

**Report: Public meeting of the UK Biobank Ethics and Governance Council
3rd December 2007
Ashmolean Museum, Oxford**

The independent Chair of the meeting, Dr Oonagh Corrigan (Lecturer in Sociology, Law and Social Science, Plymouth University), opened the session by welcoming everyone. She explained that the meeting was organised by the UK Biobank Ethics and Governance Council (EGC), a monitoring body, independent of UK Biobank, that provides advice to the project. The EGC is charged to advise UK Biobank on the interests of research participants and the general public in relation to the project. The Council is hosting a series of public meetings as one method of informing itself of these interests.

A similar meeting was held in Manchester earlier in the year, marking this as the first centre of recruitment to UK Biobank. The second centre of recruitment was Oxford where, as of 1st November 2007, over 13, 000 people from the Oxfordshire region had agreed to participate in the project. The assessment centre in Oxford has now closed having received a very positive response from the public.

Dr Corrigan stated the purpose of the meeting:

- To provide information to attendees regarding biobanking broadly and more specifically regarding UK Biobank and 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.

To this end three presentations were followed by a question and answer session which in turn was followed by a drinks reception. The presentations addressed the following subjects:

- An introduction to biobanking;
- Background and progress regarding the UK Biobank project;
- An introduction to the EGC and its work.

1. Introduction to biobanking (Dr Jane Kaye)

Introduction to speaker:

Dr Corrigan introduced Dr Jane Kaye, a medical lawyer at the Ethox Centre, University of Oxford. Dr Kaye's research is in the area of law and genetics focusing on the development of innovative technologies and the legal issues of privacy, confidentiality, data protection and negligence, as well as the broader issues of the public interest, governance and regulation. She leads the Wellcome Trust funded socio-legal project 'Governing Genetic Databases' based at the Ethox Centre.

Dr Kaye's talk drew on the findings of the Governing Genetic Databases project (she expressed thanks to her colleague Dr. Catherine Heeney for deriving the typologies described below).

1.1 What is a 'biobank'?

The term 'biobank' has many definitions in the literature, indicative of the fact that this research field is an evolving area of science. In 2001 the House of Lords Science and Technology Committee defined genetic databases as 'collections of genetic sequence information, or of human tissue from which such information might be derived, that are linked or could be linked to named individuals'. The European Commission funded EUROGENBANK project added to this description by defining genetic databases as being 'systematically organised, accessible to third persons, established for the purpose of studying and/or using and/or preserving genetic information; in addition, this purpose had to be the primary goal of the collection; the collection should consist of living organisms and/or DNA and/or sources of DNA or DNA based information'.

1.2 Are there a range of biobanks?

There are a wide variety of biobanks which differ according to various aspects of the study design. Reflecting on the findings of the Governing Genetic Databases project, these aspects might include:

- **The methodology** which may be epidemiological, cohort, clinical, longitudinal, hypothesis driven and/or prospective. These methodologies are not mutually exclusive, for example, UK Biobank is a longitudinal, prospective, epidemiological cohort study.
- **The participant group** which might comprise affected populations (i.e. individuals who have a particular disease condition), age cohorts (such as UK Biobank), birth cohorts, the general population and close relatives of individuals already involved in a study.
- **The size of the study** which will depend on the purpose of the project. A biobank which aims to investigate a rare disease may contain information and samples from only a few hundred affected individuals whereas a national project which aims to investigate common diseases (e.g. UK Biobank) may involve hundreds of thousands of people.
- **The types of data and samples collected and stored.** Data falls into the following broad categories: genotypic, phenotypic, health, social and genomic data. Samples might include: blood, urine, faeces, hair, tumours and healthy tissue and saliva. Most biobanks contain both data and samples. Indeed, many older studies which had not originally collected DNA samples have now started to do so. In some cases datasets from existing studies have had genetic studies and datasets 'bolted on'. This has implications for future management and use of the entire resource.

Studies can also differ in the way in which they are funded; the collaborations involved in their development and management and the governance arrangements:

- **Funding** can be in the form of one off grants, ongoing or fixed term pump-priming and may come from one or more sources at any one time or from different sources over time. The Governing Genetic Databases project has identified the following main sources of funding: the host university, the NHS,

a funding council (e.g. the MRC), charities (e.g. the Wellcome Trust) or the Department of Health.

It is important for biobanks to have a sustainable source of funding and for plans to be put in place for the decommissioning of a biobank when the funding or use of the biobank comes to an end.

- **Collaborations.** Reasons for collaborating in epidemiological studies include the need to acquiring sufficiently large numbers of cases to investigate subtle interactions of a range of variables. Clinical geneticists may share information with others interested in the same condition or to gain access via other clinicians to patients with a phenotype of interest. Various types of information might be shared including samples, computer records, paper records, pictures and verbal reports on the relationships between phenotype and genotypes in particular cases.

There are different types of collaborations:

- There is an official aspect to **formal collaborations**, in which researchers will use similar systems (for example, a particular computerised system underpinning or supporting the collaboration). This type of collaboration can impose harmonisation and standardisation on the types of data held by the biobank. Data and samples may also be held in a central repository, such as UK Biobank where data and samples are collected at different centres throughout the UK in a uniform way and stored centrally.

A project may be set up from the outset as a multi-site study and the collaboration is therefore official by definition. Such collaborations may be between public-public, private-private or public-private parties. The collaborations are underpinned by a number of policies and operating protocols, for example the exchange of samples might be subject to a Material Transfer Agreement that has been agreed to by all members of the collaboration. Collaborations between public and private sector, for example, between a pharmaceutical company and a health consultant or scientist based in the public sector, tend to have protocols in place defining rights and responsibilities.

- **Informal Collaborations** are often ad hoc where exchanges between the parties are informal and can involve requests over the telephone for information, data and potentially samples. They can be opportunistic, where a colleague has samples and/or data on a similar topic and there are no prohibitive barriers in place.
- **Governance** does not simple relate to laws and regulation, but also concerns the systems that are put in place to support the biobank's activities (e.g. 'good practice' guidelines).

Very few biobanks have the comprehensive type of governance system that has been adopted for UK Biobank. Some biobanks do have a steering

committee which advises on the scientific aspects of the study and also on ethical and legal matters (e.g. consent and access by third parties). These committees are primarily associated with large scale projects (e.g. epidemiological projects, cohort studies and formal collaborations).

- ***Influential laws/guidance and their interpretation.*** At an international level there is no specific, binding legal instrument that applies to biobanking. In the UK biobanks are subject to a number of laws and guidelines including: the Human Tissue Act 2004 (in particular the licensing requirement), the Data Protection Act 1998 and numerous guidelines. Some countries have legislation relating specifically to the operation of biobanks, for example, Sweden. Biobanks in the UK and internationally are required to gain research ethics committee approval before the study commences.

The availability of legal expertise varies according to the nature of the project. For example, for small scale clinical studies or units based within the NHS the head of the department or the Principal Investigator usually has responsibility for keeping up to date with, and interpreting, the official governance framework. For larger studies there will often be defined people with specific responsibility for interpretation of laws and guidance. Private companies will usually have a legal department or a 'team of lawyers' who have this responsibility.

- ***Types of Consent.*** The nature of a participant's consent is important as a means of determining the future uses of the biobank. Consent may be given for a specific study, thus limiting any future use which is beyond the scope of the initial study. Alternatively, a broad consent may be given, which is generally the case when it is anticipated that there will be multiple uses by a number of different researchers.
- ***Access Limitations (External).*** Many large studies have a data access committee which is responsible for reviewing applications for access to the biobank. Some studies have 'on-site' access for sensitive data whereby researchers are only permitted to use the data at the study site. Conversely in some cases data is 'open-access' and available to everyone, for example genomic data. However, there is currently some degree of controversy about making genetic data 'open-access' in the same way.

In some studies a researcher may only be able to gain access to data if they become a collaborator, a step which involves meeting certain criteria for entry. Finally, access in some cases can be strictly limited to the public sector, while in other cases studies, access by the private sector will be considered.

1.3 How does UK Biobank fit in with the international scene?

Research, including biobanking, is a global activity. It is possible to find that samples collected in China are processed in Paris and then analysed in the UK. Initiatives are

taking place to develop networks within networks in order to facilitate the sharing of data and samples between biobanks. One such initiative is the Canada based Public Population Project on Genomics. This project aims to harmonise and standardise the methods of collection, storage and use of samples and information between biobanks internationally so that these might be more easily shared. Such initiatives aim to maximise samples sizes so that the subtle interactions between genes, environment and lifestyles, which may not be evident in small sample sizes, can be investigated. Funding bodies are also starting to make it mandatory for researchers to make data available for other researchers.

The push to share data and samples adds a new twist to the way that research is conducted:

- Firstly, it creates a tension between collaboration and competition. In some cases researchers no longer have prolonged, exclusive use of their own data. Wide accessibility of data may raise concerns over its use by “free-loaders” or that a researcher’s data may be used by another party before it is exploited by the researcher themselves.
- New relationships are formed between researchers raising issues of trust that do not arise when researchers work independently (e.g. that the data is of good quality and will be used appropriately).
- There is a shift in research practice from local control to global accessibility through the web and from project orientated research to data management infrastructure.
- There is a need to develop new standards and procedures.
- The inadequacies of the legal framework are exposed, where regulation is only at a national level but the research activity is global.

A quote from Eric Lander (a world leader of the international Human Genome Project) is relevant to the potential that biobanks offer:- “2007 has been one of those magical years where the entire picture comes into focus. Suddenly we have the tools to apply to any problem: cancer, diabetes — a huge list of diseases. It's just a stunning explosion of data. Pick a metaphor: We've now landed on this new continent, and the people are out there exploring it, and we're finding mountains and waterfalls and rivers. We're turning on lights in dark rooms. We're finding pieces to the jigsaw puzzle.”

2. UK Biobank (Professor Rory Collins)

Introduction to the speaker:

Dr Corrigan introduced Professor Rory Collins, Principal Investigator and Chief Executive of UK Biobank and co-director of the University of Oxford's Clinical Trial Service Unit & Epidemiological Studies Unit. Professor Collins has been involved in the establishment of large-scale epidemiological studies investigating the causes, prevention and treatment of heart attacks, other vascular disease, and cancer, while also being closely involved in developing approaches to the combination of results from related studies ("meta-analyses").

Professor Collins has been involved with UK Biobank for approximately five years during which time twenty different Universities have been involved with the planning

and piloting of the project. It was only recently, in 2005, that he became Principal Investigator and Chief Executive of UK Biobank.

2.1 Prospective study design

UK Biobank is a prospective study that aims to involve 500,000 UK men and women aged 40-69 years. The project will accumulate extensive baseline questions and physical measures along with stored blood and urine samples in order to allow many types of assay in the future. Repeat assessments will occur over time in subsets of the participants to allow for sources of variation (and the potential for other enhancements to the information that was initially collected). UK Biobank will seek broad consent from participants for follow-up through all health records and for all types of health research that fit the project's purpose. Over time participants will develop certain illnesses. The target participation rate of 500,000 is a sufficiently large number of people developing different conditions to assess reliably the causes of a wide range of different diseases. The project has been established as a charitable company in order to protect the resource for the next fifty years or so. Although it is not a novel concept in its own right, UK Biobank should generate a richness of data which sets it apart from other studies to date.

2.2 Invitation to participate and the assessment centre visit

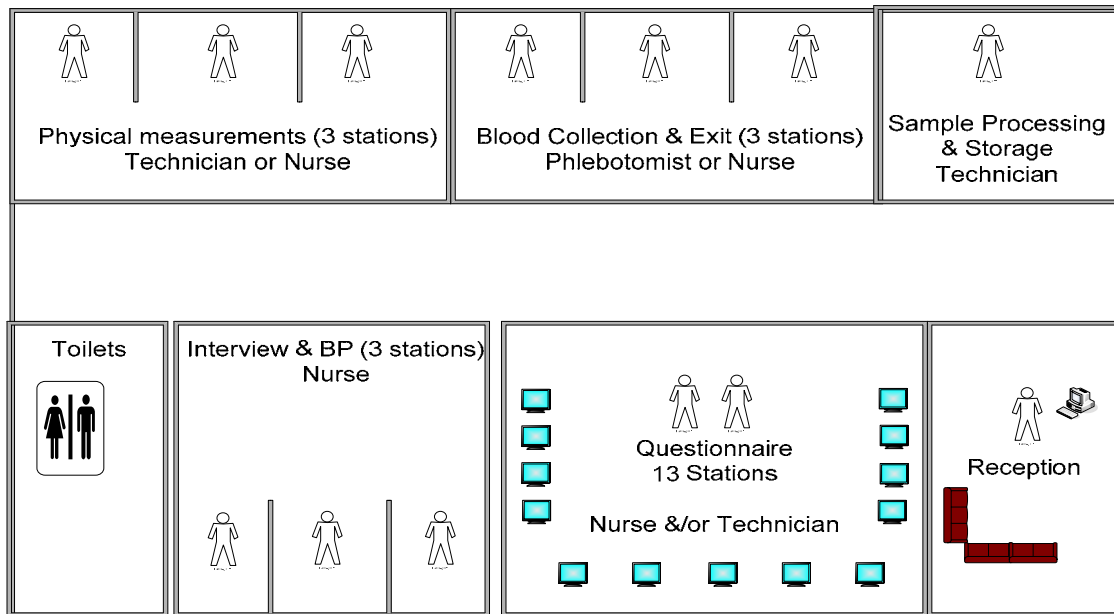
UK Biobank generates invitations to participate by processing, in confidence, contact details from central registries. The project's central invitation and appointment system aids high throughput and smooth running of the assessment centres, and reduces costs. UK Biobank has the potential to over-sample particular groups (e.g. age, sex, deprivation) through the central invitation strategy and through selective location of assessment centres.

When an individual agrees to participate in UK Biobank they are making a big commitment which includes agreeing to spend 90 minutes of their time at the assessment centre and agreeing to let UK Biobank have access to their electronic health records. During the pilot phase of the project, and during the recent months of recruitment, UK Biobank has received on average a 10% acceptance rate to its invitation to participate. As such, it is estimated that 5 million people will need to be invited in order to recruit 0.5 million participants. With a view to making participation as convenient as possible for potential participants, the assessment centres are being placed in central locations (e.g. well known shopping centre).

UK Biobank recognises the potential sensitivity surrounding the project processing potential participants' contact details (albeit in confidence). As an indicator of potential participants' concerns regarding the project, those who chose to decline participation during the pilot phase of the project were requested to provide their reasons. Of the approximately 10,000 people who responded to the invitation letter by declining to participate, 70% provided their reason. Of the 7,000 people who provided their reason for declining participation only 56 people stated concerns over the invitation (e.g. an invasion of privacy). This represents 0.1% of all invited individuals, suggesting that the method of invitation is broadly acceptable to potential participants. Subsequent to the pilot phase, the invite materials have been revised in

order to clarify how UK Biobank has gained access to, and is processing, contact details.

UK Biobank has created a streamlined assessment centre flow with the aim of accommodating approximately 110 people per day. The lay-out of the assessment centre is as follows:



UK Biobank aims to open (and close) one assessment centre per month for the next three years and to recruit 10 -15 thousand participants through each centre. Once the project is fully operational there will be six assessment centres recruiting concurrently in different regions of the UK at any given time.

2.3 Baseline assessment

Innovative methods have been developed in order to minimise the costs of recruitment and the assessment centre visit including, for example, the use of a touch screen questionnaire. There are three elements to the baseline assessment of participants: a questionnaire, physical measures and biological samples.

The strategy for questionnaire selection has been informed by the following:

- The public health importance of the relevant condition.
- The likely importance of factors for main effects, or as confounders and sources of bias.
- The reliability and validity of questionnaire measures.
- The lower threshold for inclusion on touch-screen than in interviewer questionnaire.
- The availability of alternate sources of information about the factor (e.g. previous medical and other health-related records; physical measurements; biological samples; internet diet/activity diaries).

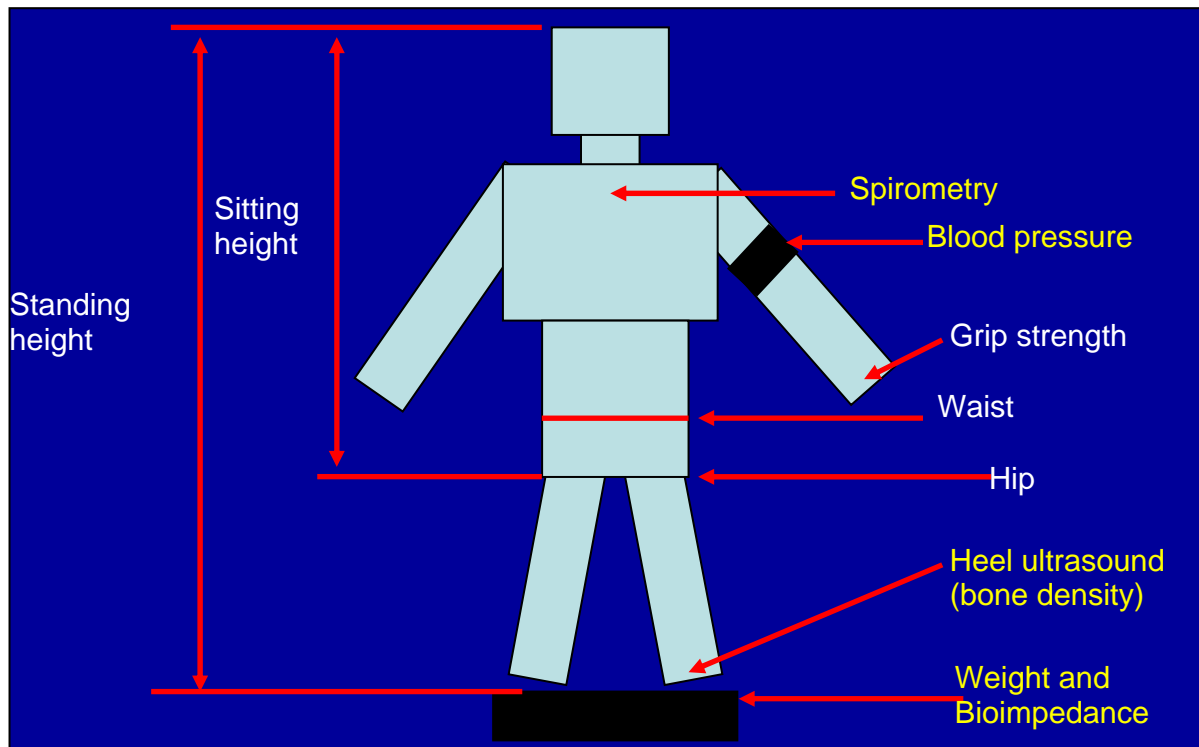
The table below describes the topic areas included in the touch screen questionnaire and the median time taken to complete the respective sections.

Topic Areas	Median Touch screen time (mins)	Topic Areas	Median Touch screen time (mins)
Socio-demographics	3.0	Ethnicity	0.2
Tobacco smoking	0.5	Family history, sib-linkage, twins	1.9
Physical Activity	4.5	Psychological state	2.4
Diet	4.6	Screen/health service use	0.3
Alcohol consumption	1.0	Sex specific questions	1.7 (f) 0.4 (m)
Sleep	1.2	Past medical history/medications	1.8
Early childhood	1.2	Other general health & disability	3.2
Environmental exposures	3.3	Cognitive Function	4.2

The strategy for physical measures selection has been informed by the following:

- Whether or not previous studies have indicated that the measure was relevant (i.e. associated with important health outcomes).
- The chosen method should be reliable (e.g. calibration system; ease of training, use, monitoring and maintenance; direct data transfer to computer).
- The feasibility of conducting measures within about 20 minutes (given limitations of available resources).
- The opportunities for enhancement (such as intensive phenotyping in subsets of participants at baseline and/or at periodic re-assessments over time).

The physical measures currently undertaken at the assessment centre are depicted in the diagram below.



The strategy for sample collection and handling has been informed by the following:

- Blood and urine are being collected because of the wide range of possible assays and wide physiological coverage that these samples allow.
- There has been a careful choice of anticoagulants and preservatives to allow widest possible range of potential future uses.
- Detailed pilot studies have been undertaken to show that sample processing procedures allow very wide range of assays.
- Storage facilities (automated -80°C and back-up liquid nitrogen) provide physical security and reliable tracking of individual samples.

2.4 Long term follow-up of health exposures and outcomes through different sources

During the assessment centre visit consent is obtained from participants for access to their past and future medical and other health-related records. These could include:

- *Death & cancer:* already available through UK central registries
- *Hospitalisations:* already available in Scotland (Scottish Morbidity Record) and in England & Wales (Hospital Episode Statistics)
- *Primary care, medications & investigations:* already available in Scotland (General Practice Administration System for Scotland and Scottish Morbidity Record), but needs Connecting for Health for national coverage
- *Other health-related information:* such as screening results, dental records, previous occupations & residences, etc

Multiple sources of information may be used to enhance the phenotyping of participants, and to identify and help validate relevant health outcomes during follow-up

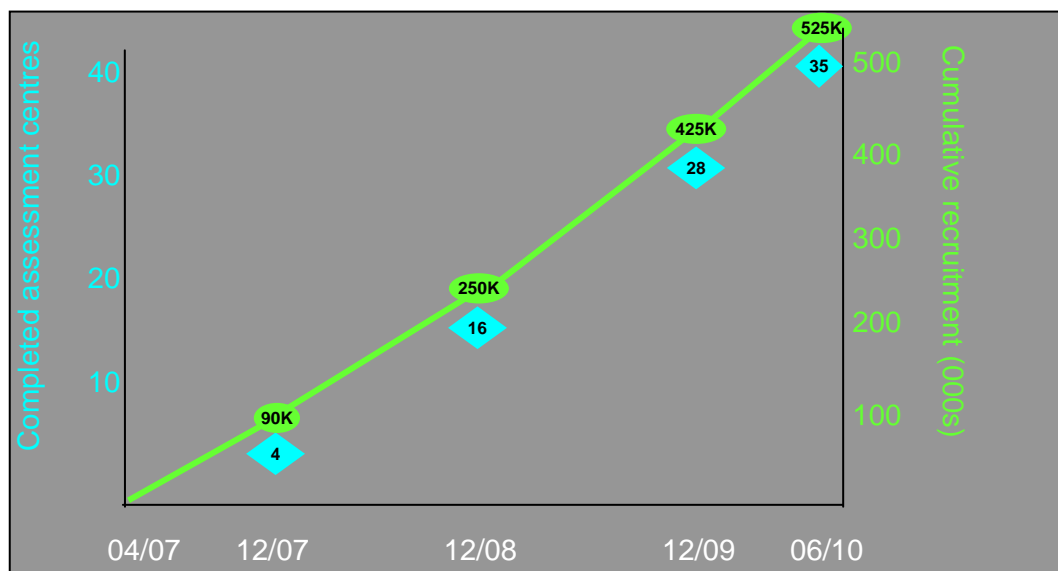
2.5 Strategy for access to the resource for health-related research

It is anticipated that the UK Biobank resource will chiefly be used for a series of case-control studies of different outcomes within the cohort (using anonymised data sets and/or samples). A timetable will be developed to indicate when sufficient cases of each condition are likely to have occurred (which could be many years from now; e.g. 10 years). Based on this timetable, UK Biobank will coordinate calls for efficient use of the resource, allowing researchers to develop proposals against this indicative timetable.

There will be no preferential access to the resource, instead its use will be promoted as widely as possible for research that fits the purpose of UK Biobank. Disease-specific proposals will be reviewed by independent expert groups, while a national Access Committee will advise UK Biobank on prioritisation. The EGC will advise on, and monitor, the access process.

2.6 Target assessment of 0.5 million participants during 2007 - 2010

Recruitment is expected to continue until mid-2010 during which time a total of 35 centres will have been in operation with a target recruitment total of approximately 500, 000 people (see the table below). Centres are currently operating in Manchester, Edinburgh, Glasgow and Cardiff, with new centres opening in Stoke and Bury in the near future.



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

Introduction to the speaker.

Dr Corrigan introduced Professor Graeme Laurie, Chair of the UK Biobank Ethics and Governance Council, Chair of Medical Jurisprudence at the University of

Edinburgh and Director of the Arts and Humanities Research Council Research Centre for Studies in Intellectual Property and Technology Law. His research interests include the role of law in promoting and regulating science, medicine and technology. In 2001 he convened a World Health Organisation working group that produced international guidelines on the establishment and maintenance of genetic databases. Professor Laurie is Chair of the Privacy Advisory Committee for Scotland, a member of the NHS Central Register Governance Board and a member of the Scottish Executive Generation Scotland Advisory Board.

Professor Laurie addressed the following questions:

- How and why was the Council formed?
- What is the purpose of the Council?
- What are the recent activities of the Council?

3.1 Why and how was the Council formed?

The UK Biobank Ethics and Governance Council was established in 2004 as what could be considered as a governance 'experiment'. During the development stages of UK Biobank the principal funders of the project (the Wellcome Trust, the Medical Research Council and the Department of Health) recognised that the scale of the project, and the possibility of public concern, required that the ethics and governance aspects of the project should be developed in parallel with the science.

An Interim Advisory Group (IAG) was established by the funders in 2003 and charged to make recommendations concerning the elements of the Ethics and Governance Framework (EGF). This Framework was intended to describe a series of standards to which UK Biobank will operate during the creation, maintenance and use of the resource and would elaborate on the commitments that are involved, not only to those participating in the project but also to researchers and the public more broadly. Professor Laurie served on the IAG.

The IAG's discussions were informed by public consultation work and resulted in the recommendation that an independent oversight committee should be established as an important element of UK Biobank's governance structure. The Ethics and Governance Council was subsequently established through a publicly-advertised, open appointments process in keeping with the Nolan Principles of Public Life. Dr Kaye indicated in her talk that law is one element of governance. By establishing a governance structure which is over and above the legal requirements, the funders of UK Biobank have opted for a 'Governance+' approach.

3.2 What is the purpose of the Council?

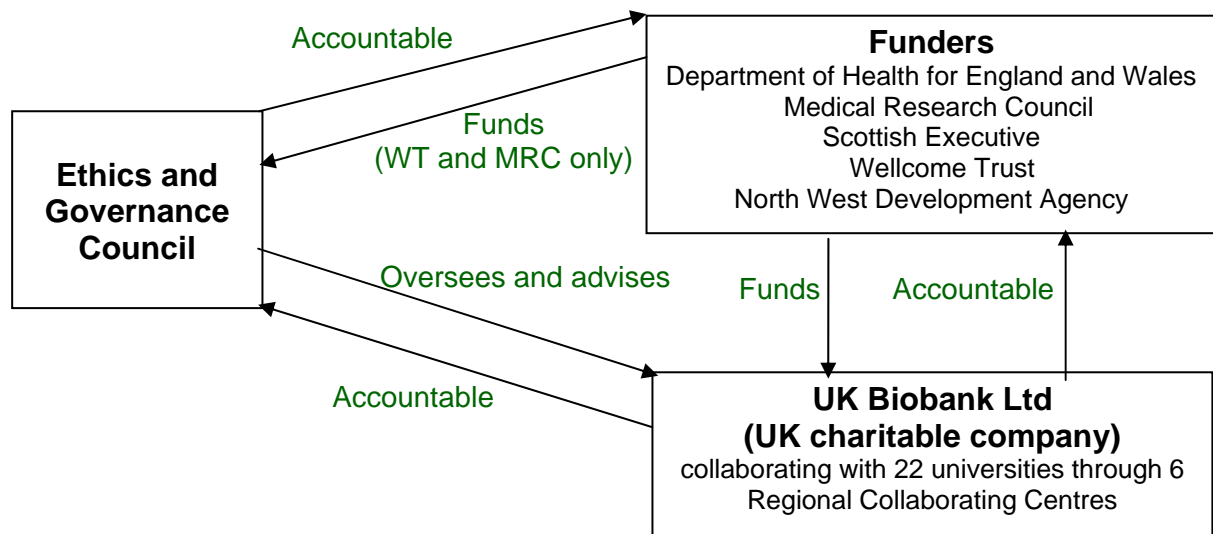
Council members come from a number of disciplines including law, ethics, biomedical science, policy, consumer issues, and lay representation. The remit of the EGC is:

- To act as an independent guardian of the EGF and advise on its revisions;

- To monitor and report publicly on the conformity of the UK Biobank project with the EGF;
- To advise more generally on the interests of research participants and the general public in relation to UK Biobank.

The Council is also charged to advise UK Biobank on any policies which relate to or flow from the EGF, for example those relating to recruitment, access to the resource or complaints handling.

The EGC's relationship with UK Biobank and its Funder can be found below.



The EGC holds a mirror up to UK Biobank, asking it to reflect on whether or not its activities are best practice. The Council also monitors the project and will communicate its own reflections informally to UK Biobank. If the Council is not satisfied with UK Biobank's response, it could make a formal statement of concern. It could escalate concerns, if necessary, by making a public statement that UK Biobank should or should not take certain action.

It should be noted that the EGC is independent of UK Biobank (i.e. it is not the project's internal ethics advisory body). As such, there are a number of activities and responsibilities which do not fall to the EGC but to UK Biobank itself. For example, the Council has not been established to:

- Assume responsibility for the ethical management of the resource;
- Speak on behalf of UK Biobank (instead the Council speaks *about* UK Biobank);
- Own and develop the EGF and associated policies.

3.3 What are the recent activities of the Council?

The EGC has been in operation for 3 years, the first 2 years of which were under the chairmanship of Professor Alastair Campbell. In those early years UK Biobank was

under development and the EGC advised on, for example, the specifics of consent, key policies and a number of operational aspects.

During Professor Laurie's chairmanship the EGC has continued to advised on UK Biobank's policies and protocols but has also established a number of 'forward looking' activities intended to proactively identify issues relating to the EGF that require attention.

Recent activities include:

- Advised on the project's participant materials. Before recruitment commenced the Council provided comment and advice on the project's proposed participant materials with the aim of making them both clear, accurate, comprehensible and in accordance with the requirements stated in the EGF.
- Advised on the project's standard operating procedures (SOPs). The Council has reviewed and advised on several of UK Biobank's SOPs, including how incidental findings (for example, significantly high blood pressure) made during the assessment visit will be managed by UK Biobank staff; how capacity of potential participants will be judged, and how complaints and enquiries will be handled.
- Commissioned work to inform the Council's advice giving. Two studies have recently been commissioned by the Council;
 - A conceptual analysis of the 'public interest' and 'public good'. The Council's remit states that it will advise on the interest of the general public, but what does it mean to advise in this way? The Access and Intellectual Property Policy of UK Biobank states that the resource will be managed as a resource for the public good. In order to fulfil its remit and to monitor and advise UK Biobank on applications for access to the resource the Council intends to develop a clear understanding of what the 'public interest' and 'public good' might mean in these contexts.
 - A study of public attitudes to access issues (including the terms of access, benefit sharing and intellectual property). The study will involve two specific age groups, one in the age range of UK Biobank participants and one younger group (i.e. those more likely to benefit from the research conducted on UK Biobank).
- Established a subgroup to advise on the development of the project's Access and Intellectual Property Policy. UK Biobank is currently revising its policy with input from a subgroup of EGC members.
- Established a subgroup to develop the Council's communications strategy. A second subgroup has been established to discuss and develop the Council's communications strategy.

It is not expect that people will simply place their trust in the Council by the very fact it exists. Instead the Council hopes to instil and earn trust by working in a transparent, independent way that accords with public interest and involves the proper scrutiny of UK Biobank.

4. Question and answer session

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

Q1 How does the concept of sharing data internationally sit with the participants' original consent and UK Biobank's commitment to maintain confidentiality?

A1 (RC) The critical point is that while UK Biobank has to be able to identify individuals, potential researchers will only have access to anonymised data and explicit consent is obtained for international use of the resource.

(GL) At the outset, participants give broad consent to the use of data and samples. We don't know who will seek access to them in the future. Consent is a process rather than a one-off event – people will be able to withdraw at a later date if they wish.

Q2 How will the project obtain participants' medical information in the future?

A2 (RC) Systems for providing access to medical information are developing all the time. Scotland is relatively far advanced with the development of unified data sources, but even in England you only have to go to one place for information about all hospitalisations, for example. UK Biobank aims to utilise the central system which is being developed by Connecting for Health. The systems will link and store General Practice, hospital and community services information and will contain past (up to a few years) and future information. UK Biobank can afford to wait until this information is available. With its single NHS service, and heterogeneous population, the UK is uniquely placed to undertake this research - with a richness of data unparalleled in other countries.

Q3 Is the data devalued because the participants are self-selecting?

A3 (RC) Studies like UK Biobank are influenced by 'healthy volunteer effect' and we have taken this into account in the study design. We aim to make the assessment centres accessible to anyone, irrespective of any incapacities. We locate centres in places that encourage a variety of participants, and we hold sessions at weekends and in the evenings so that we don't exclude particular population groups. We are not aiming for the biobank to be 'representative' but instead as different, and as 'generalisable', as possible. The central invitation system allows us to over-invite certain hard to reach categories with the aim of increasing the heterogeneity of the participant group.

Q4 The participants are a fantastic communications resource. Do the EGC or UK Biobank use it?

A4 (GL) There is an issue about the EGC contacting participants directly and using them for its own ends. Instead we target the assessment centres and hold public meetings. UK Biobank is developing a video to be shown in the assessment centres, this will contain information about the EGC's work.

(RC) We will discuss this with the EGC, but how do you communicate with half a million people? We are considering how best to alert people to new

developments and emerging issues and how best to balance the provision of information against the concern not to overburden participants.

Q5 The 'public interest' is hard to define. How does the EGC find out and assess what it is and how will UK Biobank inform people about the kinds of research that will be carried out?

A5 (RC) At the beginning we inform people about the broad purpose of UK Biobank. As the study progresses, we intend to inform participants about individual studies. People can withdraw at any point if they are unhappy about any aspect of the project.

(GL) The EGC has commissioned colleagues at Bristol University to help us with this by providing a conceptual analysis of both the 'public interest' and the 'public good'. Judgments will have to be made as to whether an individual's objections are representative of wider concerns. When thinking about how to define the 'public interest' we will consider questions such as 'how can benefits be maximised?' and 'what would the 'majority of reasonable persons' think?'.

Q6 Give us a flavour of the sort of research that might be carried out on the resource.

A6 (RC) First, research has been conducted during the establishment of UK Biobank: for example an assessment of the integrated pilot conducted in 2006 has been published on the website and detailed information about sample processing will be published in a journal soon. Second, research will be undertaken using the data and samples in the resource. In the short term, we expect that the studies will be 'cross-sectional', whereby associations in a few thousand people will be investigated between different measurement and sample results. In the future, comparisons will be made between people who develop a particular condition and people who don't. Studies will involve subsets of participants and will be looking at quite subtle factors. As the resource matures, it will enable researchers to look at a wider spectrum of disease.

Q7 How can samples be anonymised but you say that I can withdraw?

A7 (RC) Within UK Biobank, there has to be the facility via key coding to link samples and data to identifying details- this allows "withdrawals" to be effected. Access to the key codes within UK Biobank is very restricted. Data are encrypted and anonymised and firewalls are used for protection. We pay a company to try and break into the system. If any weaknesses are exposed, they are dealt with.

(GL) UK Biobank's Systems Architect attended the November EGC meeting and presented the project's information technology and information management strategy, with a focus on security. The EGC felt that the project team is paying sufficient attention to this very important area.

Q8 How will UK Biobank know if I develop diabetes or have a heart attack?

A8 (RC) At regular intervals, we will interrogate the relevant information systems to gain up-to-date details of hospitalisations, prescriptions, etc. among the participants.

Q9 If in five to ten years' time UK Biobank observes a certain propensity for particular groups to develop a certain disease, will you warn people?

A9 (RC) There will be no feedback to individuals about their individual results, beyond the results they receive at the assessment centre (e.g. blood pressure, body mass index, lung function, heel bone ultrasound). But, results of research conducted on the resource will be available on UK Biobank's website as an information source for participants and the health service alike.

(GL) This is a major issue that has been explored by UK Biobank and the EGC. The EGC concluded that participation is in a research project; it is not, and should not be confused with, a health check.

(JK) There is a study in Western Australia that is considering giving feedback via alerts to doctors, but this does beg questions about the nature of the original consent, about what kind of information is fed back (i.e. how clinically valid is the result?) and who should feed back the information (i.e. a researcher or a general practitioner?).

Q10 Who will own the samples?

A10 (RC) UK Biobank is the owner of the samples and the data, preserving the resource for health-related research.

Q11 How do you know funding will be available for 10, 20, 50 years?

A11 (Alan Doyle, Wellcome Trust) The funding bodies organised a rigorous process of international peer review at the outset and close scrutiny will, of course, continue, but it has always been understood that this project is for the long term.

(RC) Set-up costs are high (e.g. assessment centre operations and purchase of robots) but the long-term running costs should be comparatively low.

Q12 If a person withdraws, what will it mean if they have already provided information and samples? What are the mechanisms for withdrawal?

A12 (RC) There are three different levels of withdrawal. Some people might be happy for the study to retain existing data and samples for use by researchers but may not wish to be contacted again by the project team. Other people might request that their samples and data are no longer used for research. In the latter case, we would destroy samples and render data unusable. But we have made it clear from the start that we cannot guarantee that residual data (e.g. samples and/or data that have already been used as part of a research study) won't remain in the system.

(GL) It recently came to light that, due to the project's audit and archive system, UK Biobank is unable to destroy all information about participants when they withdraw. Given this the EGC and UK Biobank have been in discussions about how to address this change in process. It's important to note that the fundamental guarantee of no further use is respected and with this in mind our discussions concluded with re-wording of the Ethics and Governance Framework and the participant information leaflet.

Dr Corrigan concluded the session by thanking the participants for attending and by inviting everyone to continue the discussion over a post meeting drink.