Survey of Health, Ageing and Retirment in Europe (SHARE)

Published: 28-05-2014
Last updated: 20-04-2024

Including the collection of biological biomarkers into a social survey such as SHARE is of important scientific value as it opens up multiple research possibilities: -Identification of causal relationships: biological biomarkers can help to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON40583

Source
ToetsingOnline

Brief title
SHARE

Condition

- Diabetic complications
- Age related factors

Synonym
chronic conditions common in old age, high blood sugar

Research involving
Human

Sponsors and support

Primary sponsor: Dutch Country Team of SHARE, Prof. A. van Soest
Source(s) of monetary or material Support: We applied for funding via the National Roadmap for Large-Scale Research Facilities (submitted on September 30;2013). We expect to hear about the outcome in Spring 2014. Pilot and Pretest will have to be carried out before

that date and are likely to be funded by money stemming from NWO. Furthermore;there is financial support from the US National Institute on Aging (NIA).,U.S. National Institute on Aging (NIA)

Intervention

Keyword: chronic conditions of the elderly, Dried Blood Spots Sampling, Glycated hemoglobin, total cholesterol

Outcome measures

Primary outcome

SHARE's main aim is to provide data on individuals as they age and their

environment in order to analyse the process of individual and population ageing

in depth. SHARE is a distributed European research infrastructure which

provides data for social scientists, including demographers, economists,

psychologists, sociologists, biologists, epidemiologists, public health and

health policy experts, who are interested in population aging.

Secondary outcome

Not applicable

Study description

Background summary

The current ratio of older people to total population in Europe is higher than on any other continent * yet, the phenomenon of population aging will continue well into this century everywhere on this planet. The Survey of Health, Ageing and Retirement in Europe (SHARE, please visit our website www.share-project.org for further information), which started data collection in 2004, is the first study to examine the different ways in which people aged 50 and older live in twenty countries from Scandinavia to the Mediterranean.

SHARE is a cross-national and multidisciplinary panel study incorporating individual self-reported information regarding social, economic and health factors as well as national institutional and social policy conditions in order

to understand how we age differently within Europe. These factors are well-known determinants of healthy ageing in its broad definition which includes adequate economic and social support as well as good health.

Self-reported information on health is important as it reflects subjective impressions. When collected in different countries, however, it is typically biased because individual perceptions vary across countries as much as socio-cultural factors. This bias can be overcome through objective measures of biological and physical functions, so-called biomarkers. For this reason, biomarkers, serving as indicators of the objective state of health, are increasingly used in epidemiological and socio-economic research.

Already from its beginning, SHARE has used objective physical biomarkers well-known for their prediction of adverse health outcomes, e.g. grip strength and lung force. But even though these physical biomarkers provide some valuable insights about potential health risks, they can only give us indirect information and do not allow us to understand the underlying processes and pathways. This knowledge gap can be filled with the aid of biological biomarkers. Although there is still much to learn in this field, we already know some biological biomarkers that are strongly correlated with health. And the field is expanding.

In many clinical and epidemiological studies, biomarkers have been collected through venipuncture and venous blood analyses. Such a methodology is extremely expensive when used in field surveys such as SHARE. As an alternative, the method of Dried Blood Spot (DBS) sampling has been introduced to the research field. DBS sampling means that several drops of blood are taken by pricking, e.g. a finger, and collecting the capillary blood drops on a filter-paper card. The blood spots are left to dry and the cards are then shipped by ordinary postal mail to a laboratory, where they are stored in freezers until analyses are performed. DBS samples can easily be collected in surveys employing trained lay interviewers.

Present biotechnology allows DBS samples to be used to determine various lipoprotein or protein structures as well as tracer elements (e.g. heavy metals) in the individual. Among them, the more well-known biological markers, like glycated hemoglobin (HbA1c), a marker of diabetes, and C-reactive protein (CRP) and cytokines, markers of inflammation and associated with atherosclerosis, hypertension and cardiovascular diseases, have reliably been measured in DBS samples. More recently, DBS assays for the measurement of Vitamin D and cholesterol have been developed and validated. Low values of Vitamin D are associated with a loss of muscle mass, muscle weakness and functional decline, as well as elevated risk of osteoporosis and fracture. Cholesterol is a marker for the risk of cardiovascular diseases. DBS assays for other biomarkers are still under development and will have huge potentials in future studies.

The biomarkers collected in SHARE are expected to give novel insights into the relations between chronic conditions common in old age and behavioural and environmental risk factors under various socio-economic conditions. The inclusion of DBS sample collection in SHARE will therefore not only enrich the SHARE database but also support multidisciplinary scientific research. Moreover, we are certain that the results from the collection of biomarkers in SHARE will have a profound influence on public health policy for the benefit of individuals in Europe and elsewhere.

Study objective

Including the collection of biological biomarkers into a social survey such as SHARE is of important scientific value as it opens up multiple research possibilities:
-Identification of causal relationships: biological biomarkers can help to understand the complex relationships between social status and health and their physiological pathways.
-Pre-clinical information: biomarkers allow to identify pre-disease pathways, since the physiological processes are often below the individual*s threshold of perception.
-Measurement of respondents* health can be improved: Standard health questions in surveys are often subject to the respondents* own interpretation (of the question), own evaluation or perception (of health status), and own knowledge (of health status) and health literacy. The value of subjective health measurements is undeniable, but some research questions require objective measurements. Especially in international comparisons self-reported health data may be biased by varying country-typical response styles. Biomarkers enable researchers to validate respondents* self-reports and therefore to study the amount and determinants of under-, over-, and misreporting in large-scale population surveys.

A fundamental advantage of including the collection of biomarkers into a large-scale survey such as SHARE is the simultaneous availability of biological and socio-demographic data in a representative (i.e. non-clinical) population. Using these data, manifold research areas can be investigated, e.g. the implications of recent public policy interventions on the health of older citizens, the causal link between biological aging processes with socially and economically induced health behaviours, or the future costs of typical chronic diseases in old age, such as diabetes.

In general, we are interested in biomarkers indicating the development of diseases that occur typically from onwards the mid of live (such as cardiovascular diseases) and conditions which are influenced by life style and environmental factors. In particular, the following parameters from the collected DBS samples will be analysed:
-Glycated hemoglobin (HbA1c): this is a measure for identifying the blood sugar concentration over a longer period of time. We are not measuring the current

blood sugar level (NOT fasting blood sugar, thus respondents are allowed to eat or drink before taking the blood spots); instead, by analysing the HbA1c value from the blood spot, we find out about the average blood sugar level of the last 2-3 months, and if somebody might have diabetes or not. Diabetes is a common disease of old age and of unhealthy lifestyle. Furthermore, if diabetes is known to the respondent, the HbA1c value tells, how well the respondent is adjusted to the treatment.
-Vitamin D (Vit. D): low values of Vit. D are associated with a loss of muscle mass, muscle weakness and functional decline, as well as elevated risk of fracture (osteoporosis). Vit. D blood concentration is highly dependent on nutrition and sunlight exposure. As the latter depends on local climate and latitude, and the former on nutrition habits that differ regionally, comparing vitamin D levels in a cross-national survey may provide interesting insights in the risk of developing diseases according to where somebody lives.
-Total cholesterol: The level of total cholesterol is a good marker for the risk of developing cardiovascular diseases. These diseases often have a subtle beginning below the threshold of the person*s perception. The analyses of the total cholesterol can help to identify patients in an early stadium of cardiovascular diseases which would otherwise pass unobserved.
-C-reactive protein (CRP) and cytokines (such as TNF*, IL-6, BDNF): CRP and cytokines are inflammation markers which tell us if a respondent has an ongoing inflammation. Subdued but non-disease specific increases of CRP/cytokines are correlated with cardiovascular diseases and stress. Also ageing per se is associated with cytokine release, but at much lower levels than the elevations observed during infections. A wide range of environmental factors (e.g. smoking, infections, and obesity), genetic factors, and declining functions of sex hormones contribute to this systemic low-grade inflammatory activity in older individuals, but also age-associated diseases contribute. Both Tumor Necrosis Factor alpha (TNF-*) and Interleukin 6 (IL-6) have been associated with morbidity and mortality and are believed to reflect the underlying pathogeneses of atherosclerosis, diabetes and dementia, as well as frailty and functional decline. Many other cytokines relevant to ageing exist, e.g. Brain-Derived Neurotrophic Factor (BDNF), which is released from nerve cells during exercise and activates the brain stem cells to convert into new neurons as well as protecting existing neurons from degradation. Accordingly BDNF has been linked to dementia and depression. Lifestyle factors may affect negatively (smoking, obesity) or positively (diet, physical activity) the level of circulating cytokines. Furthermore, low socio-economic status has been linked to elevated inflammatory markers.

These data therefore allow the investigation of the correlation between socio-economic conditions and behaviour and the risk of developing certain diseases, which all are an immense economical factor for the ageing European society.

Study design

SHARE is a multidisciplinary and cross-national panel database of micro data on health, socio-economic status and social and family networks of more than 85,000 individuals (approximately 150,000 interviews) from 19 European countries (+Israel) aged 50 and over.

1. Sample size and target population

The target population for inference from SHARE is the European population aged 50 and over. For practical reasons the definition of the study population for SHARE is: Persons born in 1964 or earlier, and persons who are a spouse/partner of a person born in 1964 or earlier, who speak the official language(s) of the country and who are residents within private households, regardless of nationality and citizenship.

To achieve representation of this population, SHARE employs a sample design which involves baseline samples of the household population aged 50 and over at a particular point in time in each country, supplemented by regular refreshment samples of the sub-population of people who have turned 50 since the original baseline sample was selected.

The sample size in the Netherlands will be 4000 individuals. We will ask panel respondents as well as refresher respondents, who do an interview for the first time, to participate in the dried blood spot collection. The participation in this part of the interview is voluntary. Should a respondent refuse to have blood spots taken, no blood will be collected. Furthermore, we will not collect blood in case the interview is a proxy-interview (i.e. an interview not with the originally sampled person but with another person who knows him/her well) or if the respondent is not able to understand the information given to him/her prior to the DBS sample collection and/or to agree to the collection of blood spots.

2. Methodology (Dried Blood Spot Sampling)

SHARE is a face-to-face interview that takes place in the respondents' homes using CAPI (Computer-Assisted Personal Interviewing) software. In the middle of the interview the collection of DBS samples is conducted. Of course, the participation is absolutely voluntary (with regard to the SHARE study as well as regarding the collection of the DBS samples). All participating respondents will be asked for their (informed and written) consent to have their blood collected for DBS samples.

DBS samples are collected by taking blood from a finger prick using a small, sterile lancet * just as it is done daily by millions of diabetic people. After pricking a fingertip with the small lancet, a few drops of blood are dripped on specified (circled) areas of a card made of filter paper, i.e. a DBS filter card. The card is registered by a unique identifier in the format of a barcode printed on a sticker attached to the card and the respective barcode number is

typed into the CAPI by the interviewer. When dry, the filter card is put into a special tear-proof and water-resistant envelope. As DBS samples are sensitive to moisture and high temperatures, a small desiccant bag and a temperature sensitive strip are added to the envelope before being dispatched by postal mail to the SHARE Biobank located at the Institute of Public Health, University of Southern Denmark in Odense, Denmark.

At the beginning of the DBS sample collection each respondent is given an information leaflet (and enough time to read it), then he/she has to sign a consent form. The signed consent form is collected by the interviewer and sent to the the survey agency, while a copy of the form is left with the respondent. Both forms have the respondents' unique barcode attached.

3. Materials Needed & Blood Sample Collection

The following materials are needed in order to collect the DBS samples:
- 2 Blood spots collecting cards
- Disposable protective cloth
- 2 pairs of disposable rubber gloves
- Disposable disinfecting wipes
- 2 semi-automatic lancets
- Cotton balls
- Plasters
- Desiccant
- Small plastic bag for blood spot collecting card
- Small envelope for blood spot collecting card
- Special, water-resistant and tear-proof mailing envelope
- Barcode stickers
- Address stickers
- Temperature sensitive strip
- 2 copies of the "Dried Blood Spots Collection" consent form
- Large plastic bag for waste material

The detailed steps of the DBS sampling are the following:
1. The respondent is asked to give informed and written consent to participate in the DBS collection, if yes
2. The respondent is asked to rub and/or shake hands (warm hands ensure enough bleeding through good capillary circulation).
3. All parts from the blood collection kit are placed on the disposable protective cloth.
4. The blood spot collecting cards, consent forms and envelopes are marked with individual barcodes.
5. The interviewer puts on rubber gloves.
6. The finger to be pricked (preferably the respondent*s fourth finger on the non-dominant hand) is cleaned with the disinfecting wipe and let to dry.
7. The semi-automatic lancet is activated on a lateral side of the respondent*s finger and blood drops are collected (the puncture can be done either by the interviewer or by the respondent himself):

8. Using a cotton ball, the first drop of blood is wiped off.
9. The next large drops of blood from the respondent*s finger are allowed to drop onto the pre-marked circles of the DBS filter card (without touching them with the fingers).
10. The respondent is provided with a cotton ball and a plaster to attach firmly to the puncture site which is observed for continued bleeding (in case of which a second plaster is provided and the finger should be held firmly in an elevated position).
11. The barcode number is entered into the CAPI (double-checked).
12. The card is put aside to dry until the end of the whole SHARE interview, but for 15 minutes minimum.
13. Used materials are discarded.
14. The dried DBS filter card is posted in a special tear-proof and water-resistant envelope for biological material together with a desiccant and a temperature sensitive strip.
15. The DBS sample should be sent to the SHARE Biobank as soon as possible after the interview using the standard mail service. Meanwhile the samples have to be kept in a cool place.

4. Processing and Storage of the DBS Samples

To ensure comparability of the biomarker analysing results, all DBS samples from all SHARE countries are sent to one single biobank, namely the SHARE Biobank at the Institute of Public Health of the University of Southern Denmark in Odense.

Upon arrival at the biobank, the DBS sample is immediately processed, given arrival on a weekday. The process starts by scanning the barcode on the DBS filter card and, thus, registering the sample in a specific SHARE biomarker database together with the dates of the sample collection, the mailing stamp and the arrival at the biobank. The indicated temperature on the temperature sensitive strip * showing the highest temperature the sample was exposed to * is entered into the database as well. Once registered in the database, copies of the unique barcode are printed on stickers for later use (see below).

To minimise the risk of accidental events jeopardising the quality of the sample or resulting in a later loss of the DBS sample, the DBS card is divided into three subsamples, each registered in the database by the same unique barcode number and marked with a barcode sticker, and put in a new envelope, which is sealed inside a plastic bag containing a desiccant. Each of the three subsamples is finally stored in different freezers and their exact locations are also registered in the database. The temperature of the freezers is kept at -20°C. Experiences from the National Danish Biobank in Copenhagen show that the biological material on the DBS cards can be kept frozen at this temperature for many years without significant deterioration. An alarm will sound in case the temperatures of the freezers deviate significantly from -20°C and a biobank

staff member on call will receive a warning by mobile phone.

To ensure confidentiality, the barcode is the only "identifier" of the individual respondent. Neither the biobank nor the processing laboratory have access or connection to the SHARE interview database and do not keep any names or other personal information in their database. After the mentioned analyses have been carried out, the DBS samples will still be kept in the biobank. The respondents consent to their blood samples being stored after the ending or termination of the DBS collection in SHARE. But they may revoke their participation and request the removal from storage and the destruction of their blood samples at any time.

5. Analyses and Linkage oft the Results to the SHARE Dataset

The DBS samples collected in SHARE wave 6 will be used to carry out analyses regarding the development of diseases, which occur often from onwards the mid of life in order to enable scientific research to conduct comparative analyses of correlations between such diseases and life circumstances (such as family, occupation, retirement, social networks). At this, the main focus lies on cardiovascular diseases and diseases, which are influenced by life style and environmental factors. In particular the following pre-specified analyses will be conducted: Glycated hemoglobin (HbA1c), Vitamin D (Vit. D), total cholesterol, C-reactive protein (CRP) and the cytokines tumor necrosis factor-alpha (TNF-*), interleukin 6 (IL-6), brain-derived neurotrophic factor (BDNF).

In this context participants are given the opportunity to exclude certain analyses from being done. This, of course, also applies with regard to analyses related to scientific research questions in the above mentioned research areas, which could be answered with the help of the DBS samples in the future. Since other biological biomarkers are still under development and will have huge potentials with regard to future scientific research, the samples will be stored in the SHARE Biobank even after the pre-specified analyses have been conducted in order to maintain the possibility to carry out further scientific analyses in this field.

Finally, for scientific research purposes all the analyses results are sent to the central SHARE coordination team where the data are merged with the SHARE wave 6 database. Since the unique barcode number was entered into the CAPI during the interview, the DBS analyses results can be linked to the interview data. However * to emphasise this * the barcode numbers will not be part of any of the releases in the SHARE database used by scientific researchers.

Study burden and risks

Dried blood spots (DBS) sampling is safe and easy to perform. The method of DBS sampling was developed to safely gain a small blood sample from a newborn to

check for a disabling metabolic disease (phenyl ketonuria), which may be avoided if disclosed right after birth. In the last years, the method was adapted to field surveys taking blood from adult respondents to generate objective health data. In Sweden, self-administered DBS collection is used in diabetes control monitoring of patients living in more remote areas. In population-based ageing research in Denmark, more than 3500 DBS samples have been collected among the old and oldest old without any problems. Also in Germany during SHARE wave 4, more than 1400 DBS samples have been collected, and no problems occurred. Pricking the finger is in general associated with very low risks. Millions of diabetic people do it daily to check their blood glucose. The puncture can cause light pain or a small hematoma.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

SHARE is a face-to-face interview that takes place in the respondents' homes using CAPI (Computer-Assisted Personal Interviewing) software. In the middle of the interview the collection of DBS samples is conducted. Of course, the participation is absolutely voluntary (with regard to the SHARE study as well as regarding the collection of the DBS samples). All participating respondents will be asked for their (informed and written) consent to have their blood collected for DBS samples.

Exclusion criteria

If for whatever reasons a respondent is not able or willing to consent with regard to the dried blood spots collection, no blood will be collected and this part of the study will be skipped entirely. Furthermore, we will not collect blood in case the interview is a proxy-interview (i.e. an interview not with the originally sampled person but with another person who knows him/her well) or if the respondent is not able to understand the information given to him/her prior to the DBS sample collection and/or to agree to the collection of blood spots.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-05-2014
Enrollment:	4000
Type:	Actual

Ethics review

Approved WMO

Date:	28-05-2014
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL46467.008.14