

FACT SHEET

THE GERMAN NATIONAL COHORT

1. OVERVIEW The German National Cohort (GNC) is a joint interdisciplinary endeavor which is being implemented by a national network of 25 German research institutions. Its overall aim is to investigate the causes underlying major chronic diseases, i.e. cardiovascular diseases, cancer, diabetes, neurodegenerative/-psychiatric diseases, respiratory and infectious diseases, and their pre-clinical stages or functional health impairments. In each of 18 study centers, spread across Germany, a random population sample of 100,000 women and 100,000 men aged 20-69 years is being drawn for a broad range of baseline examinations. These include an interview and self-completion questionnaires, several medical examinations and the collection of biological material (blood, urine, saliva, nasal swabs and stool). In a random by selected subgroup of 20 % of the participants (n = 40,000) an intensified examination („Level 2“) program is being performed. In addition, in five of the 18 study centres a total of 30,000 study participants will be examined by magnetic resonance imaging (MRI). These participants will also be offered the intensified Level 2 examinations. All participants will be invited for a re-assessment after 4 years. Information about chronic disease endpoints will be collected through a combination of active follow-up (including questionnaires every 2-3 years) and record linkage. The GNC is planned for an overall duration of 25-30 years. It will provide a major, central resource for population-based epidemiology in Germany, and will help to develop novel strategies for early detection, prediction, and primary prevention of major diseases.

2. HISTORY

The planning of the GNC started in 2009, and led to a detailed study protocol that was reviewed by a panel of international experts in 2011. Between 2011 and 2013, two series of pretest studies were conducted, to test interview and examination procedures, to train field staff and to build up logistic and organizational structures for the future recruitment of study participants at each of the 18 study centers. In December 2013 the GNC was launched, starting with part A (convenience sample; followed by the overall testing of study procedures), part B (random

population sample; implementing the full range of available Level 1 examination modules) and the interim phase (random sample; all Level 1 modules implemented; successively implementing Level 2 modules). The main phase – covering all examinations selected for the study – started in October 2014.

3. STUDY OBJECTIVES

The GNC is designed to address research questions concerning a broad range of potential causes of major disease groups. The repeated collection of biomaterials in combination with extensive information from questi-



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questionnaires and medical examinations is a basic asset of its design. Overall, four general objectives are pursued by the National Cohort, and within their general scope a number of more specific research questions will be pursued:

- i. *Identification of etiological pathways from life-style and environmental risk factors to major chronic diseases and functional impairments.*
- ii. *Assessment of the geographic and socio-economic disparities in health status and disease risks in Germany and possible causes and explanations.*
- iii. *Improvement of risk prediction models for identifying individuals at increased risk of developing major chronic diseases, so as to allow personalised prevention strategies.*
- iv. *Evaluation of markers for early detection of diseases and pre-clinical phenotypes, as to develop effective tools for disease prevention.*

4. STUDY DESIGN AND METHODS (see tables)

Data collection comprises two levels of intensity. All study subjects follow a 3 hour recruitment protocol including computer-assisted personal interview, self-completion questionnaires and physical and medical examinations (Level 1). A random sub-sample of 40.000 participants (20% per study center) completes an extended protocol with additional physical and medical examinations (Level 2). Furthermore, at five centers (Augsburg, Berlin, Essen, Mannheim and Neubrandenburg) a total of 30.000 participants will be drawn from the GNC participants to undergo a high-resolution (3 Tesla) magnetic resonance imaging (MRI) protocol. This includes whole body, cardiac, and brain images, generating a comprehensive morphological and functional data

base (MRI programme). If not already included in the Level 2 sample, MRI participants are offered to take part in all Level 2 examinations in addition to Level 1. The intensified sub-cohorts (Level 2 and MRI programme) will be used to address more detailed study questions on risk factors and early clinical precursor stages of diabetes, heart disease, and neurodegenerative disorders, in particular.

5. ETHICS AND DATA CONFIDENTIALITY

The GNC is being conducted in compliance with the Federal Data Protection Acts and all other pertinent legislation and directives, and following the guidelines of the 'Opinion of the German Ethics Council' on human bio-banks for research and other relevant directives on research ethics. A data protection concept for the GNC was developed in close collaboration with the German Federal and State Commissioners for Data Protection and Freedom of Information. An independent trust center was established to ensure proper pseudonymization of the data collected from study subjects (see www.nationale-kohorte.de/datenschutz.html). An external ethics advisory board will accompany the GNC over the full study period. The 'Code of Ethics' of the GNC ["Ethikkodex"], describes general principles for the collection and use of study data (www.nationale-kohorte.de/ethikkodex.html). Also the study is under continuous surveillance by the ethical committees of the regional study centers. Special emphasis is placed on privacy, safety of data, especially genetic information and reporting of incidental medical findings.

6. FUNDING, GOVERNANCE AND MANAGEMENT

For the first study period from 2013 to 2023, which will cover baseline



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assessment and re-assessment of all 200.000 study participants, as well as a first phase of prospective follow-up for disease occurrence, the German federal and local state governments and the Helmholtz Association cover the main part of the overall budget. A total of 210 million Euros will be provided for the first 10 years of the project. This sum is complemented by considerable in-kind contributions of each of the recruitment centers.

The German National Cohort e.V. as a registered association in which all participating research institutions are members is the central governing body. The general assembly of the association elected a board of directors who are responsible for the management of the GNC. This board includes four scientific directors and one administrative director. A committee of funders acts as a supervisory board regarding general governance questions and project decisions with major financial impact. The association's general assembly has formed several committees and working groups, including an epidemiological steering committee (composed of 1-2 scientists per participating scientific institution, and representatives of central GNC facilities), and a working group for quality management. Also, a number of scientific and thematic working groups, involving many scientists from the GNC consortium and beyond across Germany, have been very active in developing the GNC study protocol. These making groups will be continued as platforms for the planning of scientific use of the GNC data and bio-specimens. The GNC receives external guidance by a Scientific Advisory Board and an Ethical Advisory Board.

7. ACCESS TO DATA AND BIO SAMPLES

Scientific analyses of data and bio-samples will be possible immediately after completion of the baseline examinations. The rules for the access to data and bio samples have been laid down in a Use and Access Policy and agreed by the General Assembly of the GNC [see <http://www.nationalekohorte.de/nutzungsordnung.html>]. Data transfer will be handled by the transfer unit of the GNC which will be fully operational in 2017. The transfer unit will also provide a central IT-platform for data analysis.

8. APPLICATION PROCEDURE FOR LEVEL 3 STUDIES

Level 3 studies are extensions of the standard GNC research program. They may include additional data collections, examinations or bio samples for all, or parts of the cohort.

They are designed, financed, and conducted by one or more study centers. Collaborations with external partners are possible.

The Use and Access Committee is in charge of evaluating the Level 3 applications according to a clearly defined policy [see <http://www.nationalekohorte.de/level3ordnung.html>] and evaluation criteria. Applications for access to data or Level 3 studies may be submitted to the executive office in Heidelberg.



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Gefördert vom Bund,
den Ländern und der
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EXAMINATION MODULES

THE GERMAN NATIONAL COHORT

Content of the face-to-face Interview

Interview

Socioeconomic & demographic

- Migration
- Education (own, partner, parents), family net income, occupation (own, partner)
- Family state, housing

Medical history:

cardiovascular diseases, metabolic d., infections, cancer, neuro-psychiatric d., respiratory d., gastro-intestinal d., allergies, skin d., musculoskeletal/rheumatological d., kidney d., surgeries

Women's questions

Psychiatric: depression (filter questions)

Self-completion questionnaires offered as Touch-screen modules

Self-completion questionnaire (touch screen)

Smoking

Alcohol

Other drugs (illegal)

Neurologic & psychiatric factors: PHQ depression and anxiety scales (PHQ9, PHQP2, GAD7), restless legs, sleep-related factors and behavior

Family med. history: parental diabetes, cardiovascular disease, asthma, Parkinson's, dementia, depression, cancer, sudden cardiac death; age at parents' death

Psychosocial factors: Personality BIG5, PHQ Chronic stress, Effort reward imbalance, Childhood trauma, Social networks & support, Occupational insecurity, Health-related QoL (SF12)

Early life factors, weight history

Screening

Use of medical services

Pregnancy

Family planning (men)

Vision/eye diseases, hearing

Tattoos, solarium, skin diseases

Environmental factors

Occupational exposure (filter questions)

Occupational exposure (filter questions)

Infections & Immune function

Animal exposure

Physical activity (GPAQ)

Symptoms questionnaires (heart failure, chronic bronchitis, gastrointestinal)

Oral health (OHIP-5, periodontal disease)

Musculoskel. pain

Musculoskel. pain



EXAMINATION MODULES

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Self-completion questionnaire (touch screen)

WEB-based / paper versions:

- Diet [2 x 24-h recall, FFQ] (web-based)
- Physical activity pattern & 24-h recall (web-based)
- Residential history (address for linkage with environmental information) (paper-based)

Physical examinations

	Module	Level 1	Level 2
Cardiovascular system:	Blood pressure and heart rate ¹ [2x]	X	
	Resting electrocardiogram [10-s ECG; 12 leads]		X
	2D/3D echocardiography		X
	Vascular Explorer [ankle-arm index, pulse wave analysis]	X	
	Long-term ECG / apnea / accelerometric device: Somnowatch plus		X
Diabetes-related:	Oral glucose tolerance test	[X]	X
	AGE reader [skin autofluorescence]		X
Cognitive function:	Test battery [memory, concentration, dexterity]	X	[TS]
Lung function:	Spirometry	X	
	Nitric oxide [FeNO] in exhaled air		X
Musculoskeletal system:	Medical examination of hip, knee and hands*		X§
Oral health:	Retinal photography: ELLEX DRF camera; visus test		X
	Hearing test [German Digit Triple Test via touch screen & headphone]		X§
	Olfactory test [sniffin'-sticks 12]		X
Physical activity/fitness:	7-day accelerometry: Actigraph GT3X+	X	
	Submaximal bicycle ergometer test		X§
	Hand grip strength	X	
Anthropometry:	BIA, body weight and height	X	
	Waist circumference	X	
	Ultrasound of the abdominal fat		X
Collection of bio samples:**	Blood [plasma, serum], urine	X	

* „1 out of 3 modules“, ** Nasal swabs, saliva and stool will be collected during main phase

ORGANISATIONAL STRUCTURE AND BODIES OF THE GNC

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Gemeinsam forschen für eine gesündere Zukunft

