The Nuffield Department of Population Health, or NDPH, was created in 2013 to carry out research and train scientists to seek answers to some of the most important questions about the causes, prevention and treatment of disease here in the UK and around the world. The department's work is vital - despite improvements in life expectancy seen in developed countries in recent decades, the health problems we face today, particularly from long-term chronic conditions, still result in avoidable suffering for millions of people worldwide.

In this interview with Kat Arney, the head of the department Professor Sir Rory Collins explains the idea behind the formation of the NDPH and its approach to research – starting with the question what do we actually mean by population health?

Rory: There are all sorts of terms that are used: public health, community health, global health. I think that in a way it's the opposite of personalised medicine. It's at group level rather than trying to be very precise. I think there is a danger in over-precision - if you put all your resources into trying to treat an individual perfectly, that assumes you know how to do that. It may well be that you get most of it right, but you get some of it wrong and you would be better off with some kind of general algorithms that you applied to the population. Some individuals may not do quite as well, but individuals on average would do much better.

Kat: There is a temptation to treat everyone as an individual special snowflake, so this kind of large-scale approach says we can get benefits by just looking at all the snow?

Rory: Yes, and also you want to think what for each individual will produce on average the best outcome. Rather than having a very small percentage of very rich people, it's a more equitable and perhaps much more effective distribution of health.

Kat: In terms of the work that goes on here, what sort of spread have you got in the approaches that you are taking and the kind of questions that you're trying to answer?

Rory: The focus of the department is on chronic disease - the diseases that are going to occur most commonly during middle and old age. We are talking about cardiovascular disease, cancer, associated diseases such as diabetes, diseases associated with cognitive function, with joints – the slow decrepitude of age. In the same way that we have very successfully pushed back when cardiovascular disease affects people, can we do the same thing with the disabling condition of dementia?

Kat: None of us can cheat death in the end, so the name of the game here is about extending healthy lifespan for as many people in the population as possible?

Rory: Yes, and the most remarkable thing I think is that people just don't realise how good it has got. If you look at the trends in terms of mortality, not just in rich countries but across the world and particularly in infectious diseases, we've been fantastically successful in getting kids through adolescence and into early middle age, so that has been very, very successful. We have to remember that the UK is just a small percentage of the world, and the things we learn can be applied - not necessarily in the same way - but can be applied worldwide and have an enormous impact.

And that I think is another aspect of the Department – not just thinking about one narrow view of an individual patient, or even an individual country. We have to think about the things that matter in different countries, and chronic disease is mattering increasingly not just in the developed world, but in developing countries. As kids get through to adolescence and early middle age then they get hit by the conditions of early middle age, so what can we learn that can be applied in those countries to

help reduce their risks of dying prematurely or being disabled prematurely? More active life and big increases in the quality of that life.

Kat: Looking in a bit more detail at the kind of work that goes on here, what are some of the focuses and the methods or approaches that the researchers in the NDPH are using?

Rory: The key approach that lies at the heart of what we do is focusing on what matters. Looking at important health conditions, the big causes of death and disability, and then trying to understand what are the major determinants of those major causes of death and disability, rather than focusing on novelty. Those are the things that if you can change them will have a big impact on population health.

There are three big epidemiological groups – there's the National Perinatal Epidemiology Unit (NPEU), which is particularly focused on understanding disability and death around the time of childbirth. Then we move much later to the Cancer Epidemiology Unit (CEU) with its focus on cancer. A lot of their work has been around the determinants of cancer in women, particularly the role of hormones.

The other group is the Clinical Trial Service Unit (CTSU), which has largely focused on randomised trials, especially in cardiovascular disease, and then more recently on ways of preventing heart attacks and strokes in the first place – blood pressure lowering and now cholesterol-lowering. The CTSU has set up observational studies both in developed countries – such as the UK Biobank project of half a million people - but also parallel studies such as the China Kadoorie Biobank, which is half a million people in China, and a similar study in Mexico – the 150,000 person Mexico City cohort.

So we are sitting on an enormous richness of data, more and more data emerging from the blood samples, genotypes, biochemical measures. It's a great training ground for the students and for research fellows to work with data. A lot of problem in the past has been not enough data. Now we have a new problem - we have so much data and data on a scale that allows real signal to emerge.

Kat: What was the idea behind bringing these slightly disparate teams together to form one coherent department?

Rory: There has been a lot of strength in Oxford in population and health science but they weren't linked together. So there was a lot of complementarity which wasn't taken advantage of. The idea of a Department of Population Health was to bring all of that together and to increase collaboration between the different groups. It was about bringing together the strengths that already existed and making it even stronger.

In addition we're providing an environment in which people could be taught, could be trained, and could have their careers developed. It is a training school for people to come and then do PhDs in that area. Many of them are now doing PhDs within the Department using the richness of the data that we have. We have really large-scale, really detailed data that allows people to get off to a running start doing a PhD in something that really matters, which is a great way to start your career.

Kat: It does very much feel like the watchword of the department is data. How has that driven the kind of things that you have done here and the successes that have come out of the department?

Rory: I think what is critical to the department is trying to understand what's really important in terms of health. What are the major causes of disease, and what are the main ways in which you can reduce the risk of bad outcomes, focusing on generating reliable evidence about the things that

matter? Rather than generate these claims of ‘a bit more of this causes a bit less of that disease’, or ‘eat more fat, eat less fat’, the department was also interested in testing causation.

Until relatively recently the only way to do that was through randomised trials – if you think blood pressure is an important determinant of stroke, what happens if you lower blood pressure? Maybe nothing: it may be that you've had blood pressure that is high for decades and then lowering it is too late. But when you do the randomised trials actually you remarkably see very rapid reductions [in stroke risk] and also slower reductions in the risk of coronary heart disease. So that provides really good evidence about causation and about reversibility.

More recently we are seeing the introduction of genetic epidemiology where the association of genetic variants with an intermediate risk factor, say with LDL-cholesterol level, can be used as a quasi-randomisation. We refer to it as Mendelian randomisation because whether or not you have the variant that produces slightly higher or slightly lower cholesterol is a random process. You can see whether people with higher or lower LDL have different levels of risk, so it can help you determine whether the association is causal.

It becomes an opportunity to see whether other risk factors may be causally related to disease and may help to determine whether one brings forward new drugs to hit a target that looks causal or not if it doesn't look causal. So epidemiology and randomised trials are becoming closer and closer together through that process.

Kat: We've talked a bit about the kind of epidemiological studies that are going on – large studies like the Million Women Study and also the work of the Clinical Trials Unit, taking large groups of people and giving them one treatment or not another treatment and seeing the differences between them. What are some of the other groups here doing, for example trying to apply these findings?

Rory: I think what's important about a department like the Nuffield Department of Population Health is the interaction between different groups. A lot of the time you see observational epidemiology being done in isolation. You see randomised trials being done as if epidemiology wasn't relevant to it. What we've been trying to do is link the two together, so first to demonstrate the treatments work, and then work out are they cost-effective?

I think we have a fantastically powerful health economics group who work closely with the trialists ensuring the right data are collected to allow them to produce generalisable health economic models that can provide information, not just in Britain but other populations too. We've got the Ethox group with Mike Parker, now being funded by the Wellcome Trust – the first Institute on ethics that the Wellcome Trust has set up, embedded within a research institute. They’re understanding the problems and coming up with practical but appropriate solutions to those problems, so they are part of the research team.

How do you assess outcomes that matter to patients, to individuals? Well you ask them what matters to them, and you develop tools to test them. And so we have an outcomes research group that has developed a lot of tools for assessing the disability associated with a range of different diseases, such as Parkinson's and joint problems, and those can be used to determine whether treatments are actually influencing the things that matter to the patients. Again, they are embedded within the research team.

And then finally there's no point in learning this if it doesn't get implemented, so there are groups that are thinking about once we've learned what works, what are the ways in which you can get

people to change their diet? What are the things that actually change when you know that change could produce improvements in health?

It goes from original idea, often generated by observational epidemiology, evaluation of whether that idea is really a causal association and can be reversed, determining its cost-effectiveness, determining its impact on things that matter to patients, and then working out how that can be implemented. And again thinking globally, thinking about the world population, not about some individual person or individual population.

Kat: What do you see as the really big challenges that the department is addressing? What's keeping you up at night?

Rory: As an epidemiologist in the past the complaint was too little data. Now the complaint is too much data, and that really is why the Department set up the Big Data Institute (BDI) here in Oxford. It's a collaboration between the Department of Population Health and the Department of Medicine, where there are experts in statistical genetics that can work alongside the experts in epidemiology within the Department of Population Health, and we are recruiting in people with skills in bioinformatics.

My observation over the last 30 years is that if you don't work together with people with different skills, there is a danger that groups will go off and solve the wrong problem. What works really well is having people with different expertise, different knowledge, and different abilities working very closely together so that the right problems are solved, and that's what the Big Data Institute within the Department of Population Health can allow us to do.

Our focus has been on cancer and cardiovascular disease, but I think if we look to the future we do certainly want to extend into the diseases of older age, around cognition and around joint and bone conditions. That focus is because they have a big impact on the quantity and quality of life - not just in the developed world but in the developing world, chronic disease is the major problem now. Infectious diseases are still a problem but they have been dealt with very, very effectively. As a consequence, people are surviving into middle age and we need to work out how to help them.

Our focus is on a global approach to the chronic diseases of middle and older age. We have created over the last 20 years too much data, and now over the next 20 years we're going to create many more answers from those data.

To find out more about the work of the NDPH, as well as opportunities for training and research positions, please visit www.ndph.ox.ac.uk