UK Biobank Prospective Cohort

• 500,000 UK men and women aged 40-69 years when recruited and assessed during 2006-2010

• General consent for all types of health research; no feedback of individual results to participants

• Extensive baseline questions and measurements, with biological samples stored for future assays

• Follow-up of health outcomes through linkage to health records and direct contact with participants

Available for academic and commercial researchers worldwide without any preferential access (and limited exclusive access for data generated by researchers)
Huge Biobank project launches despite critics

Jim Giles

Half a million British subjects to be monitored in sickness and in health.

British family doctors have started recruiting subjects for an ambitious effort to probe the interplay of genetic and environmental factors that cause disease.
Increase depth of characterization of participants in large prospective cohorts

- Detailed questions and measurement of ALL of the participants at the time of recruitment into the cohort
- Linkage to antecedent information about participants to be able to assess impact of previous “exposures”
Following the health of 0.5 million UK Biobank participants through linkage to National Health Service (NHS) records:

Regularly updated information on a wide range of diseases from NHS datasets in all three countries:

- **Deaths**: cause and date of death
  - all participants: >20,000 cause-specific deaths
- **Cancers**: site, stage, grade and date of cancer
  - all participants: >120,000 site-specific cancer cases
- **Hospital discharges**: diagnosis, procedure and date
  - all participants: 1000’s of disease cases
- **Primary care data**: diagnosis, prescription, laboratory
  - only HALF of the participants: 1000’s more cases

Scotland: 36,000 participants

England: 446,000 participants

Wales: 21,000 participants
INCREASE DEPTH of characterization of participants in large prospective cohorts

• Detailed questions and measurement of ALL of the participants at the time of recruitment into the cohort

• Linkage to antecedent information about participants to be able to assess impact of previous “exposures”

• Deeper phenotyping (e.g. remote monitor; imaging) at baseline in large subsets of the cohort (if not all of it); & repeated assessment at intervals during follow-up
Enhanced phenotyping in large subsets of cohort: e.g. imaging of 100,000 UK Biobank participants

- MRI of brain, heart and abdomen
- DEXA of bones, joints and body
- Ultrasound of carotid arteries
- Repeat baseline assessment plus enhanced cognitive assessment and cardiac rhythm monitoring

100,000 participants plus 10,000 with repeat imaging after 18-24 months (2015-22)
INCREASE DEPTH of characterization of participants in large prospective cohorts

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• Deeper phenotyping (e.g. remote monitor; imaging) at baseline in large subsets of the cohort (if not all of it); & repeated assessment at intervals during follow-up

• Collection of biological samples:
  – As much as possible to avoid depletion
  – As many different types (e.g. blood, urine, stool)
  – As many different ways (e.g. different preservatives)
Advantages of COHORT-WIDE sample assays when establishing a resource for a wide range of research

• Uncontrolled assays may deplete the available sample rapidly, preventing subsequent studies

• “Nested” case-control studies may yield assay data that are not comparable within a cohort

• By contrast, cohort-wide assays:
  – are cost-effective
  – minimise depletion
  – improve quality control
  – support different comparisons
  – yield data that are readily shareable

Case-control approaches may be lower cost in the short-term, but a cohort-wide strategy is far less “costly” in the long-term
Biomarkers that have been measured in all 500,000 participants (in blood unless indicated otherwise)

<table>
<thead>
<tr>
<th>Cardio-metabolic</th>
<th>Bones and joints</th>
<th>Cancer</th>
<th>Renal</th>
<th>Liver</th>
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<tbody>
<tr>
<td>Cholesterol</td>
<td>Vitamin D</td>
<td>SHBG</td>
<td>Cystatin C</td>
<td>Albumin</td>
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<td>Direct LDL-c</td>
<td>Rh. factor</td>
<td>Testosterone</td>
<td>Total Protein</td>
<td>Direct Bilirubin</td>
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<td>HDL-c</td>
<td>ALP</td>
<td>Oestradiol</td>
<td>Urea</td>
<td>Total Bilirubin</td>
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<td>Triglyceride</td>
<td>Calcium</td>
<td>IGF-1</td>
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<td>Lp(a)</td>
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<td>HbA1c</td>
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<td>Glucose</td>
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<td>Sodium</td>
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Haematological assays were conducted during the recruitment phase, and those assay data have already been made available to researchers.
A truly global resource: approved researchers in 72 countries
Over 700 published papers
Publications in Top Journals

- NATURE: 126
- BMJ: 33
- IJE: 28
- CIRCULATION: 22
- PLOS ONE: 39
- THE LANCET: 22
- AMERICAN JOURNAL OF HUMAN GENETICS: 13
- PLOS GENETICS: 10
- SCIENTIFIC REPORTS: 25
- MOLECULAR PSYCHIATRY: 14
- PLOS MEDICINE: 6
The UK Biobank resource with deep phenotyping and genomic data

Abstract

The UK Biobank project is a prospective cohort study of genetic and phenotypic data collected on approximately 500,000 adults from across the United Kingdom, aged between 40 and 69 years. The open resource is unique in its size and scope of recruitment. The open resource is unique in its size and scope of recruitment.
Red cell distribution width and common disease onsets in 240,477 healthy volunteers followed for up to 9 years

Luke C. Pillig, Janice L. Atkins, George A. Kuchel, Luigi Ferrucci, David Melzer

Published: September 13, 2010 • https://doi.org/10.1371/journal.pone.003504

Abstract

Higher Red Blood Cell Distribution Width (RDW or anisocytosis) predicts incident coronary artery disease (CAD) plus all-cause and cardiovascular mortality. But its predictive value for other common diseases in healthy volunteers is less clear. We aimed to determine the shorter and longer term associations between RDW and incident common conditions in participants free of baseline disease, followed for 9 years. We undertook a prospective analysis of RDW using 240,477 healthy UK Biobank study volunteers aged 43–79 years at baseline, with outcomes ascertained during follow-up (69 years). Participants were free of anemia, CAD, type-2 diabetes, stroke, hypertension, COPD, and any cancer (except non-melanoma skin cancer) at baseline. Survival models (with competing hazards) tested associations with outcomes from hospital admission records and death certificates. High RDW (≥75th centile, n = 6,989) compared to low (<75th centile, n = 22,184) was strongly associated with mortality (HR 3.16: 95% CI 2.57 to 3.74), adjusted for age, sex, smoking status, education level, mean cell volume, and other baseline covariates. Higher RDW was also associated with incident CAD and UK
Even moderate intake of red meat raises cancer risk: study finds

Six coffees a day could save your life

Inflammation may cause heart disease and depression: study

Haemochromatosis ‘bigger threat than we thought’
The work undertaken by the @uk_biobank will inform life sciences for decades to come!

Go forth and make science, people! Thanks to UK Biobank and all the participants for making this amazing resource possible!
“The sample size of this resource, combined with the breadth of data that have been collected — and that will continue to accrue as the participants age — is unprecedented.

The excitement about the opportunities to advance human genetics using UK Biobank is palpable.

The generosity of the United Kingdom in sharing this resource with the rest of the world is a shining example of the value of investing in the greater good.”