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Cohort Profile

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Cohort Profile: The LIFE-Adult-Study

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Why was the cohort set up?

Population-based cohort studies are an essential foundation for investigating associations of genetic and non-genetic risk factors with the occurrence of diseases. Several such studies have been initiated in Germany over the past decades focusing on specific phenotypes and diseases.[1–5] In 2009, the Leipzig Research Centre for Civilization Diseases (LIFE) was established to set up population-based and patient-based cohorts with

Key Features

- The LIFE-Adult-Study is a population-based cohort study investigating the prevalence and incidence of common diseases and subclinical disease phenotypes, the complex interactions between genetic and lifestyle factors regarding the co-occurrence and development of subclinical phenotypes and diseases, and the role of biomarkers to predict disease initiation and progression.
- The study comprises an age-stratified and sex-stratified random sample of 10 000 adult individuals (aged 18–79 years) from Leipzig, Germany. The baseline assessment was conducted from August 2011 to November 2014 and the first follow-up was conducted from October 2017 to August 2021. A total of 5512 individuals completed postal follow-up questionnaires and 1799 individuals participated in a physical examination follow-up programme.
- The study focuses on cardiovascular and metabolic disorders, cognition and brain function, depression, sleep disorders and electroencephalography-vigilance regulation, eye diseases, voice and allergies. The assessment programme comprises physical and medical examinations, personal interviews, self-administered questionnaires, psychometric tests, and clinical chemistry from blood and urine samples (including biobank asservation).
- Data usage requests can be submitted to: Dr Christoph Engel, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Haertelstrasse 16–18, 04107 Leipzig, Germany, e-mail: christoph.engel@imise.uni-leipzig.de.

comprehensive molecular characterization and deep disease phenotyping programmes for a broad spectrum of common diseases. LIFE focuses on the characterization of subclinical disease phenotypes and the identification of determinants predicting their progression to clinically manifest disease. It is part of the Medical Faculty of Leipzig University, enabling the participation of clinicians, epidemiologists and methodologists researchers experienced in molecular and genetic profiling, biostatistics and bioinformatics. LIFE is funded by the European Union, the European Regional Development Fund and funds of the Free State of Saxony, Germany.

One of the main cohort studies of LIFE is the 'LIFE-Adult-Study'—a population-based study of 10 000 randomly selected adult citizens of Leipzig, a city with currently ~600 000 inhabitants. The LIFE-Adult-Study pursues three major goals: (i) to assess the prevalence and incidence of common diseases and subclinical disease phenotypes, (ii) to investigate the complex interactions between genetic and lifestyle factors regarding co-occurrence and development of subclinical phenotypes and diseases and (iii) to investigate longitudinally the role of biomarkers to predict risks for disease initiation and progression. The study focuses on primarily age-related clinical phenotypes: cardiovascular disorders, metabolic disorders, cognition and brain function, depression, sleep disorders and electroencephalography-vigilance regulation, eye diseases with a focus on retinal degeneration, voice and allergies. Other major LIFE cohort studies are the 'LIFE-Child-Study' and the 'LIFE-Heart-Study'.[6,7] An up-to-date list of all publications of LIFE is available at https://www.uniklinikum-leipzig.de/einrichtungen/life/life-forschungszentrum/publikationen.

Who is in the cohort?

Details on the design of the LIFE-Adult-Study are described elsewhere.[8] Briefly, the study comprises an age-stratified and sex-stratified random sample of 10 000 residents of the city of Leipzig, who were mostly of central European descent. Participants are 18–79 years of age, with a focus on individuals aged between 40 and 79 years. Address lists of randomly sampled citizens were provided by the resident's registration office of the city of Leipzig. In the age group of 40–79 years, a total of 29 535 citizens were invited to participate in the study, of whom 31.0% took part, 29.0% refused participation and 36.3% did not respond. The remaining individuals (3.7%) could not be successfully contacted or did not participate despite declaring their willingness. Among 2386 individuals aged 18–39 years, 16.6% were willing to participate in the study, 22.0% refused to take part and 61.4% did not respond. Figure 1 shows the planned and achieved sample sizes. The baseline recruitment and examination of the 10 000 study participants were conducted from August 2011 until November 2014. A comparison of study participants with both the Leipzig population and non-participants using official statistics and short questionnaire data showed that study participants were less often elderly women and more often married, highly educated, employed, healthier and current non-smokers compared with both the Leipzig population and non-participants.[9]

How often have they been followed up?

The baseline data collection (questionnaires and physical examinations) was performed at the study centre of the LIFE-Adult-Study. All study participants underwent a core assessment programme with an average duration of 5–6 h within 1 day ('core programme'). Participants aged ≥65 years (or ≥60 years since March 2013) were invited to take part in two additional assessment programmes, particularly with magnetic resonance imaging (MRI), which were scheduled shortly after the core

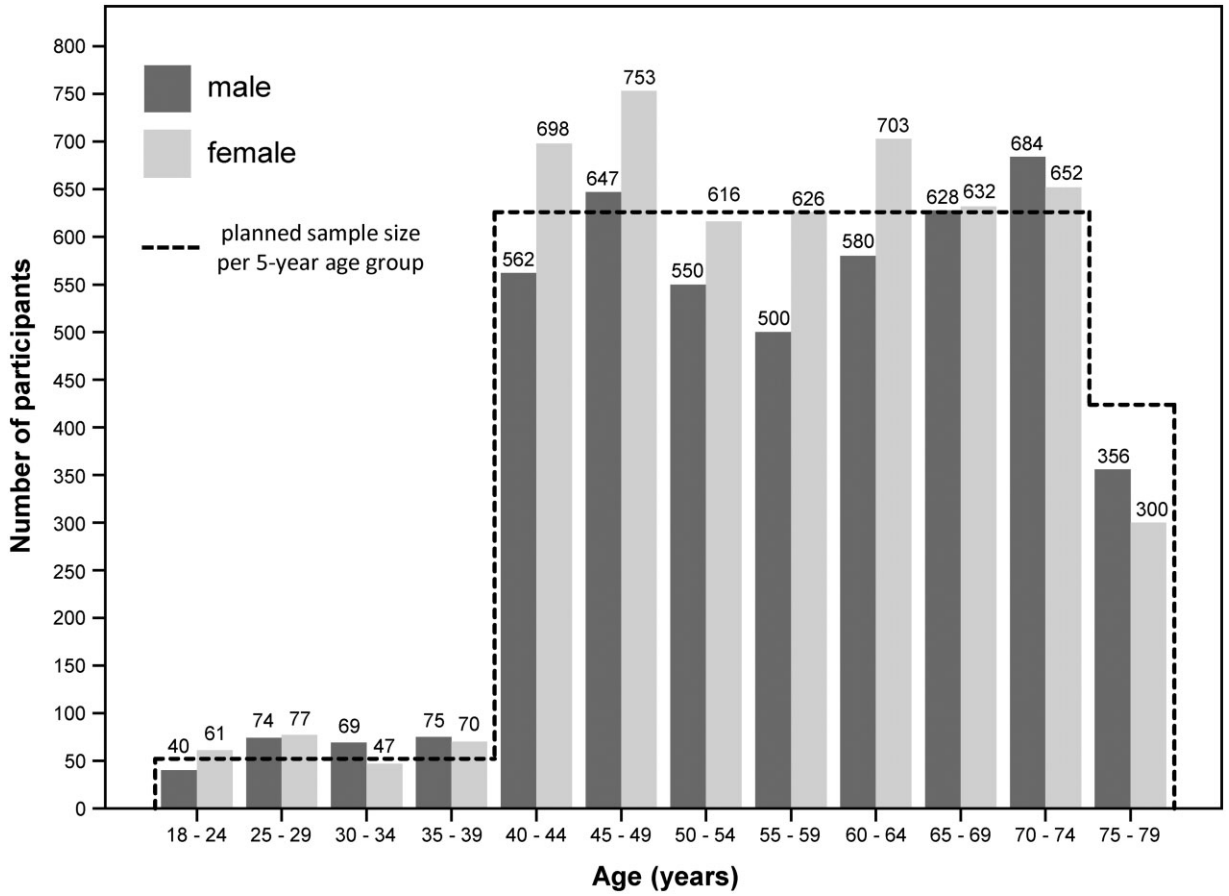

Figure 1 Planned and achieved sample size (baseline recruitment)

programme visit on 2 separate days with an average duration of 3–4 h each.

The first follow-up phase started in October 2017 with a questionnaire-based postal interview of all participants of the baseline round. In addition, participants who underwent MRI at baseline were reinvited for physical examinations at the study centre. The first follow-up ended in August 2021. A total of 6115 individuals joined the first follow-up phase, of whom 1799 also joined the examination programme at the study centre. Non-participation (3885 individuals) was due to death ($n = 450$), active refusal ($n = 788$), loss to follow-up ($n = 61$) or non-response ($n = 2586$).

Follow-up participants had a mean age of 64 years at invitation and 53% were female. Individuals who actively refused participation were older on average (69 years) and more often female (57%). Non-responders were younger (59 years) and only slightly more often female (54%) compared with participants.

What has been measured?

Baseline assessment (August 2011–November 2014)

The baseline assessment programme comprised physical and medical examinations (Table 1), computer-assisted personal interviews, computer-based or paper-based self-administered questionnaires, psychometric tests (Table 2) and clinical chemistry from blood and urine samples (Table 3). The first additional programme for participants aged ≥65 years (or ≥60 years since March 2013) focused on cognitive function and included a brain MRI. The second additional programme comprised detailed assessments of depressive symptomatology and vigilance, including multi-paradigm electroencephalography.

First follow-up assessment (October 2017–August 2021)

The follow-up programme consisted of two parts: (i) a set of paper-based self-administered questionnaires sent out to all 10 000 baseline participants and (ii) a 2- to 3-day programme of different physical examinations at the study centre. Tables 1–3 provide an overview of the physical examinations, interviews, questionnaires, tests and laboratory analyses conducted during the follow-up. A number of assessments was newly introduced, e.g. bioelectrical impedance analysis, ultrasound of lower limb arteries, 7-day

Table 1 Physical examinations and assessments of adults in the LIFE-Adult-Study cohort at baseline and follow-up

Examination	Baseline	Follow-up
Bio-specimen asservation		
Serum, plasma, dried blood spot cards, whole blood	A	S
Peripheral blood mononuclear cells (PBMC)	A	–
DNA, RNA	A	–
Urine	A	–
Anthropometry		
Classical: body weight, body height, circumference measures	A	S
3D laser-based optical body surface scan	A	S
MRI-based abdominal fat tissue volumetry	S	–
Bioelectrical impedance analysis (BIA)	–	S
Cardiovascular system		
Blood pressure	A	S
Electrocardiogram (10 s, 12 leads)	A	S
Echocardiography	A	–
Carotid ultrasound	A	S
Ankle-brachial index (ABI), pulse wave velocity (PWV)	–	S
Ultrasound of leg arteries (A. fem. comm., A. fem. superf., A. popl.)	–	S
7-day electrocardiogram	–	S
Diabetes		
Oral glucose tolerance test (OGTT)	S	–
Physical activity and fitness		
Hand grip strength	A	–
7-day actimetry	A	–
Eye		
Optical coherence tomography and fundus photography	A	S
Visual acuity measurement	–	S
Ocular biometry	–	S
Autorefractometry	–	S
Brain		
MRI	S	S
Electroencephalography	S	S
Liver		
Transient liver elastography	–	S
Miscellaneous		
Voice profile	S	–
Olfactory test (Sniffin' sticks 12)	S	S
Skin prick test (six inhalative allergens)	A	–
Measurement of skin ageing	–	S

A, all participants; S, subgroup; MRI, magnetic resonance imaging; A. fem. comm., femoral artery; A. fem. superf., superficial femoral artery; A. popl., popliteal artery.

electrocardiogram, transient liver elastography, visual acuity measurement, ocular biometry and autorefractometry.

A main goal of the follow-up was to obtain additional health-related data from external sources such as health

Table 2 Computer-assisted personal interviews (I), self-administered questionnaires (Q) and cognitive tests (T)

	Baseline	Follow-up	
Assessment	(physical)	(written)	(physical)
Socio-demographics and medical history			
Socio-demographics and socio-economic status	I	Q	I
Medical history	I	Q	Q
Family medical history	I	Q	–
Medication (last 7 days)	I	Q	I
Allergies	I	Q	–
Male and female gender questions	Q	–	Q
Immune competence	Q	–	–
Oral health	Q	Q	–
Pneumonia	–	Q	–
Language skills	–	–	I
Place of residence biography	–	Q	Q
Life style			
Smoking	I/Q	Q	–
Food frequency and alcohol consumption	Q	Q	–
International Physical Activity Questionnaire (IPAQ)	Q	Q	–
Three-Factor-Eating Questionnaire (TFEQ)	Q	–	–
Yale Food Scale	Q	–	Q
E-cigarette use	–	Q	–
Eating behaviour	–	–	Q
Sun exposition of the skin	–	–	I
Use of green areas	–	Q	–
Housing situation and noise	–	Q	–
Psychosocial aspects			
Satisfaction with Life Scale (SWLS)	Q	Q	–
Generalized Anxiety Disorder (GAD-7)	Q	Q	–
Patient Health Questionnaire-15 (PHQ-15)	Q	Q	–
SF-8 Health Survey	Q	Q	–
Life Orientation Test Revised (LOT-R)	Q	Q	–
ENRICHD Social Support Instrument (ESSI)	Q	Q	–
Personality Adjective List (16 AM)	Q	–	–
Lubben Social Network Scale (LSNS)	Q	Q	–
EuroQol Visual Analogue Scale (EQ VAS)	Q	–	–
Sense of Coherence Leipzig Short Scale (SOC-L9)	Q	–	Q
	Q	–	–

(Continued)

Table 2 Continued

Assessment	Baseline (physical)	Follow-up (written)	Follow-up (physical)
Childhood Trauma Screener (CTS)			
Use of healthcare services	Q	–	–
Barratt's Impulsivity Scale Version 11 (BIS-11)	Q	–	Q
Behavioural inhibition system/ behavioural activation system (BIS/BAS)	Q	–	Q
NEO-Five-Factor Inventory (NEO-FFI-30)	Q	–	Q
Need Inventory of Sensation Seeking (NISS)	Q[a]	–	–
Hypomanic Personality Scale (HPS)	Q[a]	–	–
State-Trait Anger Expression Inventory (STAXI)	Q[a]	–	Q
The Trier Inventory for Chronic Stress (TICS)	Q[a]	–	Q
Loneliness Scale	–	Q	–
Perceived Stress Questionnaire (PSQ)	–	Q	–
Copenhagen Psychosocial Questionnaire (COPSOQ) B3, B8, B9	–	–	Q
Occupational cognitive demands (O*NET)	–	–	Q
Employee–work requirement misfit	–	–	Q
Sleep			
Pittsburgh Sleep Quality Index (PSQI)	Q	–	Q
Multidimensional Fatigue Inventory (MFI-20)	Q	–	–
Epworth Sleepiness Scale (ESS)	Q	–	Q
Morningness-Eveningness-Questionnaire (MEQ)	Q	–	–
Sleep Questionnaire (SF-A)	Q[a]	–	–
Cognition			
Stroop test	T	–	–
Trail-Making Test A&B	T	–	T
Subjective Memory Impairment	I	–	I
Verbal Fluency Test 'Animals'	T	–	T
Behavioural Assessment of the dysexecutive syndrome (DEX)	Q	–	Q
Triangle test	T[a]	–	–
Reading the mind in the eyes test	T[a]	–	T
SIDAM	I/T[a]	–	I/T
Barthel-Index for basic Activities of Daily Living (BI ADL)	I[a]	–	I
Instrumental Activities of Daily Living Scales (IADL)	I[a]	–	I
CERADplus neuropsychological test battery	T[a]	–	T
Wechsler Memory Scale (WMS)	T[a]	–	–
Iowa Gambling Task (IGT)	T	–	–
n-back task	T	–	–
Reversal learning task	T	–	–
Mnemonic Similarity Task (MST)	–	–	T
Depression			
Centre of Epidemiologic Studies—Depression Scale (CES-D)	Q	–	Q
Childhood Trauma Questionnaire (CTQ)	Q	–	–
CIDI DIA-X Screener	Q	–	–
Structured Clinical Interview for DSM Disorders (SCID)	I[a]	–	–
Geriatric Depression Scale (15-item version, GDS-15)	Q[a]	–	Q[b]
Inventory of Complicated Grief (ICG)	Q[a]	–	–
Inventory of Depressive Symptoms (IDS-SR)	Q[a]	–	Q[b]
Leipzig Life Event List	Q[a]	–	Q
Stress Appraisal Measure (SAM)	–	–	Q
Copenhagen Burnout Inventory (CBI)	–	–	Q

[a]Only aged 60–79 years.

[b]Only participants who underwent the electroencephalography assessment.

SIDAM, Structured Interview for the diagnosis of Dementia of the Alzheimer type, Multi-infarct dementia and dementias of other etiology according to ICD-10, DSM-III-R and DSM-IV; CERAD, Consortium to Establish a Registry for Alzheimer's Disease; CIDI DIA-X, Composite International Diagnostic Interview Diagnostic Expert System.

insurances, cancer registries, general practitioners and specialized physicians. Therefore, participants were asked to provide their specific consent for record linkage. Up to March 2021, health insurance data for 1800 participants were obtained. Self-reported changes of health status are validated through a process of requesting confirmations by the treating physicians. In addition, the vital status of 98.6% of the participants was updated with the public population register.

What has it found? Key findings and publications

Tables 4–8 summarize selected characteristics of the 10 000 participants by sex and age group. Data from the

Table 3 Laboratory analyses and biomaterials

Parameter
Electrolytes: Sodium, Potassium, Chloride, Magnesium
Liver and pancreas: Alanine transaminase, Aspartate transaminase, Choline esterase, Gamma-glutamyltransferase, Bilirubin (total and direct), Lipase, Total protein, Albumin, Urea
Kidney: Creatinine, Cystatin C
Cardiac markers: Creatine kinase, Creatine kinase MB, Myoglobin, Troponine T high sensitive, N-terminal prohormone of brain natriuretic peptide
Lipid metabolism: Cholesterol, High density lipoprotein cholesterol, Low density lipoprotein cholesterol, Apolipoprotein B, Apolipoprotein A1, Trigycerides, Lipoprotein (a)
Glucose metabolism: Glucose, Insulin, C-peptide, Glycated haemoglobin (HbA1c)
Iron metabolism: Transferrin, Ferritin
Vitamins: Folic acid, Vitamin B12
Bone metabolism: Alkaline phosphatase, Phosphate, Calcium, Osteocalcine, Beta-CrossLaps, Propeptide of type I collagen, Parathormone, 25-Hydroxy vitamin D3
Endocrine function/hormones: Cortisol, Luteinizing hormone, Follicle stimulating hormone, Estradiol, Testosterone, Sex hormone-binding globulin, Dehydroepiandrosterone sulphate
Thyroid: Thyrotropin (TSH), Free triiodothyronine, Free thyroxine, TSH receptor antibodies, thyroglobulin antibodies, Thyreoperoxidase antibodies
Inflammatory mediators: Interleukin 6, C-reactive protein high sensitive
Allergy diagnostics: Specific immunoglobulin E sx1 (timothy grass, rye, birch, mugwort, *Cladosporium herbarum*, *Dermatophagoides pteronyssinus*, cat, dog), fx5 (hen's egg, cow's milk, fish, wheat, peanut, soy), total immunoglobulin E
Hematology: Complete blood cell count with differential, Reticulocytes
Urine: Albumin, Creatinine, Immunoglobulin G
Targeted metabolomics: Amino acids/acylcarnitines, Plant sterols and cholesterol precursors, Trimethylaminoxid and precursors, Oxysterols and bile acids
Targeted proteomics: Apolipoprotein profile

baseline assessments served as the basis of a large number of published data analyses and research projects (see Supplementary File 1, available as Supplementary data at *IJE* online, for a full list of publications). Selected published results are briefly presented in the following paragraphs. Additional selected results are described in Supplementary File 2 (available as Supplementary data at *IJE* online).

Brain MRI studies

A major goal of the LIFE-Adult-Study is to investigate structural and functional brain alterations and their associations with a broad spectrum of phenotypes and disease susceptibility. Using high-resolution 3-Tesla MRI, we found that higher body mass index, higher systolic blood pressure, smoking and higher HbA1c blood levels were associated with altered grey and white matter (micro) structure, even in young to middle-aged adults.[10–18] These changes translated into subtle changes in cognitive performance, such as verbal fluency and memory. Moreover, visceral fat accumulation was related to lesions in the deep white matter through higher levels of interleukin-6 in blood, indicative of low-grade systemic inflammation as a pathomechanistic link.[19] Evidence integrating measures of neuroimaging and metabolic imaging, sex hormones and cognition supports differences in women and men in the association of visceral adipose tissue with structural brain networks important for memory.[20] In women, higher estradiol levels were associated with increased structural brain network covariance and cognitive performance during mid-life. In sum, these findings highlight the need for early preventive and therapeutic strategies to reduce cardiovascular and metabolic risk factor-mediated brain damage.

Cognition studies

Another major objective of the LIFE-Adult-Study is to characterize neurodegenerative diseases and their prodromal stages based on questionnaires and neuropsychological tests (Table 2). We obtained new empirical data on the prevalence of mild neurocognitive disorder (miNCD) and types of impaired neurocognitive domains. We found a substantial proportion (20%) of older adults having miNCD.[21] We also found that memory-related subjective cognitive symptoms are very common and unspecific in the non-demented adult population aged 40–79 years.[22] We provided new age-specific, sex-specific and education-specific reference values for the cognitive performance of

Table 4 Basic characteristics of study participants at baseline examination

	Men			Women		
	18–39	40–59	60–79	18–39	40–59	60–79
	n = 258	*n* = 2259	*n* = 2248	*n* = 255	*n* = 2693	*n* = 2287
CASMIN classification	*n* = 258	*n* = 2254	*n* = 2240	*n* = 254	*n* = 2688	*n* = 2278
Low education	14 (5.4)	111 (4.9)	321 (14.3)	12 (4.7)	76 (2.8)	393 (17.3)
Medium education	149 (57.8)	1552 (68.9)	1204 (53.8)	146 (57.5)	1911 (71.1)	1474 (64.7)
High education	95 (36.8)	591 (26.2)	715 (31.9)	96 (37.8)	701 (26.1)	411 (18.0)
BMI WHO category	*n* = 258	*n* = 2253	*n* = 2231	*n* = 254	*n* = 2690	*n* = 2278
BMI <25 (normal weight, including underweight)	154 (59.7)	712 (31.6)	476 (21.3)	198 (78.0)	1286 (47.8)	645 (28.3)
BMI 25 to <30 (pre-obesity)	80 (31.0)	1030 (45.7)	1110 (49.8)	42 (16.5)	835 (31.0)	923 (40.5)
BMI ≥30 (obesity)	24 (9.3)	511 (22.7)	645 (28.9)	14 (5.5)	569 (21.2)	710 (31.2)
Waist circumference (cm), mean ± SD	*n* = 258	*n* = 2249	*n* = 2230	*n* = 254	*n* = 2687	*n* = 2275
	89.1 ± 11.0	99.3 ± 12.3	104.1 ± 11.0	80.0 ± 9.9	90.1 ± 13.4	95.6 ± 12.1
Blood pressure	*n* = 256	*n* = 2246	*n* = 2224	*n* = 254	*n* = 2663	*n* = 2259
Systolic (mmHg), mean ± SD	125.2 ± 10.4	129.7 ± 13.8	135.1 ± 17.5	113.4 ± 9.4	121.2 ± 14.9	132.1 ± 18.4
Diastolic (mmHg), mean ± SD	72.3 ± 8.7	79.0 ± 9.6	75.1 ± 10.0	68.9 ± 7.7	75.0 ± 9.5	73.6 ± 9.7
Hypertension prevalence	*n* = 252	*n* = 2233	*n* = 2193	*n* = 247	*n* = 2650	*n* = 2216
	35 (13.9)	934 (41.8)	1628 (74.2)	8 (3.2)	775 (29.2)	1534 (69.2)
Maximum handgrip strength, mean ± SD	*n* = 193	*n* = 2027	*n* = 2056	*n* = 202	*n* = 2439	*n* = 2089
	48.2 ± 9.6	47.3 ± 9.0	39.3 ± 8.4	30.2 ± 5.1	29.3 ± 6.1	24.6 ± 5.7
Smoking	*n* = 258	*n* = 2225	*n* = 2110	*n* = 250	*n* = 2640	*n* = 2107
Never smoker	127 (50.4)	835 (38.3)	828 (38.8)	144 (59.0)	1252 (48.2)	1494 (70.3)
Former smoker	34 (13.5)	670 (30.7)	1011 (47.4)	41 (16.8)	642 (24.7)	407 (19.2)
Current smoker	97 (38.5)	720 (33.0)	271 (12.7)	65 (26.6)	746 (28.7)	206 (9.7)
Medication: number of drugs taken within last 7 days	*n* = 252	*n* = 2256	*n* = 2246	*n* = 249	*n* = 2688	*n* = 2283
0	143 (56.7)	875 (38.8)	258 (11.5)	58 (23.3)	491 (18.3)	185 (8.1)
1	60 (23.8)	492 (21.8)	253 (11.3)	82 (32.9)	703 (26.2)	280 (12.3)
2–4	46 (18.3)	671 (29.7)	862 (38.4)	97 (39.0)	1112 (41.4)	935 (41.0)
5+	3 (1.2)	218 (9.7)	873 (38.9)	12 (4.8)	382 (14.2)	883 (38.7)

Numbers represent absolute counts and numbers in brackets represent percentages, unless otherwise specified. CASMIN, Comparative Analysis of Social Mobility in Industrial Nations; BMI, body mass index; WHO, World Health Organization.

older German-speaking adults.[23] Another study revealed that lower executive functioning performance in cognitively intact older apolipoprotein E epsilon (APOE) 4 allele carriers might be related to an early Alzheimer's dementia prodrome.[24]

3D laser-based anthropometry

For the first time in epidemiology, we applied laser-based 3D whole-body scanning (3D-BS) for anthropometry. This method allows the determination of >150 anthropometric variables by a single scan with a duration of ∼10 s. Most of these variables showed good intra-observer and inter-observer reliability.[25] Using self-organizing maps, we identified 15 clusters of human body shapes, most of which were sex-specific.[26,27] 3D-BS provides a more detailed description of the human body shape beyond traditional measures such as body mass index and waist-to-hip ratio. We also used 3D-BS to validate commonly used empirical formulae for calculating the body surface area, which is essential for many medical applications.[28]

Optical coherence tomography (OCT) of the retina

The retinal nerve fibre layer thickness (RNFLT) around the optic nerve head (circumpapillary RNFLT, cpRNFLT) is important to detect optic neuropathies like glaucoma and to monitor their progression. We applied OCT to provide a detailed quantitative description of cpRNFLT at a so-far unprecedented resolution of 768 angular locations.[29] In addition to age-dependent differences, we determined estimates of the true scanning diameter, which is a measure of individual eye anatomy.[29] We found a considerable sex-dependency of RNFLT, which is currently not considered in existing normative data sets.[30] In addition, we described cpRNFLT differences between right and left eyes.[31] These norms are accessible as part of the RNFLT(D)-Visualizer application via https://apps.health-atlas.de/rnflt-visualizer. We found markers of renal function and lipid metabolism

Table 5 Sleep quality at baseline examination

	Men			Women		
	18–39 $n=258$	40–59 $n=2259$	60–79 $n=2248$	18–39 $n=255$	40–59 $n=2693$	60–79 $n=2287$
Diurnal preference (D-MEQ)	$n=252$	$n=2146$	$n=1886$	$n=240$	$n=2484$	$n=1789$
Definitive evening type	4 (1.6)	15 (0.7)	0 (0.0)	5 (2.1)	11 (0.4)	3 (0.2)
Moderate evening type	43 (17.1)	121 (5.6)	22 (1.2)	27 (11.3)	134 (5.4)	42 (2.3)
Neutral type	157 (62.3)	989 (46.1)	561 (29.7)	149 (62.1)	1260 (50.7)	663 (37.1)
Moderate morning type	46 (18.3)	900 (41.9)	1072 (56.8)	56 (23.3)	952 (38.3)	884 (49.4)
Definitive morning type	2 (0.8)	121 (5.6)	231 (12.2)	3 (1.3)	127 (5.1)	197 (11.0)
Actigraphy-based sleep duration (night–day cycles[a])	$n=57$	$n=501$	$n=604$	$n=58$	$n=709$	$n=634$
Short sleep duration (<6 h)	27 (47.4)	184 (36.7)	144 (23.8)	17 (29.3)	140 (19.7)	98 (15.5)
Medium sleep duration (6–8 h)	30 (52.6)	296 (59.1)	382 (63.2)	36 (62.1)	503 (70.9)	430 (67.8)
Long sleep duration (>8 h)	0 (0.0)	21 (4.2)	78 (12.9)	5 (8.6)	66 (9.3)	106 (16.7)
Actigraphy-based sleep efficiency (night–day cycles[a])	$n=57$	$n=501$	$n=604$	$n=58$	$n=709$	$n=634$
Low sleep efficiency (<70%)	6 (10.5)	65 (13.0)	86 (14.2)	9 (15.5)	43 (6.1)	40 (6.3)
Medium efficiency (70–85%)	40 (70.2)	280 (55.9)	327 (54.1)	38 (65.5)	353 (49.8)	317 (50.0)
High sleep efficiency (>85%)	11 (19.3)	156 (31.1)	191 (31.6)	11 (19.0)	313 (44.1)	277 (43.7)

Numbers represent absolute counts and numbers in brackets represent percentages, unless otherwise specified.

[a]Night–day cycles were defined as duration from individual bedtime on Day 1 and individual bedtime on Day 2 (for further details on the actigraphic assessment, see[37]). The analysis included all individuals with at least five evaluable night–day cycles in the 1-week actigraphy.

D-MEQ, German Morningness-Eveningness Questionnaire.

Table 6 Allergy at baseline examination

	Men			Women		
	18–39 $n=258$	40–59 $n=2259$	60–79 $n=2248$	18–39 $n=255$	40–59 $n=2693$	60–79 $n=2287$
Skin prick test[a]	$n=181$	$n=1524$	$n=1316$	$n=167$	$n=1689$	$n=1298$
Ambrosia	11 (6.1)	65 (4.3)	36 (2.7)	7 (4.2)	60 (3.6)	42 (3.2)
Birch	64 (35.4)	296 (19.4)	135 (10.3)	32 (19.2)	234 (13.9)	98 (7.6)
Timothy grass	49 (27.1)	268 (17.6)	141 (10.7)	28 (16.8)	298 (17.6)	174 (13.4)
Mugwort	24 (13.3)	86 (5.6)	31 (2.4)	9 (5.4)	70 (4.1)	15 (1.2)
Alternaria	29 (16.0)	179 (11.7)	85 (6.5)	19 (11.4)	172 (10.2)	90 (6.9)
House dust mite (Dermatophagoides pt.)	49 (27.1)	131 (8.6)	95 (7.2)	23 (13.8)	126 (7.5)	44 (3.4)
Allergy questionnaire[a]	$n=233$	$n=2119$	$n=2096$	$n=224$	$n=2464$	$n=2124$
Urtikaria	18 (7.7)	104 (4.9)	72 (3.4)	16 (7.1)	247 (10.0)	161 (7.6)
Anaphylaxis	6 (2.6)	43 (2.0)	43 (2.1)	7 (3.1)	98 (4.0)	65 (3.1)
Food allergy	42 (18.0)	254 (12.0)	164 (7.8)	48 (21.4)	466 (18.9)	263 (12.4)
Insect allergy	14 (6.0)	151 (7.1)	125 (6.0)	26 (11.6)	306 (12.4)	270 (12.7)

Numbers represent absolute counts and numbers in brackets represent percentages, unless otherwise specified.

[a]Groups are not mutually exclusive.

to be independent predictors of sectoral cpRNFLT, which may improve early diagnosis of eye disease.[32]

Measurements of the speaking and singing voice

Voice range profiles are widely used in clinical practice to assess voice disorders. We employed this method in our epidemiological setting.[33] Based on the currently largest sample of 2472 speaking and singing voice profiles worldwide, we established population-based reference values of different voice parameters. We found that the fundamental frequency of females was six to seven semi-tones lower than previously described.[34] Moreover, current smokers had lower speaking voice frequencies compared with non-smokers and former smokers. An association study of the speaking voice with sex hormone levels and anthropometric parameters obtained from 3D-BS revealed that body mass index (BMI), body height, body weight, breast-to-abdomen-ratio, bioavailable testosterone and dehydroepiandrosterone sulphate were associated with the speaking voice in adults.[35]

Table 7 Selected conditions and measurements at baseline examination

	Men			Women		
	18–39	40–59	60–79	18–39	40–59	60–79
	n = 258	*n* = 2259	*n* = 2248	*n* = 255	*n* = 2693	*n* = 2287
Diabetes	*n* = 252	*n* = 2182	*n* = 2135	*n* = 244	*n* = 2599	*n* = 2125
No	225 (89.3)	1271 (58.2)	736 (34.5)	235 (96.3)	2037 (78.4)	1053 (49.6)
Yes, by medical history and/or medication	2 (0.8)	144 (6.6)	500 (23.4)	3 (1.2)	104 (4.0)	364 (17.1)
Yes, yet undiagnosed pre-diabetes	24 (9.5)	714 (32.7)	789 (37.0)	6 (2.5)	423 (16.3)	631 (29.7)
Yes, yet undiagnosed diabetes	1 (0.4)	53 (2.4)	110 (5.2)	0 (0.0)	35 (1.3)	77 (3.6)
Carotid artery characteristics						
Mean carotid intima media thickness (mm), median (IQR)	*n* = 247	*n* = 2178	*n* = 2141	*n* = 245	*n* = 2622	*n* = 2212
	0.54 (0.49 – 0.60)	0.68 (0.61 – 0.78)	0.83 (0.74 – 0.93)	0.52 (0.48 – 0.58)	0.65 (0.59 – 0.73)	0.81 (0.73 – 0.90)
Prevalence of plaque	14/243 (5.8)	751/2090 (35.9)	1604/2070 (77.5)	3/244 (1.2)	593/2567 (23.1)	1278/2154 (59.3)
Psychological and health variables						
Anxiety (GAD-7), mean ± SD	*n* = 255	*n* = 2226	*n* = 2134	*n* = 255	*n* = 2669	*n* = 2180
	2.92 ± 3.03	3.19 ± 3.26	2.83 ± 2.97	3.90 ± 3.28	4.27 ± 3.74	3.85 ± 3.27
Bodily complaints (PHQ-15), mean ± SD	*n* = 255	*n* = 2180	*n* = 2000	*n* = 255	*n* = 2594	*n* = 1966
	3.71 ± 2.80	4.38 ± 3.39	5.00 ± 3.83	5.63 ± 3.74	6.18 ± 4.02	6.58 ± 4.12
Satisfaction with Life Scale (SWLS), mean ± SD	*n* = 256	*n* = 2233	*n* = 2123	*n* = 255	*n* = 2665	*n* = 2177
	26.50 ± 5.26	25.50 ± 5.90	27.20 ± 5.06	26.80 ± 5.35	26.30 ± 5.75	26.90 ± 5.31
Optimism (LOT-R, total score), mean ± SD	*n* = 255	*n* = 2240	*n* = 2133	*n* = 255	*n* = 2663	*n* = 2163
	16.80 ± 4.00	16.20 ± 3.89	15.90 ± 3.52	17.10 ± 3.96	16.70 ± 4.02	15.90 ± 3.57
Olfactory dysfunction	*n* = 202	*n* = 1700	*n* = 1576	*n* = 184	*n* = 1998	*n* = 1607
Anosmic	1 (0.5)	47 (2.8)	177 (11.1)	1 (0.5)	33 (1.7)	112 (7.0)
Dysosmic	53 (26.2)	851 (50.1)	984 (62.4)	61 (33.2)	925 (46.3)	934 (58.1)
Normosmic	148 (73.3)	802 (47.2)	415 (26.3)	122 (66.3)	1040 (52.1)	561 (34.9)
Retinal nerve fibre layer thickness (μm), mean ± SD	*n* = 194	*n* = 1644	*n* = 1194	*n* = 191	*n* = 1981	*n* = 1267
	97.6 ± 8.8	97.6 ± 9.1	95.2 ± 10.1	98.9 ± 8.6	98.4 ± 8.9	96.5 ± 9.4

Numbers represent absolute counts and numbers in brackets represent percentages, unless otherwise specified. GAD-7, Generalized Anxiety Disorder (7 items); PHQ-15, Patient Health Questionnaire (15 items); SWLS, Satisfaction with Life Scale; LOT-R, Life Orientation Test Revised.

Table 8 Omics measurements at baseline examination

Omics layer	Technique	Sample size	References
Genetics	Affymetrix Axiom CEU1 SNP-array	7669	38–53
Transcriptomics	Illumina HT12-v4	3359	54
Proteomics	Olink Cardiovascular III	2016	–
Metabolomics (amino acids and acylcarnitines)	LC–MS/MS	9622	55
Phytosterols/zoosterols	LC–MS/MS	1689	56
Steroid hormones	ECLIA, LC–MS/MS	8329	50,57
Adipokines	ELISA	3111	–
Cytomics	10-color flow cytometry	1365	58–61

LC–MS/MS, liquid chromatography—mass spectrometry and liquid chromatography—tandem mass spectrometry; ECLIA, electrochemiluminescence immunoassay.

What are the main strengths and weaknesses?

The LIFE-Adult-Study is a large population-based epidemiological study with uniquely deep phenotyping and a comprehensive assessment of psychosocial and lifestyle factors. A specific strength of the assessment programme is its particularly detailed characterization of subclinical phenotypes, with emphasis on anthropometry, cognition, depression, vascular diseases and retinal health. To the best of our knowledge, our study was the first to employ a 3D body scanner to collect >150 anthropometric parameters from each participant within a population-based epidemiological research setting. The LIFE-Adult-Study provides the largest population-based data set worldwide on voice range profiles for the singing and speaking voice to date. Moreover, we have initiated a structured process to validate self-reported medical events by contacting the attending physicians of the participants. In addition, we have initiated a record-linkage process with the participants' health insurance companies as well as with the registers providing mortality data.

The representativeness of our study was limited due to selective participation. A comparison of study participants aged 40–79 years with both the Leipzig population and non-participants using official statistics and short questionnaire data suggested that participation was associated with higher social status, healthier lifestyle and lower burden of disease.[9] Even though analyses corrected for this bias by applying sampling weights, frequencies of major health conditions in the general population are likely to be underestimated. The external validity, i.e. generalizability, of our regional study must be considered limited with respect to the estimation of disease prevalences and incidences, as these are known to differ across different regions in Germany. However, this limitation should affect associative data analyses less.

Can I get hold of the data? Where can I find out more?

We welcome collaborations with external researchers and have already extensively shared data and biospecimens. Use and access of data comply with the FAIR criteria.[36] A data portal has been established to search for available data. Selected data sets are available on a data-sharing portal (https://www.health-atlas.de/). For access to any data or biosamples, it is mandatory to submit a detailed written proposal describing the background, objectives, methods, timelines, names and affiliations of all researchers involved; the type and scope of requested data and biomaterial; the publication and exploitation strategy; and how results and newly generated data will be returned for further use. Upon review and approval by the Use-and-Access Committee, data and samples can be provided. Specific contracts and data or material transfer agreements may be necessary, particularly for researchers from countries not bound to the EU General Data Privacy Regulation. All enquiries should be directed via e-mail to Dr Christoph Engel (E-mail: christoph.engel@imise.uni-leipzig.de).

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Ethics approval

The LIFE-Adult-Study is conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Medical Faculty of Leipzig University (approval numbers 263–2009-14122009, 263/09-ff, 201/17-ek). Written informed consent was obtained from all participants.

Data availability

See 'Can I get hold of the data?' above.

Supplementary data

Supplementary data are available at *IJE* online.

Author contributions

C.Eng. wrote the manuscript with contributions from K.W., S.Z., R.B., U.C., C.Enz., M.F., A.H., F.G.R., M.R., S.R., J.S., C.S., R.T., A.V.W., M.S. and M.L. The study was designed by C.Eng., K.W., S.Z., J.T., M.S. and M.L., who act as guarantors for the paper. C.Eng., K.W., S.Z., R.B., H.B., U.C., C.Enz., M.F., A.Ha., A.Hi., F.G.R., S.G.R.H., J.S., C.S., M.L.S., A.T., R.T., A.V., R.W., A.V.W., J.T., M.S. and M.L. designed the examination and questionnaire programme of the study. K.W. was responsible for the study centre. R.B., U.C., A.T. and J.T. were responsible for the biobank and laboratory analyses. S.Z. was responsible for secondary data validation. C.Enz., S.H. and M.R. were responsible for data management and quality control. C.Eng., K.W., S.Z., C.Enz., A.Hi., F.G.R., M.R., S.R., C.S., R.T., A.V.W. and M.S. performed the data analyses shown in Tables 4–8. M.L. and J.T. obtained funding for the study. All authors read and approved the final manuscript.

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Conflict of interest

None declared.

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