate you are a clinician and not a politician, but there must have been some political objections beforehand and there must still be some now. How much did the introduction of the scheme essentially remove some of those objections? In the same way that once we got vaccinating we saw vaccine hesitancy reduce, is there green pass hesitancy in Israel, and to what level is that there in the political system?

Professor Balicer: In the public I am sure there is. There is a subgroup of the population that resists everything associated with Covid-19 control for various reasons: disbelief in the severity of the disease; resistance to the vaccination; resistance to the state's intervention with personal freedoms; and others, which I do not agree with, but I respect that there is a segment of the population for whom these are their beliefs and they are acting upon them.

I am sure, as they were very vocal, that they were not happy with these green pass measures as they were unhappy with everything else from vaccines and in other aspects. There is a segment, but the overall echoing response was a resounding affirmation of its importance and understanding how it is of benefit for everybody involved.

In the political setting, it is difficult to grasp how different the point in time was at that time. These were considered bold, risk-taking behaviours by the Ministry of Health, unprecedented in different responses of the ministry and others to the risk associated with resurgence.

When we took that decision, it was actually going above and beyond, and taking a leap of faith in both the vaccines and the adherence to the rules, opening things that have been closed for months, sometimes for over a year. I truly can say that it was very much welcomed because it allowed us to have many of these interventions early. If we wanted to do this now, I would imagine that we might have had some different discussions.

Q2392 **Aaron Bell:** Thank you. That was my next question. The situation in the United Kingdom—I am not sure how familiar you are with our data—is that the overall rate among the English population is about 24 per 100,000 at the moment. We are not in the position Israel was in when you introduced this.

Would you recommend that we consider implementing all or some aspects of the green pass in the UK on that basis if that is our current background rate of Covid, 25% of the population have had both vaccines and about two thirds of the adult population have had one dose of the vaccine? Would you recommend in our situation that we consider implementing your scheme?

Professor Balicer: I think that would be very difficult to do. It is difficult to recommend because the decision is really very much setting-specific both in terms of what the public and the local values are, and in

balancing the risk and how risk averse the Government and the decision makers are if something going wrong, as well as the previous dynamics that were witnessed as disease came and receded and came back again. It is a lot of local experience with how this will be accepted, how much risk people are willing to take and the fine tuning of how protected the population is with one dose at this point: first of all, in view of the existing strains and variants, and with the potential of additional strains that we are now seeing, which raise some questions about whether we will have to address a slightly different reality than we are seeing right now when the wrong variants emerge.

Q2393 **Aaron Bell:** I see some concerns have been raised in Israel about the green pass being issued too soon after vaccination. My understanding is that you can issue it after the second dose. In Britain we are having 12 weeks between doses, so that might be problematic if we were to look at this sort of a scheme.

Obviously, there is a large degree of protection given by the first dose as well after two or three weeks once the antibody and the immune response has kicked in. What is the most appropriate time to consider issuing a vaccination certificate based on the scientific evidence, in your understanding, bearing in mind that we have the 12-week gap in the UK?

Professor Balicer: Again, this becomes a sticky issue because there are different vaccines used in the UK and each one of them has its data to suggest the exact vaccination effectiveness in different timeframes and depending on a single or two doses. It is a complex situation to try to condense it all together into a single recommendation.

In Israel it was pretty straightforward for us. We wanted people in those indoor settings to feel safe, and in order to feel safe we knew that there was a marked difference between the first dose and the week after the second dose. Per protocol, a week after the second dose you have high enough protection. This was deemed the appropriate approach. We have had people claim that it is worth while waiting one more week after the second dose because then the level of protection seems to be even higher. This is where risk management comes into play. We said that that might be true, but what you get a week after the second dose is good enough.

This is something that the scientific community and the professionals need to weigh together and see what level of risk is deemed acceptable, communicate that to the public, and make the decisions appropriately.

Aaron Bell: Thank you very much for your time. It has been very helpful.

Q2394 **Dawn Butler:** Thank you very much, Professor Balicer, for joining us today. Can I just clarify something? You said that the green pass is for high-risk activities. Are they high-risk activities indoors or outdoors?

Professor Balicer: Most of the settings that are included in the green passes are indoor settings—restaurants, conference halls, concerts, shows, et cetera. There are some specific outdoor settings that are included, and they are also included in the green pass approach—sports events, et cetera.

Q2395 **Dawn Butler:** Great. You also touched on people needing to get negative tests to go into the green zone. How many negative tests over what period of time? Could you just talk us through that a bit, please?

Professor Balicer: Until now, you could only go into a green zone if you have performed a rapid test upon entrance. Past tests were not considered appropriate in order to do that. We are modifying that rule now, actually today, because we deem that the overall morbidity risk is low enough for us to say that if you had a negative test three days ago it is good enough for you to come into the green zone today.

In practice, the entire country is green right now. Except for specific localities, morbidity is very rare. The overall risk is low enough for us to take this additional step. If we had high dissemination right now in the community setting, this would not have been done, but with the current dissemination rates it is a fair enough risk to absorb.

Q2396 **Dawn Butler:** Did you meet Michael Gove when he visited Israel?

Professor Balicer: Yes.

Q2397 **Dawn Butler:** What was the area that he was most inquisitive about?

Professor Balicer: I am not sure that is relevant to the talk today. I will leave it at that.

Dawn Butler: That is interesting. Thank you very much, Professor, for joining us.

Q2398 **Chair:** Thank you very much. Very good try, Dawn.

We are obviously very grateful for your evidence today and very interested in your example. For the record, for people who might be watching this or our colleagues in Parliament, summarise for us the experience of a citizen of Israel in terms of getting the green pass. What happens? How do you acquire it?

Professor Balicer: There is an app on your cell phone. I can actually show you how it is done. *[Witness held up cell phone.]* You operate it on your smartphone. As it comes up, what you need to do once—but sometimes you need to renew it—is you hit one of the buttons and you ask for a green badge. You put some of your personal details in there. It verifies this information with the central repository. The next thing you see is this little moving green video with your detail, and that is it. Over here, where I am blocking, there is my ID number. If I put my ID in this, that is good enough for people to know that I have a green pass. That is it.

Q2399 **Chair:** Very good; thank you. That is very clear. Is that information your vaccination history and also tests that have been conducted, not just the vaccination?

Professor Balicer: Just whether or not you are either vaccinated or previously have had a positive PCR to show that you have been ill with Covid-19. Those two aspects render you eligible for the green pass.

Chair: Very good. I am very grateful to hear directly from the person who leads the committee in Israel responsible for the advice on the response to the pandemic.

Science is international, and it is appropriate that we should look at what is happening elsewhere. We are looking very intently at what is happening in Israel. We are pleased and grateful that you have been talking to our Ministers as well as their scrutineers on this Committee. Thank you very much indeed for your evidence today and good luck with your successful handling of the rest of pandemic.

Professor Balicer: Thank you so much.

Chair: Thank you. That concludes this session of the Committee.