

*For 15 October 2008*

1. What was the trigger for the creation of UK Biobank and Generation Scotland and can you describe the value and the long-term aims of large biobanks?

In order to help assess the main causes of various chronic diseases quantitatively, it was recognised that there was a strategic need to establish some large blood-based prospective epidemiological studies with prolonged and detailed follow-up of cause-specific morbidity and mortality. The likely value of doing this has been illustrated by combined analyses (“meta-analyses”) of previous small prospective studies. For example, the Prospective Studies Collaboration combined data from about 60 studies involving follow-up of a total of 1 million people for an average of about 12 years. It showed that some of the classical risk factors – such as blood pressure – were much more important than had been realised. This finding has had important implications for research strategies, patient treatment and public health policy (e.g. Food Standards Agency action on reducing salt in processed food in order to reduce population levels of blood pressure). UK Biobank will allow a much wider range of risk factors for a much wider range of diseases to be identified, and studied, more reliably than ever before. This will result in substantial improvements in prevention and treatment, and reduced disability and premature death.

2. Biorepositories such as UK Biobank and Generation Scotland are expected to yield insights into the genetic basis of common diseases. What types of insights do you expect to appear first?

UK Biobank is a classical epidemiologic study (like, for example, Sir Richard Doll’s British Doctors’ Study which was able to demonstrate the full health effects of smoking by following about 50,000 doctors for 50 years). It aims to study lifestyle and environmental causes of disease, as well as genetic causes. Consequently, there is nothing fundamentally new about UK Biobank, except in terms of:

- Size: UK Biobank is much larger than almost all other studies (for example, 500,000 participants versus 50,000 in the British Doctors’ Study);
- Detailed phenotyping: The assessment of participants is very much more detailed than in any other study of similar magnitude: not just questions (as in the British Doctors’ Study) and various physical measures (such as blood pressure, as in studies that contributed to the Prospective Studies Collaboration), but also collection and storage of blood and urine samples. These samples will allow not only many standard assays (for example, blood cholesterol, again as in studies in the Prospective Studies Collaboration), but also many novel assays (not just genes but proteins, metabolites, etc), which will allow a much wider range of risk factors to be studied; and
- Detailed health follow-up: Information on participants will be obtained not only about death and cancer through national registries (as in many previous

prospective studies), but also about general practice consultations, out-patient and in-patient hospital activity, investigations and prescribing, which will allow a much wider range of diseases to be studied.

As a consequence, UK Biobank will provide a powerful resource for studying a wide range of complex diseases that are of great relevance to public health. During the first 10 years of follow-up, extensive and powerful research will be able to be undertaken on more common conditions (such as diabetes, coronary heart disease, chronic lung disease and some cancers). Subsequently, UK Biobank will provide a valuable resource for research into the causes of an increasingly wide range of conditions (such as stroke, less common cancers, joint disease and dementia).

3. How will findings that arise from biobanks be translated into clinical practice? Are there structured pathways facilitating translation?

The role of UK Biobank is to provide a resource that helps researchers to work out the causes of a wide range of debilitating and deadly conditions. Such evidence may then translate into both clinical practice and public health in much the same way as the work of Sir Richard Doll on smoking or of the Prospective Studies Collaboration on blood pressure. It may also help to identify new disease pathways that lead to new treatments: for example, both epidemiological evidence relating blood cholesterol to heart disease risk and genetic evidence for abnormalities in the LDL cholesterol receptor led to the development of statin drugs to lower “bad” LDL-cholesterol, which are now saving tens of thousands of lives each year.

Early in its inception, UK Biobank was criticised for the large-scale of funding required, and for the slow speed at which recruitment was started and became established. To what extent have these criticisms been overcome?

Given the level of investment in UK Biobank (£62 million to set up the resource), it was appropriate to spend a considerable amount of time consulting widely on its detailed planning (e.g. what questions to ask, what measurements to make, what samples to collect) and then to pilot all of the procedures before starting to recruit (including streamlined recruitment strategies, and automated sample processing and storage facilities). Recruitment started in April 2007, 100,000 participants had joined by April 2008, 200,000 participants had joined by October 2008, and recruitment should be completed by mid-2010 – ahead of schedule and on budget. (By contrast, the NIH estimated that it would cost about \$1,000 million to set up an equivalent study in the USA and has not been able to do so.)

4. We have heard that there are differences in the way that centralised healthcare records are organised in England, Scotland and Wales, and that the healthcare informatics framework in Scotland works better for assisting research than that in England. Do you agree with this? What do you see as the main differences and what makes one system better than the others?

The ability to obtain detailed health information about participants in studies like UK Biobank is key to being able to study a wider range of diseases – not just those that kill (using death registries, as in Sir Richard Doll’s British Doctors’ Study) but also the many other diseases that disable people and make them

miserable (for example, joint disease and dementia) which have been less well studied. Central health record systems are more developed in Scotland, but it is becoming increasingly possible in England and Wales to link to some centralised health records (for example, to Hospital Episodes Statistics but not, as yet, to GP records), although the bureaucratic hurdles to do so are becoming increasingly obstructive to research (see point 7 below).

5. What role has Connecting for Health, or other initiatives such as the Tayside diabetes database or the Welsh electronic healthcare system, played in bringing together healthcare information for researchers using biobanks?

See response to 5 above: The ability to obtain detailed health information for research – not just in an anonymised or grouped format but also on identifiable individuals (with appropriate safeguards) – is key to finding the causes of a wide range of diseases (as well as monitoring the safety of treatments and the health effects of other exposures). Continued government funding and support is required to ensure that the needs of health research are integrated fully into centralised health records systems as they are developed (as is the intention of the Research Capability Programme of Connecting for Health).

6. Are present IT systems sufficient for joining up information from different databases, or is further development and investment necessary? How might this happen?

No, the current systems are not sufficiently developed throughout the UK to allow such research to reach its full potential. For example, the inability to link to GP records centrally means that many diseases managed chiefly in primary care cannot be studied effectively in the large-scale studies that are needed. In addition, there are serious bureaucratic obstacles to the use of health records for research – reviewed in the Academy of Medical Sciences' 2006 report ("Personal data for public good: using health information in medical research") – which are preventing such data from being used for important health research. As is concluded in that report, there is an urgent need to improve the interpretation of current legislation, and to produce clearer new legislation, in order that health records can be used more effectively for health research with appropriate (and not disproportionate) safeguards.

7. What happens if genetic screening carried out in association with a biobank shows that an individual is at risk of either a serious curable or incurable disease? Are the patient and other family members informed, and if so, how?

After detailed consultation with the public, clinicians, researchers, ethicists and lawyers during planning for UK Biobank, it was concluded that potential participants would be invited to join the project on the understanding that there would be no feedback of their individual results to them, their families or their doctors (or, indeed, to the police, insurers or employers). The detailed reasons for this decision are given in UK Biobank's Ethics & Governance Framework, and include:

- The value of such feedback being questionable because the data would be communicated outside of a normal clinical setting and would not have been evaluated in the context of the person's medical record; and

- It might be harmful (including causing undue alarm and having potentially adverse effects on insurance and employment status) to provide feedback without prior counselling (which UK Biobank would not be able to provide because the very wide range of tests that will be done subsequently are not known at recruitment).

Instead, the overall findings and implications of results that derive from UK Biobank will be made available to participants and the wider community so that they can influence public health strategies (including, when appropriate, the introduction of screening for newly discovered risk factors).

8. What are the risks to privacy and confidentiality to participants and their families in biobank collections and how are you managing them? What role do patients and volunteers play in deciding what will happen to their samples and information supplied as part of biobank studies?

UK Biobank has put a number of rigorous procedures in place to protect the confidentiality of participants. These include: keeping information that might identify individuals (such as their name and address) separate in our databases from other information about the participants; computer security to block unauthorised access (for example, by “hackers”) to the computers that hold personal information; restricting access to personal information within UK Biobank, and having all staff sign confidentiality agreements; and removing personal identifying details from all data or samples provided to researchers.

When they join UK Biobank, participants provide consent for their data and samples to be used for any type of approved health-related research in the future (rather than for specific research). Subsequently, they will be informed of the research that is done using the resource and have the right to withdraw at any time (for example, if they have concerns about the uses of the resource). An independent Ethics & Governance Council has been set up to provide oversight of the conduct of UK Biobank, including to ensure that the resource is used in accordance with the consent that has been given.

9. Recent evidence suggests that an individual may be identified from their genomic profile, even if their genomic profile is only present in summary format amongst hundreds of other individuals. What are the real risks in using and publishing this data in medical research or when linking different databases?

There will need to be controls on access to such data (rather than making them freely available), as is the case in UK Biobank where approved researchers will have to confirm in a formal agreement that they will not make any attempt to identify individual participants or to contact them directly.

10. What role do biobanks have in educating healthcare professionals and patients?

Participation in such studies may well help the public to understand some of the ways in which access to health records for research can be used to help improve their health. As discussed above (for example, Sir Richard Doll’s British Doctors’ Study and Prospective Studies Collaboration), such studies provide information that can influence the prevention and treatment of disease both by healthcare professionals and by wider public health strategies.

