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Cohort profile: follow-up of a Berlin Aging Study II (BASE-II) subsample as part of the GendAge study

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ABSTRACT

Purpose The study 'Sex- and gender-sensitive prevention of cardiovascular and metabolic disease in older adults in Germany', the GendAge study, focuses on major risk factors for cardiovascular and metabolic diseases and on the development of major outcomes from intermediate phenotypes in the context of sex and gender differences. It is based on a follow-up examination of a subsample (older group) of the Berlin Aging Study II (BASE-II).

Participants The GendAge study assessments took place between 22 June 2018 and 10 March 2020. A total of 1100 participants (older BASE-II subsample, aged ≥65 years) with baseline data assessed at least by one of the BASE-II partner sites were investigated in the follow-up. These participants had a mean age of 75.6 years (SD ±3.8), with a mean follow-up at 7.4 years (SD ±1.5).

Findings to date Data from different domains such as internal medicine, geriatrics, immunology and psychology were collected, with a focus on cardiometabolic diseases and in the context of sex and gender differences. Diabetes mellitus type 2 was reported by 15.6% and 8.6% of men and women, respectively. In contrast, this disease was diagnosed in 20.7% of men and 13.3% of women, indicating that a substantial proportion of almost 30% was unaware of the disease. Echocardiography revealed that left ventricular ejection fraction was higher in women than in men, in agreement with previous reports.

Future plans A gender questionnaire assessing sociocultural aspects implemented as part of the follow-up described here will allow to calculate a gender score and its evaluation based on the newly collected data. At the same time, the other BASE-II research foci established over the past 10 years will be continued and strengthened by the BASE-II transition into a longitudinal study with follow-up data on the older subsample.

Trial registration number DRKS00016157.

Strengths and limitations of this study

- The GendAge study focuses on major risk factors for cardiovascular and metabolic diseases and on the development of major outcomes from intermediate phenotypes in the context of sex and gender differences.
- The Berlin Aging Study II (BASE-II) follow-up as part of the GendAge study assessments covered most of the medical, psychosocial and cognitive domains and variables assessed at baseline.
- Comprehensive and longitudinal study data offer the potential to answer a number of questions that are of crucial relevance for the health of old women and men.
- The possibility of a selection bias in the follow-up study population is a limitation, which we have made various efforts to accommodate.
- We are able to systematically quantify the sampling bias and even account for it when it comes to the question of generalisability of study results to a population as a whole.

INTRODUCTION

The original BASE-II cohort

The Berlin Aging Study II (BASE-II) was launched as a multidisciplinary study aimed at better understanding the multitude of different ways in which age and ageing evolve and identifying the underlying mechanisms and contributing factors. Baseline recruitment of 2200 adult volunteers from the Berlin metropolitan area and baseline assessments were completed in 2014.[1] The ascertainment protocol included the collection of data from different domains for each of the 2200 participants (about 75% aged 60 years and above, the *older group* of BASE-II participants), namely, geriatrics and internal medicine, immunology, genetics, psychology, sociology and economics.[1 2]

BASE-II baseline data were used in a multitude of analysis projects focusing on key questions revolving around age and ageing. Research topics of the ongoing study include, but are not limited to, cognitive ageing,[3–5] cardiovascular and metabolic health,[6–8] sarcopenia and frailty,[9 10] psychosocial factors of

ageing,[11 12] genetic risk factors of ageing and disease,[13–15] the impact of characteristics of the neighbourhood people are living in,[16] as well as indicators of biological age[17 18] and immune biomarkers.[19] For an overview of the BASE-II research foci and publications, refer to a previous work[20] and the BASE-II website (https://www.base2.mpg.de/en/project-information/publications).

Contact procedure: follow-up assessments

Of the original BASE-II sample consisting of 2200 participants, 1671 aged 60 years and above (=older group) were assessed medically at baseline between 2009 and 2014. The follow-up assessments within the GendAge study took place between 22 June 2018 and 10 March 2020 at the Charité Universitaetsmedizin Berlin. During the recruitment of the follow-up cohort, we approached all BASE-II participants of the remaining pool of 1428 subjects out of the originally 1671 subjects who completed the baseline medical assessments at an age of 60 years and older (older BASE-II group, see figure 1). Between 7 February 2020 and 13 March 2020, we additionally performed follow-up assessments in a total of 64 participants of the younger BASE-II group aged 20–35 years at baseline until these assessments were suspended because of the SARS-CoV-2 pandemic. Potential follow-up participants were contacted via telephone and an invitation letter that contained a comprehensive participant's information sheet. Letters of consent were sent at least 5 days before the scheduled first of two assessment days to all subjects who agreed to participate. As a result of a 4-week pilot phase, we reduced the maximum number of participants examined on each of the first two study days from 6 to 4, with an interval of usually 7 days between study visit 1 and 2. Largely because of this early adjustment, follow-up examinations lasted 21 months instead of the 15 months originally planned. Moreover, another wave of cognitive assessments carried out by the Max Planck Institute for Human Development (MPIB) has been tightly linked to the GendAge assessment of BASE-II participants. The cognitive session (=third study visit) followed about 7 days after the second medical examination.

What is the reason for the new data collection?

The study 'Sex- and gender-sensitive prevention of cardiovascular and metabolic disease in older adults in Germany', the GendAge study, focuses on major risk factors for cardiovascular and metabolic diseases and on the development of major outcomes from intermediate phenotypes in the context of biological sex and gender differences. Major outcomes include, but are not limited to, myocardial infarction (MI), heart failure and diabetes mellitus type 2 (T2D), as well as mortality and quality of life. Gender was quantitated in two ways: by a retrospective approach, based on available data at study entry (2009–2014) and already published (GenderScore-I, GS-I)[21] as well as by a comprehensive gender questionnaire covering a range of sociocultural gender characteristics as a central instrument (GenderScore-II, GS-II). This questionnaire contains an adapted version of the gender questionnaire developed by Pelletier and colleagues covering most of the four gender aspects described by the Women Health Research Network of the Canadian Institute of Health Research (gender roles, gender identity, gender relations and institutionalised gender).[22 23] The variables finally constituting the GS-I were chronic stress, marital status, risk-taking behaviour, personality attributes: agreeableness, neuroticism, extraversion, loneliness, conscientiousness and level of education.[21]

What will be the new areas of research?

There is new knowledge showing that sex differences play a role in all major diseases, their prevention and treatment.[24] Other studies showed that gender as the sociocultural dimension of being a woman or a man affects disease and treatment outcomes and also well-being.[22 25] The new areas of research cover the systemic inclusion of sex-specific analysis and the inclusion of gender. Ageing interacts with sex and gender differences in health, but it is not clear, which mechanisms are most important.

GendAge aims to better understand, which mechanisms affect cardiometabolic morbidity, mortality and quality of life among older adults in a sex-sensitive and gender-sensitive manner.

While on different occasions follow-up data were ascertained for questionnaire and cognitive data,[5 26–30] as being part of the GendAge study, this cohort profile update describes the first comprehensive follow-up assessments in a BASE-II subsample (older group) that also includes

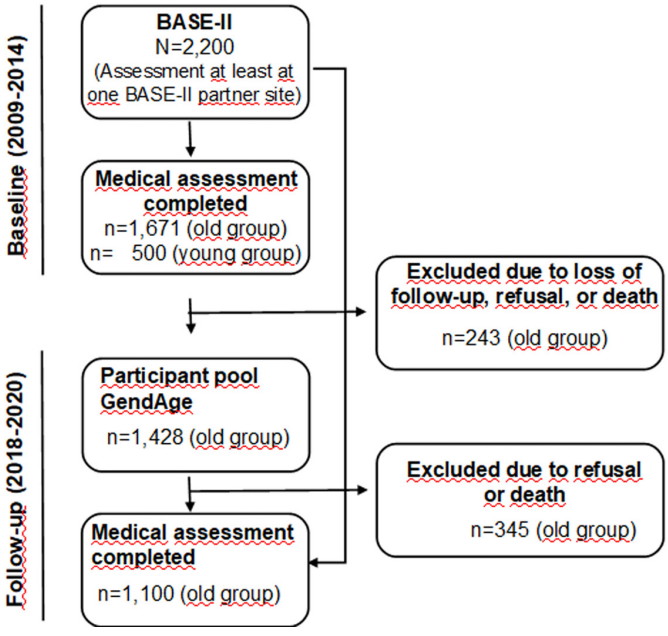

Figure 1 Flowchart explaining the final Berlin Aging Study II (BASE-II) sample with follow-up assessments completed in GendAge. A total of 17 of the 1,100 participants examined atfollow-up were not medically examined at baseline but were examined at least atone of the other BASE-II study sites.

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a reassessment of central variables in the areas of internal medicine and geriatrics.

COHORT DESCRIPTION

As presented in the flowchart (figure 1), following the contact procedure until the participant pool was exhausted resulted in a total of 1100 participants of the older BASE-II group investigated in the follow-up. These participants had a mean age of 75.6 years (SD ±3.8, range 64.9–94.1 years), with up to 10.4 years of follow-up (mean follow-up at 7.4 years, SD ±1.5). At follow-up, almost all of the older participants were retired (97.3%) as compared with 86% at the time of baseline assessment. At baseline, BASE-II participants were characterised by higher education and better self-reported health status than the general population of Berlin and Germany.[1] At follow-up, this selection seems to have increased, with 68.8% of the participants reported to have a high school degree (51% at baseline) and about 61% rated their health as *very good* or *good* (40% at baseline). The rate of divorce had been above average at baseline with 29% and had dropped to 21.7% at follow-up, which is still significantly above the German and Berlin average (ie, 12.0% and 17.4%, respectively),[31] while the proportion of widowed participants increased from 5% at baseline to 10.5% in the follow-up dataset of older BASE-II participants. As shown in table 1, differences between men and women are evident with respect to the sociodemographic status and psychosocial functioning in the follow-up cohort: Men reported significantly higher school degrees and higher satisfaction with life in general than women. Interestingly, self-rated health did not differ between men and women, which matches to the overall morbidity estimated by an adapted version of the Charlson morbidity index,[17 32] which also did not differ between men and woman (p=0.98, table 1). This morbidity index, however, increased between baseline and follow-up (p<0.001, Wilcoxon signed-rank test and data not shown). Differences between men and women exist in the follow-up dataset with respect to the prevalence of some, but not all cardiovascular risk factors and diseases (table 1). Men, for example, had a higher BMI and a higher proportion of men reported to have T2D and MI than women. No significant differences between men and women were evident in the reporting of hypertension, peripheral artery disease and stroke. With the aim of investigating human ageing processes in BASE-II under consideration of different disciplines and longitudinally, the baseline investigation aimed at the most comprehensive data collection possible. At follow-up, most of these data in the field of geriatrics, internal medicine and psychology were again part of the study protocol (for a select overview, see table 2).

Findings to date

With a focus on cardiometabolic diseases in GendAge, we extended the broad range of data assessed in this area at baseline by echocardiography. Data on right and left ventricular and atrial morphology and systolic and diastolic function and vascular stiffness were obtained. Left ventricular ejection fraction was higher in women than in men, in agreement with previous reports.[33 34] Furthermore, increased LV mass and volumes in men before and after indexing to body surface area were confirmed, underscoring major sex differences in cardiovascular pathophysiology.[35]

With the aim of achieving a particularly high-quality standard in the assessment of participant's medical history at baseline and follow-up, including past and current diseases, the information given by the participants was recorded from study physicians as part of a structured one-to-one interview, allowing to consider its plausibility. This, however, does not cover the gap between reported (anamnestic) diseases and the diseases diagnosed in the course of the study. This is exemplified by T2D, which was reported by 15.6% and 8.6% of men and women, respectively. In contrast, this disease was diagnosed in 20.7% of men and 13.3% of women based on the American Diabetes Association guidelines 2019,[36] indicating that a substantial proportion of almost 30% was unaware of the disease (table 1).

As part of our endeavours, we have developed a retrospective gender score taking BASE-II baseline data reflecting sociocultural aspects (eg, level of education, marital status and chronic stress) into account. This retrospective gender score (GS-I) was associated with a number of clinical and psychosocial variables and performed better in predicting differences in a subset of variables (eg, depression and life satisfaction) compared with biological sex.[21] In addition, we have implemented a comprehensive gender questionnaire as part of the follow-up assessments described here, to calculate a prospective gender score as proposed by Pelletier and colleagues.[22]

Peripheral blood mononuclear cells were prepared from 903 participants at follow-up, of which 845 were fully analysable (58 were dropouts) and frequencies as well as absolute counts of recent thymic emigrants (RTEs), T_{EMRA} effector T cell subsets (T_{EMRA}) and cytotoxic $CD4^+$ T cells were directly assessed. While RTEs are known to decrease with ageing,[37] alterations in T_{EMRA} and specialised cytotoxic $CD4^+$ T cell compartments can be indicative of age-related perturbations of systemic T cell immunity.[38] The immunological screening has so far revealed significantly higher frequencies of RTEs in women as compared with men, indicating a higher thymic T cell production even at the advanced ages of the GendAge participants. In men, more $CD45RA^+$ re-expressing T_{EMRAs} were detected than in women (table 1). These cells are associated with chronic viral infections (eg, CMV) and can serve as a signature of immune-senescence.[39] We found no significant difference in the frequencies of cytotoxic $CD4^+$ T cells. Together, these preliminary findings confirm the better immune status of aged women as compared with men. A detailed analysis of the datasets will identify additional correlates of sex and gender, ageing and the immune system.

Table 1 Selection of BASE-II follow-up characteristics as assessed of theGendAge study

	Total number of observations	Women* (N=573, 52.1%)	Men* (N=527, 47.9%)	P value†
Age (years)	1100	75.7 (±3.5)	75.5 (±4.0)	0.276
Highest school degree				
Elementary school	1095	35 (6.1%)	18 (3.4%)	<0.001
Intermediate school		183 (32.0%)	104 (19.9%)	
High school		354 (61.9%)	401 (76.7%)	
Family status				
Married	1098	218 (38.0%)	386 (73.5%)	<0.001
Not married, in partnership		12 (2.1%)	19 (3.6%)	
Single		60 (10.5%)	33 (6.3%)	
Divorced		187 (32.6)	51 (9.7%)	
Widowed		89 (15.5%)	26 (5.0%)	
Other		7 (1.2%)	10 (1.9)	
Employment status				
Retired	1055	540 (97.6)	486 (96.8)	0.689
Self-rated health				
Very good	1096	56 (9.8%)	65 (12.4%)	0.499
Good		284 (49.7%)	262 (50.0%)	
Fair		166 (29.0%)	143 (27.3%)	
Poor or very poor		66 (11.5%)	54 (10.3%)	
Satisfaction with life in general	1097	7.9 (±1.6)	8.1 (±1.4)	<0.05
Digit Symbol Substitution Test‡	1095	41.37 (±8.48)	39.21 (±9.67)	<0.001
Verbal learning test	925	41.6 (±12.3)	44.0 (±12.8)	<0.01
Depression (ever diagnosed)	1095	122 (21.3%)	63 (12.0%)	<0.001
BMI	1098	26.6 (±4.7)	27.4 (±3.7)	<0.01
Physical inactive§	1096	67 (11.7%)	65 (12.4%)	0.781
Diabetes mellitus type II (self-reported)	1097	49 (8.6%)	82 (15.6%)	<0.001
Diabetes mellitus type II (diagnosed/ American Diabetes Association guidelines 2019)	1097	76 (13.3%)	109 (20.7%)	<0.01
Metabolic syndrome (diagnosed, American Heart Association/ International Diabetes Federation/ National Heart, Lung,and Blood Institute criteria 2009)	1074	252 (45.5%)	327 (62.9%)	<0.001
Hypertension	1097	296 (51.7%)	311 (59.2%)	<0.05
Myocardial infarction	1097	11 (1.9%)	24 (4.6%)	<0.05
Stroke	1096	13 (2.3%)	20 (3.8%)	0.158
Peripheral artery disease	1094	8 (1.4%)	15 (2.9%)	0.138
Morbidity index	955	1.0 (IQR 2.0)	1.0 (IQR 2.0)	0.981
Pulse wave velocity (m/s)	932	11.21 (±0.92)	11.04 (±0.91)	<0.01
Left ventricular ejection fraction (%)	773	64.12 (±6.24)	62.92 (±5.76)	<0.01
Left ventricular mass (g)	691	135.24 (±31.87)	179.76 (±38.96)	<0.001
Left ventricular mass index (g)¶	690	78.55 (±16.83)	91.22 (±17.96)	<0.001
Left ventricular end-diastolic volume (mL)¶	773	54.10 (±12.24)	63.67 (±13.58)	<0.001
Frailty (Fried)				
Not frail	1087	260 (45.4%)	251 (47.6%)	0.542
Pre-frail		280 (48.9%)	248 (47.1%)	
Frail		28 (4.9%)	20 (3.8%)	
Maximal hand grip strength (kg)	1098	20.5 (±4.4)	35.1 (±6.8)	<0.001

Continued

Table 1 Continued

	Total number of observations	Women* (N=573, 52.1%)	Men* (N=527, 47.9%)	P value†
Recent thymic emigrants (naïve CD4⁺ T cells)	395**	64.69 (±16.34)	51.03 (±13.69)	<0.001
T_{EMRA} (effector memory T cells re-expressing CD45RA)	395**	32.82 (±19.96)	34.94 (±21.29)	0.309
Cytotoxic SLAMF7+CD4⁺ T cells	181††	6.02 (±5.98)	6.05 (±6.60)	0.974

*Data are presented as N (%), mean±SD or median (IQR).
†Differences between women and men were assessed using the parametric t-test, the non-parametric Mann-Whitney U test or the χ^2 where appropriate.
‡Assessed at study visit 1.
§Assessed with the question, 'Are you seldom or never physically active?'.
¶Adjusted for body surface area.
**845 expected to be available after completion of the analyses.
††629 expected to be available after completion of the analyses.
BMI, body mass index.

The gender questionnaire implemented as part of the follow-up assessments described here will allow to calculate a gender score and its evaluation based on the newly collected clinical and psychosocial follow-up data. At the same time, the other BASE-II research foci established over the past 10 years will be continued and strengthened with the transition of BASE-II into a longitudinal study with follow-up data on the older subsample.

Other measurements

Similar to baseline, we determined numerous routine laboratory parameters from blood and urine (table 2), and also stored blood plasma/serum and urine samples for future analyses. Genomic DNA was already extracted from EDTA-blood and buccal swab samples from GendAge participants, which will be used, for example, for the profiling of genome-wide DNA methylation signatures and new genome-wide single nucleotide polymorphism genotyping experiments (table 2). In between the two assessment days at the Charité, participants were asked to fill out a comprehensive psychosocial take-home questionnaire and return this at their second Charité visit.

At baseline, the BASE-II included a group of 600 younger subjects aged 20–35 years serving as a reference population,[1] of which 500 completed baseline medical assessments. Between 7 February 2020 and 13 March 2020, we performed follow-up assessments in a total of 64 participants of this younger group until these assessments were suspended because of the SARS-CoV-2 pandemic. These younger participants had a mean age of 36.8 years (SD ±3.5, range 29.3–44.1 years), with up to 10.7 years of follow-up (minimum 6.1 years, mean follow-up at 8.2 years, SD ±1.6). Follow-up for these younger BASE-II participants essentially followed the protocol used for the 1100 older BASE-II participants. Because this younger group is not primarily part of the analyses planned in GendAge, further details about this group will be described elsewhere.

The cognitive session carried out by the MPIB lasted about 4.5–5 hours (third study visit). Subjects were tested in groups of 4–6 individuals. The cognitive battery included 17 measures of learning and memory performance, attention/processing speed, working memory, executive functioning and perceptual speed (see table 2). Within the week between study visit 2 (Charité) and 3 (MPIB), accelerometers (ActiGraph wGT3X-BT) have been used to track participants' physical activity and sleep in a subset of our participants (n=750).

After the cognitive session, participants were invited to take part in a one-to-one interview on a different day. This additional individual assessment took up to 60 min and serves as a cohort comparison between the BASE and BASE-II study populations. This additional data collection will also contribute to the BASE-II cognitive waves, allowing us to further investigate individual differences in ageing trajectories (for an overview, refer to previous work[20]).

Furthermore, and as part of a collaboration with the Lifebrain study, a consortium of European studies funded by the EU Horizon 2020 Framework Programme,[40] we collected blood samples using dried blood cards, in order to determine laboratory parameters with identical methods used for all Lifebrain participating sites. Lifebrain aims at identifying determinants of healthy lifespan development by integrating and harmonising data and results from 11 large and predominantly longitudinal European samples from seven countries. This has yielded a database of fine-grained measures focusing on brain and cognition from more than 7000 individual participants.

The GendAge study was approved by the Ethics Committee of the Charité–Universitätsmedizin Berlin (approval number EA2/144/16) and all participants gave written informed consent. GendAge is registered in the German Clinical Trials Register (Study-ID: DRKS00016157). The cognitive battery was approved by the Ethics Committee of the Max-Planck-Institute and the genomics experiments were approved by the Ethics Committees of the Charité (approval number EA2/144/16) and the University of Lübeck (approval numbers AZ19-390A and 19-391A).

Table 2 BASE-II follow-up assessments during the two GendAge study visits and the cognitive sessions (third study visit)

Type of assessment/domain	Example assessments/tests
Physical examination and medical history	Medical history structured by organ systems, medication, body weight, height, lifestyle (including smoking status, alcohol consumption, physical activity)
Physical status and functional tests	Tinetti Mobility Test, Timed up & Go Test, Barthel Index (ADL), Lawton Instrumental Activities of Daily Living Scale (IADL), hand grip strength, anthropometric parameters, pulse wave velocity/ arterial stiffness (Mobil-o-Graph), echocardiography, ECG, spirometry, motion monitoring (Actigraph), dual-energy X-ray absorptiometry (DXA)
Psychological screening tests	Mini Mental State Examination (MMSE), Digit Symbol Substitution Test (DSST)*, Center for Epidemiologic Studies Depression Scale (CESD)
Questionnaires	EPIC (Food-Frequency Questionnaire), Gender Questionnaire, Pittsburgh Sleep Quality Index, Rapid Assessment of Physical Activity, SARC-F, SF-36
Laboratory values†	Blood, serum or plasma: 25-hydroxyvitamin D, apolipoprotein A1, apolipoprotein B, basophiles, calcium, cortisol, creatinine, creatine kinase, C-reactive protein, cystatin C, dehydroepiandrosterone, eosinophils, erythrocytes, ferritin, folic acid, gamma-glutamyltransferase, glucose 1, glucose 2‡, glutamate, oxalacetate transaminase, glutamate-pyruvate transaminase, HbA1c, high-densitylipoprotein cholesterol, hematocrit, haemoglobin, homocysteine, international normalised ratio, iron, low-densitylipoprotein cholesterol, leucocytes, lipoprotein (a), lymphocytes, magnesium, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, monocytes, neutrophils, oestradiol, osteocalcin, partial thromboplastin time, RDW, sex hormone-binding globulin, testosterone, thrombocytes, thyroid-stimulating hormone, thyroxine, total cholesterol, triglycerides, triiodothyronine, urea, uric acid, vitamin B_{12}, zinc. Urine: albumin, creatinine, desoxypyridinoline, test strip: bilirubin, blood (erythrocytes), glucose, ketones, leucocytes, nitrite, pH value, protein, specific weight, urobilinogen Dried blood cards: arsenic, brain derived neurotropic-factor, cadmium, chromium, fatty acids (C12:0, C14:0, C15:0, C16:0, C16:1n7, C17:0, C18:0, C18:1,t6-11, C18:1,c9, C18:1,c11, C18:2,n-6, C20:0, C18:3,n-6, C18:3,n-3, C20:1,n-9, C20:2,n-6, C22:0/C20:3,n-6, C20:4,n-6, C20:5,n-3, C24:0, C22:5,n-3, C22:6,n-3, unknown), HbA1c, hsCRP, lead, mercury, nickel, total cholesterol
Genomics	Genome-wide single nucleotide polymorphism genotyping using the 'Global Screening Array' (Illumina); genome-wide DNA methylation profiling using the 'Infinium MethylationEPIC' array (Illumina)
Psychosocial questionnaire	Well-being, positive affect and negative affect, emotion regulation, stress, personality, control beliefs, domain-specific control, time perception, embitterment, loneliness, solitude, social activities, network structure, sexuality, risk behaviour, etc
Biobanking	Blood plasma and serum, urine, DNA extracted from EDTA-blood and buccal swaps
Cognitive tests (third study visit)	*Episodic memory* (Picture-Word-Task, Face-Profession-Task, Object Location Task, Scene-Encoding, Verbal learning and memory test), *Working memory* (Letter Updating, Spatial Updating, Number-N-Back), *Executive functioning/processing speed* (Multi-Source-Interference Task, Digit Symbol Substitutions Test*), *Fluid intelligence* (Letter series, Number series, Practical Problems), *Subjective Health Horizon Questionnaire* (SHH-Q)
Immunological assessment	Cryopreservation of whole blood (SmartTube system) or isolated peripheral blood mononuclearcells, and serum samples. Direct ex vivo staining of recent thymic emigrants (RTE, CD31+CD45RA+CD4+T cells), TEMRA (CD45RA+CD8+T cells), Tregs (CD25bright CD127- CD4+T cells), cytotoxic CD4+Tcells, among others using four different panels: (1) ImmunoCount Panel (CD45, CD3, CD56, CD19, CD16, CD14, CD123, CD1c); (2) RTE panel (CD3, CD4, CD8, CD45RA, CCR7, CD31, CD95, CD11a); (3) TREG panel (CD3, CD4, CD8, CD25, CD127); (4) Effector T cell panel (CD3, CD4, CD8, CD45RA, CCR7, SLAM-F7, IL-6R, CD57, PD-1). Panels were measured on MacsQuant 10 (Miltenyi), MacsQuant 16 (Miltenyi) or LSR II (BD)

*Assessed at study visit 1 and visit 3.
†Blood samples were drawn after a fasting period of at least 8 hours (if not otherwise indicated).
‡Post-load (75 g glucose, 2 hours), not assessed in participants with known diabetes.
BASE-II, Berlin Aging Study II.

Strengths and limitations

The BASE-II follow-up assessments covered most of the medical, psychosocial and cognitive domains, and variables assessed at baseline, and thereby taking the BASE-II characteristic of an exceptionally broad and in-depth data collection to a next, longitudinal level. In addition, and in the context of the GendAge focus on cardiometabolic disease, we extended the assessments in this area, for example, by including high-quality echocardiography resulting in a unique data collection. This strength with respect to comprehensive and longitudinal data offers the potential to answer a number of questions that are of

crucial relevance for the health of old women and men. Thus, GendAge will make important contributions for improvements in understanding the health and well-being of older adults in both genders. BASE-II was initiated as a multidisciplinary study with expertise in a broad range of fields relevant for ageing research (eg, internal medicine and geriatrics, biology, psychology, genetics, immunology, socioeconomics and now in GendAge further extended by sociocultural aspects of gender). The past 10 years of BASE-II research have shown that multidisciplinary collaboration is not only a statement of intent, but a fruit-bearing working posture and a clear strength of BASE-II.

Sampling bias is a challenge which cohort studies have to deal with, and this is especially an issue in the follow-up of older study populations such as the older group of BASE-II participants. To address this, we have made a considerable effort (eg, offering a taxi service for participants not able to travel independently) to include as many participants in the follow-up as possible. Additionally, and similar to baseline, we are able to systematically quantify the sampling bias and even account for it when it comes to the question of generalisability of study results to a population as a whole (eg, Berlin or Germany), due to the evaluation of selectivity and representativeness via the German Socio-Economic Panel Study (SOEP).[1] Despite these possibilities, we cannot rule out the possibility of a selection bias completely, which certainly is a weakness of this study, a weakness that applies to all cohort studies relying on voluntary participants who have been non-randomly recruited. With our direct comparability to the national representative SOEP study, we are in a position though to quantify the amount of selectivity and, if need, take measures to correct and adjust our results.

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PI Ilja Demuth at ilja.demuth@charite.de to obtain additional information about the GendAge study and the data-sharing application form.

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