English Longitudinal Study for Ageing (ELSA)
Genetic Data Access Procedures

The English Longitudinal Study of Ageing (ELSA) is a panel study of a representative cohort of men and women living in England aged 50 or over. It is a collaboration between the Department of Epidemiology and Public Health at University College London (UCL), the Institute for Fiscal Studies (IFS), Natcen Social Research (NatCen) and the University of Manchester, with additional input from the University of East Anglia. It is multidisciplinary in orientation, involving the collection of economic, social, psychological, cognitive, health, biological and genetic data. The study commenced in 2002 and the cohort is followed up every two years, with periodic refreshment to maintain the age profile. Data are collected using computer assisted personal interviews and self-completion questionnaires, with additional nurse visits for the assessment of biomarkers every four years. The original sample was 11,391, ranging in age from 50 to over 90 years. ELSA is managed by a management board made up of representatives from the participating institutions (see appendix for list of members). It was designed as a sister study to the Health and Retirement Study (HRS) in the USA, so is harmonised with ageing studies in other countries to facilitate international comparisons. It is also linked to financial and health registry data. The dataset is openly available to researchers and analysts soon after collection, and is available from the UK Data Service (http://www.esds.ac.uk/longitudinal/access/elsa/l5050.asp). A profile of the cohort was published in 2013 (http://www.ncbi.nlm.nih.gov/pubmed/23143611).

ELSA encourages and facilitates data sharing with all *bona fide* researchers. For a definition of *bona fide* research, please see http://www.nshd.mrc.ac.uk/data/bona_fide_researchers.aspx.

1. Genetic Resources in ELSA: the ELSA DNA Repository (EDNAR)

There are two main sets of genetic data in ELSA. First, a genome wide microarray assay (GWAS study) was carried out in 2013/14 with funding from the ESRC. This involved genotyping of around 8,000 ELSA participants with the Illumina Omni 2.5-8 chip. The same chip has been used in the HRS, allowing for direct comparisons. This provides information on 2.5 million single nucleotide polymorphisms (SNPs), which is expanded to over 4 million SNPs by imputation.

Second, genetic data has accumulated through genotyping in a number of specific candidate SNPs and variable number tandem repeats (VNTRs) on 6,000 participants. These include an Illumina bundle of 1,536 SNPs in 3,300 participants, which has contributed data and become part of a number of national and international consortia including the UCL-Edinburgh–Bristol consortium (UCLEB), and the International consortium of Blood pressure (ICBP). The 6,000 DNAs previously extracted have contributed to a number of study designs including replication for findings in genome wide association studies, large scale investigations of gene by environment interactions, analyses using the Mendelian randomisation paradigm, and targeted candidate pathway analyses. A list of research publications that include EDNAR data can be found on the ELSA website at the following address http://www.elsa-project.ac.uk/publications/case/related.

DNA from ELSA is stored at Source BioScience. The GWAS was carried out by UCL Genomics, and working samples of extracted DNA are held by LGC Genomics so that they can carry out genotyping on specified SNPs. THE GWAS has been deposited in the European Genome-phenome Archive (EGA).

2. Genetic Data Access

The over-riding aim of our data access procedure is to facilitate access to genetic data in a transparent and streamlined manner. We will not consider the issue of potential overlap between research projects, but applicants are encouraged to review the list of publications that have used genetic data, and the brief summary of approved applications to use the resource, which can be found at http://www.elsa-project.ac.uk/.

Data access will be regulated by the ELSA Genetic Data Access Committee (EGDAC). This is chaired by Professor Andrew Steptoe (UCL), and composed of members of the ELSA management board and experts from UCL and other institutions (see appendix for the list of members). The EGDAC reports to the ELSA Management Board. Dr Nina Rogers (n.rogers@uclac.uk) is the first point of contact for all enquiries concerning use of ELSA genetic data.

We expect that three types of applications will be made:

Type a: Applications for the ELSA GWAS data without additional phenotypic information, in order to provide genotyped control data.

Type b: Applications linking the ELSA GWAS or existing candidate gene polymorphisms with ELSA phenotypic data.

Type c: Applications to commission genotyping, because not all SNPs have been genotyped.

We envisage that the vast majority of applications will involve use of existing genetic data.

3. Evaluation of applications

Applicants are invited to download and complete the Word application form, which should be sent to Dr Nina Rogers (n.rogers@ucl.ac.uk). Applications will be evaluated by the EGDAC. This committee meets monthly, but decisions can be made between meetings. Evaluation of applications is based on the following:

Type a: These are relatively straightforward, access to data will be provided to *bona fide* researchers.

Type b: Favourable decisions about these applications depend on the suitability of the ELSA phenotypic data for the topic under investigation and the potential for identification of the participant despite de-identification of the data.

Type c: The EGDAC consider the same factors as in Type b, but will also take into account the significance of the research question, demonstration of appropriate power to do the analyses, and the amount of material that the application requests and the amount of the sample remaining.

Applicants should allow three months for this process, though most should be completed within one month.

4. Conditions for the use of ELSA genetic material

a. The samples and related data and intellectual property rights belong to the universities (UCL, Institute of Fiscal Studies, the University of Manchester and NatCen Social Research).
b. If any commercial revenues result from the Recipient's use of the materials, UCL shall be entitled to a fair and reasonable share of any such revenues that accrue to the Institution or the Recipient.
c. The applicant accepts that the EGDAC will make reports to the ELSA management group, which makes annual reports to the ESRC and NIA. The names and institutions of persons either given or denied access to the biological materials and associated phenotypic data and the basis for the decisions will be summarized in this annual report.
d. The applicant will acknowledge the ESRC, NIA, UCL Genomics, LGC Genomics and Source BioScience where appropriate. The following language should be used

'Samples from the English Longitudinal Study of Ageing DNA Repository (EDNAR), which receives support from the National Institute on Aging (NIA) and the Economic and Social Research Council (ESRC), were used in this study. We thank contributors and the ELSA participants'.

e. Data provided to the applicants can only be used for the purposes originally stated and must not be used in any other way without re-application to the steering committee.
f. No data should be passed on to any third party unless they were specified in the original application.
g. No applications that request sole access to a specific phenotype will be accepted.
h. Any grant applications based on the genotyping data should include a covering letter from the Chair of EGDAC stating that the project has been approved by the committee or will be considered on a specific date.

5.
Grant applications

Applicants who require agreement before submitting grants should bear in mind that the EGDAC must receive the completed research proposal form at least one month before the submission deadline. It is the responsibility of the researcher to ensure compliance with their funder's terms and conditions with respect to their use of EDNAR data.

Supervisors are ultimately responsible for their PhD students in the same way that PIs are responsible for their researchers. We therefore request that any proposals for PhD projects are submitted jointly with the supervisor rather than the student themselves.

6.
Charges for access to genetic data

ELSA receives funding from the National Institute on Aging and a consortium of Government Departments coordinated by the ESRC to support data collection and basic data management. This does not extend to providing support for individual projects, and researchers will be expected to meet the additional costs for data access and provision. All researchers accessing EDNAR data will be charged on a cost recovery basis: This cost will vary depending on the amount and type of data. Please note, we cannot give discounts to PhD students or for any other reason. Once a proposal has been approved and the applicant informed of the cost these **are non-negotiable**.

Costs will be determined on a project-by-project basis and will reflect the true costs to the ELSA team of providing the resources requested. Once a proposal has been agreed in principle an accurate costing will be provided. Example costings for data requests are provided below. Data will **not** be provided until an invoice has been settled or a purchase order number is received by our finance department.

Costs are reviewed on an annual basis and the current costs are fixed until the end of March 2015.

VAT will be charged where applicable.

Charges for data requests

Type of data request	**Charge (+VAT where applicable)**
ELSA GWAS data without phenotypic information	No charge
Applications linking ELSA GWAS with phenotypic data: - up to 40 phenotypic variables - every additional 40 phenotypic variables	£800 £50
Applications linking ELSA candidate gene polymorphisms with phenotypic data - up to 50 polymorphisms and phenotypic variables - every additional 40 phenotypic variables	£800 £50

7. Requests for new genotyping

Potential users should note that the DAC favours keeping the DNA resources together to ensure their conservation. It should also be noted that we will favour applications that commission genotyping at the EDNAR (using genotyping resources at KBioscience, UK). Projects that request new genotyping are expected to have researched the possibility of genotyping at KBioscience, through the EDNAR. For further information and clarification you can contact Dr. Nina Rogers (n.rogers@ucl.ac.uk)

Access to data and requests for Genotyping

Genotyping will be carried out by KBioscience, (unless there is a strong scientific justification for genotyping elsewhere) who, in collaboration with the EGDAC, will collate requests and perform genotyping in a timely manner. Timing of genotyping will be determined in collaboration with the applicant, but may be influenced by priorities established by the steering group and those set by the NIA. The costs of genotyping incurred by UCL will be reimbursed by the applicants. These costs will include those associated with cherry picking samples, should protocols require.

Access to data and DNA

1. No application can request to cover more genes than is reasonable or have sole access to a specific phenotype. New genetic data should be lodged with the EDNAR repository as soon as possible (and within three months of measurement).
2. Any grant applications based on the data and biological samples should include a covering letter from the Chair of EGDAC stating that the project has been approved by the committee or will be considered on a specific date.
3. Data and biological samples provided to the collaborators can only be used for the purposes originally stated and must not be used in any other way without re-application to the steering committee.
4. The costs of laboratory and data extraction services incurred by University College London in providing DNA and phenotypic data will be paid by applicants in addition to the charges

listed in section 6. These costings will be kept to a realistic level rather than reflect current commercial expenses. DNA will only be released once these have been agreed by the applicants and respective parties and reimbursement has been forthcoming. These costs may include costs of re-plating/ picking samples, transport of sample, costs associated with checking methodology and quality assurance.

5. All approved applications will be asked to agree and sign an NIH approved material transfer agreement (MTA) before transfer of samples.
6. All approved applications for DNA sample will initially receive two 96 well tray for piloting their methodology and quality assurance. There will be a priori agreement of acceptable error rates between the applicant and the EGDAC. Once the steering group is satisfied that this first phase has been successfully completed, applicants will proceed to the second stage where they will receive a full or sub-set of DNA samples as required by the protocol.
7. A short progress report (1 side A4) should be made to the EGDAC after the first year or halfway through the project, whichever is sooner. This report should explain any problems with achieving the project objectives (specifically where new measurements are being made on biological samples) and where appropriate how many samples have been completed. The ELSA management board will use the application and approval procedures in reports to the NIA and ESRC.
8. Delays in completion of the project and/or resulting publications, and reasons for such delays, should be notified to the EGDAC.
9. Any residues of biological samples or excess materials must be returned to the Source Bioscience by the end date of the project. Delays in the return of sample and reasons for EGDAC.
10. The expense of transferring both from and back to Source BioScience or any other site must be met by the applicants unless prior agreement is reached with the EGDAC.
11. The applicants must notify the committee of any potential errors discovered with using the materials.

ELSA Genetics Data Access Committee (EGDAC):

Professor Andrew Steptoe (chair)
PI of ELSA, Department of Epidemiology and Public Health, UCL

Dr Nina Rogers
ELSA Project Manager, Department of Epidemiology and Public Health, UCL

Paul Bradshaw
Head of the longitudinal surveys group, National Centre for Social Research

Professor Nicholas Christakis
Professor of Sociology and Medicine, Yale Institute for Network Science, Yale University

Professor Aroon Hingorani
Professor of Genetic Epidemiology, Institute of Cardiovascular Sciences, UCL

Dr Michelle Miller
Associate Professor (Reader) of Biochemical Medicine, Warwick Medical School, University of Warwick.

Dr Jing Hua Zhao
Senior Scientist, MRC Epidemiology Unit, Cambridge.