

Access matters / hypothesis-testing or hypothesis-generating applications

The purpose of this note is to provide guidance to researchers as to how UK Biobank deals with hypothesis-generating applications.

1. To date, the majority of research applications to UK Biobank have involved a researcher applying to use UK Biobank data to investigate a specific hypothesis: namely an investigation of a particular supposition that appears to explain a group of phenomena or is advanced as a basis for further investigation. This hypothesis is then tested by a prospectively defined experiment, often by the application of an assay to selected phenotype cases and controls.
2. The advent of modern day “omics” (including genomics, proteomics, metabolomics, transcriptomics etc.) in tandem with the development of high throughput assays has given rise to the development of hypothesis-generating research (for example, many GWAS studies are hypothesis-generating). Hypothesis-generating research does not require a pre-selection of either phenotypes or genotypes, rather the research looks for patterns or perturbations in the data which can then form the basis for a more specific hypothesis which in turn can then be tested.
3. Such hypothesis-generating research takes place in basic science and clinical practice, as well as in clinical research. Hypothesis-testing and hypothesis-generating research projects are not mutually exclusive, just different approaches for the conduct of research and they can often be complementary: the idea behind hypothesis-generating research is essentially to generate and identify a hypothesis(es) which can be tested.
4. UK Biobank exists to facilitate basic, translational and clinical research. It welcomes applications, which may be either hypothesis-generating or hypothesis-testing or indeed a combination of the two. The issue for UK Biobank is to ensure that the scope of an application is appropriately defined. This is the purpose of the guidance to researchers set out in this note.
5. *UK Biobank’s essential access criteria*
 - 5.1 The fundamental access test as set out in UK Biobank’s Access Procedures is that the Resource is available “for all types of health-related research that is in the public interest”. In order to be able to apply the test in a meaningful way a research application must involve a project with an identifiable and defined purpose, scope and output. Accordingly, UK Biobank would like to re-iterate that ***all research applications to UK Biobank must articulate a definable purpose, scope and output.***
 - 5.2 To illustrate this, UK Biobank has set out below:
 - 5.2.1 certain types of application which do not fall within this classification (and thus may not be approved); and
 - 5.2.2 how it will deal with hypothesis-generating applications.

6. *Types of application which UK Biobank will not approve*
 - 6.1 Certain types of research applications would not possess a definable purpose, scope and output, for example an application to study:
 - 6.1.1 (subjectively) whatever the researcher determines he/she wishes to research; or
 - 6.1.2 (objectively) anything about anything.
 - 6.2 Applications which are framed in such a way would not be approved by UK Biobank, as it would not be possible for UK Biobank:
 - 6.2.1 to review such an application in order to determine whether it was “health related” and/or “in the public interest”;
 - 6.2.2 nor from a practical perspective would it be possible to determine when it would be finished.
7. *Some practical guidance for hypothesis-generating research*
 - 7.1 The question for UK Biobank is whether the application can be appropriately defined. For example, an application to develop statistical methods, whereby the output of the research is the development of statistical models which measure the correlation between an individual’s genotype and phenotype would (in principle) represent an acceptable application. The scope may be very broad but it is definable.
 - 7.2 UK Biobank considers that there is no inherent reason why hypothesis-generating research cannot be suitably defined. Further, UK Biobank recognises that once a suitable hypothesis(es) has been generated (perhaps using a subset of the dataset provided), the researcher may well want to test it (using a different dataset).
 - 7.3 In order that UK Biobank can keep abreast of this hypothesis-testing research, which the researcher then goes onto investigate as a result of their hypothesis-generating project:
 - 7.3.1 As a working presumption, UK Biobank will not require the researcher to submit a separate application; but
 - 7.3.2 it will require that the researcher notifies UK Biobank in advance about the hypothesis-testing research in order to confirm that such research is compatible with UK Biobank’s access criteria (namely that the hypothesis is health related research in the public interest), and provides suitable timelines for the conduct of the research and the return of results.

UK Biobank’s Access Sub-Committee retains a keen interest in this topic and will keep it under review and amend / update as necessary.

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