# What makes UK Biobank special?

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For **UK Biobank** see http://www.ukbiobank.ac.uk

In a prescient move more than a decade ago, the Medical Research Council and Wellcome Trust decided to establish the large UK Biobank prospective cohort to support the investigation of risk factors for the major diseases of middle and old age.[1,2] Recruitment of more than 500 000 men and women aged 40–69 years was successfully achieved during 2006–10 and their health is being followed long term. On March 30, 2012, the UK Biobank resource is launched for use by all researchers—without exclusive or preferential access—for any health-related research that is in the public interest.

The challenges of understanding the determinants of common life-threatening and disabling diseases are substantial. Such conditions are typically caused by many different exposures that might each have moderate effects and interact with each other in complex ways.[3,4] To investigate a wide range of exposures, extensive information needs to be collected through questionnaires and physical measurements, as well as by storing biological samples that allow many different types of assay (eg, genetic, proteomic, metabonomic, or biochemical). Moreover, to study reliably the sort of effects of different exposures that it is plausible to expect, many thousands of cases of a specific disease may be required.[4]

Prospective cohorts have a number of advantages for the comprehensive and reliable quantification of the combined effects of lifestyle, environment, genes, and other exposures on health outcomes.[3,5] In particular, exposures can be assessed before they are affected by disease or its treatment, or by a person's response to developing disease. Diseases can also be studied that are not readily investigated by retrospective studies (eg, dementia or rapidly fatal conditions). Moreover, the overall beneficial and adverse effects of a specific exposure on the life-time risks of multiple health outcomes can be considered (eg, associations of obesity with different causes of death[6]). Prospective studies do, however, need to be large because only a small proportion of the participants will develop any particular disease.

Some large prospective cohorts have used cost-effective strategies to obtain reliable information about disease associations with exposures assessed only by questionnaires (eg, the Million Women Study in the UK).[7] Others have focused on the assessment of certain types of exposure on specific outcomes (eg, diet and cancer in the EPIC study of 500 000 people in Europe).[8] Generalisable associations of exposures with disease can be obtained without including representative samples of particular populations.[9] Instead, what matters is that sufficiently large numbers of individuals with different levels of exposures can be investigated. Establishing prospective studies in different populations will extend the range of exposures that can be considered: for example, the 500 000 person Kadoorie Biobank[10] in China involves a population with lower cholesterol concentrations than can be reliably studied in most developed countries, and the 150 000 person Mexico City Prospective Study[11] involves a population with higher prevalence of obesity.

UK Biobank has been designed to allow the assessment of the relevance of many different exposures to a wide range of health outcomes (including not just mortality and cancer, but also many other conditions that cause disability). The questionnaires, physical measurements, and biological samples collected from participants were chosen—following extensive consultation—to allow detailed assessment of exposures in the whole cohort.[1,12] Enhanced phenotyping has been done in large subsets (eg, retinal imaging in about 100 000 participants), and further enhancements are either ongoing (eg, repeated diet recall surveys via the internet; physical activity

| | Year of follow-up | | |
|---|---|---|---|
| | 2012 | 2017 | 2022 |
| Diabetes mellitus | 10 000 | 25 000 | 40 000 |
| Myocardial infarction and coronary death | 7000 | 17 000 | 28 000 |
| Stroke | 2000 | 5000 | 9000 |
| Chronic obstructive lung disease | 3000 | 8000 | 14 000 |
| Breast cancer (female) | 2500 | 6000 | 10 000 |
| Colorectal cancer | 1500 | 3500 | 7000 |
| Prostate cancer | 1500 | 3500 | 7000 |
| Lung cancer | 800 | 2000 | 4000 |
| Hip fracture | 800 | 2500 | 6000 |
| Rheumatoid arthritis | 800 | 2000 | 3000 |
| Alzheimer's disease | 800 | 3000 | 9000 |
| Parkinson's disease | 1000 | 3000 | 6000 |

Estimates based on UK age-specific and sex-specific rates with adjustment for potential healthy cohort effects and losses to follow-up.[1,4]

***Table:*** **Approximate numbers of incident cases of exemplar diseases expected to accrue in first 15 years of follow-up in UK Biobank**

monitors sent by mail) or being planned (eg, imaging of brain, heart, and body). Prospective studies typically collect either large amounts of data on small numbers of participants ("data depth") or small amounts of data on large numbers of participants ("data breadth"). UK Biobank has achieved both data depth and data breadth.

By embedding UK Biobank within the UK's National Health Service, a wide range of disease outcomes can be identified through routine medical records. Information will also be sought directly from participants about disorders that are typically under-reported (eg, cognitive decline and depression). Misclassification of disease cases can reduce statistical power to assess associations and the failure to characterise disease subtypes can reduce biological specificity. Diagnostic accuracy is to be increased in UK Biobank by using more intensive methods (eg, retrieval of imaging data and tissue samples) for the validation and classification of health outcomes. The table shows the numbers of cases for a selection of diseases that are expected to occur during the first 15 years of follow-up, with similarly large numbers developing other important disorders.[1,4] Hence, over time, UK Biobank will become of value for the investigation of an increasingly wide range of diseases. Opportunities also exist for early results to emerge from studies based on prevalent disease and other information recorded at baseline.

It is hoped that researchers from around the world will now start using the UK Biobank resource (with the participants' identity appropriately protected) to generate findings that lead to better strategies for the prevention, diagnosis, and treatment of a wide range of life-threatening and disabling disorders.

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I am Principal Investigator and Chief Executive of UK Biobank. As stated above, however, no one has exclusive or preferential access to the UK Biobank resource. I declare that I have no conflicts of interest.

1 UK Biobank. Protocol for a large-scale prospective epidemiological resource. March 21, 2007. http://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf (accessed March 15, 2012).
2 Palmer LJ. UK Biobank: bank on it. *Lancet* 2007; **369:** 1980–82.
3 Manolio TA, Bailey-Wilson JE, Collins FS. Genes, environment and the value of prospective cohort studies. *Nat Rev Genet* 2006; **10:** 812–20.
4 Burton PR, Hansell AL, Fortier I, et al. Size matters: just how big is BIG?: quantifying realistic sample size requirements for human genome epidemiology. *Int J Epidemiol* 2009; **38:** 263–73.
5 Grimes DA, Schulz KF. Cohort studies: marching towards outcomes. *Lancet* 2002; **359:** 341–45.
6 Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009; **373:** 1083–96.
7 Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet* 2003; **362:** 419–27.
8 Riboli E, Kaaks R. The EPIC Project: rationale and study design. European Prospective Investigation into Cancer and Nutrition. *Int J Epidemiol* 1997; **26** (suppl 1)**:** S6–14.
9 Manolio TA, Collins R. Enhancing the feasibility of large cohort studies. *JAMA* 2010; **304:** 2290–91.
10 Chen Z, Chen J, Collins R, et al, on behalf of the China Kadoorie Biobank (CKB) collaborative group. China Kadoorie Biobank of 0·5 million people: survey methods, baseline characteristics and long-term follow-up. *Int J Epidemiol* 2011; **40:** 1652–66.
11 Tapia-Conyer R, Kuri-Morales P, Alegre-Diaz J, et al. Cohort profile: the Mexico City Prospective Study. *Int J Epidemiol* 2006; **35:** 243–49.
12 Elliott P, Peakman TC. The UK Biobank sample handling and storage protocol for the collection, processing and archiving of human blood and urine. *Int J Epidemiol* 2008; **37:** 234–44.

# Metal-on-metal failures—in science, regulation, and policy

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Worldwide there is dissatisfaction and fear among patients because commonly used implantable devices such as hip and breast implants, or defibrillator leads, fail. Metal-on-metal implants used for hip resurfacing or replacement are at the epicentre of the controversy because weaknesses in regulatory systems for medical devices have been exposed.[1,2] Initially the Australian and England and Wales registries reported failures associated with ASR (Articular Surface Replacement), a specific metal-on-metal device for hip replacement.[3,4] Subsequent reports highlighted common failures associated with large-head metal-on-metal implants in evidence from registries and comparative studies.[3,5,6] In *The Lancet*, Alison Smith and colleagues[7] now strengthen and extend the evidence that large-head metal-on-metal failure is not implant specific—it is a class effect. By use of data from the National Joint Registry of England and Wales, Smith and colleagues were able to assess more than 400 000 primary hip-replacement procedures, of which 31 171 employed stemmed metal-on-metal prostheses that were commonly used between 2003 and 2011. There was a 5-year revision rate of 6·2% (95% CI 5·8–6·6) in patients who had received metal-on-metal prostheses, substantially greater than that with other types of device and more elevated for prostheses with larger head sizes. Although the risk estimates are