^UCL

REVIEW OF COHORT RESEARCH

Research Domains

Populations & Lifelong Health

www.ucl.ac.uk/research/domains

Background

In recognition of an exceptional concentration of investigator-led population and clinical cohort studies and expertise health informatics research at UCL, together with national pre-eminence in these areas, UCL Faculty of Population Health Sciences has made cohort-based research a central component of its academic strategy.

The importance of scientific research in humans for illuminating disease mechanisms with a view to development of new diagnostic and predictive tests, as well as new treatments, is well recognised by industry. Policy makers also acknowledge the key role of cohort research in guiding social and public health interventions.

Despite this, the high cost of cohort research in comparison with other areas of biomedical endeavour, means there is a continuing need to justify funder support for such studies. Particularly so in an era of investments in large national initiatives such as UK Biobank and the Francis Crick Institute which, though perceived as competing, may actually be complementary.

New opportunities have also emerged that sharpen the competitive edge of population science compared to other fields of biomedical research. These include:

- The low-cost and high fidelity of genomic and other –omics technologies that can now be applied on a population scale using fresh or archived human biological specimens

- New mobile technologies that allow measurement of physiological parameters and habitual activities in large population studies, outside of the research clinic

- More detailed, safe imaging modalities such as magnetic resonance imaging

- Linkage to routine clinical phenotyping and health outcomes through anonymised linkage to participants' electronic health records

- New research methods such as Mendelian randomisation analysis that permit improved causal inference from observational studies in humans.

Aims

With this background, UCL Faculty of Population Health Sciences initiated a review of UCL cohort research in order to inform future strategic development and investment. The review has the following aims:

- To identify the extent of population, clinical and electronic health record cohort resources at UCL

- To identify areas of good practice, leading edge science, and health and wealth impacts, that may be shared more widely

- To capitalise on areas of synergy and connectivity between cohort studies

- To identify key challenges faced by investigators working in the field of cohort research

- To raise awareness of cohort studies among other disciplines, to facilitate new research collaborations and maximize use of cohort resources

- To scope the wider landscape of cohort research to identify new resources and investment opportunities to support cohort research

- To ensure the value of cohort research at UCL is maximized.

Review process

Professor Graham Hart (Dean, UCL Faculty of Population Health Sciences) asked Professor Aroon Hingorani (Director, UCL Institute of Cardiovascular Science; UCL Professor of Genetic Epidemiology) to lead the review, supported by Sarah Welsher (Strategic Coordinator, Populations & Lifelong Health Domain, Office of the Vice-Provost (Health), UCL School of Life and Medical Sciences).

Professor Hingorani assembled a steering committee (see Appendix 1 for membership) to help define the form and content of the review. The steering committee agreed the review should be conducted as follows:

- Two meetings of the steering committee to define the scope of the review

- An internal symposium with wide participation from cohort researchers to share successes and best practice, discuss the key challenges facing UCL cohort research, and identify opportunities for maximizing the value of cohort research

- A meeting of the steering committee to review the outcome of the symposium and to refine the scope and content of the review

- Circulation of an initial draft review for comment by the steering committee and key stakeholders

- A follow-up meeting of the steering committee to finalise the review

- A final version of the review for consideration by the UCL School of Life and Medical Sciences Senior Executive Group.

The steering committee agreed that this process should be followed by an externally-facing meeting to bring together UCL's population science expertise with key partners, including funders (MRC, Wellcome Trust, NIHR etc.), policy makers, and the biotech and pharmaceutical industry, to showcase the cohort resources and expertise and re-emphasize the importance and usefulness of cohorts to biomedical research and health and social policy.

A key part of part of the review process, the UCL Clinical and Community Cohorts for Improved Population Health – a One Day Symposium was held on 16th June, 2014. One hundred and twenty seven delegates attended the symposium, from a wide range of UCL population and cohort studies, as well as other disciplines, including delegates from the Institute of Education (now UCL Institute of Education). The symposium comprised plenary lectures, workshops and panel discussions. Sessions included experiences of lead investigators overseeing newly developed and established populations cohorts, clinical cohorts, and virtual cohorts assembled using electronic health record linkage. The experiences of investigators working in consortia of cohort studies: as well as participants were also shared. Workshops covered data management and data sharing, capacity building, enhancement of cohorts with biological data, use of cohorts as a framework for intervention trials, as well as the development of cohorts from trial populations. A final session covered emerging technologies, encompassing methylation profiling, transcriptomics, and metabolomics. A comprehensive symposium report can be found in Appendix 3.

Cohorts at UCL

More than 2.2 million people in the UK are currently participants in population-based cohort studies[1], and 14 of these cohorts are hosted by or have links to UCL's Faculty of Population Health Sciences and Institute of Education. This includes the oldest and the newest British birth cohort studies, and the largest tri-ethnic cohort in the UK.

UCL also curates or otherwise takes a leadership role in 27 intensively characterised clinical or electronic health record cohorts (with over 1000 patients/participants), focussed on infectious diseases (particularly HIV and TB), obesity, cardiovascular disease, ovarian cancer, and the health of premature infants. These cohort studies benefit from our expertise in basic bioscience, clinical science, and epidemiology – all the way through to applied public health and policy-related research.

Details of these cohort studies can be found in Appendix 2.

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[1] MRC, 2014. Maximising the value of UK population cohorts: MRC Strategic Review of the Largest UK Population Cohort Studies. Available online at www.mrc.ac.uk/news-events/publications/maximising-the-value-of-uk-population-cohorts/

Key issues arising

The steering committee noted that cohort research at UCL appears to be flourishing, with numerous examples of pioneering research, collaborative working and evidence of health and wealth impacts.

However, the steering committee and symposium participants also identified several critical issues facing cohort research at UCL. These include:

- Limited availability of clinical space for cohort resurveys such that non-UCL space is frequently used for such work with corresponding cost

- Mounting pressure on space for sample management and storage with each cohort developing its own solution to sample management risking inefficiency, duplication and higher cost

- Difficulties in recruiting and retaining key cohort support staff including data scientists, statisticians, research nurses and research co-ordinators because of:

- the limited pool of individuals with the necessary skills and experience
- the lack of established career development pathways
- insecurity of employment arising from the ebbs and flows in grant funding

- Difficulties in accessing health record data which are needed for the analysis of outcomes. These difficulties have increased as a result of concerns raised by the care.data initiative

- Limited skills capacity in converting raw health record data in to usable research datasets

- The mounting workload imposed by the need for greater sharing of cohort data in line with funder requirements

- The lack of established mechanisms for knowledge-sharing between cohorts

- The difficulty in maintaining the visibility of early and mid-career scientists in large scale work undertaken by cohort consortia

- The need for a better interface between population and discovery science to facilitate forward and reverse translation

- The need for a better interface between population and analytical science to ensure genomic, transcriptomic, proteomic, metabolomics and physiological measures can be readily accessed by cohort investigators

- The need for a pathway through which new technologies can be identified, tested and applied in population studies

- Potential advantages and disadvantages of a stronger interface with industry

- Ensuring the visibility of cohort research in the wider biomedical research environment and maintaining the justification for continued follow up of cohort studies in a constrained funding environment.

Review recommendations

Following meetings of the Cohort Review Steering Group and the 'UCL Clinical and Community Cohorts for Improved Population Health' one day symposium, the Steering Group propose the following recommendations:

- The Domain should highlight the existing cohort resources and expertise we have at UCL, on a web page, to ensure they are easily discoverable. This should link to other cohort directories, and complement – rather than duplicate - the work of the Public Health Research Data Forum and CLOSER.

- The Faculty should consider the options and cost-effectiveness of various alternatives for provision of clinical facilities within UCL for biomedical examination of cohort participants. This could be achieved through the development of a clinical phenotyping unit.

- The Cohort Review Steering Group should consider the SLMS-wide review of biobanking governance, led by Adrienne Flanagan, and suggest a cohort representative is involved in any further work in this area.

- The Faculty should consider a review of structures to recruit, retain and support the career development of data scientists, statisticians, research co-ordinators and other key support staff, as well as mid-career scientists for future cohort management and leadership.

- Consideration should be given to development of a cohort support unit akin to the clinical trials unit model. This could be built into the vision for a clinical phenotyping unit, and perhaps included as part of the BRC submission.

- The Faculty should consider playing a role in addressing skills-gaps, particularly in developing a new cadre of data scientists with skills spanning – omics technologies and the ability to translate raw health record into usable research outcomes.

- The Faculty should also consider development of a cross- disciplinary 4 year PhD programme (including social and biomedical sciences), to bring together supervisors and a strong student body.

- The Faculty should consider developing a UCL-wide forum for cohort research to help promote connection, collaboration and knowledge sharing between cohorts, and interaction with discovery science, analytical science, health informatics and health economics. Such a forum might be hosted and supported by the Population Health Domain. Activities related to this initiative might include mentoring, cohort secondments, cohort research days, and short term observerships for PhD students and early career post-docs to gain experience in working across cohorts. It might also act as a mechanism through which to engage with Francis Crick Institute and the NHS.

- Given the limited pool of research council and charity funding, and the emerging recognition of the important role that cohort studies and electronic health record datasets can play in the development of new health technologies (including predictive and diagnostic biomarkers), in drug development, and in trial design, the Faculty should give close consideration to the type of systematic interactions it might seek to make with the biotech and pharmaceutical sector, so as to share in healthcare innovation. Models for such interactions exist elsewhere in the UK, and in other countries.

- The Faculty should consider how best to increase the translational opportunities of cohort studies for impact.

- A review of how our research is already impacting policy and practice, and promotion of the BMJ/MRC Framework for design and evaluation of complex interventions to improve health, would be useful.

Appendix 1

Cohort Review Steering Group Membership

Professor Aroon Hingorani
Chair UCL Cohort Review, UCL Institute of Cardiovascular Science

Professor Philip Beales
UCL Institute of Child Health

Professor Martin Bobak
UCL Institute of Epidemiology & Health Care

Professor Eric Brunner
UCL Institute of Epidemiology & Health Care

Professor Nishi Chaturvedi
UCL Institute of Cardiovascular Science

Professor John Deanfield
UCL Institute of Cardiovascular Science

Professor Carol Dezateux
UCL Institute of Child Health

Professor Graham Hart
Dean, UCL Faculty of Population Health Sciences

Professor Harry Hemingway
UCL Institute of Epidemiology & Health Care

Professor Alun Hughes
UCL Institute of Cardiovascular Science

Professor Mika Kivimaki
UCL Institute of Epidemiology & Health Care

Professor Diana Kuh
UCL Institute of Epidemiology & Health Care

Professor Sir Michael Marmot
UCL Institute of Epidemiology & Health Care

Professor Usha Menon
UCL Institute for Women's Health

Professor Amanda Mocroft
UCL Institute of Epidemiology & Health Care

Professor Richard Morris
UCL Institute of Epidemiology & Health Care

Dr Juan Pablo-Casas
UCL Institute of Cardiovascular Science

Professor Alison Parks
UCL Institute of Education

Professor Christine Power
UCL Institute of Child Health

Professor Caroline Sabin
UCL Institute of Epidemiology & Health Care

Professor Amanda Sacker
UCL Institute of Epidemiology & Health Care

Professor Andrew Steptoe
UCL Institute of Epidemiology & Health Care

Professor Goya Wannamethee
UCL Institute of Epidemiology & Health Care

Professor Peter Whincup
St George's, University of London

Sarah Welsher
UCL Populations & Lifelong Health Domain Coordinator

Appendix 2

Population Cohorts

British Cohort Study 1970
Dr Mark Hamer & Dr Alice Sullivan (IoE)
www.cls.ioe.ac.uk/page.aspx?&sitesectionid=795&sitesectiontitle=Welcome+to+the+1970+British+Cohort+Study+(BCS70)

British Regional Heart Study
Professor Richard Morris, Professor Goya Wannamethee & Professor Peter Whincup (St Georges)
www.ucl.ac.uk/pcph/research-groups-themes/brhs-pub

British Women's Heart and Health Study
Dr Juan Pablo-Casas
www.lshtm.ac.uk/eph/ncde/research/bwhhs/

English Longitudinal Study of Ageing (ELSA)
Professor Andrew Steptoe
www.elsa-project.ac.uk/

Gemini: Health and Development in Twins
Professor Jane Wardle
www.geministudy.co.uk/

Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) Study
Professor Martin Bobak
www.ucl.ac.uk/easteurope/hapiee.html

Life Study
Professor Carol Dezateux
www.lifestudy.ac.uk/

Millennium Cohort Study
Professor Emla Fitzsimons
www.cls.ioe.ac.uk/page.aspx?&sitesectionid=851&sitesectiontitle=Welcome+to+the+Millennium+Cohort+Study

National Child Development Study (1958)
Professor Chris Power, Professor Elina Hyponnen & Professor Alissa Goodman (IoE)
www.cls.ioe.ac.uk/page.aspx?&sitesectionid=724&sitesectiontitle=National+Child+Development+Study

National Survey of Health & Development (1946)
Professor Diana Kuh
www.nshd.mrc.ac.uk/nshd__65.aspx

Northwick Park Heart Study
Professor Steve Humphries

ONS Longitudinal Study
Dr Nicola Shelton
www.ucl.ac.uk/celsius/about-the-ls

Southall and Brent Revisited (SABRE)
Professor Nishi Chaturvedi
www.sabrestudy.org/?cat=11

UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS)
Professor Usha Menon
www.instituteforwomenshealth.ucl.ac.uk/womens-cancer/gcrc/ukctocs

Whitehall II (Stress and Health Study)
Professor Mika Kivimaki
www.ucl.ac.uk/whitehallII

Clinical Cohorts

AALPHI: Adolescents and Adults Living with Perinatal HIV Cohort
Dr Ali Judd
www.ctu.mrc.ac.uk/our_research/research_areas/hiv/studies/aalphi/

Antiretrovirals, Sexual Transmission Risk and Attitudes (ASTRA)
Dr Fiona Lampe
www.astra-study.org/

Bariatric Cohort
Dr Rachel Batterham

Clinical Cohorts in Coronary disease Collaboration (4C)
Professor Harry Hemingway
www.ucl.ac.uk/cardiovascular/research/preventions-outcomes/clinical-epidemiology-cardiovasculat-disease/accordian-files/clinical_cohorts_coronary_disease_collaboration

Concerted Action on SeroConversion in AIDS and Death in Europe (CASCADE)
Professor Kholoud Porter
www.ctu.mrc.ac.uk/cascade/

Collaborative HIV Paediatric Study (CHIPS)
Dr Ali Judd
www.chipscohort.ac.uk/default.asp

Data Collective on Adverse Events of Anti-HIV Drugs (D:A:D)
Professor Caroline Sabin & Professor Andrew Phillips
www.ucl.ac.uk/iph/research/hivbiostatistics

European Pregnancy and Paediatric HIV Cohort Collaboration (EPPICC
Dr Claire Thorne
www.penta-id.org/hiv/eppicc-studies.html

EPICure: Population based studies of survival and later health status in extremely premature infants
Professor Neil Marlow
www.epicure.ac.uk

EuroSIDA
Professor Amanda Mocroft
www.ucl.ac.uk/iph/research/hivbiostatistics

European Collaborative Study
Dr Claire Thorne
www.eurocoord.net

Hypertrophic Cardiomyopathy Outcomes (HCMO)
Professor Perry Elliott

Italian Cohort of Antiretroviral Naïve Patients (ICONA)
Dr Alessandro Cozzi-Lepri
www.ucl.ac.uk/iph/research/hivbiostatistics

Management of Post-Transplant Infections in Collaborating Hospitals (MATCH)
Professor Amanda Mocroft
www.cphiv.dk/MATCH

National Study of HIV in Pregnancy and Childhood (NSHPC)
Professor Pat Tookey
www.ucl.ac.uk/silva/nshpc

National Institute for Cardiovascular Outcomes Research (NICOR) Registries
Professor John Deanfield
www.ucl.ac.uk/nicor

A Prospective, Observational Study to Examine the Effects of Ageing on the 'Pharmacokinetic and Clinical Observations in People Over Fifty' (POPPY)
Professor Caroline Sabin
http://clinicaltrials.gov/show/NCT01737047

Prognostic value of Interferon Gamma Release Assays (IGRA) in predicting active TB among individuals with (or at risk of) latent TB infection (PREDICT)
Professor Ibrahim Abubakar
http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=8489

Royal Free Hospital Cohort
Dr Fiona Lampe & Dr Colette Smith
www.ucl.ac.uk/royalfreehivdb

TB: HIV
Professor Amanda Mocroft
www.cphiv.dk/TBHIV

Thrombosis Prevention Trial
Professor Steve Humphries

UK Collaborative HIV Study (UK CHIC)
Professor Caroline Sabin & Professor Andrew Phillips
www.ukchic.org.uk/

UK Seroconvertors Register
Professor Kholoud Porter
www.ctu.mrc.ac.uk/our_research/research_areas/hiv/studies/ukr/

Ukraine Paediatric HIV Cohort Study
Dr Claire Thorne
www.ucl.ac.uk/ich/research-ich/mrc-cech/research/studies/HIV-ukraine-paediatric

Electronic Health Records Data

CALIBER
Professor Harry Hemingway
www.caliberresearch.org/

UK HIV Resistance Database
Professor David Dunn
www.ctu.mrc.ac.uk/hivrdb/public/default.asp

Cohorts by category

Population Cohorts

Birth cohorts:
1970BCS
Life Study
MCS
NSHD/1946BC
NCDS/1958BC

Occupational:
Whitehall II

Twins:
Gemini

Ethnic minorities:
SABRE

Older cohorts:
ELSA

Diet/specific health outcomes:
BRHS
BWHHS
HAPIEE
NPHS
UKCTOCS

Other:
ONS LS

Clinical Cohorts and Electronic Health Records Data

Infectious diseases:
AALPHI
ASTRA
CASCADE
CHIPS
D:A:D
EPPICC
EuroSIDA
European Collaborative Study
ICONA
MATCH
NSHPC
POPPY
PREDICT
Royal Free Hospital Cohort
TB:HIV
UK CHIC
UK Seroconvertors Register
Ukraine Paediatric HIV Cohort Study
UK HIV Resistance database

Obesity:
Bariatric cohort

Cardiovascular disease:
4C
CALIBER
HCMO
NICOR
Thrombosis Prevention Trial

Newborn health:
EPICure