

**Report: Public meeting of the UK Biobank Ethics and Governance Council
22nd March 2010
The Town Hall, Sheffield**

The independent Chair of the meeting, Professor Aurora Plomer (Chair in Law and Bioethics, Sheffield University) opened the session by welcoming everyone. The meeting has been organised by the UK Biobank Ethics and Governance Council (EGC), an independent advisory committee that was established in November 2004 to oversee the UK Biobank project. The EGC is charged with advising UK Biobank on the interests of participants and the public and holds public meetings as a means of gauging what interests people have in relation to the project.

Nationally, as of 22nd March 2010, a total of 442,000 people have agreed to participate in the project. The Council decided to hold a public meeting in Sheffield because members of the public are currently being invited to participate in the project, with 10,000 people having already agreed to take part. UK Biobank expects to reach its target of half a million participants in Summer 2010.

The purpose of the meeting was:

- To raise awareness and encourage debate among attendees about biobanking broadly, and more specifically regarding UK Biobank and the role of the EGC.
- To invite comments and questions in relation to the ethics and governance aspects of UK Biobank. These comments and questions will be used to inform the EGC's advice to UK Biobank.

The following subjects were addressed in three presentations, followed by an open Question and Answer session:

- An introduction to biobanking (Professor Aurora Plomer);
- Background and progress regarding the UK Biobank project (Dr Tim Sprosen Chief Scientific Officer of UK Biobank);
- An overview of the EGC and its work (Professor Graeme Laurie, EGC Chair and Professor of Medical Jurisprudence at the University of Edinburgh).

1. Introduction to biobanking (Professor Aurora Plomer)

The term 'biobank' first appeared in the academic literature in 1996 but it was only after 2000 that the term was used with any frequency. Although 'biobank' is used to describe various biological repositories, it originally referred to large population banks of human tissue and related data. A number of definitions have been applied including:

- A collection of biological samples which are permanently preserved. (Icelandic Act on Biobanks)
- An organised collection of human biological material and the information associated with the material stored for one or more research purposes and capable of being linked. (Hungarian Biobank)

- Biological material from one or several human beings collected and stored indefinitely or for a specified time and whose origin can be traced to the human or humans from whom it originates. (Swedish Act on Biobanks)

While definitions may vary biobanks have a number of common features including:

- Materials collected include both physical biological samples and associated personal data including medical and lifestyle data
- Size of collection (large)
- Lifespan (several decades)
- Purpose (to facilitate prospective health-related research)

UK Biobank is a large-scale prospective epidemiological resource that aims to recruit 500,000 participants. It is one of several initiatives taking place throughout the world with other examples including the:

- Icelandic Health Sector Database
- Estonian Genome Project
- Banco Nacional de ADN in Spain
- European Prospective Investigation into Cancer and Nutrition (EPIC)
- US National Children's Study

The nature of biobanks gives rise to a number of ethical and governance questions, many of which will likely be addressed in the following presentations and will arise in the Question and Answer session. These cross-cutting questions include aspects of:

- Consent
- Commercialisation
- Security
- International Access

2. UK Biobank (Dr Tim Sprosen)

Recruitment was launched in Sheffield six months ago with between 10 – 15,000 invites being sent out per week, initially to people living 2/3 miles from the city centre. Potential participants are offered an optional appointment which they can confirm, change, decline or ignore. A dedicated Participant Resource Centre is available to deal with any queries and handles on average 1,200 calls per day. Since the launch of the project 3 years ago, UK Biobank has recruited 442,000 of its target 500,000 participants.

Participation involves a 2 hour assessment centre visit during which UK Biobank staff are available to answer any questions, in particular during the consent process. UK Biobank aims to facilitate research on a wide range of diseases and this is reflected in the breadth of information that participants are asked to provide (including details of their diet, smoking habits, family history and activity). The assessment includes a number of measurements such as blood pressure, lung function, body mass index and innovative measures including heel ultrasound. This final test provides a measure of bone density and is thought to be a predictor of future bone fractures. By testing participants now, and then following their health over time, UK Biobank hopes to provide evidence for how effective the test is as a

predictor of future fractures. Finally, participants are asked to provide a sample of blood, urine and saliva.

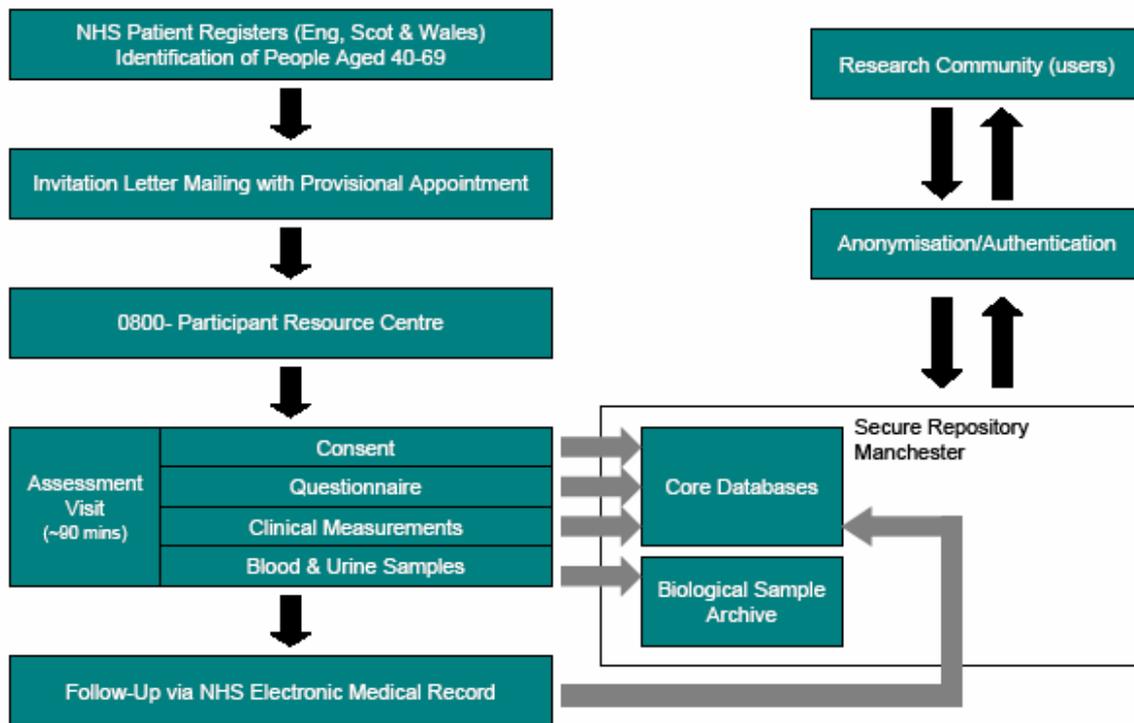


Figure 1. Overview of UK Biobank processes (including the identification and invitation of potential participants, elements of the assessment visit and data storage and use)

Participants provide consent for UK Biobank to access their NHS and other health-related records and to have their data and samples stored by the project and used for health-related research over the next few decades. Participants also consent to being re-contacted by UK Biobank, for example if the project would like to ask more questions, but any such additional involvement is entirely optional.

Assessment centres take about 2 weeks to set up and are usually based in city centre locations (the Sheffield centre is next door to the Bus Interchange, a few minutes walk from the train station). The project uses touch-screen technology for both the consent process, the questionnaires and cognitive function tests. Most aspects of the visit are optional, although in order to participate individuals must agree to provide consent and a blood sample. Assessment centres are open from 8am until 6.30pm and are attended by approximately 100/110 people per day per centre.

UK Biobank runs an awareness raising campaign at the launch of each new assessment centre, including bus advertising and making contact with local charities, social organisations and Councils. The project invites local GPs to attend a launch event in order to inform them about the project and the fact that their patients might receive an invite to participate.

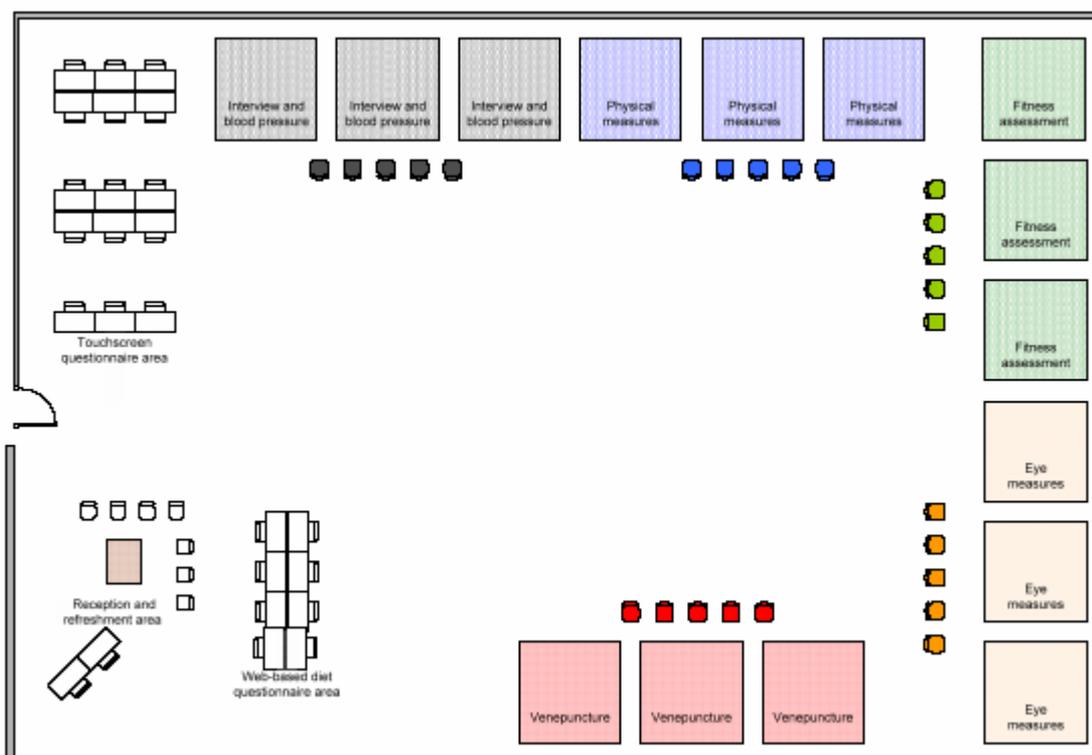


Figure 2. Example floor plan for a UK Biobank assessment centre

The idea of establishing a large resource for medical researchers arose almost 10 years ago. Implementation of UK Biobank began in 2003 and recruitment was launched in 2007. The project is being established in such a way that it can maintain the resource and manage researcher access for the next few decades.

The data and samples held by UK Biobank will be used by researchers to investigate why some people develop diseases whereas others do not. It will do this by gathering information on a range of risk factors through the baseline (and future) assessments and by acting as a resource for researchers who want to investigate the relationship between genes, environment and lifestyle and the onset of disease. For example, once at least 10,000 participants have developed dementia researchers can compare these cases with a group of people who are matched for age, sex and location but who have not developed the condition. This will allow researchers to look for any differences between the two groups (e.g. was the cognitive function test score lower for those who went on to developed dementia as compared to those who did not? Are there any biological markers which are distinct for those who developed dementia as compared to those who did not?)

	Age	40-49	50-59	60-69	All
Sex	Male	11%	16%	19%	46%
	Female	13%	19%	22%	54%
Income	<£18k	4%	6%	14%	24%
	£18-52k	13%	19%	20%	52%
	>£52k	9%	11%	4%	24%
	All	25%	35%	40%	100%

Figure 3. Distribution of participants by ages, sex and income

UK Biobank is well positioned, and well timed, to collect data for some investigations. For example, the use of mobile phones has increased rapidly over the last few years although the long-term health effects of such use are unknown. By collecting data now, when some but not all participants use a mobile phone, UK Biobank will be able to compare individuals who use mobile phones against those who do not. Had the project been established some years earlier, when few people owned a mobile phone, or in the future, when most people will have a mobile phone, this comparison could not be made.

Resources like UK Biobank are needed as an important step in helping to tackle the public health issues currently facing society (including the rise in obesity, binge drinking and changes to working practices). In terms of obesity, the data collected at the assessment centre already show correlations between lifestyle choices and body mass index (see figure 4). For the future UK Biobank might be able to help researchers investigate not only the causes of obesity but also how and where people put on weight (facts that have implications for disease outcome).

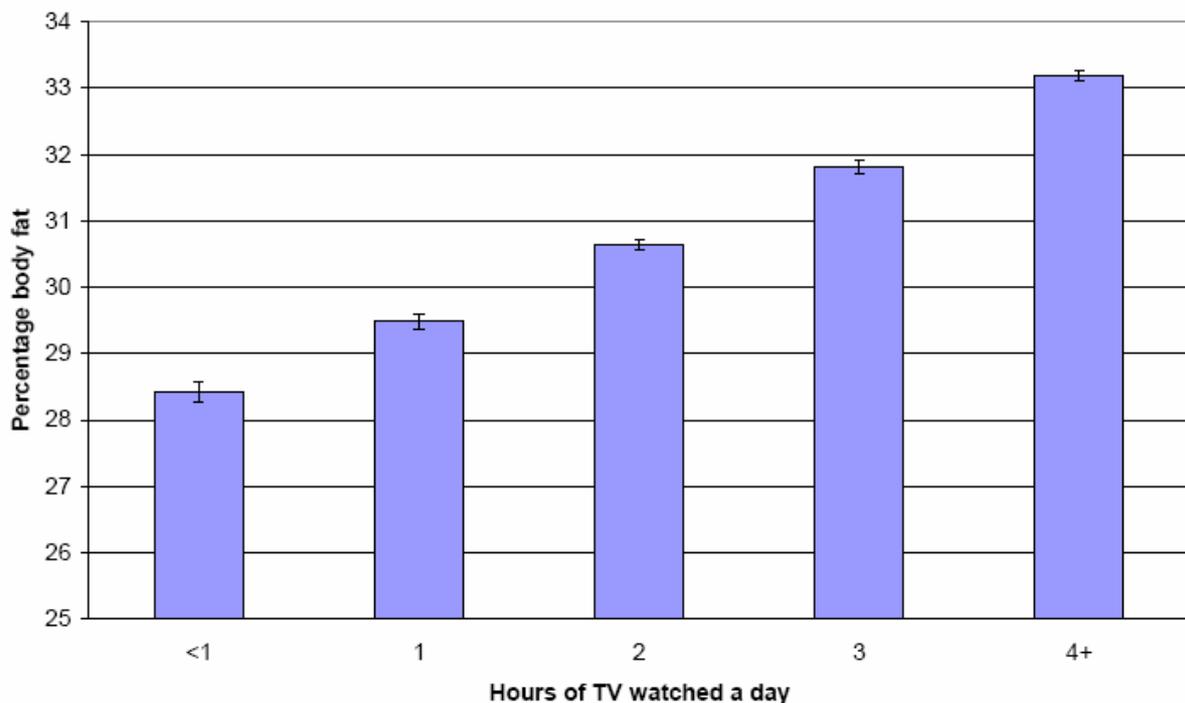


Figure 4. Analysis of baseline data showing percentage body fat compared with hours of TV watched a day

UK Biobank is planning a number of future developments which will be used to enhance the scientific value of the resource. For example, a diet questionnaire has been developed and introduced to the baseline assessment for the last approximately 100,000 participants. Participants will be re-contacted over the coming years and asked to fill-out this online questionnaire, which provides a snap-shot of the participants previous day's food intake. The project will also re-contact a subset of 20 – 25,000 participants every 3/4 years and ask if they are willing to undertake a repeat of the assessment visit. The future assessments will likely take place in a mobile assessment unit which was launched recently in Swansea with funding by the Welsh Government. Finally, UK Biobank is currently developing a proposal to invite

100,000 participants to undertake whole body, heart and brain magnetic resonance imaging.

3. The Ethics and Governance Council (Professor Graeme Laurie)

During their set-up and operation, biobanks must navigate up to 43 pieces of regulation and comply with rules at the international level (including data protection and human rights protection). Regardless of these arguably excessive requirements, the principal funders of UK Biobank (the Wellcome Trust, the Medical Research Council and the Department of Health) decided that an independent advisory and monitoring committee should form an integral part of the project's governance model. This decision responded to the fact that we do not know how, where or when the data and samples held by UK Biobank will be used. This presented a problem for the funders given that researchers would normally be required to provide participants with specific information about the use of their data and samples as part of an informed consent procedure.

In light of the anticipated duration of UK Biobank, and the uncertainties about future use, the funders considered it important to develop a system to protect participants in the short and long term. In 2003 the funders convened an Interim Advisory Group to advise on the ethics and governance framework under which the project should operate. This Group made two key recommendations:

First they advised that UK Biobank should adopt an Ethics and Governance Framework (EGF) which lays out explicitly its commitments to participants, the public and other stakeholders. This public document explains that consent will be sought to 'participate in UK Biobank' and states that since it is impossible to anticipate all future research uses, consent will be sought for research in general that is consistent with UK Biobank's purpose (rather than for specific research). This model of 'broad' consent requires important complementary obligations from the researcher including that participants will be kept informed of the research being conducted using the resource and that participants can withdraw at any time and for any reason.

The EGF is a living document which will change over time to reflect UK Biobank's development and the changing legal and social landscape in which the project operates. Version 3 of the Framework, which is available on UK Biobank's website, describes key aspects of recruitment (including the selection and approach of potential participants and the elements of consent), confidentiality commitments and the project's policy on who and how researchers can access the data and samples (including the principle that exclusive access will not be granted to any party).

The Group's second recommendation was that a permanent and independent Ethics and Governance Council should be established to advise the project and to monitor its conformity with the EGF. Such a Council was proposed as an additional safeguard for participants and the trust that they place in UK Biobank by providing advice on the public and participants' interests and on revisions to the EGF (e.g. in relation to changes in the law).

In advising, reviewing and reporting on UK Biobank's activities, the EGC serves as a "mirror" for UK Biobank, providing critical and constructive advice. As the EGF

states, 'Normally the Council will communicate its reflections and criticism informally. If the Council is not satisfied with UK Biobank's response, it could make a formal statement of concern (e.g. to the Board or funders) or, if necessary, make a public statement that certain action should or should not be taken.'

The Council has advised UK Biobank throughout its set-up and recruitment phase and is currently in its fifth year of operation. The recent activities of the Council include:

- Monitoring complaints and enquiries received by the project
- Reviewing the project's data security provisions
- Advising UK Biobank on its access and intellectual property procedures
- Reviewing the project's proposals for follow-up of participants (through NHS and other health-related records)
- Advising UK Biobank on its proposal to invite some participants to attend a future assessment visit involving Magnetic Resonance Imaging (including what feedback, if any, should be provided)
- Commissioning work to inform the Council's advice
- Convening a workshop to look at different methods through which participants and the public can be involved in UK Biobank and the Council's decision-making

The Council's work can be summed up in the following three words:

- Independence
- Scrutiny
- Acting in the public interest

Question and answer session

The presentations were followed by a Q&A session during which the following questions were raised:

Q1 UK Biobank promises to be an exceptional resource for researchers. How will the access process be policed?

A1 [TS] The broad principles of UK Biobank's access policy are contained in the EGF. The project's main priority is to promote the best possible use of the resource for public benefit. Approximately 10,000 cases will be required for the majority of diseases before the gene and lifestyle interactions can be reliably investigated and it will take 4/5 years for such numbers to accrue for the most common diseases. In the intervening time UK Biobank will establish its access procedures, including a peer review process. Importantly, we must be mindful that the samples are depletable and so their use must be carefully managed. It is likely that sample analyses will be performed in central laboratories (under contract to UK Biobank) rather than samples being sent out to individual researchers.

[GL] The EGC has developed a list of questions which it has recommended UK Biobank address during the development of its access and IP procedures. These questions, which are available on the EGC website for public comment, include such aspects as which criteria will be used to judge applications and what benefit-sharing arrangements UK Biobank might adopt.

[TS] Requests for access will be judged on the scientific merit of the application, on the researcher's reputation and on whether the research fits the aim of UK Biobank. These days the divide between academic and commercial research is increasingly artificial as many universities have commercial interests. In any event, all applications will be held to the same criteria and all will be required to place their research findings back into UK Biobank in order to enrich the resource over time.

Q2 How will aspects of intellectual property be managed (e.g. property rights arising from use of the resource)?

A2 [TS] UK Biobank is currently developing its intellectual property (IP) policy. It should be noted that UK Biobank aims to help researchers identify the causes of disease in order to prevent their onset (rather than having a primary focus on identifying treatments that might be patentable).

[GL] UK Biobank has indicated that it will have no claim over inventions (and any associated IP rights) that researchers have developed as a result of using the resource. However, the project will prevent researchers from using such IP rights to unreasonably block health-related research. The EGC has advised UK Biobank to word its policy more broadly by stating that 'normally' there will be no reach through rights but with the possibility that this option might be used in appropriate circumstances.

Q3 When attending the assessment centre I was told that UK Biobank does not intend to identify the genetic makeup of participants. Can you confirm that this is true?

A3 [TS] The information leaflet sent to all people invited to participate makes it clear that samples will be stored for future analysis, including genetic tests. My apologies that you were misinformed at the assessment centre.

Q4 As I understand it, the EGC is a watch-body and acts in an advisory capacity. To whom is UK Biobank responsible?

A4 [TS] UK Biobank's protocol and consent process have been formally reviewed and approved by a Research Ethics Committee. The project is required to report annually to this Committee and to submit any protocol changes for approval.

Q5 To which ethical standards are you expecting researchers to adhere? What checks will you make on researchers who request access?

A5 [TS] Access to data and/or samples will be granted under licence for scientifically and ethically approved research consistent with UK Biobank's purpose. Licences will be for specific uses under strict terms and conditions in standard access agreements, including compliance with the consent given and the standards described in the EGF. Users will be provided with reversibly-anonymised data and samples only and, under licence, will be forbidden to try to identify and/or to re-contact participants. UK Biobank is the legal owner of the resource and as such has certain rights, such as the right to take legal action against unauthorised use or abuse of the data or samples.

Q6 Have you conducted any qualitative research on the participant experience? I ask because I felt 'processed' during my assessment visit. From speaking to others who have participated my feeling is that people can be challenged by the things they are asked to do as part of the visit and the feedback form can be unexpected.

A6 [TS] We endeavour to make the visit as efficient as possible but also to give people the opportunity to ask any questions that they may have. We are mindful of the time and commitment that people give to UK Biobank when they agree to participate and we try to make the visit a pleasant experience. The current visit has been informed by a post-visit survey in which participants were asked about their assessment experience. Comment cards are available in all centres, and are completed by approximately 40% of participants. Where a problem arises the issue is escalated to a senior member of the team and where necessary changes are made to the visit process.

UK Biobank aims to ensure that participation is not perceived as a health check. However, as the EGF explains, it would be impractical and inappropriate to conceal from participants some of the measurements taken during their assessment visit (e.g. blood pressure). As a result of our discussions with the EGC, we report a number of measurements against standard population ranges and try to avoid providing an interpretation (because the assessment centre staff do not have access to a participant's medical record against which to evaluate the finding). Participants are advised to visit their GP if they are concerned about a particular measurement (e.g. high blood pressure).

[GL] The EGC considers it very important that UK Biobank surveys its participants. What do people understand about what they have signed up to? Do people understand that their health will be followed-up over time through their NHS and other health-related records? Also, people may have different expectations which should be explored, including what constitutes an acceptable frequency of re-contact.

Q7 How does UK Biobank and the EGC see itself dealing with media interest in the project?

A7 [TS] People put a lot of trust and responsibility on UK Biobank's shoulders when they agree to participate and as such it is very important for the project to be clear on its purpose and transparent in its decision-making. The team at UK Biobank believes that the project can deliver its aim of 'Improving the health of future generations'. We need to be clear about expectation and avoid media hype as UK Biobank may not be able to deliver in the short term. For example, it will take over 10 years before there are enough cases of dementia within the cohort for this disease to be investigated. UK Biobank's expectations are high and so to should the expectations of the project's participants and funders.

[GL] The EGC has not looked at the role of the media. Consent should be seen as an ongoing process and there must be an ongoing commitment to keep participants involved and informed. If UK Biobank can build and maintain a good relationship with participants this should hopefully negate any media hype (be it positive or negative).

Q8 How will UK Biobank control the data it holds (e.g. genetic information)? Unless UK Biobank performs all the meta-analyses, some data will be sent out to researchers at some point. Surely at this point of release you have effectively lost control of the data?

A8 [TS] UK Biobank's principle is to retain full control of all access to, and uses of, the resource and not to trust anyone else with identifiable data. Researchers will be provided with reversibly-anonymised data and sample only and it will be a contractual offence to identify, re-contact or try to find out additional information about a participant.

It is possible that, by the time access is open for case-control studies in about 5 years time, UK Biobank could be in a position to perform the data and sample analyses on behalf of the researchers. This would avoid the need to send the samples and primary data outside of UK Biobank.

[GL] There is no such thing as zero risk. Various strategies are available to minimise the risk of inappropriate data use by third parties including a contractual agreement which, if breached, could result in UK Biobank denying the researcher any further access, pursuing civil actions or informing the major funding bodies of the incident in order to prevent the research from gaining future funding. Under the provisions of the Data Protection Act UK Biobank is only permitted to send data to a country which has UK-equivalent data protection provisions.

Q9 We heard that UK Biobank hopes to carry out a number of enhancements including MRI. Will participants be re-consented for this future aspect of the study?

Q9 [TS] Participants provide consent to be re-contacted by UK Biobank in the future. We are investigating the possibility of inviting 100,000 participants to have a whole body, heart and brain MRI scan to address important questions such as what anatomical features are indicators of future disease processes? This additional aspect of the visit is optional and a specific consent will be sought.

UK Biobank recently introduced a number of enhancements to the baseline assessment visit, including a diet questionnaire and a hearing test. The hearing test was considered important because, although overlooked by other studies because it is not a cause of death, hearing loss has significant implications for quality of life.

Q10 I was surprised by the questions in the touch-screen questionnaire. Do you wish now that you had asked other questions?

A10 [TS] The questionnaire was developed through a process of consultation with scientists working in a variety of disease areas. Many of the questions have been validated, such as those relating to smoking and diet, whereas other questions are more speculative, such as those relating to mobile phone use. With all studies of this kind, a researcher would want to ask more and different questions but ultimately a limit needs to be set. It may be interesting in the future to go back to certain groups of people e.g. heavy drinkers and ask them more questions.

Q11 What happens once a participant has died, in particular if family members object to the uses of their relatives data/samples?

A11 [TS] Participants provide consent for UK Biobank to link to their NHS record and to let their samples and data be used for research, even after their incapacity or death (unless they withdraw from the project).

[GL] The Information Commissioner has recently taken the view that the common law duty of confidence applies after death and this has been supported by the Information Tribunal. Contrary to this the provisions of the Data Protection Act 1998 do not apply to information relating to deceased persons but genetic information from a deceased person might nonetheless relate to his/her living relatives and these people are entitled to protection of these data under the Act, but it is not clear how this will work in practice. UK law, which is currently bad at recognising that information can 'belong' to two or more people, will need to change as we learn more about genetic determinants and UK Biobank will need to think about its legal responsibility to living family members.

Q12 We've heard a lot tonight about protecting the participants' interest but what about UK Biobank's engagement with potential researcher users?

A12 [TS] In the past resources were created by people with an interest in using the data and samples. This is not the case for UK Biobank, the purpose of which is to establish and maintain the resource for use by other researchers. UK Biobank aims to raise awareness in the scientific community and to prompt researchers to ask themselves 'can UK Biobank answer my research question?'. UK Biobank aims to be a good custodian of the samples and data by keeping participants engaged and researchers aware of the resource's potential.

Q13 From where does the Wellcome Trust source its funding?

A13 [TS] The Wellcome Trust is an independent charity founded with an endowment from Sir Henry Wellcome in the 1930s. Wellcome co-founded a multinational pharmaceutical company which, after a takeover and merger, has become part of the modern day GlaxoSmithKlein (in which the Wellcome Trust has a small percentage of shares). The Wellcome Trust is the largest charity in the UK and a major funder of research.

Q14 Bearing in mind that UK Biobank will be a valuable resource for commercial companies, who within the governance model controls and monitors profits arising from use of the resource?

A14 [TS] UK Biobank is a charitable company and as such is not able to make a profit.

[GL] The literature shows that while people tolerate profit this depends on whether it is considered to be excessive. Further, people are more likely to be sympathetic to the creation of profit if there is some form of benefit-sharing. Arguably UK Biobank should provide for the possibility of some downstream profits coming back to the project in exceptional circumstances, although this is a difficult situation to manage given UK Biobank's charitable status.

Professor Aurora Plomer closed the meeting by thanking everyone for attending and inviting them to continue their discussions over a drink.