

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), the National Centre for 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/5050.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 7412 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/>.

The ELSA study has joined Managing Ethico-social, Technical and Administrative issues in Data ACcess (METADAC), which are operationalised through a committee known as the METADAC Access Committee. METADAC governs access to phenotype, genotype and 'omic' data and samples from five UK longitudinal studies. Meetings to review applications are held at six-weekly intervals. A more detailed description of the METADAC, its key structural features and decision-making can be found here (<https://www.metadac.ac.uk/metadac-about/>). Dr Olesya Ajnakina (o.ajnakina@ucl.ac.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. For this type of application, no applications are needed as the data can be either directly downloaded from the European Genome-phenome Archive (EGA) (<https://www.ebi.ac.uk/ega/home>) or requested by contacting Dr Olesya Ajnakina (o.ajnakina@ucl.ac.uk).

Type B: Applications linking the ELSA GWAS or existing candidate gene polymorphisms with ELSA phenotypic data. This type of the application will require a full application made and submitted to METADAC. The application form and guidelines can be found here - <https://www.metadac.ac.uk/data-access-committee/application-forms/>. The applicants are strongly encouraged to read the application guidelines and application assessment criteria that can be found here - <https://www.metadac.ac.uk/data-access-committee/application-assessment-criteria/>. The METADAC email for any questions - metadac@newcastle.ac.uk

Type C: Applications to commission genotyping, because not all SNPs have been genotyped. This type of the application will require a full application made and submitted to METADAC. The application form and guidelines can be found here - <https://www.metadac.ac.uk/data-access-committee/application-forms/>. The applicants are strongly encouraged to read the application guidelines and application assessment criteria that can be found here - <https://www.metadac.ac.uk/data-access-committee/application-assessment-criteria/>. The METADAC email for any questions - metadac@newcastle.ac.uk. Please note, *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 Table 1. 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

3. 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 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'.
- d. 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.
- e. No data should be passed on to any third party unless they were specified in the original application.
- f. No applications that request sole access to a specific phenotype will be accepted.
- g. Any grant applications based on the genotyping data should include a covering letter from the METADAC stating that the project has been approved by the committee or will be considered on a specific date.

4. Grant applications

Applicants who require agreement before submitting grants should bear in mind that the METADAC must receive the completed research proposal (application Type B) 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 genetic 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.

5. 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. This charges for data requests are outlined in **Table 1**.

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. VAT will be charged where applicable.

Table 1. *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: <ul style="list-style-type: none"> - Up to 40 phenotypic variables - Every additional 40 phenotypic variables 	£500 £50
Applications linking ELSA candidate gene polymorphisms with phenotypic data <ul style="list-style-type: none"> - Up to 50 polymorphisms and phenotypic variables - Every additional 40 phenotypic variables 	£800 £50

For any further questions please contact Dr Olesya Ajnakina (o.ajnakina@ucl.ac.uk).