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EDITORIAL

Osteoporosis epidemiology in UK Biobank: a unique opportunity for international researchers

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With the launch on March 30, 2012 of the UK Biobank resource "for use by all researchers [nationally and internationally]—without exclusive or preferential access—for any health-related research that is in the public interest" [1], the international osteoporosis community gained a unique and invaluable dataset: 500,000 adults aged 40–69 years, comprehensively phenotyped, including blood and DNA, and QUS assessment at the heels. With the funding in late 2012 of the Imaging Enhancement pilot, 6–8,000 of what will eventually be 100,000 individuals will undergo DXA at whole body, spine, hips and knees, plus vertebral fracture assessment, along with MRI brain, heart and upper abdomen, and carotid ultrasound. In this editorial, we review the unique resource afforded by UK Biobank, and its immense present and future value to investigators of metabolic bone disease and other musculoskeletal conditions.

The need for such a resource is clear. Non-communicable diseases such as osteoporosis, osteoarthritis, diabetes, cardiovascular disease, and dementia are already an immense burden in the developed world, and are increasingly prevalent in developing populations, as more Westernised lifestyles and diets are adopted [2]. Life expectancy is increasing in many areas of the globe, bringing a new emphasis on the promotion of healthy ageing. To meet this aspiration, achieving greater understanding of the interactions between non-communicable diseases in older populations, the identification of novel risk factors and the elucidation of potential early biomarkers of later disease will be essential. To date, there has been no real opportunity to examine prospectively, in a single adequately sized and phenotyped cohort, a wide range of outcomes and the potential interplay between them. With access now available to all bona fide researchers anywhere in the world, UK Biobank represents just such an opportunity for the osteoporosis and musculoskeletal research community.

UK Biobank is a large prospective cohort established by the UK Medical Research Council and Wellcome Trust as an international resource for the investigation of risk factors for major diseases and morbidities of middle and older age. Five hundred thousand men and women, aged 40–69 years, were recruited nationwide between 2006 and 2010. The baseline assessment was extensive, with detailed information gathered on prevalent disease, diet, lifestyle, socioeconomic factors, education, medications/supplements (by questionnaire) and specific measurements such as blood pressure, weight, height, bio-impedance, grip strength, and ultrasound measures of heel bone density. Venous blood samples were collected [3], including DNA, and results of a panel of standard biochemical, haematological and immunological assays which are likely to be of interest to a wide range of researchers, along with chip-based genotyping data, will become available during 2014–

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2015. Large subsets of the full cohort have undergone additional investigations such as retinal imaging by optical coherence tomography and objective physical fitness and activity monitoring. The baseline assessment is being repeated every few years in subsets of about 20,000 participants to enable calibration of measurements, adjustment for regression dilution, and estimation of longitudinal change. The UK Biobank database is linked with NHS information systems in order to capture data relating to incident disease outcomes (the estimated accrual of exemplar common diseases is demonstrated in Table 1). UK Biobank combines unprecedented size, breadth, and depth for a prospective longitudinal cohort study. As incident cases accrue, it will allow musculoskeletal health outcomes to be related to a uniquely broad range of risk factors through case–control studies nested within the overall cohort [1].

Toward the end of 2012, funding for the pilot stage of the Imaging Enhancement was secured from MRC/Wellcome, which will allow detailed imaging acquisition on 6–8,000 volunteers from the original UK Biobank cohort to commence in late 2013. This comprehensive imaging assessment will include 3T MRI of the brain; 1.5T MRI of the heart and upper abdomen; carotid Doppler; and DXA of whole body, lumbar spine, hips, together with vertebral fracture assessment and imaging of both hips and knees; subject to successful completion of the pilot, the intention is to extend to a total of 100,000 participants across England. This enhancement will also include a repeat of most of the baseline assessment, including questions relating to pain and fracture. This breadth of phenotypic information in such a large cohort will yield a unique opportunity to investigate risk factors for disease both within and across organ systems.

DXA scanning in UK Biobank will contribute five novel measures as follows: (1) bone mineral density, (2) hip strength analysis, (3) prevalent vertebral fractures, (4) measures of osteoarthritis-associated joint changes (which is not possible from MRI within the time constraints on protocols to be implemented during the visit); and (5) body composition. Compared with heel ultrasound, DXA is better validated in a wider range of populations, shows lower intra-operator variation, and yields a better-characterised measurement of bone mineral. An additional benefit of DXA measurements of bone density in the imaging subset should be the potential for calibration of baseline heel ultrasound measurements, increasing their reliability across the whole cohort. Hip strength analysis allows calculation of biomechanical parameters such as cortical thickness and femoral neck bending strength, yielding valuable adjunctive mechanical indices [4]. The questionnaire data on medical history and smoking/alcohol intake will enable some risk stratification for fracture, but this will be greatly refined by addition of DXA-derived bone mineral density [5]. Vertebral fracture assessment will, with further analysis by applicant researchers, enable documentation of prevalent vertebral deformity [6]. The DXA instrument will have the capability to acquire images of hips and knees which are comparable in quality to those from traditional radiographs, and can be used for diagnosis of radiographic osteoarthritis, employing Kellgren–Lawrence scores or novel techniques such as Active Shape Modelling [7]. DXA provides a rapid assessment of body composition (5–10 min), which is better validated than is bioimpedance, and additionally allows site-specific estimation of total and proportionate fat content, together with measures of bone and lean mass [8, 9]. DXA will complement MRI measurement of visceral body fat by generating a comprehensive assessment of total and compartmental body composition that is rapidly usable with no further processing. MRI will deliver more detailed site-specific volumetric measures, but will require substantial further processing post-acquisition.

UK Biobank access procedures are documented on the website (www.ukbiobank.ac.uk); fees are modest and reflect only the need for recovery of costs associated with data processing and provision. A short initial application is required,

Table 1 Estimated numbers of incident cases (out of 500,000 baseline recruits) of exemplar common diseases

Condition	Incident cases			
	by 2012	by 2017	by 2022	by 2027
Diabetes	10,000	24,000	40,000	68,000
Myocardial infarction and coronary death	7,000	17,000	28,0000	47,000
Stroke	2,000	5,000	9,000	20,000
COPD	3,000	8,000	14,000	25,000
Hip fracture	1,000	3,000	6,000	17,000
Rheumatoid arthritis	1,000	2,000	3,000	5,000
Breast cancer	3,000	6,000	10,000	16,000
Colorectal cancer	1,000	4,000	7,000	14,000
Prostate cancer	1,000	4,000	7,000	14,000
Lung cancer	1,000	2,000	4,000	8,000
Alzheimer's disease	1,000	3,000	9,000	30,000
Parkinson's disease	1,000	3,000	6,000	14,000

followed by a more detailed full application, and then a material transfer agreement. Any additional assays, subject to sample availability, are at the expense of the applicant, and the results fed back into the central dataset so that they are available for subsequent researchers. There is currently a great potential for cross-sectional investigations based on prevalent disease. As cases of incident disease accrue, and the Imaging Enhancement is completed, there will be enormous possibilities for the international musculoskeletal community to undertake uniquely powered ground breaking studies, both within bone and joint, and linking with other organ systems, to comprehensively investigate the determinants of later disease.

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Conflicts of interest NH is Lead for DXA Assessment on the UK Biobank Imaging Working Group and a co-author of the UK Biobank Imaging Enhancement proposal. PM is Chair of the UK Biobank Imaging Working Group and oversaw the Imaging Enhancement proposal. He is a part-time employee of GlaxoSmithKline Research and Development, Ltd. and receives research funding from the MRC. RC is Principal Investigator and Chief Executive of UK Biobank, and a member of the Imaging Working Group. CC is a co-author UK Biobank Imaging Enhancement proposal.

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