

UK Biobank

Unlocking the statistics of ill health

Professor Sir Rory Collins discusses his role as Principal Investigator and Chief Executive of UK Biobank, a major future-focused national health resource and registered charity that aims to improve the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses.

UK Biobank is leading the way by developing a powerful resource for researchers to help improve our future health. Recruiting half a million people aged 40–69 during 2006 to 2010 for a large cohort study, UK Biobank is collecting vital data to increase knowledge about a wide range of serious illnesses, such as cancer, heart diseases, stroke, diabetes, arthritis, osteoporosis, eye disorders, and depression, as well as forms of dementia. The 500,000 participants had physical measures made and answered detailed questions about themselves. UK Biobank also collected samples of the subjects' blood, urine, and saliva for future analysis and are now tracking the participants' health over time through medical record systems. Moving forward as the study continues, UK Biobank is building this powerful resource to allow other scientists from around the world to use it to discover why some people develop particular diseases and others do not. ▶

What is your role as the Principal Investigator and CEO of UK Biobank?

The aim of UK Biobank is to establish a large prospective cohort that allows researchers from around the world to find out more about the causes of many different diseases. In order for the resource to be as useful as possible for researchers, we first had to recruit a large number of participants; between 2006 and 2010, 500,000 people aged 40–69 joined the project. We then had to find out as much as we could about them – that involved asking them lots of questions about their lifestyle, environment, and health, and making lots of measurements of the participants (including things like blood pressure); as well as collecting blood, urine and saliva for future assays. Finally, we then have to find out about all of the many health conditions that the participants develop subsequently. This involves UK Biobank linking (with consent) with different electronic health record systems, to find out about deaths, cancers, hospitalisations, and GP care among the participants.

My role is to coordinate the team responsible for building this resource, making it more useful for researchers, such as generating genotype and other assay data available from all the participants, and turning health record data into specific information about particular health outcomes. My role also includes encouraging and facilitating use of the resource by researchers, so that UK Biobank generates lots of novel findings that help to improve human health.

Could you tell us about some of UK Biobank's key current projects?

As the team responsible for building the UK Biobank resource, our recent focus has been on enhancing its value for research. For example, we have been using web-based questionnaires to find out more about the participants' diet and work history as potential "exposures" that could impact on the development of particular conditions. Similarly, we have been measuring the amount and intensity of their activity by getting them to wear accelerometers.

With regards to finding out about diseases that participants develop during follow-up, our focus has been on getting access to all of the different health record systems that can provide such information. We then have to use the data from these different systems (which are not necessarily accurate or complete) to determine whether the participant really has had a health outcome,



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such as a stroke or breast cancer. We also need to ascertain the particular type, for example if the health outcome is a stroke due to a blood clot or a bleed, or breast cancer with or without hormone receptors. We need to determine these details because exposures may be specifically related to a particular type of disease – for instance, something that makes blood less likely to clot may result in lower risk of strokes that are caused by clots, but higher risks of strokes due to bleeds. By characterising the participants' exposures and their diseases very specifically, we will make the resource much more useful for researchers to find out about specific causes of disease.

UK Biobank recently launched the world's biggest body-scanning project. How do you hope this will shed new light on major diseases?

The largest previous imaging studies that have been conducted involved less than 10,000 individuals (typically far fewer) and tended to focus on one part of the body (e.g. the heart or the brain). By contrast, 100,000 of UK Biobank's participants will have Magnetic Resonance Imaging (MRI) of their brain, heart and body, and low-power DEXA X-ray of their body, bones and joints, as well as an ultrasound of the arteries in their neck. Researchers will be able to combine this imaging data with all of the other information that we have collected about the participants' previous exposures, including genotype and assay data, and their subsequent health conditions. This uniquely detailed large-scale resource should allow very many novel findings to emerge.

As one obvious example, body mass index (BMI) derived from weight and height is known to be strongly associated with the risk of having a heart attack or a stroke. However, we also know that BMI does not provide a good assessment of the amount or distribution of fat in the body. For example, someone with a lot of muscle, but little fat, will have a high BMI. Also, people with the same BMI may have very different amounts of fat around their body organs, or so-called "visceral" fat, which

is thought to be more relevant to obesity-related conditions. By contrast, body MRI provides very specific information about fat amount and distribution; so the assessment of such large numbers of people will allow researchers to assess the relevance of fat to disease far more specifically than has ever previously been possible. Likewise, detailed brain imaging (which provides information not only about structure but also about function) may well – when combined with information on cognitive function and genotype – allow causes of dementia to be identified.

What impact do you think UK Biobank has made to date for improving the prevention, diagnosis and treatment of serious and life-threatening illnesses?

UK Biobank has been designed as a "prospective" cohort. By using this term, I mean that UK Biobank involves first assessing "exposures" at the start in very large numbers of participants, then looking to see whether there are differences between the exposures of participants who develop a particular condition subsequently during follow-up, and those who do not develop the particular condition. This approach allows researchers to identify novel causes of different diseases.

However, UK Biobank's approach requires not only the assessment of very large numbers of people, but also sufficient duration of follow-up, in order for large enough numbers of participants to have developed any particular condition. The participants in UK Biobank had their baseline assessment of exposures conducted in 2006–2010, so they are only now starting to have had enough follow-up for there to be large enough numbers of some of the more common conditions (such as heart attacks and certain types of cancer). Consequently, although many researchers from around the world have already started to use the resource, and an increasing number of reports on their results are being published, my view is that it will only be in the next 5-10 years that the promise of UK Biobank will be realised.

Does UK Biobank have any exciting new projects in the pipeline?

Having been able to get additional funding to genotype all of the participants in UK Biobank, as well as to measure biochemical markers in their blood and urine samples (such as cholesterol levels), it has become clear that this is a particularly effective way to increase the accessibility of the resource to researchers. That is to say, rather than require individual researchers to find funding for assays, UK Biobank obtains funding to conduct assays that can be widely used by many different researchers.

As a result, we are now seeking additional funding to conduct further sets of assays – for example, looking for markers of exposure to infectious agents, which may be related to risks of cancer and cardiovascular disease. We are also working with researchers who would like to conduct prolonged assessment of cardiac rhythm disturbances (because many “arrhythmias” come and go, they are not detected by a single ECG recording) using a novel device, which can be worn without interfering with normal activities (as we did previously for physical activity). It seems likely that new technology will allow us in the future to assess an increasing range of different exposures among participants.

How would you describe UK Biobank’s long term strategy?

UK Biobank is ALL about the long-term. It has involved the funders – UK government’s Medical Research Council and Wellcome Trust UK charity – to take a long-term perspective. They have invested substantial amounts of research funding (about \$200M so far), with the expectation of little return in terms of life-changing research findings during the first 15 years of the project. Our job now is to make sure that researchers take advantage of the funders’ vision, and turn that investment into new knowledge that in turn helps to reduce death, disability and misery caused by many different conditions.

In 2011 you were knighted by the Queen for your services to science. What did it mean for you to have recognition of your fantastic achievements in the areas of heart attacks, other vascular disease, and cancer?

The reality was that my knighthood was recognition of the work of all of the UK Biobank team. On a personal note though, it was particularly special that my mother was able to attend the ceremony and see that her long-term “investment” in me (like that of the funders of UK Biobank) had paid off!



What would you personally like to see happen in the future at UK Biobank?

UK Biobank has been established to be a resource for academic and commercial researchers to use, without preferential or exclusive access, for any type of health-related research that is in the public interest. My hope is that in the next 5–10 years we will see an increasing number and range of findings emerge from UK Biobank, from many different researchers based all around the world, about the causes of many different diseases and of ways to prevent and treat them.

• *Rory Collins became co-director of Oxford University’s Clinical Trial Service Unit in 1985, BHF Professor of Medicine & Epidemiology in 1996, and UK Biobank Principal Investigator in 2005. His work has been in establishing large-scale epidemiological studies of causes, prevention and treatment of heart attacks, other vascular disease, and cancer.*



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