

Applying for linked data from the Lifelines Cohort Study and IADB.nl database



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Lifelines Cohort Study

Lifelines is a longitudinal cohort study collecting data and samples from over 167,000 participants over a period of thirty years. The Lifelines cohort comprises residents of the northern parts of the Netherlands covering three generations: 15,000 children (0-18), 140,000 adults and 12,000 elderly (65+). The collected [data and samples](#) are a valuable source for scientific research and for the development of policy focused on healthy ageing.

Every five years, participants undergo several physical measurements and fill out questionnaires. In addition, participants are invited to complete a follow-up questionnaire once every 1.5 years, resulting in large follow-up data. You can find an overview of the collected data and samples for [children](#) and [adults](#) at www.lifelines.nl/researcher.

Researchers worldwide can apply for the use of Lifelines data and/or samples for scientific research (see Appendix A for criteria).

IADB.nl database

The University of Groningen IADB.nl pharmacy prescription database is a growing database that contains prescription data for almost 20 years from 1994 till 2017 from approximately 70 community pharmacies and covers an estimated population of 730,000 patients (situation August 2018). Registration in the database is irrespective of health care insurance and age, gender and prescription rates among the database population have been found to be representative of the Netherlands as a whole, and the database has been widely used for research. Each person is individually tracked throughout the database period and prescription records contain information on the date of dispensing, the quantity dispensed, the dose regimen, the number of days the prescription is valid, the prescribing physician (GP or specialist) and the Anatomical Therapeutic Chemical code (ATC code). Each patient has a unique anonymous identifier; date of birth and gender are known. Due to the high patient-pharmacy commitment in the Netherlands, the medication records for each patient are virtually complete, except for over the counter (OTC) drugs and medication dispensed during hospitalization.

Data linkage by Statistics Netherlands (CBS)

In order to minimize the transportation of identifying personal data and to organize the process of linking Lifelines data to IADB.nl data in a way that is legally and ethically allowed, Statistics Netherlands (Dutch: Centraal Bureau voor de Statistiek; CBS) acts as a so-called trusted third party (TTP). There is a specific Dutch law for Statistics Netherlands to allow for such health care data linkage. Importantly, Statistics Netherlands has know-how and experience in storing, pseudonimizing and encrypting data for analysis as well as data output.

In August 2018, a set of data on medication use from the IADB.nl database was uploaded to Statistics Netherlands. Data of 730,000 persons are now available with information on medication use from 1994 till 2017.

Lifelines does not store any data at Statistics Netherlands, but an infrastructure has been built ensuring that uploaded Lifelines data is pseudonimized and processed smoothly and safely prior to linkage. Statistics Netherlands has already a linkage file available (reference date 28-2-2017; n=167,487) to link the Lifelines data to the IADB.nl data files.

The requested Lifelines and IADB.nl data will be made available to researchers via the Remote Access/ On site secured virtual work environment of Statistics Netherlands. More information about this work environment can be found at the [Statistics Netherlands website](#). The usual formalities, procedures and costs of Statistics Netherlands apply for the use of this working environment.

The procedures on data request and data access are described below.

Procedure on data request

Submitting a research proposal

Researchers can apply for access to linked Lifelines and IADB.nl data by submitting a research proposal. For this, the standard application process of Lifelines is followed. The [application process](#) is explained in more detail on the Lifelines website. The required application form can also be found there. The completed application form should be submitted together with the Lifelines data selection through the online [Lifelines data catalogue](#). If you have any questions regarding the application process, please contact the Research Office of Lifelines (research@lifelines.nl).

To ensure complete and timely data delivery from IADB.nl, researchers must submit the [IADB.nl protocol](#) to info@iadb.nl in parallel with the Lifelines application. This protocol is used to register the research and to make sure the right data formats are prepared and the design and analyses are agreed. It is sufficient if this is, at this stage, a preliminary version of the protocol.

Reviewing the research proposal

First, both Lifelines and IADB will review the research proposal (for review criteria see appendix A). When the proposal has been approved by both parties, Lifelines will confirm the approval via email.

Secondly, the researcher must contact Statistics Netherlands (microdata@cbs.nl) and send them a completed [application form of Statistics Netherlands](#). In this form you indicate what data you want to use for your research project. This will typically be Lifelines data and IADB.nl data, sometimes combined with microdata from Statistics Netherlands. If the project is also approved by Statistics Netherlands, the research project can be carried out definitively.

Contract, offer and RMAA

Upon approval of the research proposal by Lifelines, IADB and Statistics Netherlands, the necessary documents will be drafted and send to the researchers:

- Statistics Netherlands will send a project agreement. Researchers are asked to return the agreement signed and send it also to Lifelines. Lifelines will include this project agreement in the appendix of the Lifelines agreement (RMAA; see below).
- Statistics Netherlands will send an indication of costs that includes costs for: project start-up, pseudonimization of participants, temporary use of the remote access environment of Statistics Netherlands and the use of microdata files of Statistics Netherlands (if applicable). More information about what costs Statistics Netherlands charges can be found in the [Service Catalogue](#). Based on this indication of costs, Statistics Netherlands will send a separate offer to the researchers.
- Lifelines will send a Research Material Access Agreement (RMAA). The signed project agreement of Statistics Netherlands will be included in the appendix.
- Together with the RMAA, Lifelines will send an offer to the researchers that includes: 1) €3,500 for the use of the Lifelines data and for uploading the required data to Statistics Netherlands, and 2) €1,000 for the use of the data on IADB.nl medication use.

- After the contract has been signed off, the researchers need to finalize the IADB.nl protocol (see [IADB.nl](#)) and submit it as a final version to make sure the right data formats are prepared and the design and analyses are agreed.

Lifelines data will be released when the offer and RMAA have been returned to Lifelines signed by the researchers (legally represented by the head of their academic department or institute), IADB.nl (legally represented by the University of Groningen) and Lifelines. Please make sure that in all documents, the roles of representatives of institutes, recipient and PI are consistent and clearly defined.

Procedure on data access

For each approved project, the requested Lifelines data will need to be uploaded to Statistics Netherlands. Prior to this step, Lifelines will allow researchers access to the data via a Lifelines workspace for the period of 1 month. Researchers are asked to use this month to:

- Minimize the amount of variables to be uploaded (strict selection of variables such as SNPs, use of sum scores rather than raw data);
- Minimize the number of data files (preferably to 1) via merging;
- Get acquainted with Lifelines data and discuss any issues/questions with Lifelines data management (as this is more difficult after linkage);
- Log all minimalization and merging actions, for example in syntaxes, so that Lifelines data management can trace them back.

After the linkage file has been checked by a Lifelines data manager, Lifelines will upload the file to Statistics Netherlands. Statistics Netherlands will then pseudonimize the participant ID's in the uploaded data file in such a way that they can be linked to patient ID's in the IADB.nl database available at Statistics Netherlands. This step takes approximately 2 weeks. After Statistics Netherlands has informed IADB.nl that the Lifelines data is ready for use, IADB will add these data to the project database (SQL server) within the virtual work environment of Statistics Netherlands. Since the combined Lifelines and IADB.nl data is only accessible via the SQL server, all analyzes must be performed on this SQL server. Support during execution of research

During the execution of the research project, researchers can receive the following support:

- IADB.nl database: the staff of the IADB.nl will help with the protocol, registration of the study, training and testing of using the data. Staff can be reached via info@IADB.nl
- Lifelines Biobank and Cohort Study: questions regarding the Lifelines data can be sent to the data managers of Lifelines (data@lifelines.nl)
- Microdata service Statistics Netherlands: questions regarding the use of the remote access environment of Statistics Netherlands can be sent to microdata@cbs.nl.

Research and Data Management Plan (RDMP)

All data analyses and results that are exported from the CBS environment to the researcher must be returned to IADB (info@IADB.nl) and Lifelines (data@lifelines.nl), where they will be stored according to IADB (RuG RDMP) and Lifelines standards.

Evaluation of the research project

All research projects that make use of Lifelines data are evaluated. Researchers will receive an invitation for filling out a short evaluation questionnaire during the execution of the project. Based on the results of these evaluations, Lifelines strives to continuously improve our services.

Publications

Researchers are obliged to publish the results of their research project in scientific journals or printed scientific meetings. Agreements on the use of the Lifelines and IADB.nl data and the rights/ obligations with regard to publications are described in the RMAA. If researchers have also used data from Statistics Netherlands, they must also follow [the agreements on publications of Statistics Netherlands](#).

Lifelines and IADB.nl should also be informed about upcoming publications and other news coverage of your research via the Lifelines Research Office (research@lifelines.nl) and IADB.nl office (info@IADB.nl). In this way we can prepare for any questions from the Lifelines participants and we can help you to share your research results with the general public via our website and / or social media.

Reference paper

The linked data from the Lifelines Cohort Study and IADB.nl database have already been used in a first study with the aim to assess the concordance of the self-reported medication use as collected by Lifelines with information of the prescription database IADB.nl. Please refer to this paper in your publications:

- Sediq R, van der Schans J, Dotinga A, Alingh RA, Wilffert B, Bos JHJ, Schuiling-Veninga CCM, Hak E. [Concordance assessment of self-reported medication use in the Netherlands three-generation Lifelines Cohort Study with the pharmacy database IADB.nl: The PharmLines Initiative](#). *Clinical Epidemiology*. 2018;10: 1-9.

Appendix A: Lifelines Review Criteria

Applicant

- Proposals can only be submitted by a senior (non-commercial) researcher. “Senior” is defined as holding a PhD degree or similar qualification.
- Applicant is currently active in research as shown by at least one publication in an international scientific journal during the last 12 months.

Application

- The application form is completed.

Quality

- It should be possible to write a scientific paper on the results.
- Unlike grant proposal reviews, it is not about the best proposal but about minimum scientific criteria: problem adequately described, research question clearly defined, approach that can answer this question.

Data

- The research question can be answered by the available data within Lifelines, IADB.nl and Statistics Netherlands.
- All requested data are needed to answer the research question(s) and match the proposal.
- When data is requested for which additional agreements are made with the researcher who is the intellectual owner or who has paid for the collection of the data, the appropriate actions as stated in the document ‘Additional agreements for data/material use’ are carried out towards this researcher and the applicant.

Legal and ethical issues

- There are no ethical issues to conduct the proposed research.
- In case data of children (<12 yrs) are requested, an employee of Lifelines should be involved in the Research Project.
- There must be no group privacy-issues.

Feasibility

- It is possible to grant access to the requested data through the regular processes.
- It is possible to establish the requested data linkage within a reasonable period of time.