Procedures for (inter)national collaborators submitting applications for research with NTR data or biological samples.

The Netherlands Twin Register (NTR) consists of individuals who have agreed to participate in twin-family studies and is managed by the Department of Biological Psychology, VU University Amsterdam (see: https://tweelingenregister.vu.nl/). The NTR was established in 1987 and has enrolled around 120.000 twins and a roughly equal number of their relatives. The majority of twin families have participated one or more times in survey studies on a host of epidemiological variables including social demography, personality, lifestyle, somatic and mental health, and subsamples took part in biomaterial collection (e.g. DNA samples) and dedicated projects for e.g. neuropsychological, biomarker, and behavioural traits. The recruitment into the NTR is fully inclusive without any restrictions on enrolment.
The NTR is committed to actively seek the commitment of its participants to science and their continued involvement in NTR research by maintaining a website, electronic newsletters, and the *MijnNTR* portal that provides feedback to participants on the types of research data they have supplied and the scientific impact they have contributed to.
The NTR resources, e.g. the longitudinal phenotyping, the extended pedigree structures, and the multi-generation genotyping allow for future twin-family research that will contribute to gene discovery, causality modelling, and studies of genetic and cultural inheritance of behavioural traits and mental and physical health.

Because the NTR is an (inter)national resource of huge scientific value, we are receptive to collaboration with academic and industry-based researchers. Researchers that contribute unique expertise or unique facilities are specifically welcomed. To facilitate scientific collaboration, all NTR data has been reorganized in a uniform NTR data repository, annotated using the FAIR (Findable, Accessible, Interoperable, Reproducible) principles. Regardless of the type of research interest, all potential collaborations on data contained in the NTR repository must be first reviewed by the NTR Data Access Committee (NTR-DAC).

For each project, a Data Sharing Request (DSR) should be submitted by an applicant with a PhD, MD or equivalent degree embedded in a reputable research institute/organisation. The applicant and NTR agree on the financial reimbursement for the NTR beforehand. The access fees will be determined by data management using a three tier heuristic based on the size and complexity of the requested datasets (costs range from € 1900 for small datasets [< 550000 valid data points] to € 5700 for large datasets [> 1100000 valid data points or datasets including omics data or data derived from omics data]; excluding VAT). These fees are needed to support maintenance of the NTR data collection, data cleaning, data annotation, and data management and other costs to support the NTR infrastructure. Before projects start, a publication/reporting plan, including a proposal for the intended authorships[1], should be in place.

The procedure for researchers who would like to request **phenotypic information** is as follows:

- Pseudonymised data will be supplied for research purposes and/or publication and shall not be used for any other purposes.
- The data shall only be used for the analyses agreed upon in the research proposal. The data shall not be passed on to third parties.
- Researchers moving to a different institute before expiration of the timeline for submission of the manuscript should reapply for data access from their new institute.
- The data may not be linked to other NTR data or other phenotypes, without prior approval of NTR.
- No attempts will be made to identify persons.

[1] Authors may not be able to contribute as much as they intended due to unforeseen circumstances. In reverse unnamed co-authors may have contributed substantially to the paper(s) justifying co-authorship under ICMJE conventions.

The procedure for researchers requesting **biological samples** is as follows:

- Pseudonymised samples will be supplied on loan for research purposes agreed in advance and shall remain the property of the NTR at all times. Leftover materials shall be sent back or destroyed after consultation with the NTR.
- The samples shall only be used for the analyses submitted in the research proposal. The samples shall not be passed on to third parties.
- Parties shall agree upfront what to do in the event of chance findings.
- The data measured in the samples shall also be made fully available to the NTR database after a mutually agreed period of time.
- The data may not be linked to other NTR data or other phenotypes. Linking of new data to other phenotypes will be done by the NTR.
- No attempts will be made to identify persons.

The procedure for researchers wanting to analyze **genomic data** (e.g. SNPs, methylation marks, gene expression levels, or DNA/RNA sequences) is as follows:

- Pseudonymised data will be made available for research purposes and/or publication and shall not be used for any other purposes .
- The data shall only be used for the analyses agreed upon in the research proposal. The data shall not be passed on to third parties.
- The data will be linked to the other requested phenotypes in the DSR by the NTR.
- The data may not be linked to other NTR data or to other genotype databases, without prior approval.
- For privacy and security concerns, we request you to perform analyses on individual-level (imputed) genome-wide data exclusively on local NTR servers.
- No attempts will be made to identify persons.

Data Sharing Requests for phenotypic information, genomic data, or samples will be evaluated by the NTR-DAC. Criteria are (1) adequate funding for NTR to prepare the requested materials, (2) fit to the research mission of the NTR as stated in the information letters and informed consents, (3) research plan conforms to appropriate IRB permission, (4) requested data are not part of ongoing quality control processing in ongoing NTR research, (5) demonstrated skills of the researcher to handle twin-family data, and/or (6) collaborative participation by the relevant NTR researchers.

Data transfer can be initiated only after receipt by NTR of a completed and signed Data Usage Statement VU researchers), Data Sharing Agreement (external researchers) or Material Transfer Agreement (biological samples, external researchers).

With kindest regards, on behalf of the Netherlands Twin Register

NTR Data Access Request Committee:
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