UK Biobank Ethics and Governance Council
Forty-seventh Meeting

Meeting at Wellcome Trust
Jenner, 215 Euston Road, London, NW1 2BE

Monday 3 October 2016 at 11.30am

Agenda

1. **Apologies**

2. **Minutes** of the forty-sixth meeting held on 27 April 2016

3. **Matters arising**
(i) Tracking of requests to UK Biobank
(ii) Final draft Memorandum
(iii) Research publications
(iv) Draft paper on access to stored tumour tissue

4. **Report on the biannual funder, UK Biobank and EGC planning review meeting**

5. **Updated EGF**

6. **Update from UK Biobank** (Mr Jonathan Sellors, Company Secretary and Dr Naomi Allen, Senior Epidemiologist)
(i) Report on access applications:
   - Access Sub-Committee Minutes
   - Access update reports
(ii) Imaging update
(iii) Other enhancements (genotyping, web questionnaires etc.)
(iv) Health outcome linkage and adjudication report
(v) Communications report including reflections and discussion on the AGM
(vi) Any other developments and outstanding recommendations from EGC46

7. **IT and data security report** including update on the access systems review (Dr Mark Effingham, Chief Information Officer)

8. **Future work programme and format of meetings**

9. **Report on meetings attended and upcoming activities**
(i) UK Biobank Board of Directors meeting 30/06/16 and 30/09/16

10. **Any other business**

11. **Date of next meeting** EGC meeting, 15 March, Wellcome Trust, London
EGC away day, 16 March, location tbc, London

UK Biobank Ethics and Governance Council
Forty-seventh Meeting

3 October 2016
Wellcome Trust, London

Present: Baroness Helene Hayman (Chair), Dr Eric Meslin (Vice Chair), Dr Sheelagh McGuinness, Mr David Walker, Dr Susan Wallace, Mr Turlogh O'Brien and Professor Sally Macintyre.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) and Ms Limbanazo Matandika for the whole day. Dr Joe McNamara (MRC) for items 5-11.

Speakers from UK Biobank: Mr Jonathan Sellors, Company Secretary and Dr Naomi Allen, Senior Epidemiologist, UK Biobank for items 6-7. Dr Mark Effingham, Chief Information Officer, UK Biobank for item 7 only.

1. Apologies

Apologies were received from Professor Søren Holm, Professor Nils Hoppe, Dr Anton Enright and Dr Jon Fistein (MRC).

Dr Jon Fistein will soon step down from his role at the MRC. The EGC Chair extended the Council's thanks to Dr Fistein for all his input.

This meeting was observed by Ms Limbanazo Matandika, an MSc student from Malawi who is visiting Wellcome's Policy Team doing work on biobanking and data governance.

2. Minutes of the forty-sixth meeting held on 27 April 2016

The Council approved the circulated minutes.

The Minutes record that the funders agreed to re-consider the options with regard to performing the EGF audit (against metrics) and the access audit (from the EGC's three strand oversight model) as part of the funders' existing audit of UK Biobank, looking in particular at the frequency and timings of the audits. It was initially envisaged that the access audit would take place around 18 months after the adoption of the three strand oversight model (i.e. summer 2016). Noting that UK Biobank is establishing a new access system, the funders asked whether an audit in the short term would be useful. Members agreed to return to this question after an update from UK Biobank's Chief Information Officer Dr Mark Effingham (item 7).

3. Matters arising

Tracking of requests to UK Biobank

Members noted that the majority of items will be covered elsewhere on the agenda.

Final draft Memorandum

The final draft Memorandum has been agreed between UK Biobank and the EGC and sent to the funders for their approval.

Research publications

At the April EGC meeting a concern was raised regarding some research publications that seem to suggest that UK Biobank is representative and that state the 'prevalence' of disease in the UK population. It was noted that this assertion is inappropriate given the response rate. To assess the extent to which this is a problem the Secretary undertook a review of the publications listed on UK Biobank's website.

Members considered a paper on the outcome of the review which concluded that the vast majority of papers did not mention the representativeness of the cohort or extrapolate to suggest population prevalence. Many papers cited the response rate with some going on to caution that their findings may not generalise to the whole UK population. In general, for those papers that did discuss prevalence this was in the context of disease occurrence in the study population only. Only a handful of papers (from 2013 and 2014) mention prevalence in a way that seemed to suggest population prevalence. In general these papers did cite the response rate as a source of potential bias. One paper prompted a response from members of the UK Biobank Eye Consortium which made the point that because 'UK Biobank is not a population sample, it is inappropriate to cite an estimate of frequency as true population prevalence'.

Ahead of the meeting Professor Rory Collins advised that the issue of UK Biobank not providing prevalence rates is quite often picked up by the Access Sub-Committee (ASC) and fed back to researchers. However, since it was decided in the Access Procedures not to try to monitor or review papers before publication, it is not possible to ensure that some such claims won't slip through the net. Mindful that there are new members, Professor Collins arranged for the issue to be mentioned to the ASC.

Members discussed the extent to which this topic does or should fall within the EGC's remit, in particular given that these papers are being produced in a peer reviewed academic community that is self-policing. The Council recognised the topic to be on the fringe of its remit but members agreed that it is an ethical issue if there is any risk of misrepresenting what UK Biobank is or if researchers disseminate information that misinterprets results derived from the resource. The EGC agreed to contact UK Biobank with a few suggestions.

Action: The Secretary will contact UK Biobank to suggest that:

- it might consider putting a description of the cohort characteristics on the UK Biobank website, including the response rate.
- the ASC may want to think about requiring researchers to include a standard paragraph in their papers so there is no inadvertent misrepresentation.
- researchers could be asked to provide a lay summary of their results, reflecting the practice of requiring a lay summary of their project at the application stage. Many of the abstracts on UK Biobank's website are technical and may not be accessible for the general reader.

Action: The EGC Chair will discuss this matter informally with the new ASC Chair, Professor Martin Bobrow when they meet for an introductory conversation.

Draft paper on access to stored tumour tissue

Members considered a further draft of the EGC paper on access to stored tumour tissue which now includes a review of the literature and a commentary on the issues around re-contact. At the April EGC meeting it was also agreed that the paper should include the results of a participant survey. While UK Biobank has yet to undertake the survey work, the paper was presented to members as an interim version which will be updated in light of the participant engagement work in due course.

The Secretary advised that colleagues from the Million Women Study (MWS) have approached Wellcome's Policy Team to ask if they are aware of any analysis on the point of whether stored tissue can be considered part of the health record. Members agreed to share the paper with the MWS and that, once finalised, the paper should be published and shared with other cohorts.

Action: The Secretary will share the paper with the MWS.

Members returned to this topic when UK Biobank colleagues joined for the afternoon session:

Dr Naomi Allen explained there is considerable research interest in collecting tissue to look at molecular signatures of tumours, which are very heterogeneous. Only by looking at the genetic profile can you characterize different tumours and find risk factors for different tumours. UK Biobank has received overwhelming interest from the research community to have access to tumour samples. Given this, UK Biobank undertook a pilot involving the pathology department in Newcastle that aimed to answer the question 'Can we link participants with local pathology databases?'. They found that for the majority of participants treated a link could be made to their histopathology report. Half of the cohort are treated in 10 major hospitals. As a next step, UK Biobank will contact these hospitals in order to find out whether it is possible to get the written histopathology reports.

Participants might well have given (or refused to give) consent for research when they had the tissue removed in the clinical setting. For example, Dr Allen advised that the Oxford Tissue Biobank, a research facility of the University Hospitals Trust, since 2003 has asked patients undergoing a biopsy if they agree or not to having the

tissue used in research. Samples will only be released if the patient consented for such use and it is a considerable manual effort to collect these consent records. UK Biobank is assessing how feasible it is to do this and how best to engage participants with the proposed work. It is estimated that the refusal rate for use of biopsy samples in research is 1 in 1,000.

Discussing the limitation of a participant survey, it was agreed that it would be preferable for UK Biobank to conduct qualitative work that provides participants with a detailed explanation of the situation and gives the opportunity for in depth contextual discussion about what route UK Biobank should take. Even this work has its challenges, however, for example finding a representative sample that is not dominated by people with strongly held views.

The EGC Chair suggested that the formation of a UK Biobank and EGC working group would be a good way to take the discussion forward.

Action: Dr Allen will write up UK Biobank's thinking on this issue and this will be brought back to the EGC for discussion.

4. Report on the biannual funder, UK Biobank and EGC planning review meeting

The biannual meeting took place on 13 September and was a useful occasion for representatives of the EGC, UK Biobank and funders to discuss current issues.

Action: Before the next biannual planning review meeting, the Secretary will seek members' input on potential agenda items.

5. Updated EGF

Prior to this meeting the EGC provided comments on the content and presentation of the online update of the EGF and these were well received by UK Biobank. Members agreed that UK Biobank had done a good job in preparing an informational update for participants.

Action: Mr Jonathan Sellors will revise and re-circulate the online updated EGF.

The revised EGF serves the useful purpose of updating participants (and others) on UK Biobank's progress. As a separate exercise the EGC considers it necessary to update the EGF as a governance document so it reads as a contemporary, credible document. Such a document would help the EGC to fulfil its role as guardian of the EGF. The funders suggested that the EGC should set out its position in a paper explaining the need for a revised governance document.

Action: The Secretary will draft and circulate a paper on the revision of the EGF.

6. Update from UK Biobank (Mr Jonathan Sellors, Company Secretary and Dr Naomi Allen, Senior Epidemiologist)

Report on access applications

The TIME Study is being used as a pilot for how UK Biobank should handle studies that request re-contact with participants. 18,000 participants who self-reported they had hypertension were emailed by UK Biobank on behalf of the Dundee University research group. The study involved participants potentially changing the time they take their medication and follow-up through health records. 6% of the re-contacted participants contacted the researcher and 3% were eligible to take part (e.g. they took the right kind of medication) and were enrolled. As part of its follow-up work, UK Biobank will now re-contact the initial 18,000 participants and ask for their views on being re-contacted e.g. did they mind and are they happy to be re-contacted in future? The survey results will inform UK Biobank's general approach to re-contact studies.

The broader issue of whether UK Biobank is the best or most appropriate recruitment tool was discussed. Dr Allen advised that from a scientific point of view it is useful to recruit from an existing cohort for whom there is data and samples; the participants will likely be more inclined to join a further study. Recruiting in this way gives more added value than trying to recruit blind. For example, the TIME study had attempted to recruit using flyers but had minimal response. There is also value to UK Biobank as data will be returned to the resource.

Recognising the potential for reputation risk to UK Biobank and in turn to the funders, it was agreed that, for this type of request, it might be necessary for UK Biobank to require a very high standard of the researcher and this may include UK Biobank being able to input into the drafting of the study's participant materials.

Imaging update

UK Biobank is currently achieving the required response rate; 30% of those approached contact UK Biobank with 26-27% being eligible and attending the assessment. Participants give positive feedback saying they enjoy the four hour visit and would stay longer.

UK Biobank is continuing to monitor people who receive feedback. The rate of incidental findings is stable at 1-2%. The imaging pilot findings will be published shortly.

Other enhancements (genotyping, web questionnaires etc.)

The web questionnaire on mental health has just finished. The questionnaire was piloted as some questions were quite sensitive, however, the questionnaire was well received with a 35% response rate. Members recognised the sensitivity of asking questions about mental ill-health and how this could make participants more interested in the security of their data.

Health outcome linkage and adjudication report

UK Biobank has achieved significant progress in relation to achieving cohort-wide primary care data coverage. Primary care data was received for 170,000 English participants from TPP (one of the three main GP system suppliers) in September 2016. Updated primary care data for 27,000 of the 36,000 Scottish participants was received in May 2016 and will be received later in September 2016 for almost all of the 21,000 Welsh participants. By the beginning of the final quarter of 2016, UK Biobank therefore expect to hold primary care coded data covering >200,000 participants.

In August 2016, UK Biobank signed a contract with a further system supplier Apollo Medical Systems in collaboration with InPractice Systems (INPS) to commence work to extract primary care data for the about 30,000 further English participants, and currently expect to receive these data in the first quarter of 2017. Discussions with the third main English GP system supplier, EMIS, are progressing. Allowing time to establish the technical, information governance and contractual arrangements, it will likely take several further months to obtain these data; UK Biobank hopes to obtain EMIS data (currently covering an estimated 245,000 English participants) in late 2017.

Communications report including reflections and discussion on the AGM

Two participant events are planned for Newcastle in October and November. These will be afternoon tea events and have been arranged to coincide with the launch of the imaging centre. The meetings are very popular and have proved to be an effective way to communicate with participants. One of the most common questions is ‘What’s my data being used for?’. This speaks to the Council’s earlier suggestion that UK Biobank could usefully have a participant portal through which participants could see their past contributions to the project (e.g. which questionnaires they have completed) and how their data have been used.

The communications report included an update from Mr Andrew Trehearne (Head of Communication) on feedback received in relation to the Annual General Meeting and some questions to consider for next year’s event. Discussing the questions, members agreed on a number of points to feedback to UK Biobank.

A member asked how and what UK Biobank tracks in the media and whether this matters to the funders (e.g. as a way to demonstrate the impact of UK Biobank). The funders advised that impact would be looked at closely as part of the core funding renewal.

Action: Mr Sellors offered to ask Mr Trehearne how and what UK Biobank tracks in the media and to report back.

Any other developments and outstanding recommendations from EGC46

There were no other issues.

7. IT and data security report including update on the access systems review (Dr Mark Effingham, Chief Information Officer)

Access Management System (AMS): The AMS has been fit for purpose and researchers give positive feedback. However, from the internal perspective of the access management team it is not very flexible or intuitive. Given the increase in registrations and applications, UK Biobank is looking at the people, process and technology involved in the access process and trying to improve the whole system. The aim is to speed up the time between receipt of an application and the researcher receiving the data/samples. One aspect of this is to move away from having both a preliminary and main application for data only applications and to administering this through a single application instead.

Re-contact applications: At its last meeting the EGC asked if re-contact applications could be flagged automatically in the new access system, in preference to the current manual process. Dr Effingham advised that a system of work flow and messaging is being built into the system so it could be set up so re-contacts automatically generate a message to log in. However, applications should probably go through a basic level of review through the Access and Scientific Teams to make sure they are re-contacts, before being flagged to the EGC. Members were comfortable with this approach.

IT and data security systems: Dr Effingham provided an overview of the IT and data security systems and UK Biobank's current standing in relation to relevant ISO accreditations and penetrance testing. A security awareness module is being deployed to all staff, covering physical security, working on the move and cyber security and this year UK Biobank's business continuity testing has been extended to include cyber security across the Clinical Trial Service Unit, the Co-ordinating Centre and the Participant Resource Centre.

Institutional datasets (e.g. of the genotyping data): A Material Transfer Agreement is signed at the institutional level. If a researcher wants to access these data they would be given access via a bridging file. The data identifiers would be specific to the researcher's application meaning it could be tracked back to their application if data were being used for an unauthorised purpose.

Participant portal: When asked about any plans to provide a participant portal, Dr Effingham commented that a set of more transactional participant services is something worth moving towards in future. This way participants could see what their participation in UK Biobank has given rise to.

Returning to a question raised under item 2, members agreed that the proposed funder audit of UK Biobank's access systems should wait until the new AMS is bedded in.

8. Future work programme and format of meetings

Having moved from four to two meeting a year, and with no significant piece of work concluded in 2016 (e.g. the tumour tissue paper), it was agreed that the EGC Annual Review should be published mid-2017 covering an 18 month period.

An EGC away day will take place in March 2017 and will be an opportunity to think about ways of working and the scope and particular aspects of the EGC's work. It was suggested that it might be helpful to have an invited speaker.

Minor revisions were made to the EGC website in 2015 but members consider that the site is still in need of improvement.

Action: The Secretary will look at speaker options for the away day and follow-up with Wellcome's Web Team regarding the EGC website.

9. Report on meetings attended and upcoming activities

The EGC Chair attended the June and September UK Biobank Board of Directors meetings and noted that the issues relevant to the EGC had been discussed during the course of the current meeting.

The Secretary and member, Professor Sally Macintyre, attended the Human Tissue Authority annual meeting and noted that the presentation on Genomics England had been most relevant.

10. Any other business

The funders advised that the core funding renewal process for UK Biobank is underway; the international review panel will meet in November. To meet the scale of the potential commitment a wider pool of funders has been identified. This will bring advantages as well as practical and governance considerations, including how the EGC should engage with the wider group.

11. Date of next meeting EGC meeting, 15 March, Wellcome Trust, London
EGC away day, 16 March, location tbc, London