



So what I'm going to do is tell you a little bit about why we wanted to have some of the UK Biobank, specifically to address some of the questions which we can't address in some of the studies we do in our centre.

So therefore I'm going to give you a bit of background about arthritis and then when we ask for some of the data we actually had two sort of research questions. One was looking at the outcomes in arthritis and the other one was looking at some of the risk factor so who is developing arthritis, what are those factors.

So just a bit about the background the term rheumatoid conditions there are about over 100 different sorts of rheumatoid conditions and they can affect everybody even children can get arthritis, up until the older age. Sometimes there is an inflammation component involved and then we talk about arthritis so examples are rheumatoid arthritis and psoriatic arthritis and that is something we are especially interested in in our centre, so we know if we just look in the general population about half percent of one percent of the population will have either psoriatic or rheumatoid arthritis and as mentioned it is an autoimmune disease. So what does that actually mean an autoimmune disease?

A bit of background, so normally our immune system fights against external agents so if there's a virus your body responds to that, there is some cells and there's some activation. We try to temper down some of the inflammation from the external factors, but with autoimmune that means that we actually fight against some substances or some tissues within our own body so that the balance where we normally have good and bad cells within our body, that sort of tips towards the bad cells. Imbalances in our immune system might cause inflammation which is one of the important factors in arthritis.

So this is just a representation of one of the bones in our body so up there if the bone both above and below then there are some sort of tendons and muscles around your joint so just to make sure you are stable as well, and of course for the movement of your joint. Then this part which is called the synovium and the synovium fluid and that's where often these bad cells accumulate and cause some damage so some of these cells there is a lot of inflammation in the synovium so some of your

joints may be quite stiff that maybe become very swollen or tender as well, but also some of these cells may go into your cartilage or your bone and that causes quite a lot of damage.

So where is this damage in general actually it can be almost everywhere but in rheumatoid arthritis and psoriatic arthritis it often starts in your hands in the smaller joints or in some of your joints in the feet but can also involve your knee joints or hip joints or sometimes elbow or your shoulders. Although we talk about rheumatoid arthritis and psoriatic arthritis they are different sort of diseases, of course in psoriatic arthritis it includes the name psoriasis so these people also have psoriasis so there's some involvement of your skin I'm so this is an example picture of of somebody which would've involvement of the skin of one of the fingers. There's another sort of difference, when I said the cell can cause damage to your joints here you can see like little bites out of your bones and of course you can imagine it is very painful and some of these bones become kind of stiff and deform as well. So what do we want to sort of know and why do we want to look at these questions in UK Biobank.

As mentioned in the introduction it has a huge impact on patients' quality of life because it's a chronic disease there is some medication available but there's no cure for arthritis yet. So we saw already that a lot of people may have damage in the joint as consequence there are some differences and difficulties when people do daily tasks, task, people have difficulty opening a bottle of milk and walking stairs just walking outside people also have problems at work. We know for example that about forty to fifty percent of patients have to stop working within the first five years of diagnosis, but it also may cause some other diseases sometimes due to the disease itself but sometimes due to the medication these people use because the medication is specially directed towards the immune system and that may cause other problems as well. We also know that a lot of people with arthritis have other diseases especially these people have a lot of problems with their hearts so cardiovascular diseases sometimes lung diseases as well, so what we are especially interested in is what is actually how often does it occur people with these co morbidities and how does that affect how you function in daily life as well.

So some previous studies have already looked at it so why do we want to look again that the UK Biobank. So I think one of the problems is that a lot of people doing these studies just look in patients with arthritis or just look in the general population and you can't always compare these studies together. Also often as said in the beginning many people with arthritis just look at rheumatoid arthritis or just look in psoriatic arthritis, so again it is sometimes difficult to compare these diseases in one study. There is also not that much information on the impact of the additional diseases on physical activity from previous study, so I think that's why we applied for the UK

Biobank. To get that information in the good sort of structured way where everybody was asked the same questions about physical activity and about other diseases and arthritis as well. One of the first questions we want to investigate is people with arthritis how often do they have cardiovascular disease or lung disease is there a difference between different sort of rheumatic diseases, but also how different is that with the general population of those we don't have any arthritis and then in addition we want to look at what is then the impact and on physical activity in daily life.

So to answer this question this question we look at those who said they had arthritis and those who didn't have arthritis. So the first thing is then to compare the number of people with cardiovascular disease in in both populations you almost expect that that would probably be higher in the arthritis population but we don't know yet. Then of course the next step will then be to look at those who have arthritis and for example cardiovascular disease what impact may that have on physical activity and is the impact lower or the same of those who don't have any arthritis but still have cardiovascular disease so it that way we try to understand how the impact is of all of these diseases on daily functioning because that that's quite important for people. You want to go out to you want to be able to I make a meal and see your friends as well go for a walk outside and so for that we will see specifically look at activities in the home and activities outside the home and also some of the demands of those who are still working.

So the only thing we have done so far is briefly look how many people reported to have arthritis or one of the other rheumatological conditions in the UK Biobank and as you see here there is about 1.2 percent said they had rheumatoid arthritis. As you remember from the first slide we did say that we expect about one percent of the people to have rheumatoid arthritis we still need to confirm some of these findings because we also going to look at the medication some of the people used. Osteoarthritis, so again that is damage of the joint that's more common and that's also what we know is more common than some of the other types and psoriatic arthritis we see here that that the percentage open to is slightly lower than what we expect from the general population and as other types of rheumatological conditions like gout or lupus, what we are going to look at. We just also briefly had a look at physical activities so you may remember this question when you were asked about general activities, so walking for pleasure, so most people did that and about 30 percent of you did that on a regular basis other exercises by 21 percent of you said okay we do some regular exercises like swimming or cycling and there were only a few percent about four and a half percent who did really strenuous sort of sports and I think that that's representative of any sort of and within the whole population about 22 percent at they did some light DIY on a regular basis as well so

this information is something we going to link with the other information so that's one of the questions we want to address.

The next question is another important question and that's looking at sort of what are the factors that may why you get develop rheumatoid arthritis or psoriatic arthritis and other factors not. We already know from some of the studies and also from the Wellcome Trust studies, which was mentioned in the first presentation whether you will get rheumatoid arthritis, but that's not the whole story no. There are other risk factors smoking is probably also one of the biggest risk factors but some studies also found something linked with obesity some diets have been found to be linked with the development of rheumatoid arthritis but also things like blood transfusion as well but all these are fairly small part and they are definitely not a whole picture so even that there may be somebody who has all the sort of the bad sort of lifestyle habits and have some of the genetic factors they still will not develop arthritis, so there is a big question mark still that we need to investigate. So again what has been done in previous studies a lot of people just look at genes or they just look at some of these other lifestyle factors they don't really often combine all these factors in one study the other thing is that some study finds for example an association between obesity and the development of rheumatoid arthritis but other studies don't so it's really important to sort of repeat these analysis in a good sort of dataset where we either can confirm some of this analysis or even identify new factors which are quite important but we don't know yet.

So the question we are going to address in the next one and a half to two years are, especially when the genetic data is available as well so which of these lifestyle factors and there may be some factors we never thought about before and they may come up as one of the risk factors are associated with the development of rheumatoid arthritis and we do sort of the same question in patients to look at psoriatic arthritis so for that we need to do so a slightly different. We can't just start with everybody included and seen for the first time so what we need to do is look at those patients who develop arthritis after they were seen so take all those patients who didn't say they has arthritis at the beginning and then of course we've a number of patients were assessed at repeat follow-up so then we look at that sort of second follow-up visit and look at those who developed arthritis but again a lot of people will not have developed arthritis. The next step will then be to compare at all these factors so look at the genes, look at some of these factors which we already know are probably associated but there may also be some other factors of all those questionnaires you had to complete that may come up and that gives us some good clue what's going on and why people develop arthritis. For us the main thing is the uniqueness of the UK Biobank is it can address some of the questions hopefully to identify new factors or confirm some of these factors with that we can advise

people of the general population maybe to reduce smoking or do more exercise depending on what factors we identify, also if there are some certain genes and a person have some of this lifestyle factors then we could say ok the chance that you will develop rheumatoid arthritis for example is so high so we are going to give you short term treatment with some of the arthritis medication, but you need to be very careful because some of these medications are very costly and they also have some consequences because people may have some adverse events because of these medications. So that that's sort of looking ideally you want to sort of change the way some people some of the lifestyle factors, but it could be that you give some advice and short term treatment as well so that's the first part and then of course the information about outcomes is very important because we don't really know how all these factors are linked, rheumatoid arthritis some of the other diseases and how big actually the impact is on daily living as well. So within the next two years we hope to address both of these questions.

Of course it's not something I do by myself within the centre so Mike Cook who is here as well he's started to do the analysis and Jamie Sergeant and John Bowes, who has genetic background, is part of this research team