

Bench philosophy (10): UK Biobank

Handling 15 Million Aliquots

UK Biobank processes thousands of blood and urine samples each day as part of a long-term initiative aimed at improving the prevention, diagnosis and treatment of a wide range of serious illnesses including cancer, heart disease, diabetes, arthritis and forms of dementia. Long term, this resource will provide scientists with the most detailed database ever collated to help determine why some people are susceptible to certain illnesses while others are not.

In recent years, there has been an explosion in our understanding of the way in which our bodies function at a cellular level, as well as the complex influence our genes and our environment have upon health and disease. A large-scale and long-term resource, comprising of, say, half a million people's lifestyle and medical records, together with a good set of baseline measurements and samples, would provide a deep vein of health-related information for scientists to mine for many years to come.

The idea of this type of epidemiological study is not new; in a seminal piece of research the late Sir Richard Doll followed the lives of 40,000 doctors, until their death, and was able to prove a link between smoking and lung cancer (Doll *et al.*, (2004) *British Medical Journal* 328(7455): 1519). This powerful study went on to underline the strength with which smoking is linked to a number of cancers and helped identify the pivotal role smoking plays in heart disease, stroke and many other life-threatening disorders. Many of these findings were unexpected at the time his study started.



Initiated the British doctors study in 1954:
Sir Richard Doll

A new visionary project is now underway to build a major resource for scientists' future use. Launched in April 2007, UK Biobank is a major UK medical research initiative, set up to develop an extensive resource for long-term medical studies. The project is hosted by the University of Manchester and has funding from the Medical Research Council, the Department of Health, the Scottish Government, the Wellcome Trust and the Northwest Regional Development Agency. It is also supported by the NHS and involves a partnership of 22 UK universities.

Over five years, UK Biobank aims to recruit 500,000 Britons aged 40-69 (around one per cent of the adult British population) and follow their health for the next 30 years and more. Detailed information about lifestyle, work, health and medical history will be collected from each participant, along with consent for access to the participants' medical records throughout their life. Basic physical parameters like weight, height, blood pressure and lung function will also be recorded, which together with blood and urine samples taken from the participants, will establish a resource that is unprecedented in its abundance of baseline data that can be applied to a broad range of medical studies. The National Health Service (NHS) in the UK plays a crucial role within the overall scheme. By embedding UK Biobank within the NHS, which provides the overwhelming majority of health care in the UK, a very wide range of conditions could be identified and validated through routine medical records.

Thinking big numbers

The key strengths of UK Biobank are the enormous sample volume and the extensive amount of health information, collected over a substantial period of time. Over the course of 10 to 20 years, subsets of the 500,000 people will suffer from different diseases and UK Biobank will have a package of information, together with blood and



Blood samples taken from participants.

urine samples, which can be made available to research groups in various disease areas. All information is made anonymous so that the participants cannot be identified, and the researchers are required to meet strict ethical and scientific criteria to access the resource.

UK Biobank predicts that, within ten years, it will have collected about 20,000 cases of diabetes mellitus, more than 10,000 cases of heart attack and coronary death, more than 5,000 cases of chronic obstructive pulmonary disease and 5,000 cases of breast cancer. By the fifteenth year of follow up there should be at least 5,000 cases of stroke, Alzheimer's disease, Parkinson's disease, and colorectal and prostate cancers. The resource will continue to mature with time, gathering more strength as people's health is followed for longer periods through their normal health records. The huge range of opportunities that UK Biobank will provide to creative-thinking scientists is potentially endless, particularly when considering the massive advances in research technologies that will occur over this period of time.

A prospective study, such as that being undertaken by UK Biobank, for the comprehensive and reliable qualification of the combined effects of lifestyle, environment, genotype and other exposures on a variety of outcomes, has a number of advantag-

es. It allows a wide range of conditions to be studied and type of exposure can be assessed prior to disease development, avoiding recall bias.

Prospective studies are also better able to assess illnesses that cannot readily be investigated retrospectively, such as dementia and fatal conditions, and can include all cases of those diseases that have high case-fatality rates, such as heart attacks and strokes. The inclusion of multiple endpoints in a study allows broader consideration of both the risks and benefits associated with a specific exposure, such as the full effects of smoking on a wide range of diseases. Prospective studies can also provide a more straightforward source of comparable disease-free controls. An established large-scale prospective cohort is subsequently a valuable resource for assessing the relevance and influence of various factors upon the health of the general public.

All these samples: What next?

Clearly, an efficient processing system is absolutely essential to handle and store the enormous number of samples that are collected daily. Six tubes of blood and one tube of urine are collected from each participant and shipped overnight to UK Biobank's central facilities in Manchester where they are processed the following day. The seven tubes are split into 28 tubes for storage so, with an average daily target of 600 to 800 participants, this creates roughly 20,000 1.4 ml storage tubes each day, i.e. 15 million over the duration of the whole project.

There were two key issues in the selection of a system to process these samples, the first of which was the reliability and throughput required to process 20,000 tubes in a day. This was critical because more samples, resulting in another 20,000 storage tubes, arrive the following day and, as a labile substance, blood must be processed within 24 hours of collection. The other key consideration was the data audit trail, ensuring full traceability of all samples using barcodes and supported by a LIMS.

The system at UK Biobank uses 11 Tecan Freedom EVO liquid handling workstations integrated with various modules, such as barcode scanners and storage hotels for tube plates, to achieve fully automatic processing of the different blood and urine tube types. Some of the workstations are automated within laminar flow cabinets to maintain sterility of blood samples that may be used to prepare immortalised cell lines. Once the blood or urine tubes are loaded, the entire process is automated, saving la-



UK Biobank wants to collect blood and urine samples from 500,000 participants – that's more than five times the number of people that fit into the famous Wembley Stadium.

bour and eliminating the possibility of human error. The system identifies the sample tube type by its barcode, decaps the tube and aliquots the various blood or urine fractions into smaller, 2D-labeled, 96-well format storage tubes. The samples are stored at two geographically separate sites so that even if a catastrophic event at one site destroys the stored samples, no samples of any participant would be completely lost. Two workstations have been designated for each sample type, so effectively there is a running standby to ensure that the daily throughput can be achieved even if one platform is out of operation. Due to this strategy, combined with good reliability, UK Biobank has never suffered a situation where samples could not be processed.

A pilot study was performed in 2006 to demonstrate that the project and the proposed procedures were viable, after which the facilities and infrastructure were gradually put in place before starting the project in April 2007. The throughput has since been ramped up and there are now six regional assessment centres recruiting participants around the UK.

The participants' relationship with the project starts when they attend one of UK Biobank's assessment centres. Assessment typically takes 90 minutes and involves a lifestyle questionnaire through a touchscreen computer, donating small samples of blood and urine and allowing some health-related measurements to be taken, such as

blood pressure, lung function, bone density, height and weight. UK Biobank emphasises that the NHS will only provide relevant contact details for potential participants in the first instance and that UK Biobank will only follow participants' health after receiving their explicit approval.

By the people, for the people

The voluntary nature of the project means that UK Biobank is dependent on people's altruism to take part. Of course, many participants will benefit personally – because some useful findings will emerge during their own lifetime and be of direct benefit to them – but primarily this is a project to help future generations.

Though it is not possible to volunteer for UK Biobank, the initiative has already generated lots of positive feedback and goodwill among members of the public. People who are interested in the project can find out more at www.ukbiobank.ac.uk.

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Fancy composing an installment of "Bench Philosophy"?

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