Crohn’s & Colitis UK 2021 AGM - KEYNOTE

Sue Cherrie, Chairman

Good morning everyone. It's lovely to see so many of you arriving. Thank you for joining us.
It's wonderful so many of you been able to join us for our AGM. It's a while since we've had one.

Sue then introduced herself and the panelists and went on to give some housekeeping details and a summary of the programme.

So over to our first item, which is a warm welcome to Dr. Tarik Ahmed, who is consultant gastroenterologist at the Royal Devon and Exeter NHS Foundation Trust and honorary Associate Professor of Gastroenterology at the University of Exeter. Tariq is leading a research team looking at the impact of two biologic medicines on COVID-19 infections, vaccinations and immune response in people with Crohn's and Colitis. So, thanks to the Dr. Tariq and many others working on the project gastroenterology services, it's ensured that this important research is really has been put as part of a COVID-19 urgent response study programme.
This enormous effort has brought results very quickly. And these have influenced public health decisions. The speed of it is unprecedented and the charity has been delighted to support it. The results influence government, in meetings and with the vaccine minute minister and NHS leaders. Together, we are working to make sure we make sure that your needs are heard at this very strange time. Dr. Ahmed, over to you. Thank you.

Dr Tariq Ahmad

Thank you very much for that kind introduction and welcome to everybody who's dialled in today.

08:07

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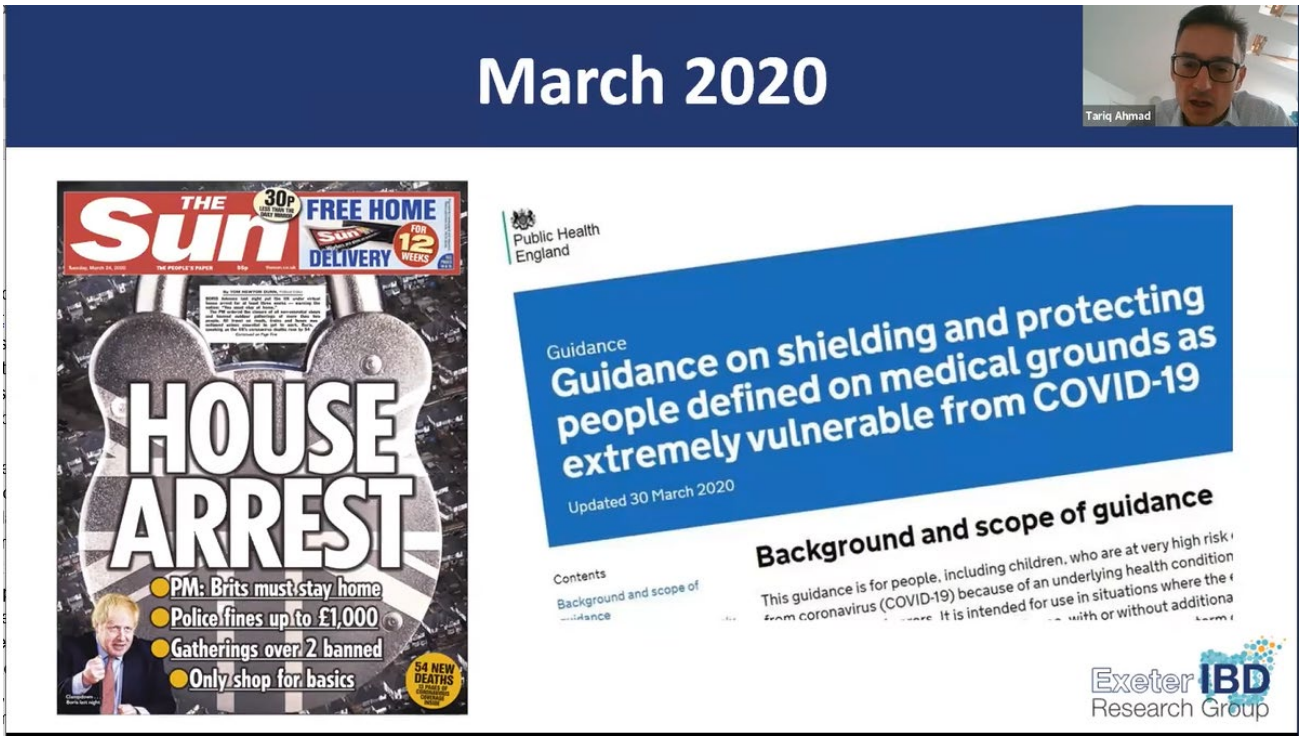
As I've already been introduced as a gastroenterologist, most of my time I'm working with patients in Devon, but probably half of my time at the moment is spent running this study CLARITY IBD. This is the acronym for a rather longer, more difficult to digest title of Impact of Biologics and Immunomodulatory Therapy, from SARS cov to infection and immunity in patients with inflammatory bowel disease. As has been already said, this is one of 95 urgent Public Health Studies that's been running over the last 18 months. And urgent public health means that our study along with the others have been prioritised for resource. All of these studies are focused on COVID-19 whereas much of the other research in the UK stopped over this period of time is only just recently restarted.



Wind back 18 months to March 2020. This was of course a very difficult time for all of us, but particularly for people and their families living with inflammatory bowel disease where house arrest really meant house arrest for many months, particularly for those people with inflammatory bowel disease and other immune mediated diseases. It wasn't the disease itself that put people at risk, but the fear was it was the treatment itself that was putting people potentially harm from COVID-19.

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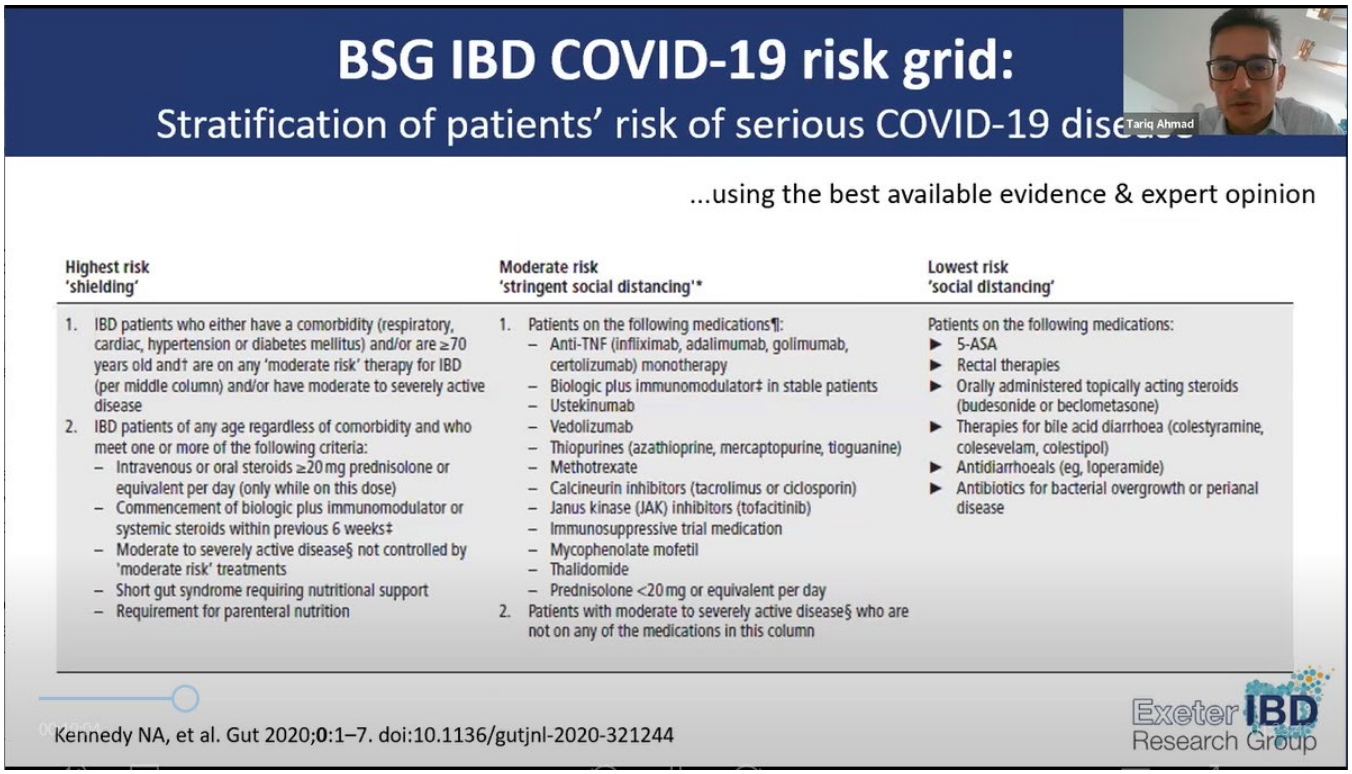

Back in March 2020 the British Society of Gastroenterology tried to help stratify people as to their risk of COVID-19, according to the drugs that they were taking. People were designated into these three different groups:

- high risk, who were told to go away and shield,
- moderate risk, you were told to follow stringent social distancing measures, and
- the lowest risk people who were felt to be at the same risk as the general population.

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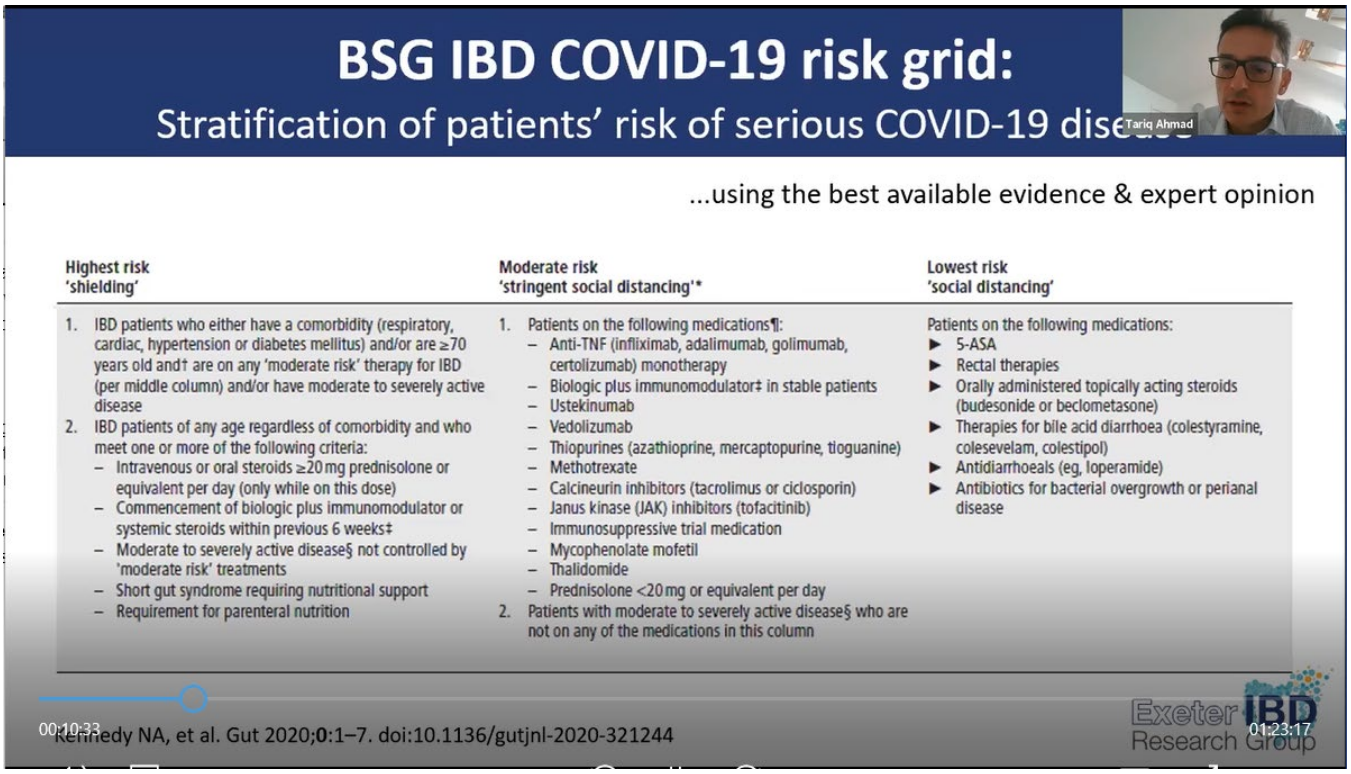

But at the time, there was very little data to justify these groups so it's based really on limited information and expert opinion.
To allow patients to understand which group they fell into the IBD registry, BSG and Crohn's and Colitis UK got together to come up and develop this risk tool using that risk group that I just showed you, and putting it into a format that could be easily digested.

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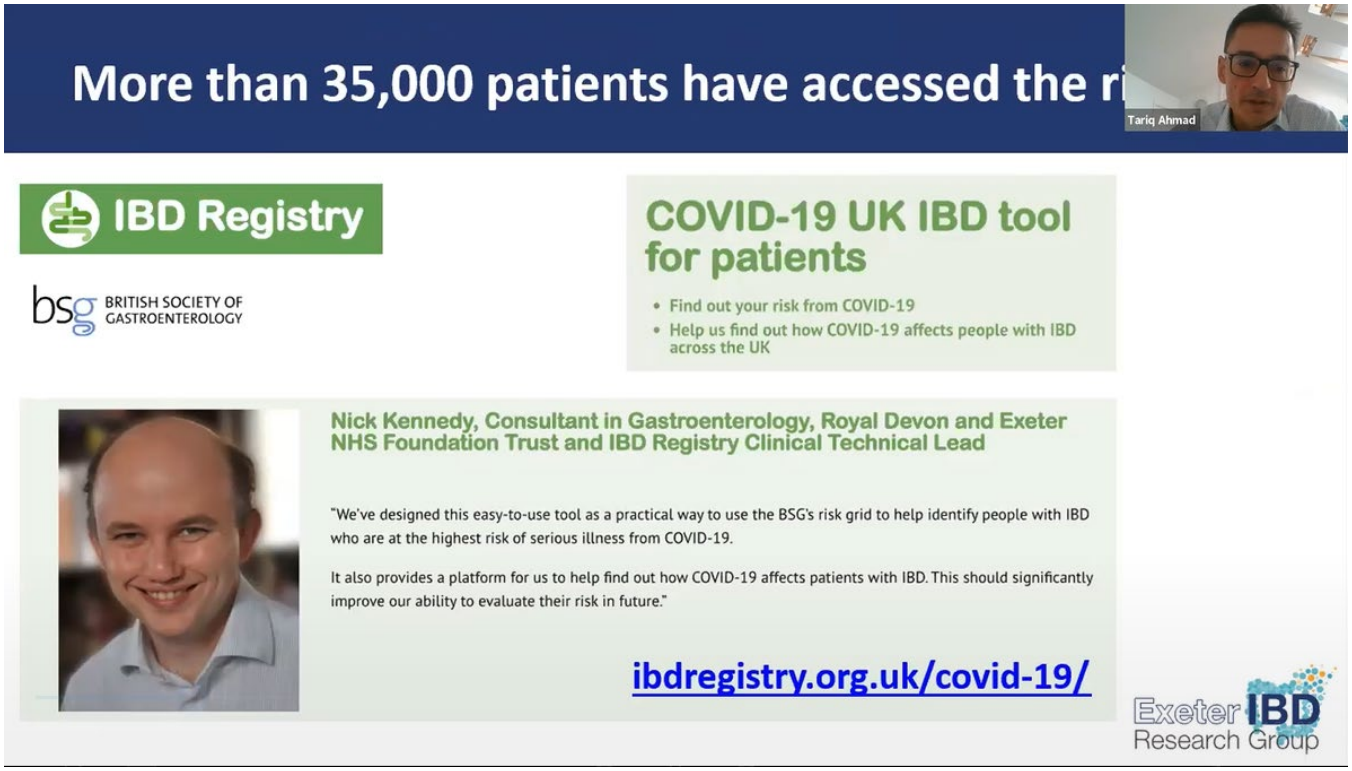
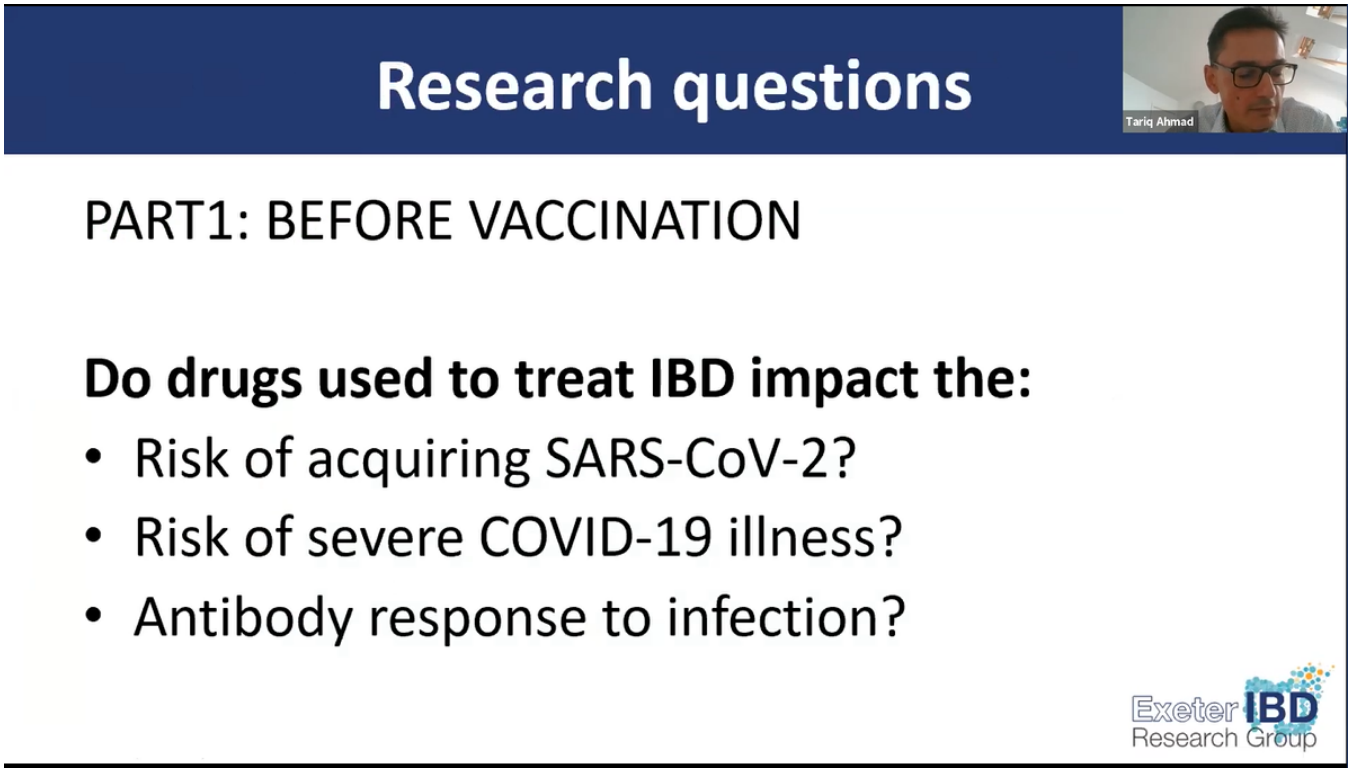


This was led by Nick Kennedy, one of my friends and a colleague in Exeter. When I last looked more than 35,000 people with inflammatory bowel disease across the UK, have used this tool to find out which group they fall into.



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About this time back in March, April 2020, that we felt that we needed to try and fill in some of the data holes, because there really wasn't much information to guide us. We're talking now about a period before vaccination was available. The key questions that we wanted to ask were for the drugs that we use in IBD: do they impact the risk of getting the virus; the risk of having a severe COVID-19 illness; and also, particularly in this project, looking at antibody response following infection. Do the drugs impair the normal protective antibody response that follows infection?

We put together a team of a crack team of people. Nick Powell from Imperial. Nick, from Exeter, Claire, has been my project manager running many projects across the UK over the last 10 years, James Goodhand, who is rather shy doesn't like to show his face much but he does a lot of the work behind these studies, Rachel Nice, who runs our laboratory, and Seb Shaji Professor of Gastroenterology in Hull.

This study rolled out as you'll see, rolled out in 92 hospitals across the UK, involved 92 Consultant Gastroenterologists and more than 400 research and IBD nurses. The cost of the study was met by various pharmaceutical companies who, at the beginning of the pandemic, were very prepared to help support this effort, and of course by the National Institute for Health Research who provided the costs for all the nurses.

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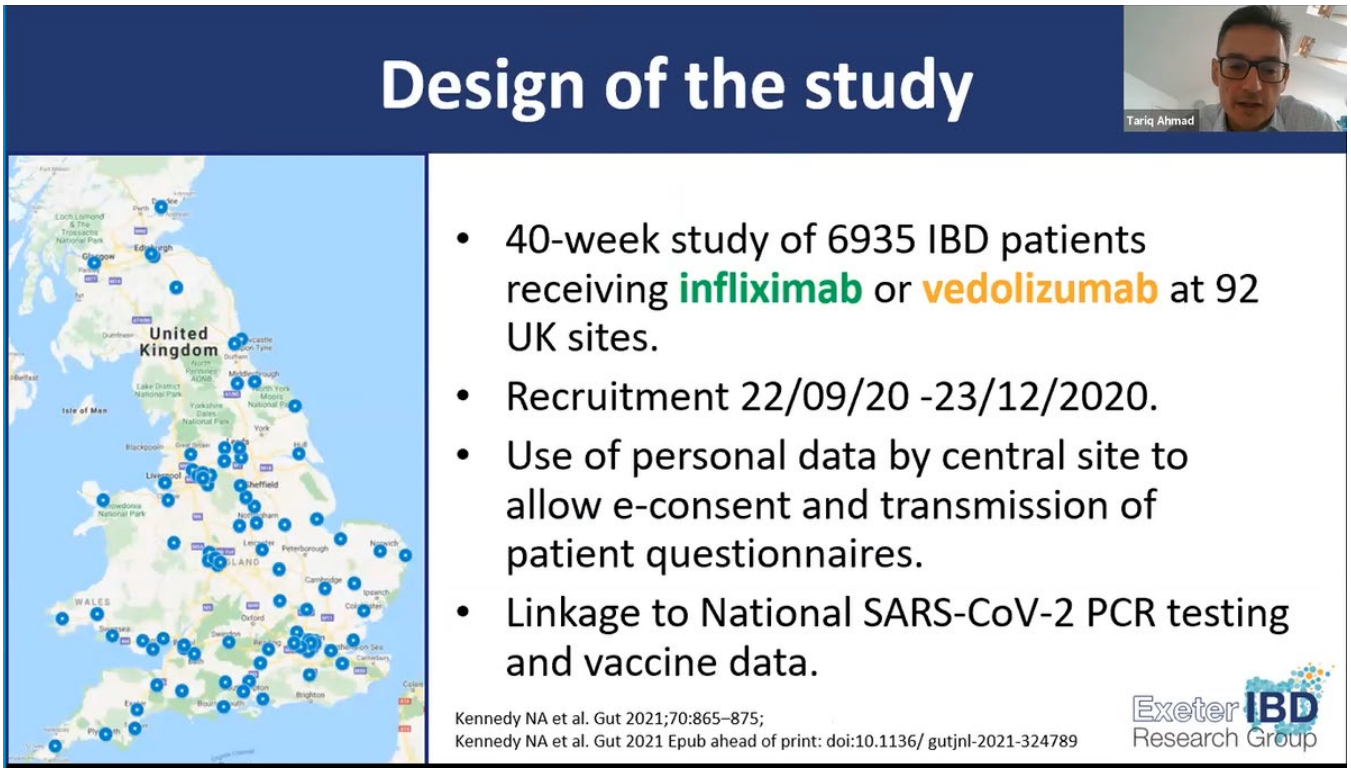

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We initially designed a 40 week study. What we wanted to do was to follow consecutive people treated with infliximab, or vedolizumab at 92 UK sites, and these are shown on the map on the left hand side. We chose these two drugs because:

- **Infliximab** over the last 20 years research has shown that this drug increases the risk of infection, particularly respiratory infections, and also impairs the normal protective response to certain vaccines. It's a relatively mild effect but nevertheless, it has been widely shown.
- **Vedolizumab**, a much newer agent, in contrast has not been shown to be associated with serious infection or to impair vaccine response. Effectively, the people treating being treated on vedolizumab that were our control group in this study.

We recruited just under 7000 patients in a 12 week period running up to Christmas last year. This was record recruitment, certainly for any IBD study, I think anywhere in the world. One of the key differences about this study was we sought permission to hold participants personal data. It meant that was unusual, because normally a central site doesn't have that access to that information but it was important. They allowed us to contact participants directly with questionnaires and consent forms. It also allowed us to link our data with the nationally held PCR testing and vaccine data. It was crucial to have people's personal data is kept very safely under very strict conditions but it does enable us to deliver this project efficiently.

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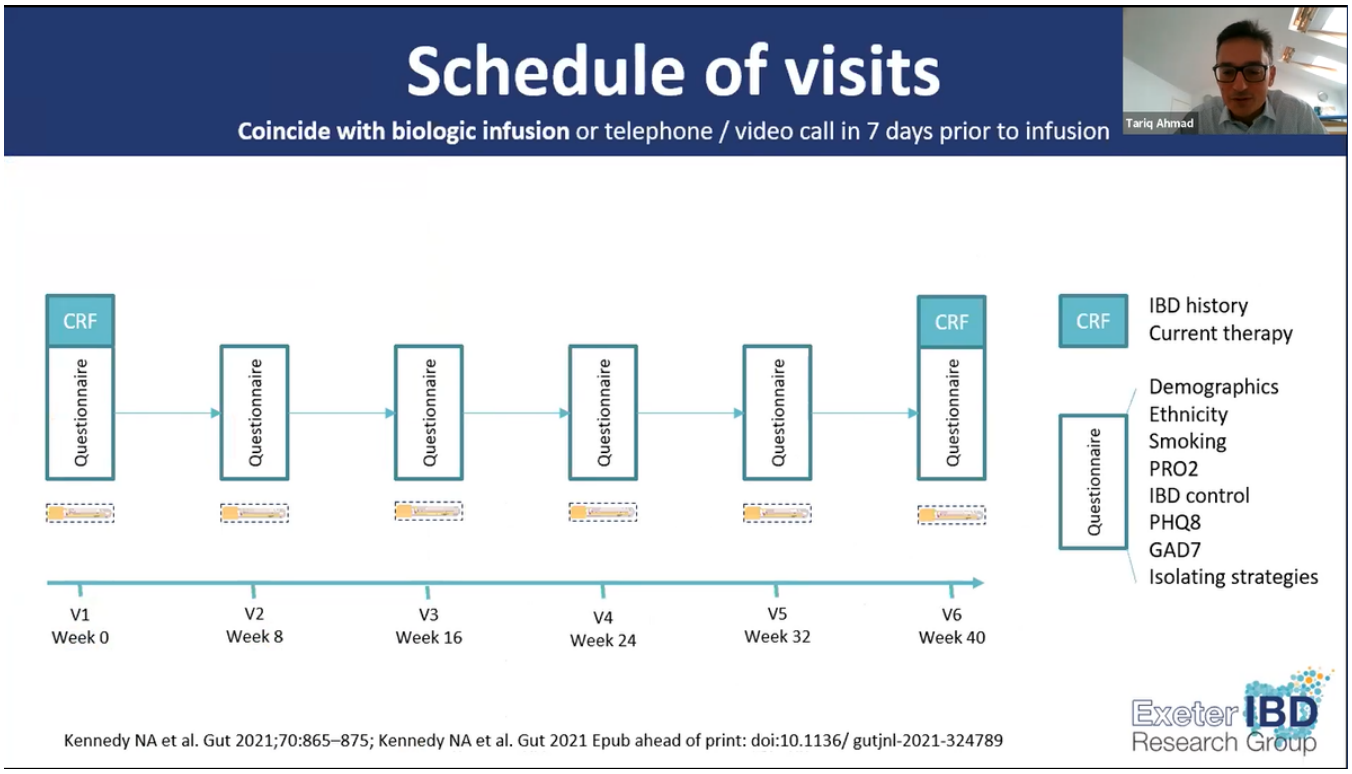

This is the rough design of the study. Essentially the patient did the work and that was completing a questionnaire every eight weeks. I know that many of the participants who got rather fed up with the questionnaires, but we have tried to improve them and shorten them a bit as time goes on. Every eight weeks when participants attended for an infusion a blood sample was taken and sent to Exeter. Along with the questionnaires, detailed information about symptoms, hospitalizations related to COVID, as well as information regarding disease activity, and levels of anxiety and depression amongst people living with IBD.

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The samples were sent to our laboratory in Exeter. Now this laboratory is situated in the main NHS biochemistry department. Every day, hundreds of parcels containing blood samples would arrive for us to unpackage and process. The advantage of running it in our NHS laboratory rather than a research lab was that the samples were subject to the same stringent quality control measures that NHS blood samples are.

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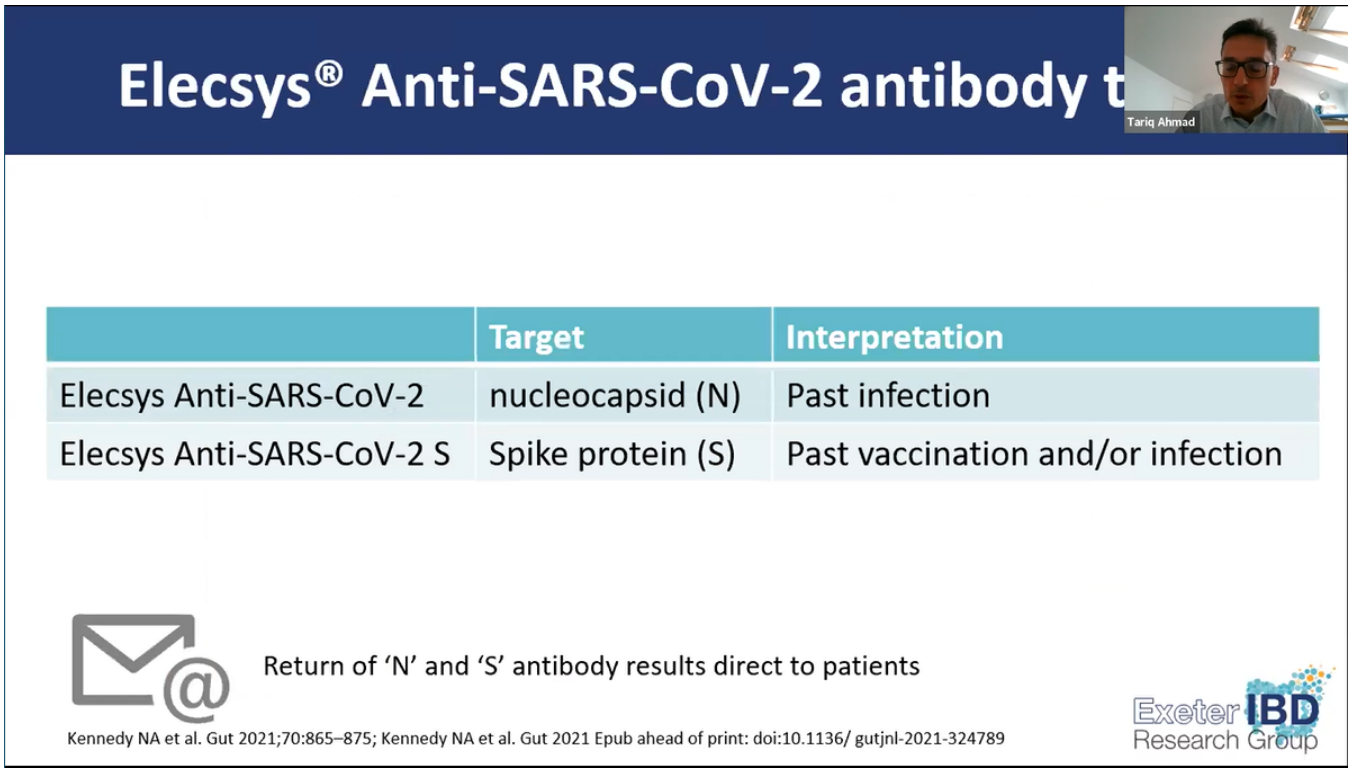

Blood samples were tested for antibodies to COVID. We use two tests. The first test we use was one against the N protein or nucleic acid. This told us whether people had had evidence of past infection. Following vaccination, we introduced another test against the spike protein of the virus. This told us whether people had had either a past vaccination or a past infection. We use the combination of these tests to look for infections in people who've been vaccinated, ie breakthrough infections. What was different about this study is we have returned the results to patients directly so people would send a text message to participants to say your result is ready, please log in, and you can have your antibody test results.

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Home finger prick testing

Exeter IBD Research Group

During the pandemic, understandably, people were reluctant to come to hospital to have their infusions and a number of hospitals switched patients from intravenous to subcutaneous preparations of infliximab, and vedolizumab. These preparations both became available during the pandemic. In order to keep these patients in, we realised that we needed to have some form of home blood monitoring system available, so we developed fingerprick testing. It's not perfect, it does require some dexterity, but it has enabled us for some patients, who have been healing at home to carry out blood tests, put them in the post, and then we can process the antibody levels on that sample. In fact, we've now extended this service to for standard blood test monitoring and drug level monitoring for our patients who live far from Exeter.

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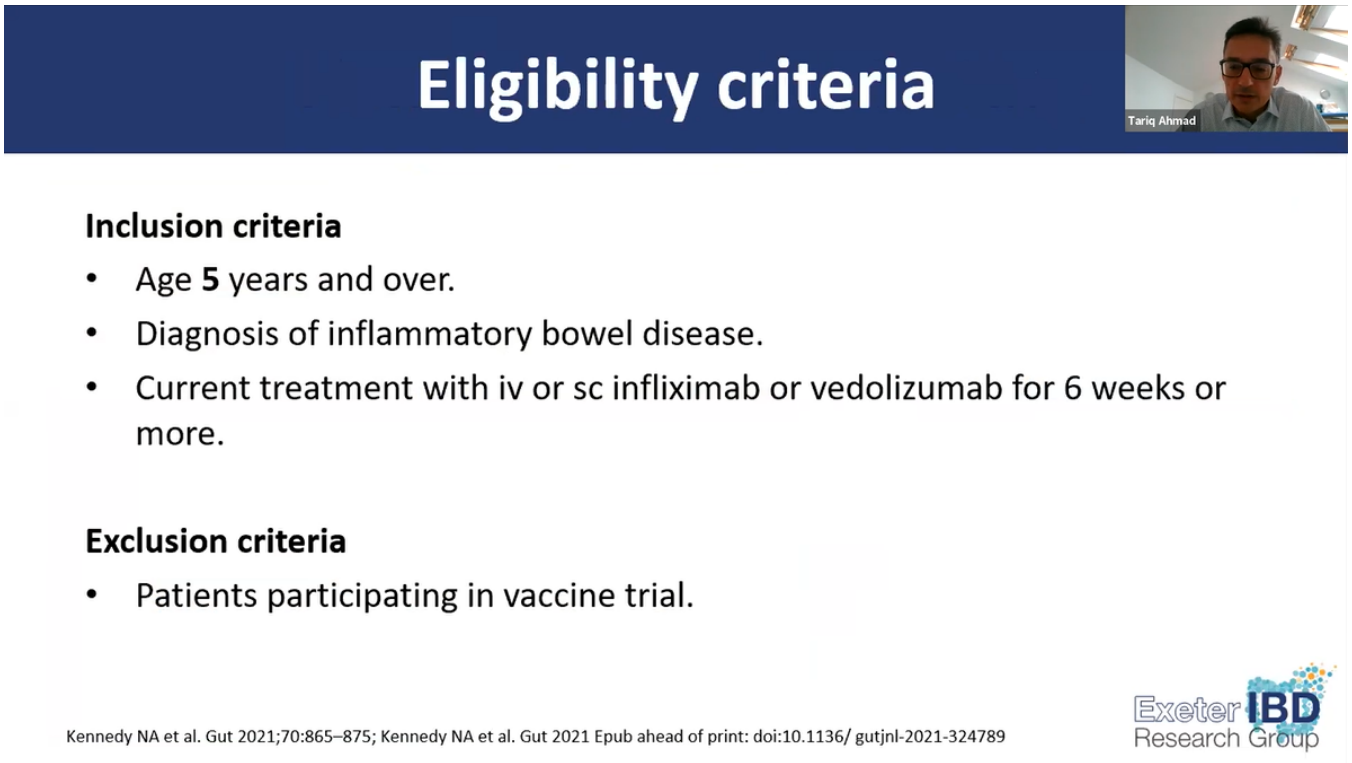

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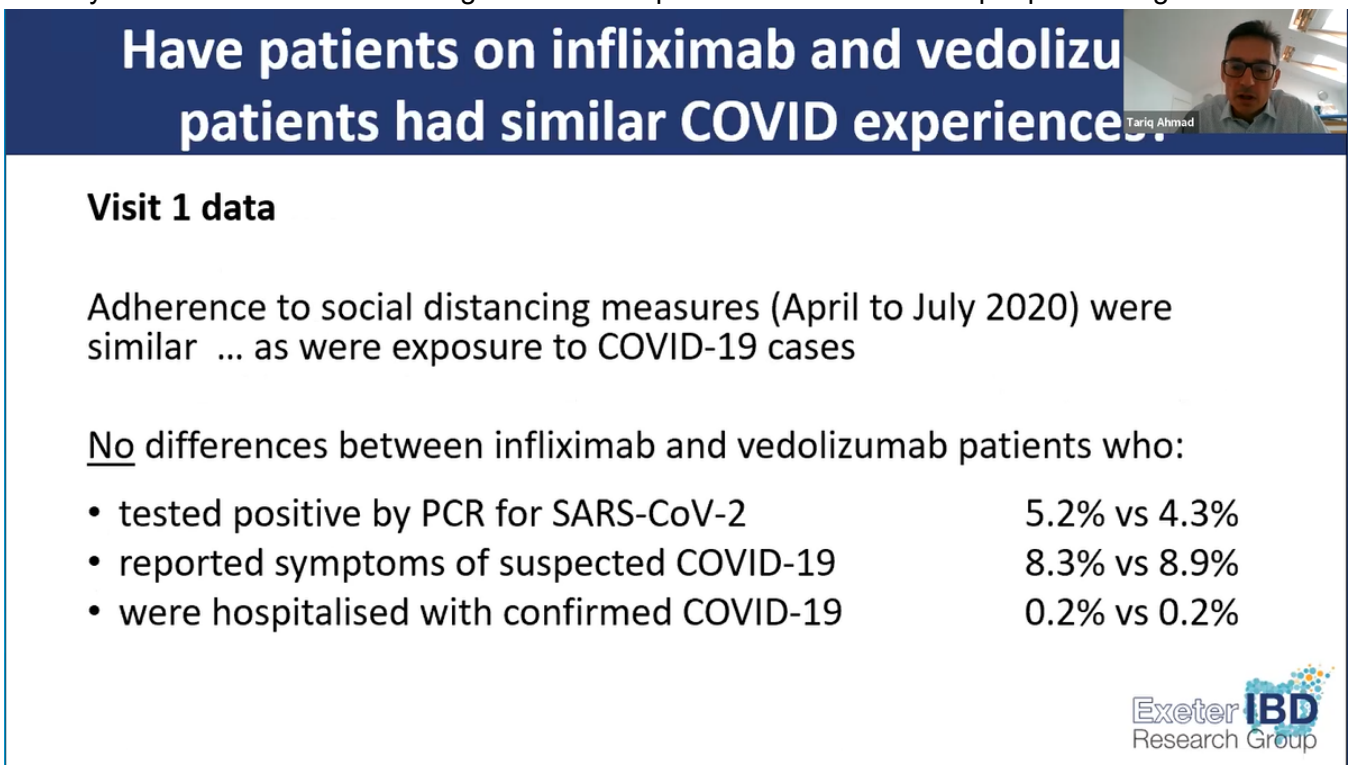
Here is the inclusion criteria We studied adults and children aged five years and over and they had to be treated with either intravenous or subcutaneous infliximab or vedolizumab for at least six weeks, we excluded people who are taking part in a vaccine trial. And there weren't many people who were actually allowed in because the drugs themselves prevented most of these people coming in.



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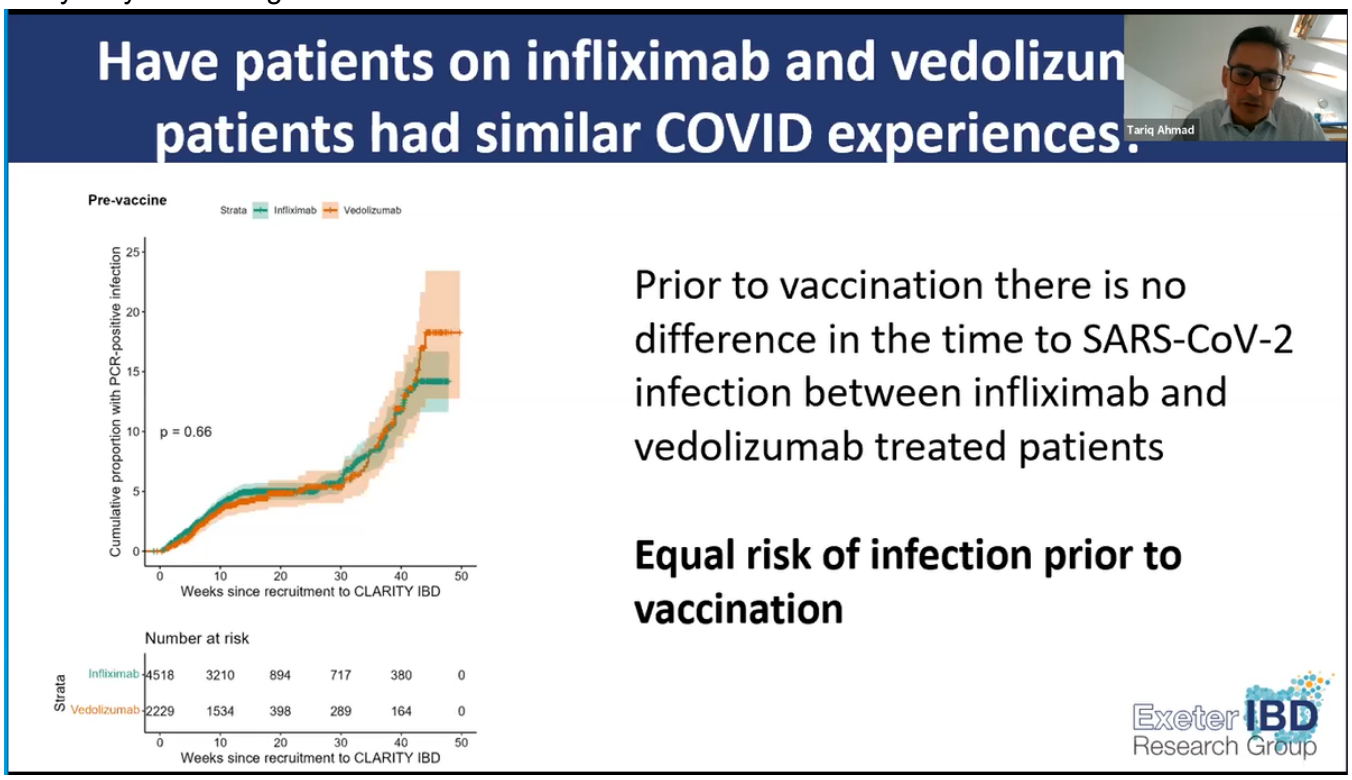
The first question that we asked is, have patients treat with infliximab or vedolizumab had similar COVID experiences? To answer this question, we simply looked at the data from the very first study visit, so study visit one on recruitment. What we saw was that there were no differences in the social distancing behaviour adopted by patients treated with either drug and there was no difference in exposure to covid 19 cases. Overall, there was no difference between PCR infection confirmed infection in people treated with either drug 5.2% versus 4.3%. Because vedolizumab patients were assumed to have no increased risk compared to the background population. This suggests that probably infliximab patients also have no additional risk. At the beginning of the pandemic, testing wasn't widely available, as you will remember. So we also asked about suspected COVID-19 based on their symptoms, and again, there was no difference. In terms of hospitalization rate, reassuringly, at the end of 2020 was very low, 0.2% of participants and no difference between the two groups. So that was really very reassuring.



We've updated this now and nine months on this graph. Its' a bit difficult to understand, but essentially it looks at the time to positive PCR infection. This includes everybody up until the time of their first vaccination. What we see is that prior to vaccination, there's no difference in the time to infections, the numbers of infections are no different prior to vaccination, suggesting that there's an equal risk of COVID-19 infection in both groups, which of course, is reassuring.

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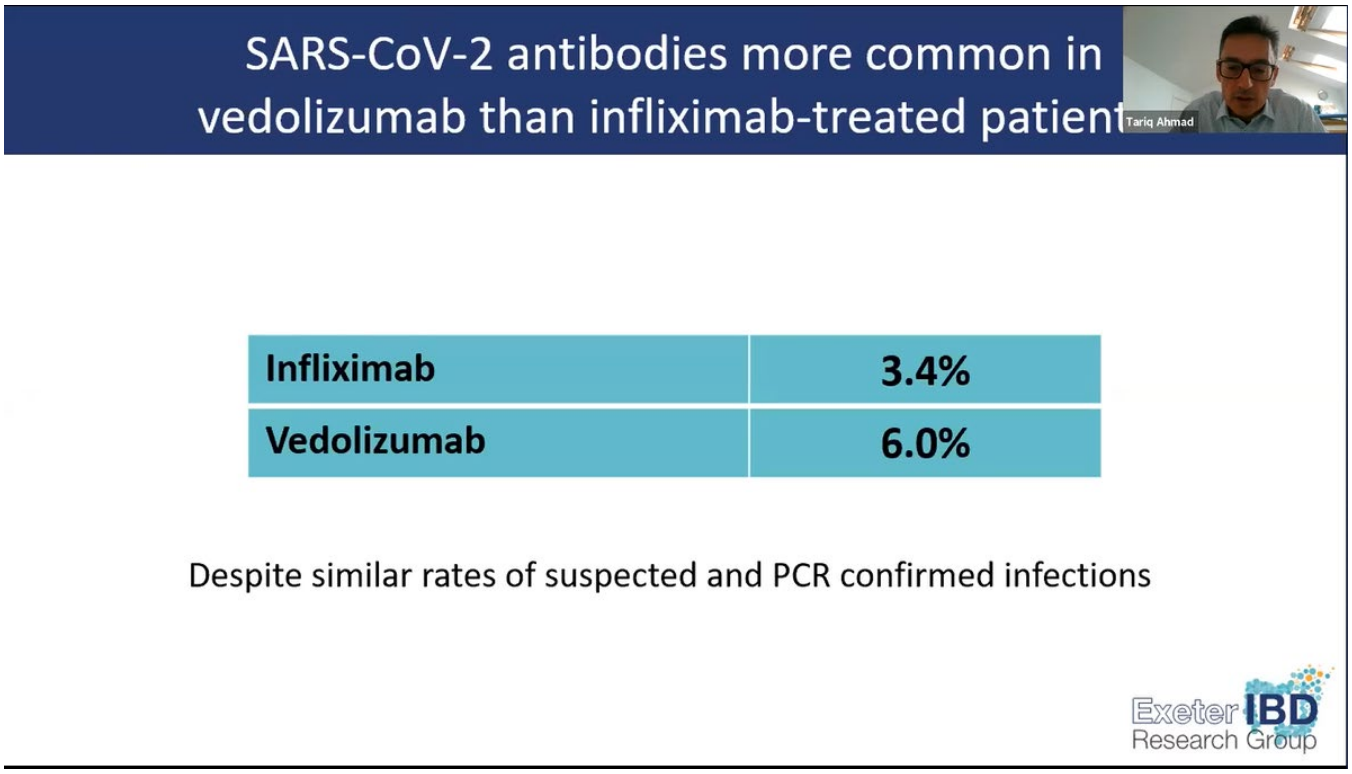

However, despite similar rates of suspected and confirmed infections, antibody levels going back to December 2020 were detected in 6% of vedolizumab patients, but just 3.4% of infliximab patients, suggesting that although there's no difference in infection rates, antibody levels are impaired in people treated with infliximab, so that protective antibody level is seen much less frequently in infliximab treated patients.

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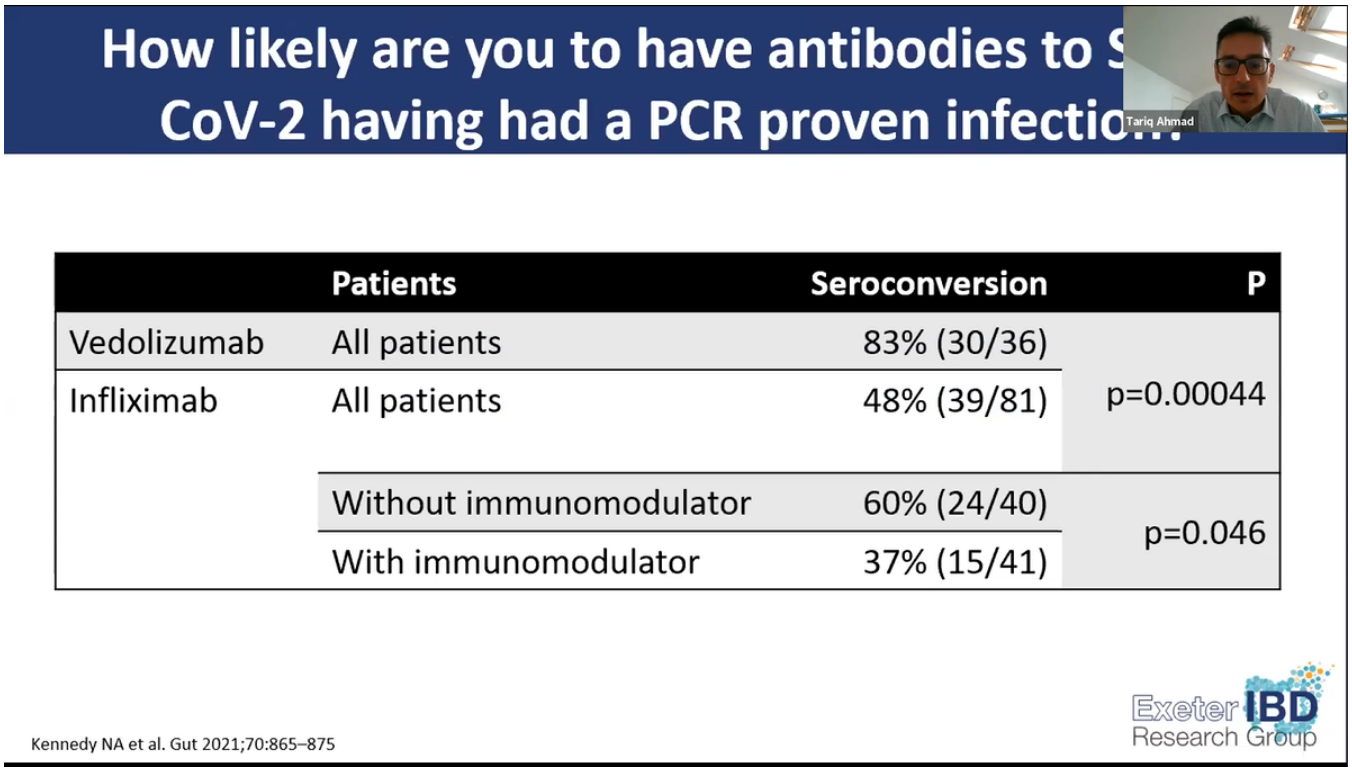

Now, what did that mean? Well, it meant perhaps, that infliximab treated patients may be susceptible to having another infection. I think more importantly, it hinted that there may be a problem with vaccine responses. We then looked in more detail at patients with PCR confirmed infections. And we saw that in vedolizumab treated patients, more than 80% had antibodies that was very reassuring, but in people with infliximab, under half had antibodies after a confirmed infection. If you're on infliximab, and an immunomodulators, such as azathioprine, this rate was even lower.

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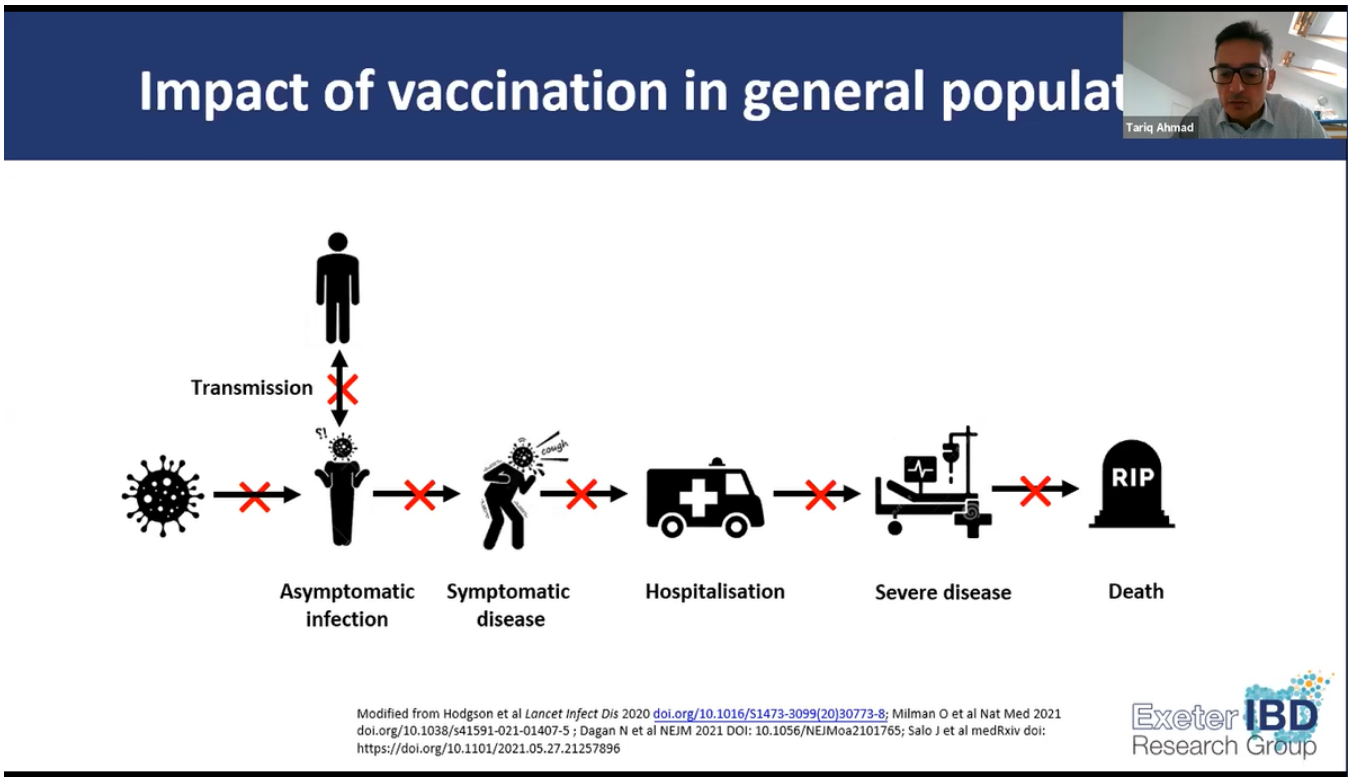

Vaccination then arrived in December 2020 and that was very exciting. Certainly in the general population, we had reassuring data that vaccination prevented asymptomatic infection, symptomatic disease, hospitalizations, severe disease and death. Then later, in the summer of this year, we learned that the vaccination also reduces person to person transmission. But of course, all of this information was from the background population or healthy individuals and it wasn't focusing predominantly, or at all, on people treated with immunosuppressant drugs. The next part of CLARITY addresses the question about vaccination in people with inflammatory bowel disease treated with these drugs.

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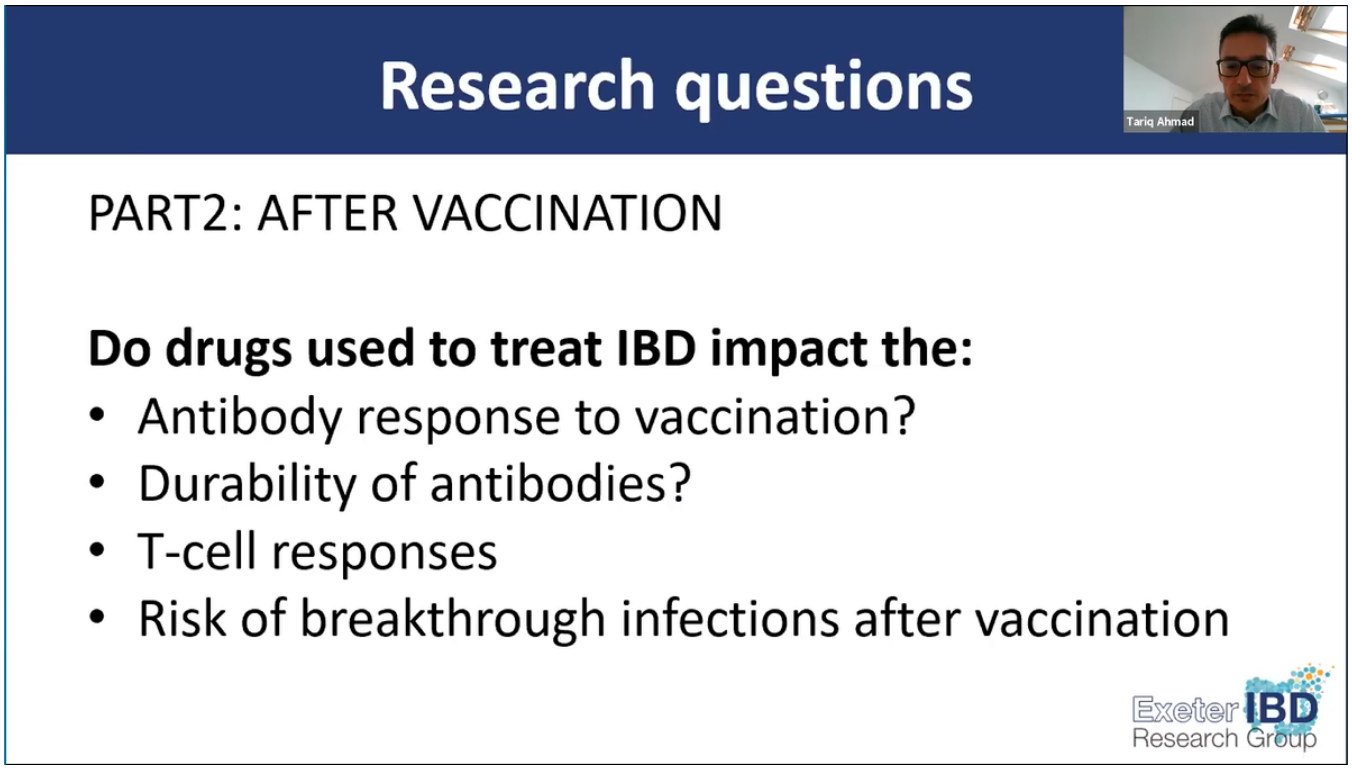

Our questions were:

- do the drugs we use affect antibody response to vaccination,
- the durability of antibodies do they decline faster?
- T cell responses because of course, it's not all about antibody responses, but also T cell responses, and
- importantly, the risk of breakthrough infections after vaccination.

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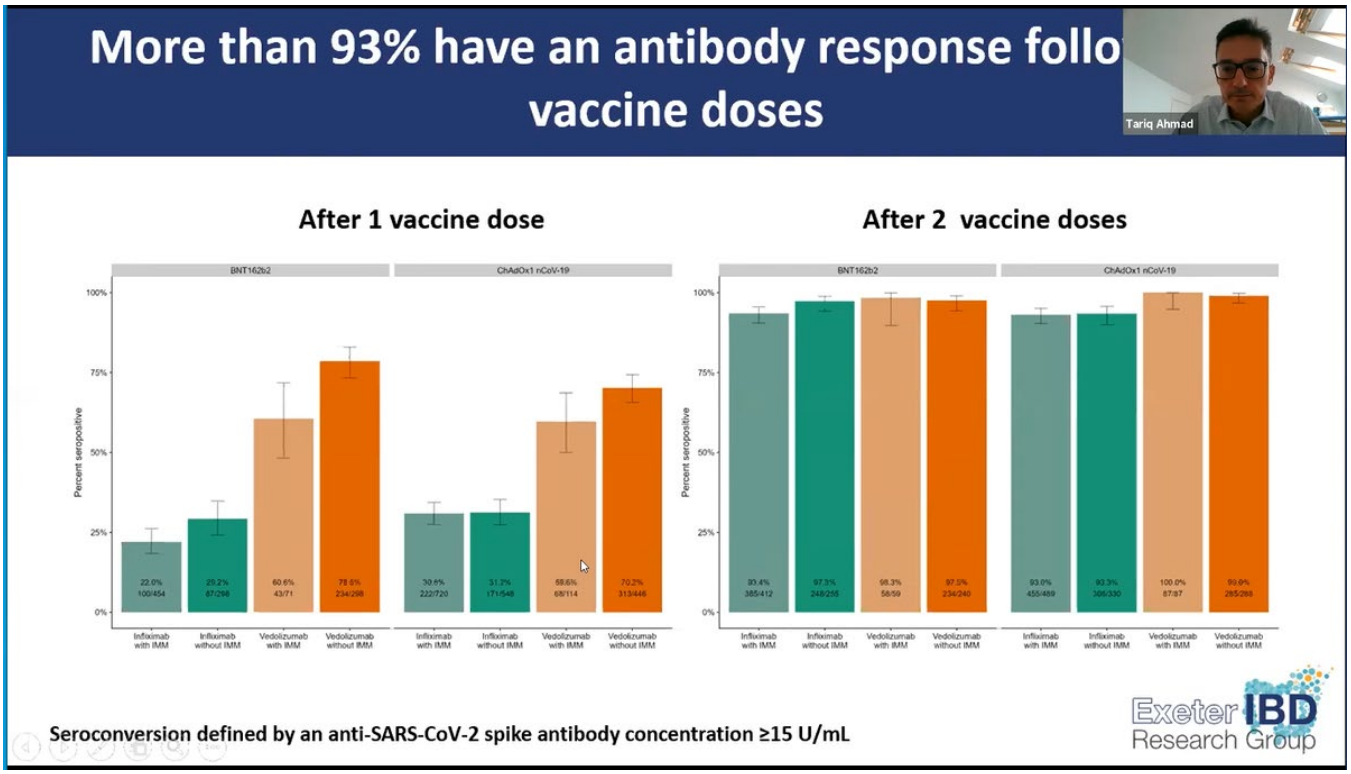

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The data on this graph shows antibody responses for the proportion of people who've reached a certain threshold after one vaccine dose. What we saw, after one vaccine dose, is that a large proportion of people treated with infliximab (shown in the blue here) have very low antibody levels. We see this both with the Pfizer vaccine and the AstraZeneca. One vaccine dose doesn't appear to elicit significant antibody responses in patients treated with infliximab. This was a bit of a concern when this this data first came out, and we urged people to continue to get their second vaccine dose. Fortunately, after two vaccine doses the vast majority of people, more than 90%, Seroconverted or reached the threshold that we believed would offer some protection. Most of the most of this work predates the Delta virus. We now know that for even healthy people, one dose of vaccine just isn't enough to offer protection against the Delta variant.

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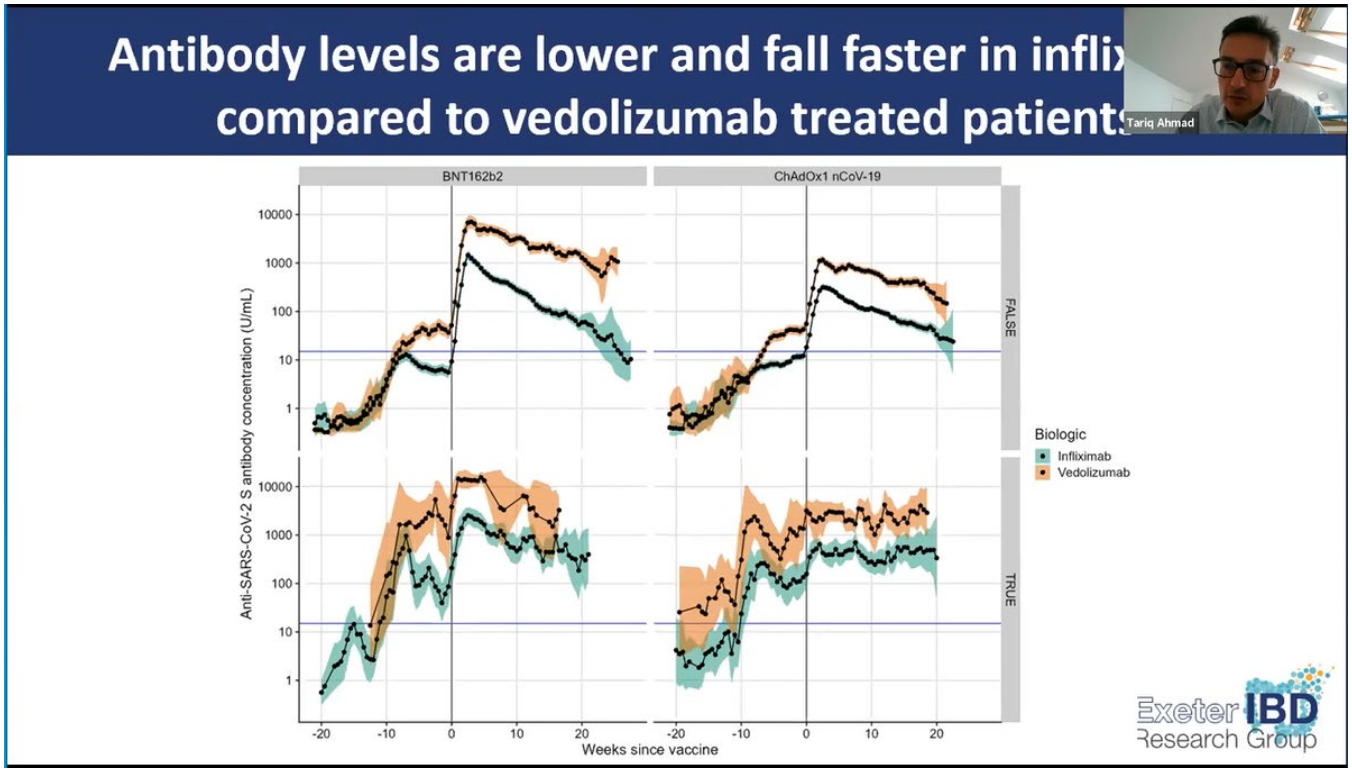

Although after two doses of vaccine the short term antibody responses were good, we then wanted to know what happened over time. Now this is a complicated diagram, but I'm going to try and take you through this. On the left hand side, we've got the people vaccinated with Pfizer, and on the right we've got people vaccinated with the AstraZeneca vaccine. People treated with infliximab are shown in green, and people treated with vedolizumab this orange brown colour. This represents the average antibody concentration for the whole group of people treated with infliximab and a whole group of people treated with vedolizumab. After the second dose we see a massive jump up in antibody levels that are significantly lower in infliximab compared to vedolizumab patients, six fold lower. But as you can see, over time, antibody responses rapidly fall such that by 24 weeks, half the people cheat with infliximab have fallen below this threshold that we think may offer protection. We see a similar issue with the AstraZeneca vaccine over time levels fall of course, even in healthy people we see this, but it appears with that infliximab patients they fall off much faster. The bottom half the screen is looking at people who had a prior infection before their two doses of vaccine, ie they'd had three encounters with the virus, one the two virus and two vaccinations. What you can see here is that an after three contacts, they have much more sustained antibody levels. So, if you've had an infection, this is good news, because clearly, you have a much more long lasting protection. It also hints that a third dose or a booster dose may achieve similar more sustained antibody responses.

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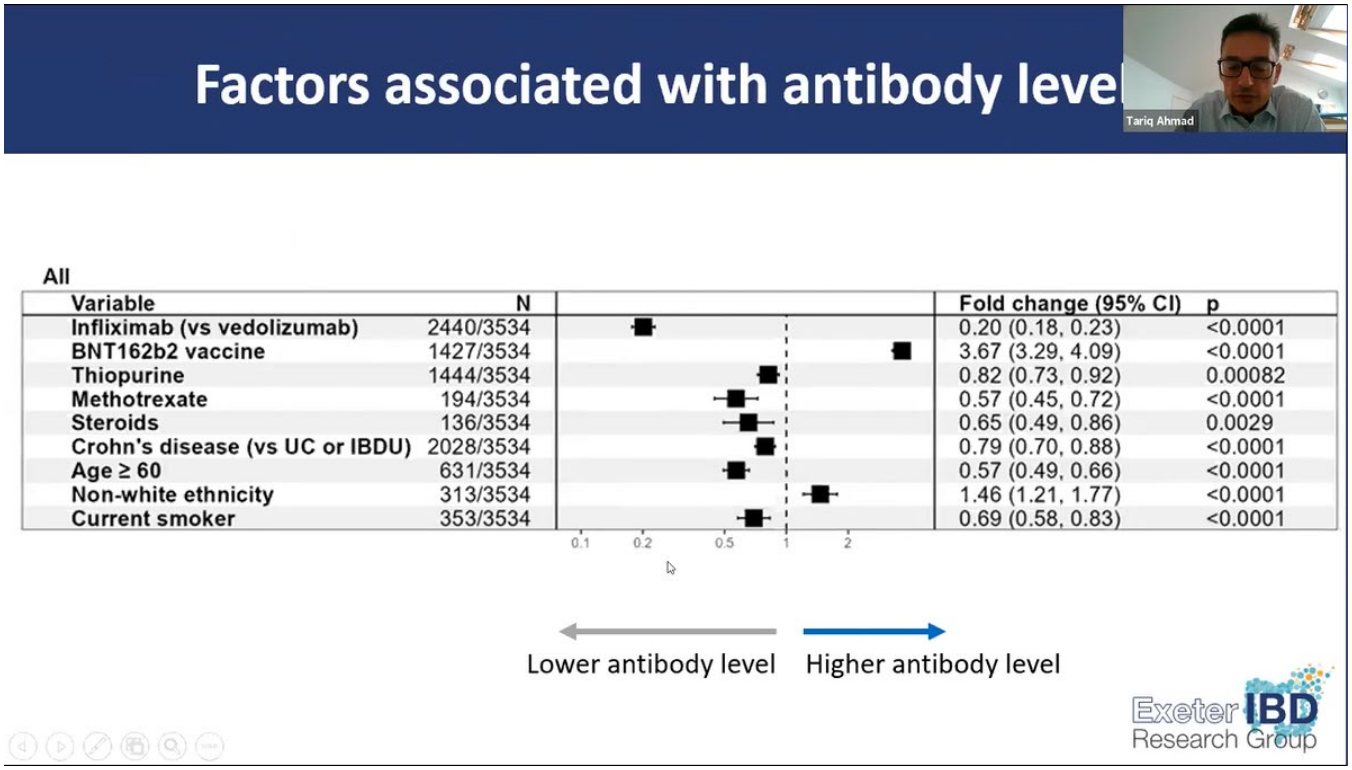

We also looked at other factors. Apart from drugs there are other factors which impact antibody levels. You can see here on this graph factors on the left hand side of this dotted line cause lower antibody levels, factors on the right hand side increased antibody levels. You can see that with infliximab that the further you are away from this dotted line, the bigger the impact of this factor. You can also see that infliximab exerts the strongest effect, and having the Pfizer vaccine compared to the AstraZeneca is the biggest sort of positive factor. But there are some other factors here:

- being on a thiopurine, or methotrexate or steroids, all lower your antibody levels, but not to the same extent as infliximab.
- having Crohn's disease compared to Ulcerative Colitis,
- being older as we've known this from a number of other studies, and
- being a current smoker. I've not seen that in any other work to date but smoking seems to lower your antibody level, there may be a confounding factor that we've not discovered to explain this but I think it's another reason to stop smoking.

If you look at the other half of this graph, you can see that being of non-white ethnicity is associated with higher levels. So this is one good news story for people of non-white ethnicity when most of the news story has been pretty negative.

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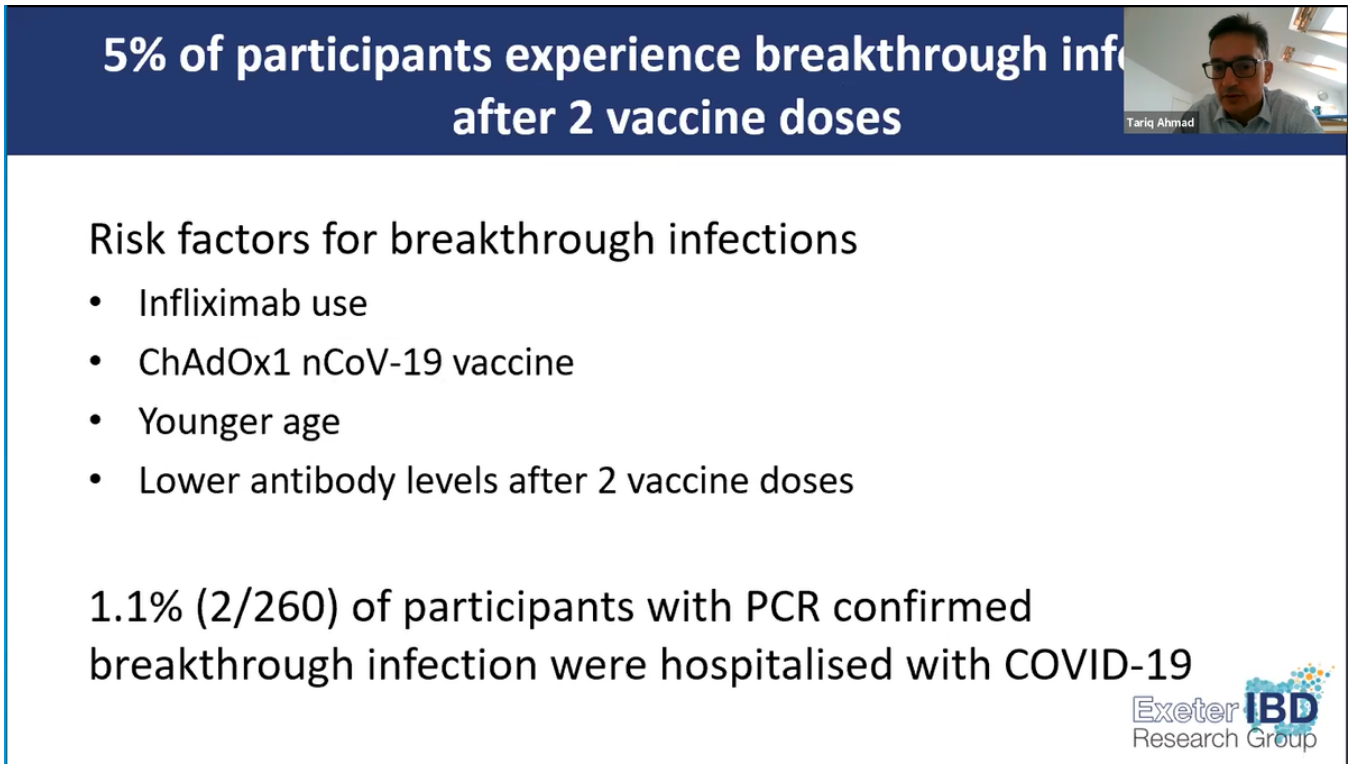

I've shown you data on antibody levels but what really matters is whether people are having further infections after vaccination. In our cohort 7000 patients 5% have had a breakthrough infection despite two doses of vaccine. These are people who've had a positive PCR test more than two weeks following their second dose of vaccine. We've looked at the risk factors for what the factors are that these people have that others don't? Again, it's:

- people on infliximab,
- people that have been vaccinated with the AstraZeneca vaccine rather than the Pfizer vaccine,
- people who are younger are more risk undoubtedly. I think this is explained by the fact that younger people are likely to be less cautious than older people.
- also, interestingly, those people who've had a lower antibody level after the second dose, suggesting perhaps that knowledge of your antibody level after second dose might potentially identify which people are at risk. This is still far from being clinically useful, but it's an interesting observation.

So that's the bad news 5% breakthrough infections, but the good news is that only two of the people with breakthrough infections in our study were hospitalised with COVID-19. The rest were mildly symptomatic, managed to manage at home without too many difficulties. So although a 5% breakthrough rate might look alarming, the risk of severe disease is very, very low following vaccination.

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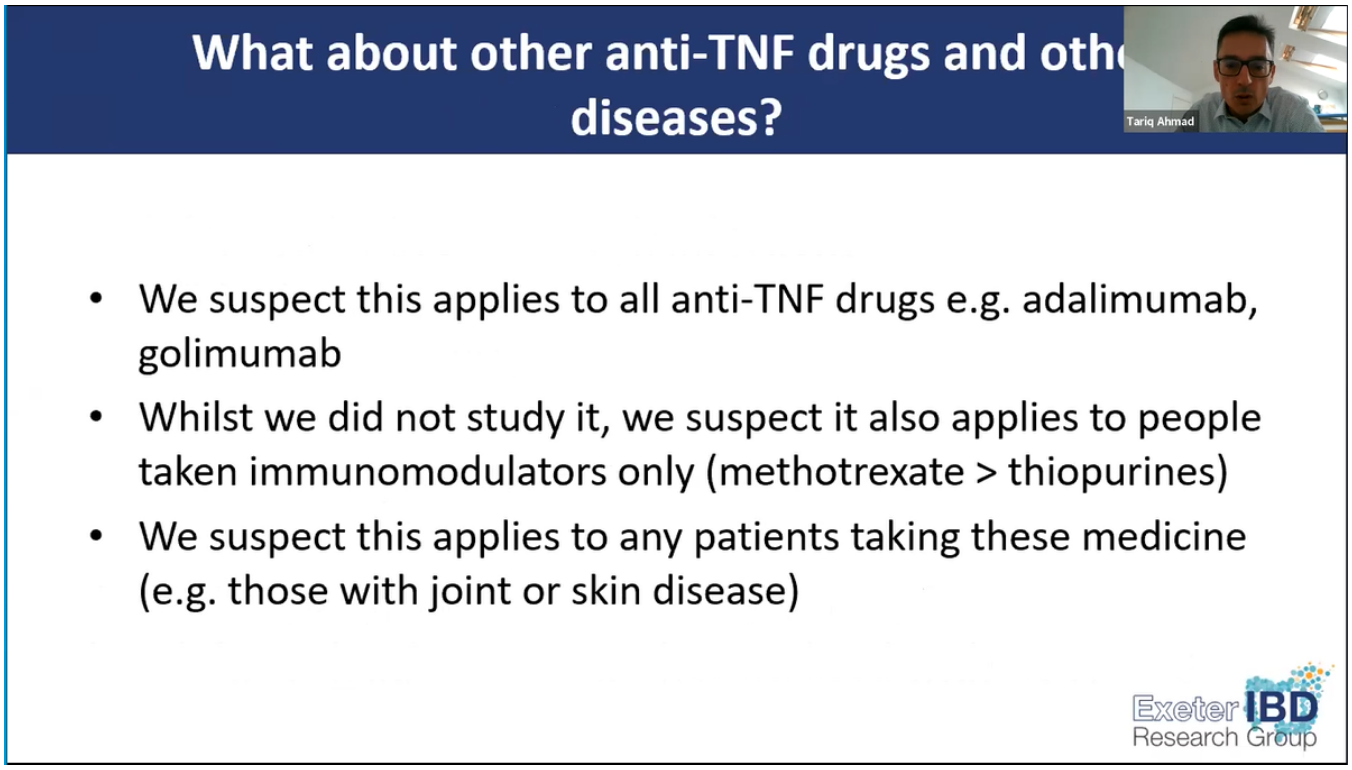

What about other anti TNF drugs? We use adalimumab and golimumab as alternatives to infliximab, and what about the use of these drugs in other diseases? Well, we are reasonably confident that this applies to all anti TNF drugs. This is a class effect. We have done some work with adalimumab showing pretty similar results. What about other drugs? We've shown that if you're in this study so far, that if you're taking azathioprin, or mercaptopurine, or methotrexate alongside infliximab that it increases your risk of reducing antibody formation even further. We haven't studied here using these drugs alone without infliximab, but we're certain that these drugs also will reduce antibody levels, but not to the same extent. We also believe that, and we see that other studies have shown that this applies to other diseases. Patients who are taking these medicines for skin or joint problems, also see the same effect.

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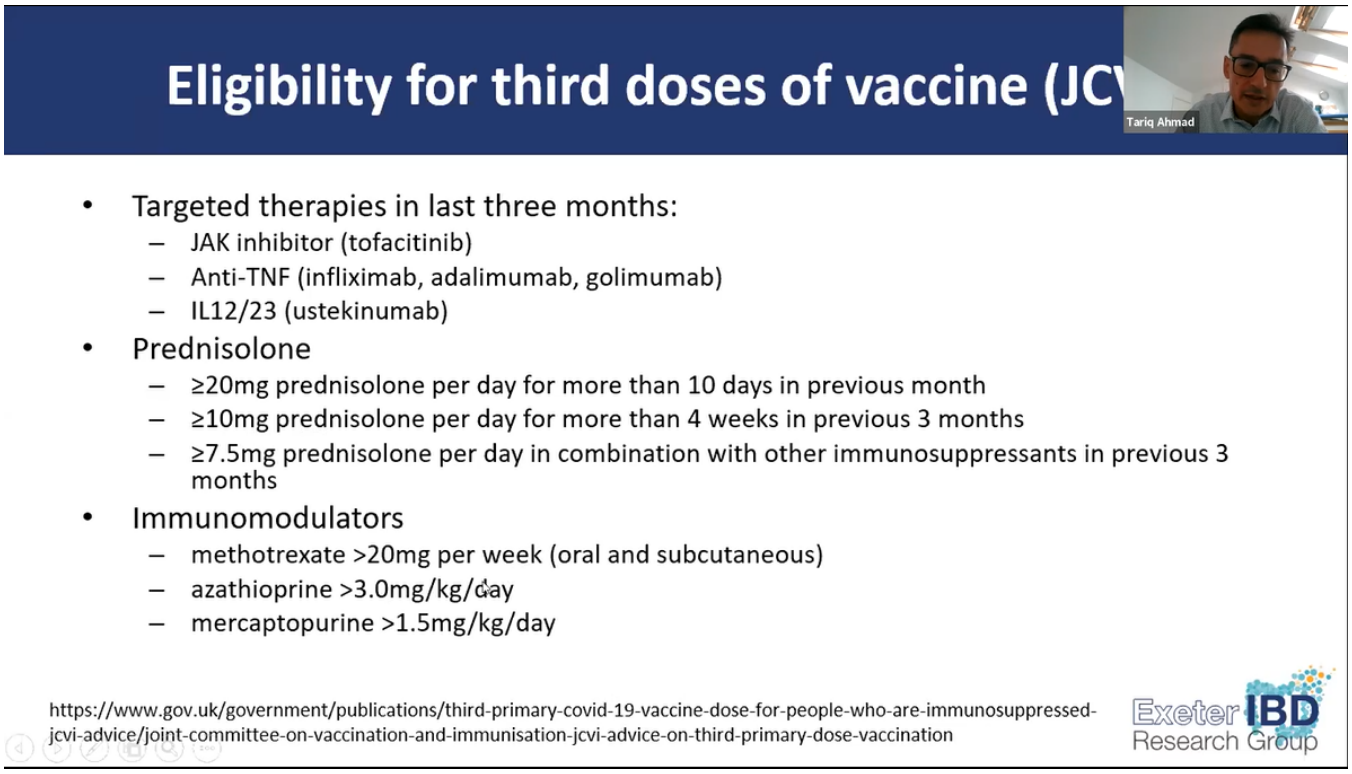

I wanted just to at the end here to give some information about third vaccine doses because I'm sure this is of interest to you. So here is the JCVI guidance on who is entitled to a third dose. This is the official guidance. I'm going to show you on the next slide, what the British Society of Gastroenterology is recommending. The JCVI has said that anybody who has taken a targeted therapy in the three months prior to either vaccine dose is eligible for third dose. You'll see here that this includes anti TNF and includes Ustekinumab. Vedolizumab isn't specifically mentioned on this list, but they state in this document that this list of drugs is not exhaustive. It also includes people taking prednisolone around the time of their vaccination, and they needed to be taking:

- more than 20 milligrammes for more than 10 days in the in the month prior to either dose, or
- 10 or more milligrammes per day for more than four weeks in the previous three months, or
- greater than 7.5 milligrammes in combination with one of the other immunosuppressants.

Now with immodulators, many patients with inflammatory bowel disease are taking these drugs alone and the JCVI suggested that unless you are taking high dose of these drugs, you didn't need a third vaccine dose.

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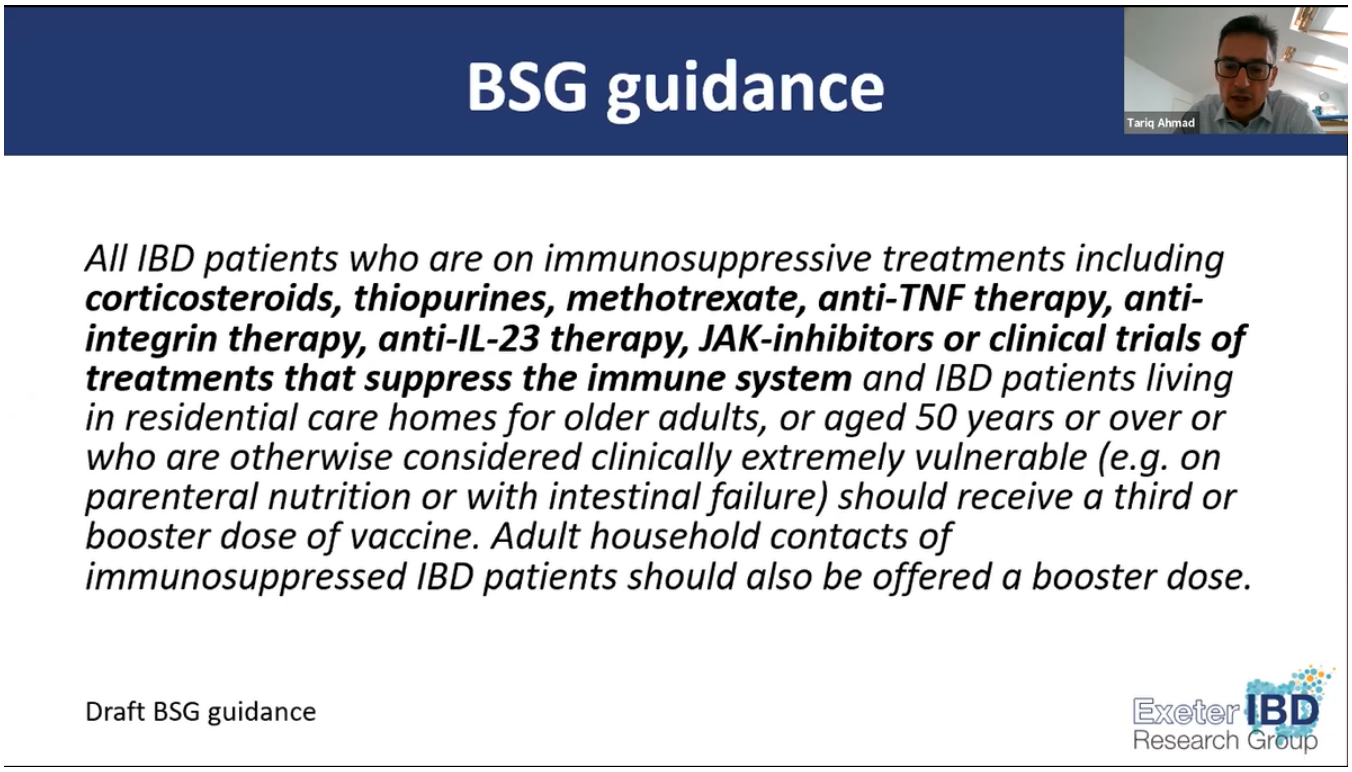

However, this is the current draft British Society of Gastroenterology guidance. It is not as yet published, but I think it will be published next week. It's not quite so clearly defined and I think it will bring in a greater number of patients. I suspect that most gastroenterology teams around the country will follow the BSG guidance rather than the JCVI, although that will be left to individual units to decide. You'll see anybody taking any of these drugs are eligible will be offered a third dose. Of course, the third dose needs to be distinguished from a booster dose. A booster dose is going to be offered to everybody 50 years or over anyway, but that will probably occur slightly later than the third dose offered to the extremely clinically valuable group or those on the drugs that we've just discussed. So many patients living with IBD will be offered a third date imminently and I suspect that many people have already been contacted over the last 24 hours and offered a time to come and have this done.

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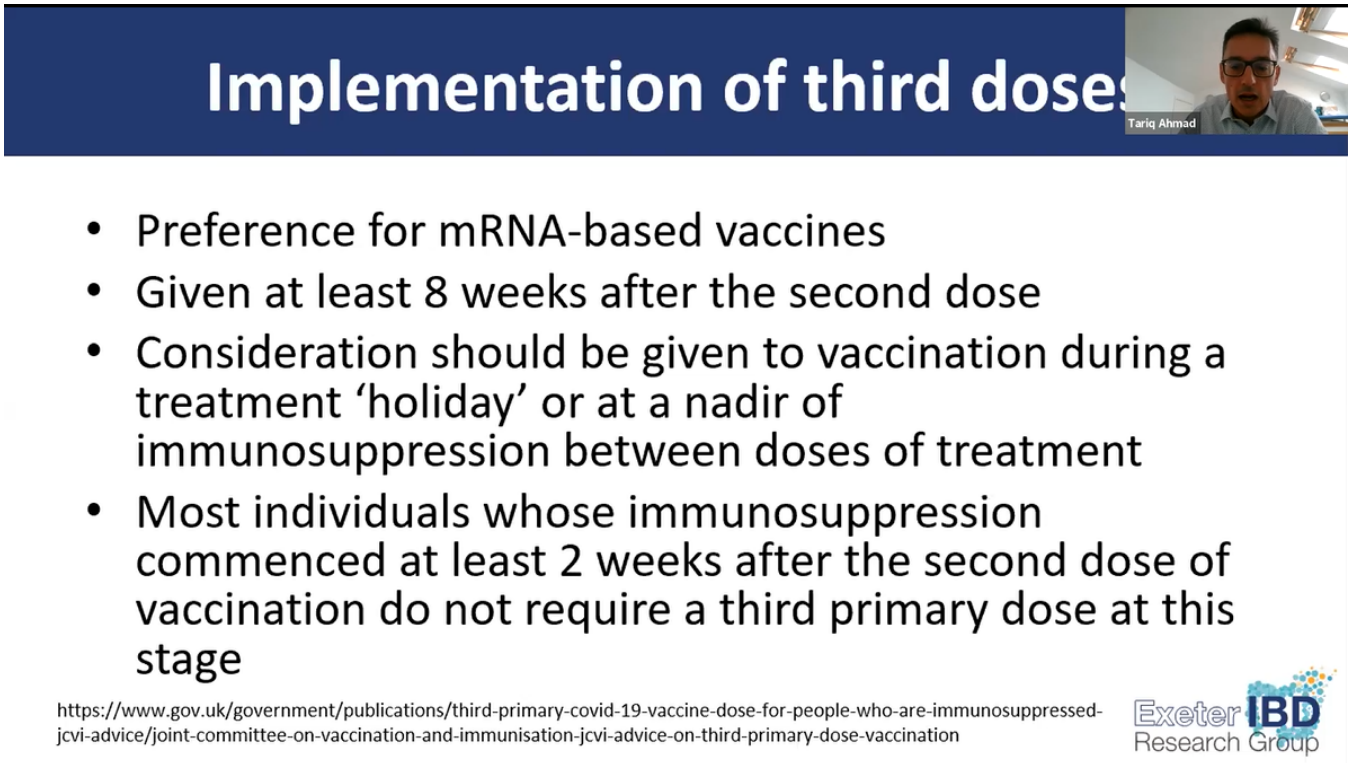

A bit more about the implementation and the third dose. There's going to be a preference for the mRNA based vaccines. So that's the Pfizer dose and I think our data supports that that would be a better option for people on these medicines. It needs to be given at least eight weeks after the second dose. If you've only had a second dose four weeks ago, it's advisable to wait a further four weeks. This is the this is the slightly tricky step, that it should be given either in a treatment holiday or when the level of the drug is lowest in the blood. What that means is because we've seen this impact of medicines on antibody levels we want to try and time the dose of vaccination where possible when the drug level is noticed, and for infliximab, if you're on an eight weekly cycle of drug, this means being vaccinated between weeks four and week six. That's going to require quite a lot of coordination with vaccine centres to get that right. Is it essential? No, it's not. I think it's better just to get the dose, but if you wanted to time this perfectly, that's how you do.

The other point to mention is that if you've been diagnosed with inflammatory bowel disease relatively recently, or started immunosuppressive relatively recently, if it was more than two weeks after your second dose, you really don't need to worry about the third dose. This is really about people on treatment, prior to and running up to a dose of vaccine.

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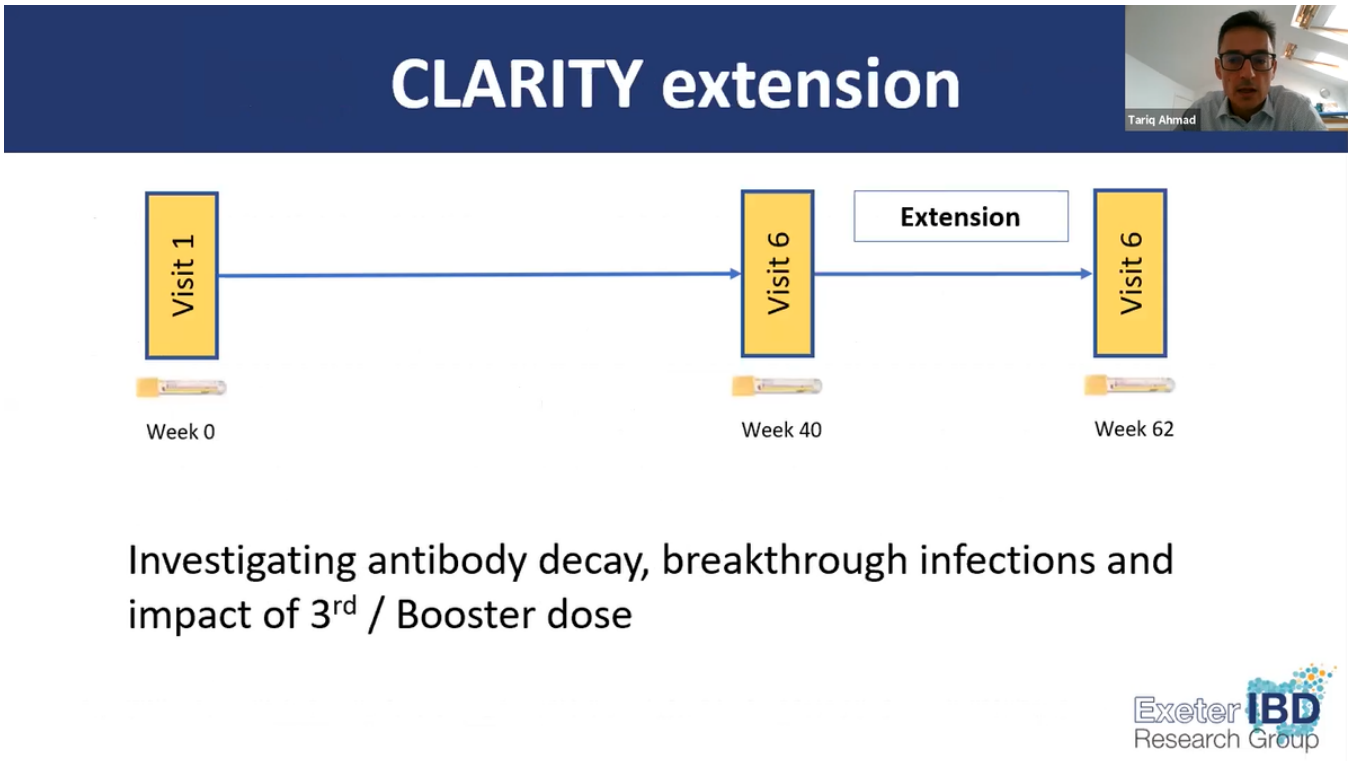

In order to capture what happens to participants in in the clarity study after a third dose, we have decided to extend the clarity study for a further 24 weeks. And that started last week. This requires participants to be re-consented to stay in the study, we hope that people will, and they're not too fed up with receiving messages from us. This will allow us to look exactly what happened for individual participants following a third dose.

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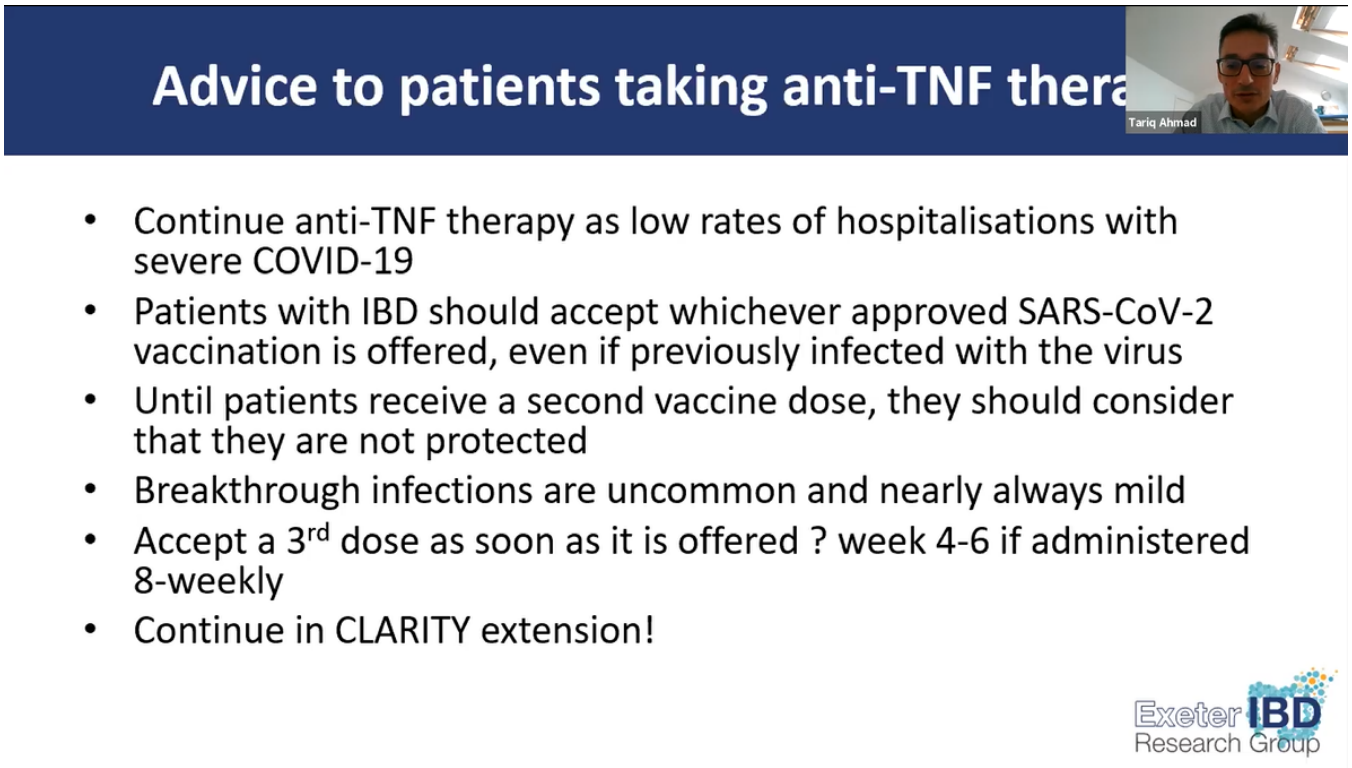

I wanted to finish by giving some specific advice to patients taking anti TNF therapy, because I didn't want to leave people on this drug feeling alone and the first messages continue anti TNF therapy. That doesn't appear to be any risk any additional risk of COVID-19 associated with taking these drugs. So the rate of hospitalizations, the rates of severe COVID-19 are low, particularly if you've had two doses of vaccine. So please continue taking the drug, it is probably one of our best treatments that we have available to us. Patients with inflammatory bowel disease should accept whichever vaccine is offered, even if they've previously been infected with the virus. So don't assume that because you've had the virus, you don't need a vaccine, I would definitely still have the vaccine. Importantly, if you're young, and you've only relatively recently got your first dose, then assume you're not protected until you've had your second dose. After that, I think you can feel much more confident.
I've shown you some information about breakthrough infections, but they are still relatively uncommon. And they are nearly always mild. So don't be alarmed by that data. Accept a third dose as soon as it's offered and as I've said, if you're on an eight weekly schedule on infliximab, then try and get it weeks four to six. If you're taking adalimumab, I would probably try to get it in the second week but I don't think it's so essential. Finally, if you're one of the 7000 CLARITY participants, please do stay with us in the extension and we will continue to provide you with your antibody data. So thank you very much Crohn's and Colitis UK, to the participants and all the nursing staff around the country who've done so much to deliver this study. Thank you.

QUESTION SECTION

Thank you very much, Tarik, that was absolutely fantastic. And as you can imagine the comments and the questions were pouring in as he was speaking. So we've got an opportunity to just pose a few questions to you just for the audience's you know, we asked people if they wanted to send some

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questions in beforehand. And we've had questions actually, during the talk. We're not going to get to them all. Undoubtedly. So I'm just going to post a few here now that to reassure everybody what we will do after the meeting and into next week, it's go through the questions and make sure that we can make them available to you as we can. So just starting off, if you're going into a flare. Should you still take the vaccine at that point?

39:54
Yeah, absolutely. And so we have looked at this and showing you the data, but vaccination doesn't it Here to impact disease activity. And as far as we can see, disease activity doesn't impact vaccine response. Of course, if you're given a course of steroids to treat your flare, or if you're started on a new drug, then that that may impact the the response to vaccination. And if your disease is relatively mild, and you can hold off treatment for a week or two, then that might be advisable. But I think if you're unsure, you should take advice from your local team. And certainly what we're doing for people who we know are need to start, say, for instance, in flexing that we've seen them this week, and they're not too bad, they can probably wait a couple of weeks, we've arranged for them to have their third dose this weekend, or early next week, so that they can hold off for a couple of weeks before starting treatment.

41:05
That's great. Thank you. And just you mentioned about the breakthrough infections, and few people wanted to know, how does that compare with the general population? I mean, are there more breakthrough? infections coming through people who are being treated with biologics? Or is it you know, about the same?

41:25
Yeah, that's a very good question. And and we, I can't give you an accurate answer to that right at this minute. But we are in the process of comparing our data to a healthy population. Data from another study, we've already done that to look at antibody responses. So we've used data from the virus watch study, to show that antibody decay. On federalism, that is no different to the healthy population, what we haven't done quite yet is look to see whether the rate of breakthrough infections is is different from the background population are not.

42:08
Great. And another one, which has come up time and again, actually in conversation throughout this period, do you think that people are many people children choosing to shield and having to shield? Do you think that's affected the results here? Because they're less exposed, actually to infections? etc?

42:28
Yes, so. So the question that was sent out, did capture information about human behaviour every eight weeks. And so we've tried to control for that, for that in the comparison of infliximab versus bellisima. But it does make it difficult to compare it with any other data. And so yes, it is a major confounding factor, of course.

42:55

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So we might get some results around that we might get some indications going forward. But it is a tricky one, obviously, to deal with. I'm just thinking about the wider impact. And obviously, people are shielding has sufficiently gone, people are being asked to go back to work more. Is there anything in the results that you can think should, you know, you'd advise people to look out when they're thinking about returning to work, or even education?

43:26
So I think I think patients with inflammatory bowel disease treated with these medicines should adopt the same measures that all of us should. I think, particularly if you look at schools, I, I think education, the benefits, education of B and F got to be weighed against the risks of keeping children away. And I would encourage people to try and not worry too much about the risks associated with these therapies. The the real impact we seen is regarding antibody responses, I haven't shown you the T cell data today, but that is reassuring, too. So I think I'm I'm hopeful that if patients, people with IBD, can get a third days that they will be protected. And I wouldn't worry on Judy, about getting back to work and getting back to school.

44:28
Yeah, so that's an important message really, isn't it? Because, you know, the impact of having to kind of moderate, you know, change your lifestyle so hugely just to on the basis of fear is is really quite

44:44
Yeah. The guidance that came out originally from the BSG and for the government, obviously was cautious advice, cautious recommendations with in the absence of any knowledge and any data and I think it's that's come out I think people should feel more comfortable.

45:02
Excellent. And then perhaps not necessarily something you can really answer, but it's definitely a live topic at the moment. People who probably are in the know they're in the third dose group and haven't heard anything. Which should they be hearing something from their consultant? Should they be hearing from the GP? What's happening?

45:27
Yes. So it's up to individual hospitals and teams to identify people who are eligible for a third date and to forward that data on to their GPS, anti vaccine, vaccine centres, different hospitals, those clear from the chat that I'm involved in, that different hospitals are doing different things. And we're so for instance, in our hospital, we're working directly with a local vaccination centre, and to get our patients prioritised not only with inflammatory bowel disease, but people with limited logical and dermatological conditions to get them prioritised over the next week or so. So it will vary. I don't think people should worry, I think they're gonna get a call or a letter inviting them to a vaccine central to the GP surgery in the next two weeks.

46:20
Right. Okay. And you know, as you say, it is vary in across the country, and certainly, for anybody who is keep an eye on our website as well, because we are doing some work around this issue, and trying

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to ensure that everybody who needs to be is being identified and contacted and getting that dose. So I guess one last thing, just to mention the BSG guidance, the British society gastroenterology guidance, which he said is slightly different to what's been published by the government that is actually now live on the British society website. So we're post for everybody who's listening, we'll post something into the chat with that link. Again, because it's slightly different, your your view is that the the consultants and specialists will be taking the BSG line and making sure that you know, everybody who needs to be is getting that dose.

47:22
Sir, the difficulty with the chase vi guidance is it's actually quite difficult to work out whether somebody is eligible, working back in time to data vaccine, which may be many months ago to work out whether they were on a certain dose of steroid or, or what have you. So it's very difficult. It's much easier, I think, to take a less stringent view and ensure that people are identified and vaccinated. So I think the easier option is the BSG option. And I know that the rheumatology Sati dermatology Sati and Arenal started taking a very similar line as the BSG. Whether the JCI wanted to wanted that to happen or not, I'm not certain, but I think it's going to be easier to implement.

48:18
Brilliant. Thank you so much Tareq. We're right on time, for Endian. And just to reassure, again, everybody, we know that there are lots of lots of additional questions, and we're going to do our best to signpost, you or answer those questions after today, that it's been fantastic seeing all of the, you know, the enthusiasm and engagement with the talk. And I am now going to hand over to sue to just give the thanks to you and speak later. Thank you, Sue.

48:52
Yeah, thanks so much, Tariq. That was really excellent. And the hopefully we've only really touch the tip of the iceberg in terms of how many questions we've had, but we knew it would stimulate a lot of interest. But I'm sure it's been a very reassuring talk for everybody. But thank you again, for giving up your time. We really appreciate it. Thank you very much. Nice to see you. Well, everyone, we're going to move on now to our AGM. The format format of that is, I'm going to lead on a review of last year. I'll be followed by Tom Brady, our Treasurer who's going to look briefly at our financials, they'll be opportunity to ask us some questions there. So again, if you've got any questions, put them through your q&a area. And then we move on to the exciting bit the resolution. And for those of you who haven't had the opportunity to vote to be able to do that, and we will, the meeting will be brought to a close by Sarah who's going to give us a presentation of our strategy and reviewing what There we are. So Andrew, if you could put that on my first slide, please.

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