Ken Audio Presentation – 22 September Evening

	Okay, right, good evening. My name is Ken Muir I'm an Epidemiologist. I work not too far away from here at the University of Manchester and it's my great pleasure to come along this evening and share with you a little bit of the work that we've started with some of the fantastic resource that you've heard about this evening. The UK Biobank Data Set.
_00:00:24_	But, I have a confession and I'd like to start and share it with you. I got the email from Andrew and Jenny asking me to come along. They said it was a Central Manchester hotel, about 8.30 at night and there would be a microphone provided. So I thought to myself this sounds promising because they've obviously heard about my reputation as a stand-up Elvis impersonator! So my confession is I'm slightly disappointed because it doesn't look like that's what you want.
_00:01:01_	So I'm going to start with a choice. It's not dead yet! So my choice before you is which would you prefer, my Elvis impression or a short talk on risk?!
_00:01:15_	Good you got the right answer.
_00:01:06_	*… Elvis!!*
_00:01:18_	Best of both worlds yeah. No, no, actually as you'll notice I have got a cold so I'll save the Elvis impression for next time!
_00:01:31_	So let's get down to the serious business. Now what am I really here to do? First thing to say is that I am nothing in one sense to do with UK Biobank. I'm not paid by them, I'm not influenced by them, I'm independent. So I'm more like you tonight. I am here from altruism trying to give something back as a big big thank you to all of you who have participated in this really tremendous study. So that's really my main aim for today and that is to thank all of you for taking the time to join in what is a landmark study.
_00:02:12_	You've started to hear quite a bit about what the data are that's been collected on you and what you've not heard so much about so far is how that data might be used and indeed is starting to be used. So in the next 15 minutes I'm going to tell you about some of the work that we're doing using your data and your data is supplemented by another 495,000 people that aren't present here this evening.
_00:02:42_	So that' really one of the take home messages. One of the things about this study is it collects all types of data on really large numbers and that's the way that science will advance in a robust and good way. Lots of studies are done with small sample sizes.
_00:03:00_	So this is my starting point for my talk. This is a slightly elderly gentleman, actually he's aged 80 in this photograph and what you'll notice about him is two things maybe. First of all he is in a wheelchair, second he's got his eyes closed. So this gentleman actually suffers from many chronic diseases of aging. He's had a fall so he's off his legs and he has to get about in a wheelchair. His eyes are shut because he has macular degeneration, a common degenerative condition of the eye that results in premature blindness in large numbers of us as we age. The thing you can't recognise about him is he also probably has prostate cancer. So as we get older unfortunately many of us develop quite serious chronic illnesses and one of the values of UK Biobank is to allow

	us to study at scale in a really truly fantastic number of people what might cause diseases like macular degeneration, prostate cancer, arthritis.
_00:04:13_	So my plan for the next 15 minutes is to do the following: I want to very quickly bring you up to speed with what goes before Biobank, what we knew before Biobank was set up, a little background to the science for 5 minutes. I then want to quickly introduce you to the rather fascinating world of risk calculators. I say that because that's what I do and hopefully you will share my enthusiasm by the end but maybe you won't and the most interesting part of my talk will be the discussion that we have afterwards as to how useful you think this could be and I'm perfectly happy for you to tell me this is absolutely useless and it's my job to convince you that it may not be.
_00:05:01_	Perhaps again the most interesting newer aspect of UK Biobank is that addition of the genetic data and we all have certain fears and certain suspicions about genetic data and how it can be used and what it secretly tells us about ourselves that we don't even know.
_00:05:22_	So I'm going to quickly introduce you to genetic data and show how it can add to risk prediction models and be used for good. And we don't have a lot of time to go into the background so you're going to have to live with me as we sort of canter through many of these concepts.
_00:05:38_	The final thing to say is, I've put this in blue because this is optional, we probably would have our most interesting discussion around some further thoughts at the end of this and depending on whether Andrew allows I'll continue or I'll stop and take it in open questions.
_00:05:55_	So let's get on with this. The starting point is really, as I said, the first point to look at is background to the science. What do we know robustly or reliably before we did UK Biobank? So you'll have seen each day those of you that read the Daily Mail or the common press, there will be some horror story out there, I don't know what this one says "Tomato's fight cancer, red wine does this, butter is bad for you then again butter is good for you, margarine is the answer etc. etc." So we are bombarded with health messages. I'm going to share this with you. Most of them may not be reliable! The main reason why they may not be reliable is normally because they're based on very small sample sizes. A typical study might have 300 cases, 300 controls and there's a whole problem how you collect data accurately and therefore you get uncertainty and instead of looking at one study, a definitive study such as Biobank, we have to look at 10 or 20 small studies, a lot of variation.
_00:07:09_	So what do we know for certain? I'm going to share three facts with you. The first is as shown in this map. So we've already had the example of prostate cancer, common cancer in males, this would be true of breast cancer etc. In terms of most of the epithelial cancers will show a distribution like this. This is a map of incidents and increasing warmth of the colour is increasing incidents. What do we notice about the so called developed countries? Warmer colours reds/oranges higher incidents. So cancer if we look on a worldwide perspective is not a universally occurring disease, in fact it's vanishingly rare in some countries. So what we can take home from this is something that is going on in Western countries, some aspects of our lifestyle are leading on to increased risks of all of the common cancers that you know and you'll

	know somebody that suffers from.
_00:08:11_	The difficulty with this sort of observation is it doesn't tell us within that general observation what are the specific lifestyle factors that lead onto that risk. The only way you can do that is to look at a very detailed data set such as UK Biobank.
_00:08:29_	Let me show you a rather complicated graph. Some of you like graphs I'm sure, some of you not quite so comfortable with them. What this shows is essentially that if the bar is above the yellow bar (I can't get the pointer to work but never mind, oh there we are). If the bar is above this yellow bar then what it's telling us is there is a genetic component to these types of cancers and all of the work that I'm going to present tonight is on cancer but we're also doing studies of arthritis, dementia and other chronic conditions but, in the interests of time lets focus on cancers and what do we notice for example about breast cancer? What's called the familial relative risk is about double the base line risk of one. What does that mean? What that means is if there is a cancer in any of your first degree relatives your mother, your sister and you are a woman then you are at nearly double the risk of developing breast cancer yourself. If we look at prostate cancer. If there's a prostate cancer in your first degree relatives again you're about double the risk and if you happen to suffer from lymphocytic leukaemia there's a particularly high genetic component to it.
_00:10:01_	Now the problem with this data again it's the same as the map. It doesn't tell us which of the genes involved it just tells us that there is a genetic component and what we'll be able to do with the UK Biobank data is look at what are the specific genes that are involved.
_00:10:18_	This is my final introductory slide and this is quite an interesting one and we could spend 15/20 minutes looking at it. I'm just going to cut to the chase and the chase is this Chinese people living in China have a very low rate of this particular cancer which is prostate cancer. It would be much the same for breast cancer, colon rectal cancer, any of the common cancers. Chinese people that move to the United States of America within 10-15 years their rates of cancer go up drastically and move towards that of people that have lived in the United States all of their life.
_00:11:02_	So what does this tell us? It tells us two important things. It tells us that it's nothing to do with your genetics protecting you, it's telling you it's to do with the environment in which you live because Chinese people are not inherently protected from cancer it's just they're living in a lifestyle that doesn't influence cancer.
_00:11:26_	So what do we know from this? We know that genetics are important, we know that your lifestyle is very important and what we need to do is characterise both in much more detail and work out what drives a particular disease and this is again an important take home message and started to come out of the early discussions. It used to be, 10 years ago before Biobank, we tended to think of diseases as either having an environmental component that drove their aetiology or a genetic component and there are examples of that. We've heard about smoking and if you smoke, almost regardless of your gene type 9 out of 10 smokers will develop a cancer. And there are some diseases that are principally genetic. You'll have all heard of these breast cancer causing genes, the BRCA Genes [_00:12:21_] and if you've got a BRCA mutation running in your family 9 out of 10 of those women that carry the bad BRCA

	Gene will develop breast cancer almost regardless of their lifestyle. So there are examples where either the environment your lifestyle dominates or your genetics dominates but the take home message is it seems that for the majority and by majority I mean 80 or even 90% of cancers may be about 95% of dementia cases a lot of cardiovascular disease is driven by a mixture of your environment, your lifestyle and the genetic factors and these two come together and interact and drive your individual risk and that's the real strength of UK Biobank. For the first time we have both broad scale information on lifestyle and broad scale information on genetic factors.
_00:13:23_	Why is that so good? Well, why it's so good in this next five minutes I'm going to talk about risk calculators and show basically what they are which is a way of putting that sort of data together. So for five minutes if you'll bear with me I'm going to briefly introduce you to risk calculation.
_00:13:47_	Now, what a risk calculator does is it works at the level of the individual and what we know about ourselves is we are completely unique and we all have a different lifestyle, a different diet, a different activity and we all have a unique genetic make-up and so what we need to do instead of making generalizable risk statements about what to do to prevent cancer, we need to get down to the individual and work out what is right for you, what is right or you and what is right for you and I can guarantee that they will not be the same. So we're moving into the area of what's called personalised medicine or personalised prevention. We will at the end of the analysis we do with UK Biobank data be able to tell you individually what you should best be doing.
_00:14:44_	So risk calculators and I am aware of the time with going last in the program, I knew I'd be squeezed for time so I'm still going to canter on regardless, we will finish in 10 minutes so please bear with me. What a risk calculator does is it takes a range of factors and totalises your risk. So you don't really need to follow this bit but I'm going to go through it.
_00:15:10_	So this is a risk calculator for prostate cancer which has come up and I've chosen as my example tonight. We take a man, his age is 65 that contributes 40 points to his total. His ethnicity happens to be white that contributes 10 points so he's got a running total of 50 points. You can see what's going to happen he adds up all of these risk factors together and gets a total number of points and for that individual with that particular constellation of factors we can read of his risk of high grade prostate cancer which is nearly 50%.
_00:15:49_	Now some of you in the audience mainly the men but many women, will know about PSA which is the test that's been used up till now, will know that PSA is normally the single marker test that's used and if you're PSA is less than 4 you will go forwards and be told that you haven't got prostate cancer. But when we put all of these factors together, it doesn't matter what the factors are to some extent, we would come to quite the opposite conclusion. One in two men with that combination of factors will have an aggressive prostate cancer.
_00:16:27_	So this is the strength of the approach of using risk calculators that instead of using one test alone, combine tests, produce a summary score and give us an individualised more precise estimate or risk. So these are used quite a bit in the clinical situation. Increasingly what we're doing is developing them for use in the community.

_00:16:52_	So let me show you a further example of prostate cancer. This one is a risk calculator based on the known risk factors in your lifestyle only that would influence prostate cancer risk. So they are age, ethnicity, family history, diet and some genetic markers and what we can do is take any of you now, put you through a risk calculation program and compute your individual risk and we can do that for any disease.
_00:17:22_	And here's one brave volunteer that went through that process, namely myself and what I'm going to share with you is my result. My result is this bar here and this is the reference bar. This is the highest possible risk that you can have of prostate cancer and if you are down here you've got the lowest possible risk in any population. My risk is slightly above normal. So how we can use these calculators further is we can advise the individual i.e. me, on what I might think about doing in my lifestyle. So the two simplest things I can do is if I eat 5 servings of foods that contain… eat less than 5 servings of food that contain fat I will drop my risk down a good chunk from there to there and if I increase my consumption of tomatoes which at the end of the day isn't too hard to do, I can drop my risk down to quite a low level. This is my prescription. If we put any of you through you may get different advice and that's what we are trying to do using your data in the UK Biobank data set.
_00:18:40_	So that's what the strength of UK Biobank is it allows us on a huge number of individuals to work out these risk prediction models and potentially take those forwards. What's further very interesting within UK Biobank is we can also look at the contribution of genetic factors to the overall risk and what you saw from the earlier slides was we now know our risk is driven not only by our lifestyle but also by our individual genetic factors.
_00:19:14_	So very quickly I'll share with you genetic factors that are studied in UK Biobank and I'm still okay to carry on? Yeah. So quickly what UK Biobank has measured is about 600,000 genetic markers in each and every one of you and of the half million people that have participated. So it has captured virtually all of your genetic code. So we can look in that huge genetic information as to which markers associate with which disease. Where or why is that useful? I'll quickly show you.
_00:19:57_	So again let's focus on prostate cancer. This is a set of chromosomes taken from any of your blood cells and what we've found out with a number of leading groups lead by a lady called Roz Eels is that in fact not all of the 600,000 genetic markers have got anything to do with prostate cancer it actually comes down to, so far, about 100 markers only influence your prostate cancer risk. Similarly for breast cancer a different set of 150 or so markers predict breast cancer risk. For colorectal cancer a different number and a different set of markers.
_00:20:40_	So let's by way of example show us how we can use these genetic markers to further refine your risk prediction. This is what it means in reality. This is what's called an age incidents curve for prostate cancer and this is age on this axis and this is your cumulative risk of that axis. This red line here is the age incidents curve of any man carrying a majority of the bad risk genetic markers. If you happen to be that unlucky man by age 55 your risk is already starting to go up and by age 80 or 90 about 1 in 3 of those men will develop prostate cancer. These are the unlucky ones. Equally there are lucky, there are winner in this and if you happen to carry the good markers that those 100 low side as they're called, virtually none of those men will develop prostate

	cancer. So the genetics themselves as well as the environmental factors need to be put together and combine that to estimate your combined risk and that's what a risk calculator does.
_00:22:04_	So what we can move from is instead of treading the population as all being the same and the disease occurring in so called random individuals, what we can now do is stratify almost, well actually from birth whether you are predisposed to one disease or another and follow those individuals up appropriately. So on the basis of the blood test that you've done and what we already know, we can categorise your underlying predisposition to prostate cancer, breast cancer and dementia and therefore target the surveillance of those individuals and this is the likely future in 10 years' time. Instead of a cancer seemingly occurring at random in a population of 1,000 individuals, we will ultimately end up with about 80% of the cancers occurring in the 20% that are most genetically predisposed. There will still be occasional cancers occurring in the residual population but it changes entirely how we will surveil [_00:23:13_] for diseases like prostate cancer. Instead of having to screen the whole population we can screen specific strata and do that at a much greater/regular interval and that will change the effecting of the screening programs and of prevention programs.
_00:23:34_	So that's what we are doing. We are currently analysing the epidemiological data set, we are starting to receive the genetic data set and we are putting all of that together into risk calculators.
_00:23:54_	So by way of a conclusion and then leading onto general discussion I wanted to put some questions to you. Do you think that this is an ethical thing to do? Do you think it's a useful thing to do? Would you, for example, find these models useful if we can tell you your future risk of dementia or cancer? Quick show of hands if you think it's a useful application?
_00:24:21_	Let me refine the question and we'll finish in two seconds. If I refine the question to say do you want to know your individual risk if we can do something about it does that make it even better?
_00:24:37_	*Yes.*
_00:24:37_	And that's the key isn't it? There's no point in telling you and worrying you, you're at risk unless we can do something about it. So again what we're doing with UK Biobank data and other data sets is looking at what interventions actually then work. So not only can we tell you you're at risk we can give you lifestyle advice to reduce that risk.
_00:25:00_	*But will you tell the insurance company?*
_00:25:02_	Good question. Now we're going to hold that because that's a very important aspect of this. So my final question is would you like to know your risk if ultimately we can give you a pill that will save you changing your lifestyle, doing more exercise and all the things that you've not so far really manged to do, would that be the holy grail?
_00:25:26_	And this future use of providing this risk information is the challenge and how best we use it in an ethical way and in a useful way is something that we need to grapple with as a population.

_00:25:40_	So let me come right back to the start. Your data is fantastically useful. UK Biobank is a tremendous resource it's extremely well managed, it's an extremely well run study and we are privileged to be accessing that data and starting to do some of the work that I've described to you this evening. I welcome any questions and thoughts that you have. Thanks
	ENDS _00:26:05_