

# UK Biobank Ethics and Governance Council Forty-eighth Meeting

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

Wednesday 15 March 2017 at 11.30am

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## Agenda

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1. **Apologies**
2. **Minutes** of the forty-seventh meeting held on 3 October 2016
3. **Matters arising**
  - (i) Tracking of requests to UK Biobank
  - (ii) Research publications
  - (iii) EGC website
4. **Report on the biannual funder, UK Biobank and EGC planning review meeting**
5. **UK Biobank core renewal** (Dr Joe McNamara, MRC and Ms Katherine Littler, Wellcome)
6. **Update from UK Biobank** (Professor Rory Collins, Chief Executive Officer)
  - (i) Report on access applications:
    - Access Sub-Committee Minutes
    - Access update reports
    - Re-contact for third party studies - TIME Study survey results
  - (ii) Review of the access process and systems (including revision of the procedures)
  - (iii) Imaging update
  - (iv) Other enhancements (genotyping, web questionnaires etc.)
  - (v) Health outcome linkage and adjudication report
  - (vi) Access to stored tumour tissue
  - (vii) IT and data security report
  - (viii) Any other developments and outstanding recommendations from EGC47
7. **Communications update** (Mr Andrew Trehearne, Head of Communications)
8. **Dementias Platform UK** (Professor John Gallacher, Director, DPUK)
9. **Report on meetings attended and upcoming activities**
  - (i) European Medicines Agency workshop: Identifying opportunities for 'Big Data' in medicines development and regulatory science 14/11/16
  - (ii) Meeting between Helene Hayman and Martin Bobrow, new Chair of the ASC 22/11/16
  - (iii) UK Biobank Board of Directors meeting 16/12/16
  - (iv) UK Biobank and Dementias Platform UK Liaison meeting 25/01/17
  - (v) Meeting with Dr Tohru Masui and Dr Yusuke Inoue from Japan Biobank 16/02/17
  - (vi) Health Research Authority event 'Human tissue, big data, proportionate consent' 28/02/17
10. **Any other business**
11. **Date of next meetings**
  - Annual meeting - 29 June 2017, Manchester Town Hall
  - EGC meetings - 17 October 2017, 21 March 2018 and 17 October 2018, Wellcome, London

**UK Biobank Ethics and Governance Council  
Forty-eighth Meeting**

**15 March 2017  
Wellcome Trust, London**

Present: Baroness Helene Hayman (Chair), Dr Eric Meslin (Vice Chair), Mr David Walker, Dr Susan Wallace, Professor Søren Holm, Professor Nils Hoppe, Dr Anton Enright, Mr Turlogh O'Brien and Professor Sally Macintyre.

In attendance from EGC Secretariat: Ms Adrienne Hunt.

Observers: Ms Katherine Littler (Wellcome Trust) and Dr Joe McNamara (MRC) for the whole meeting.

Speakers from UK Biobank: Professor Rory Collins for items 6 and Mr Andrew Trehearne for items 7-8.

Speaker from Dementias Platform UK: Professor John Gallacher for items 7-8.

1. Apologies

Apologies were received from Dr Sheelagh McGuinness.

2. Minutes of the forty-seventh meeting held on 3 October 2016

The Council approved the circulated minutes.

3. Matters arising

*Tracking of requests to UK Biobank*

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

*Research publications*

At a previous EGC meeting a concern was raised regarding some research papers 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. The Secretary subsequently undertook a review of all the abstracts on UK Biobank's website, the results of which were discussed by the Council at its October meeting leading to the following suggestions:

- UK Biobank might consider putting a description of the cohort characteristics on the UK Biobank website, including the response rate.

- The Access Sub-Committee (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. This was suggested as many of the abstracts on UK Biobank's website are technical and may not be accessible for the general reader.

Prior to the current meeting Professor Rory Collins responded to the suggestions, indicating that:

- It would be a good idea to put a note on the UK Biobank website about it not generally being able to provide prevalence estimates because it is not a representative sample.
- UK Biobank's Company Secretary, Mr Jonathan Sellors, would put on the agenda for the ASC meeting the idea of requiring/proposing some standard text for inclusion in papers, or alternatively providing a reminder to researchers that they should be careful about not claiming that the UK Biobank resource can provide reliable prevalence estimates in most circumstances.
- With respect to summarising the findings of research that comes out of UK Biobank in lay terms, UK Biobank already have some initiatives ongoing. UK Biobank's Head of Communications, Mr Andrew Trehearne will be asked if, in addition, he could ask the researchers to provide a few sentences that describe what they've found in lay terms so that this too could be available on the website.

**Action:** When asked at the present meeting about progress on the above, Professor Collins offered to follow-up on where they had got to.<sup>1</sup>

#### *EGC website*

Having agreed at the March meeting that the EGC website should be redesigned, members reviewed and endorsed an initial mock-up of the new site.

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

The biannual meeting took place on 1 March and was a useful occasion for representatives of the EGC, UK Biobank and funders to discuss current issues, including the GSK/Regeneron exome sequencing application. At the meeting the EGC Chair asked how UK Biobank will communicate with participants about the application, noting that commercial involvement can often be a sensitive issue. Ideally this should be proactive (sent prior to the press release) and not reactive. Katherine Littler had advised that UK Biobank is developing a 7 page Q&A on issues that might arise for participants; in part this builds on questions that the funders

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<sup>1</sup> After the meeting UK Biobank published a paper 'Access matters: representativeness of the UK Biobank resource' at <http://www.ukbiobank.ac.uk/resources/>

asked UK Biobank to address when the application was being considered. Agreeing that this should be sent to participants and published on the website as soon as possible, members agreed to return to the subject later in the day when UK Biobank colleagues joined the meeting.

**Ethics and Governance Framework (EGF):** UK Biobank has prepared an online update of the EGF which will be made available on its website as a way 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. At the invitation of the Board the EGC re-drafted the feedback section of the EGF by means of example. The proposal was circulated to the funders and UK Biobank in advance of the planning review meeting and will be discussed at the March Board of Directors meeting.

5. UK Biobank core renewal (Dr Joe McNamara, MRC and Ms Katherine Littler, Wellcome)

The funders convened an international panel to review UK Biobank's activities over the last 5 years and to make recommendations regarding the project's 5-year core renewal application. The funding panel agreed that UK Biobank had done an excellent job over the last 7 years and recommended funding in full. UK Biobank is in the process of responding to the panel's recommendations including the need to explore training opportunities (e.g. informatics PhDs), succession planning and long term IT infrastructure plans.

Given the extent of the proposed costs a consortium of funders has been established to meet the commitment including Cancer Research UK, the British Heart Foundation and the National Institute of Health Research (Department of Health). Wellcome and MRC will continue to be core funders and the EGC's funder contacts.

6. Update from UK Biobank (Professor Rory Collins, Chief Executive Officer)

*Report on access*

**Revision of the Access Procedures and Material Transfer Agreement (MTA):** UK Biobank has assessed how the ASC's approach to data and sample access has changed and ascertained that some aspects of current practice are not reflected in the current MTA. For example, applications have traditionally been specific, narrow and hypothesis-testing but release of the genotyping data prompted applications that are broader in scope and hypothesis-generating. A review has identified what aspects need to be modified in light of the GSK/Regeneron and other academic applications e.g. the period of exclusive use if researchers have put in a lot of time and/or money into generating data. A revised contract is now in place and was used in relation to the GSK/Regeneron application. UK Biobank will modify the Access Procedures to ensure they take account of the changes to the MTA, taking advice from the funders and EGC.

**Sample strategy:** UK Biobank's strategy has been (as far as it is possible) to turn the samples into non-depletable data that can be made available to all researchers. The ASC has rejected some applications because the requests, while convenient for the researchers, were not sufficient for UK Biobank's purpose when taking into account the sample depletion. A case cohort strategy was discussed by the International Scientific Advisory Board (ISAB) which involves a super control group that you measure against. While often seen as an efficient strategy the ISAB decided this was not ideal – it would deplete the super control group samples and more importantly assays performed in a control group at one time are not necessarily comparable when done at a different time. Systematic difference can be avoided if assays are performed simultaneously. UK Biobank has therefore decided to take a case-control approach, implementing calls for nested case-control research when there are sufficient incident cases for a given disease among the participants. Recognising that UK Biobank will still receive ad hoc applications for samples, over the next year the ASC will develop a more detailed sample strategy proposal, including the criteria it will use to judge applications. Input from EGC will be sought during this process.

When asked about current practice for the adjudication of applications that request samples, Professor Collins advised that the ASC considers the validity of the research, scientific value and how much sample is required. The ASC receives a report from the laboratory team regarding how much sample is left and the implication of the request on the resource. While the ASC has this information as standard, how they manage decisions on sample release is currently ad hoc.

**Re-contact for third-party studies – TIME Study survey results:** As part of its follow-up work to the TIME Study, UK Biobank invited the re-contacted participants to fill in a web-based survey of their views on being re-contacted. A third responded, with the vast majority indicating that they were happy to be contacted about the possibility of participating in the TIME Study. However, there was a lack of clarity among the respondents about how much UK Biobank was or was not involved with the research. This finding highlights that when participants are re-contacted for invitation into third-party studies, it is imperative that the introductory information from UK Biobank is absolutely clear; and, in particular, it needs to be made clear that UK Biobank and the third-party study are different entities operating under different rules, for example with regard to the way data may be used and stored. Recognising the potential for reputation risk to UK Biobank and being mindful not to overburden participants, members agreed UK Biobank should carefully vet requests of this kind and require a very high standard of the researcher. This may include UK Biobank being able to suggest revisions to the study's participant materials.

UK Biobank has received third-party re-contact requests from the Dementias Platform UK, including a proposal to invite participants to take part in an interventional trial. A member asked if participation in a trial would skew UK Biobank as a general observational study and whether UK Biobank would need to know what trials participants are taking part in and which arms they are on. Professor Collins responded that most interventions don't work or have only small effects and often for transient and short periods of time. The impact therefore is likely to be small in comparison to other changing effects e.g. if a participant stops smoking.

It was agreed that further consideration should be given to whether re-contact studies should be able to receive follow-up data periodically from UK Biobank (e.g. from the participant's health record) or if they should be required to collect this themselves. Also, the feedback implications of any third-party study should be considered in relation to UK Biobank's policy of providing no feedback of health information to participants beyond the measurements they receive at the assessment centre visit.

It was agreed that a small working group of UK Biobank, EGC and funder representatives should meet to discuss these issues and formulate a strategy for external re-contact applications, including adjudication criteria. The group could also consider how best UK Biobank should manage the process so it's entirely clear that the third-party study is a separate initiative.

**Action:** A small working group will be formed to take this work forward.

*Review of the access process and systems (including revision of the procedures)*

See item 'Revision of the Access Procedures and Material Transfer Agreement (MTA)' above.

*Imaging update*

About 15,000 participants have been imaged at the centre in Cheadle, where assessments are ongoing. A second centre in Newcastle will open in April with a slow ramp up period to get staff used to the process. Plans for the third centre in Reading are progressing.

The rate of incidental findings is stable at 1-2%. UK Biobank continues to follow-up what happens to people who get feedback via questionnaires. UK Biobank is in discussion with a journal regarding the publication of a paper on the pilot experience.

**Action:** Professor Collins will provide the EGC with the draft publication.

*Other enhancements (genotyping, web questionnaires etc.)*

**Cardiac rhythm monitoring:** UK Biobank is piloting cardiac rhythm monitoring for people aged over 60 who are not known to have atrial fibrillation. The pilot, which is taking place during the imaging sub-study, involves participants wearing a type of band aid for a period of two weeks, which incorporates a chip that records the data. 60% of the imaging participants are eligible and so far 75% of those have agreed to wear the monitor. 1,200 individuals have participated to date and funding is currently being sought to expand this work to 20,000 participants.

**Web questionnaire:** A new web questionnaire on irritable bowel syndrome and pain is being developed and should be implemented this year. Recognising that only those participants with email address are asked to respond to the questionnaires, members asked about UK Biobank's progress in relation to getting more and up-to-date email addresses from participants. As part of the annual newsletter, UK

Biobank prompts participants to provide their email address if it has changed. Postal address information is received periodically from the NHS.

**Genotyping:** Recently, UK Biobank contacted the UK Biobank research community to outline key principles for the full cohort genotyping release that ensures no preferential access for any group. This was a significant challenge given that there are several petabytes of data and over 100 researcher groups that already have approval to use them. UK Biobank's approach (developed with the European Genome-phenome Archive) involves researchers downloading the encrypted genotyping data files over a period of few weeks and at the end of this period all the researchers will – at the same time – be provided with the necessary information to de-encrypt the files and get access. It is anticipated that these data will become available in the second quarter of 2017.

#### *Health outcome linkage and adjudication report*

Members noted the follow-up report and the significant progress in relation to primary care data. The next challenge is to make these data available to researchers. UK Biobank's current priority is the development and implementation of methods for the processing, integration, annual updating, description and display of the different primary care datasets that it has received, which are provided using a range of different formats and coding systems.

#### *Access to stored tumour tissue*

The EGC's analysis lead it to cautiously consider there to be a *prima facie* case for treating tumour tissue as part of a participant's 'health record' (in terms of the consent given by participants at enrolment for UK Biobank to access their health records). However, a range of views were expressed by participants when this was discussed during the participant panel at UK Biobank's Annual General Meeting (AGM) in 2016 and more recently when UK Biobank conducted a survey at one of its participant events. Of note, however, the overwhelming majority were in support of the work.

Professor Collins proposed that the next step is for UK Biobank to consider the scientific value of the samples and whether this justifies the significant challenges of getting access to them. For example, formalin fixed samples are not good for sequencing. Practical challenges include the considerable manual effort to collect the consent records that participants signed when they might well have given (or refused to give) consent for research when they had the tissue removed in the clinical setting.

If the samples are of value, further and deeper engagement work will be required (e.g. qualitative work that provides a detailed explanation of the situation and gives the opportunity for in-depth contextual discussion about what route UK Biobank should take) as a way of providing an evidentiary base for UK Biobank's proposed approach. Members suggested that UK Biobank could also add this aspect to the consent form participants are asked to sign when they attend the imaging sub-study, including an option to opt-out of tissue sample collection. This would give UK

Biobank a sense of how many people chose to opt out. If very few take this option it may add weight to an argument for a general opt-out.

#### *IT and data security report*

Members noted the report.

#### *Any other developments and outstanding recommendations from EGC47*

UK Biobank is investigating the possibility of assaying a set of infectious disease biomarkers, including HIV. Members asked if the proposal requires up-front consideration of the ethical issues given the relevance of the results not only to the individual participant but also those close to them. Professor Collins advised that the data would be treated the same as the haematology results and will not be fed back to participants or anyone else. Members noted that a research project has previously been subpoenaed to give information in a trial of an individual with HIV.

During the imaging assessment, some participants have been asked to complete a questionnaire on brain donation and a large proportion of respondent were open to the idea. Recognising this would be a significant new venture, members consider that the proposal would require detailed attention if it was to go ahead.

#### 7. Communications update (Mr Andrew Trehearne, Head of Communications)

Mr Andrew Trehearne provided an update on UK Biobank's communications activities, including circulation of the annual newsletter, participant meetings, the AGM and that evening's House of Lords event, which was hosted by the EGC Chair.

The AGM will take place at the Manchester Town Hall on 29 June. Members reiterated an earlier recommendation that the AGM should include a public interest accountability exercise as per the traditional idea of an AGM, when an organisation might update on its activities, how it has spent money and the prospects for the year ahead.

Discussion returned to the issue of how researchers represent UK Biobank in their publications and the EGC's recommendation to require the inclusion of a standard paragraph in each paper and to improve accessibility of the resource characteristics on the website (see item 3 above). Mr Trehearne advised that researchers are required to incorporate a standard sentence in their publications stating that they have used UK Biobank; this could perhaps be expanded to include characteristics of the resource. There is a lot of information on the DataShowcase and the 'scientist' section of the website but this could be pulled together to improve accessibility.

#### 8. Dementias Platform UK (Professor John Gallacher, Director, DPUK)

Professor John Gallacher presented on DPUK's aspirations for collaboration with UK Biobank and its desire to draw on the range of information in the resource including

genetic, lifestyle, imaging and the answers to the cognitive function questionnaire. DPUK has received funding from the MRC to repeat image 10,000 participants who have already been imaged by UK Biobank. This will create a sub-cohort of participants with very rich imaging data and the expectation is that some of the participants will be invited to take part in experimental medicine trials.

As with all re-contacts, these will need to be carefully managed. Participants should receive very clear information about why they are being re-contacted, what taking part involves and the relationship between DPUK and UK Biobank. Care will be needed to ensure that the invitation process does not reveal to participants (either explicitly or by implication) information about which they were previously unaware (e.g. APOE4 risk factor status).

**Action:** Members agreed to send a note to UK Biobank indicating the EGC's support for the aims of DPUK and its proposed use of UK Biobank, bearing in mind that the implementation requires significant and detailed consideration which should feed into UK Biobank's work to develop a policy on re-contact for third-party studies more broadly.

#### 9. Report on meetings attended and upcoming activities

*European Medicines Agency (EMA) workshop: Identifying opportunities for 'Big Data' in medicines development and regulatory science 14/11/16*

The EGC Chair presented a talk at this EMA event entitled 'Ethical and Governance Aspects of Research Data: experience from UK Biobank'. A report of the meeting has been published.

*Meeting between Helene Hayman and Martin Bobrow, new Chair of the ASC 22/11/16*

The EGC Chair and Professor Bobrow had a constructive introductory conversation.

**Action:** Professor Bobrow will be invited to the October EGC meeting.

*UK Biobank Board of Directors meeting 16/12/16*

The EGC Chair attended the December Board meeting and noted that the issues relevant to the EGC had been discussed during the course of the day.

*UK Biobank and Dementias Platform UK Liaison meeting 25/01/17*

Members noted a draft report of the DPUK liaison meeting, which the EGC Chair and Secretary attended.

*Meeting with Dr Tohru Masui and Dr Yusuke Inoue from Japan Biobank 16/02/17*

The EGC Secretary met colleagues from Japan biobank to discuss a variety of matters, including the governance and use of biobanks in Japan and how these compare to UK Biobank.

*Health Research Authority (HRA) event 'Human tissue, big data, proportionate consent' 28/02/17*

Professor Søren Holm and the EGC Secretary attended to HRA event, Professor Holm in his capacity as member of the National Research Ethics Advisors Panel.

#### 10. Any other business

Members will meet on 16 March to discuss the EGC's remit and reflect on its work one year on from the 2015 review. The funders provided a one-page note to feed in to the Council's deliberations.

A member suggested that it would be useful to assess whether UK Biobank is in conformity with the recently published World Medical Association 'Declaration of Taipei on ethical considerations regarding health databases and biobanks'.

#### 11. Date of next meetings

Annual meeting - 29 June 2017, Manchester Town Hall

EGC meetings - 17 October 2017, 21 March 2018 and 17 October 2018, Wellcome, London