Constances and the German National Cohort

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The German National Cohort – Study design in brief (1)

Population based cohort -- Age range 20-69 yrs

Three levels of intensity:
- Level 1: 200,000 participants
- Level 2: 60,000 participants
- MRI: 30,000 participants

18 recruitment centers, wide geographic spread
5 MRI centers

Major diseases:
- CVD; Type 2 Diabetes; Cancer; Neurologic and psychiatric diseases; Respiratory diseases; Infectious diseases

The German National Cohort
18 study centers – eight regional clusters

The German National Cohort – Study design in brief (2)

- **Baseline assessment:** questionnaires, physical examinations, cognitive function tests, collection of bio-specimens (blood, urine, saliva, nasal swabs, stool)

- **2.5 hours** assessment programme at **level 1** and **4 hours** intensified assessment programme at **level 2**

- **4-5 years for 1st recruitment**, then 4-5 years of **re-assessment**

- Calibration sub-study (N=6,000 recruitment and re-assessment)

- Combination of **active follow-up** (mailed questionnaires, each 2-3 years) and **passive follow-up** (linkage with registries)

The German National Cohort – Questionnaire Data

- Socio-demographic and Socio-economic factors
- Occupation
- Medical history

- Medication (IDOM, ATC)
- Women's questions (menstrual, reproductive history, hormone use)
- Smoking, Alcohol
- Physical activity
- Health-related Quality of Life (WHOQoL, EQ5D)
- Neurologic/ psychiatric disorders (MINI screening, CES-D, ASI-3, RLS, headache, sleep)
- Psychosocial factors (Personality, chronic stress, trauma, work stress (ERI), social networks & support)
- Infections, immune status

The German National Cohort – Physical and Medical examinations (Excerpt)

- **Anthropometry:**
  Height, weight, waist and hip circumference

- **Cardiovascular:**
  Blood pressure, heart rate, 12-lead ECG, 3D-echocardiography, carotid ultrasound (IMT), arterial stiffness, ankle-brachial index, retinal photography.

- **Diabetes:**
  Oral glucose tolerance test

- **Lung function, physical activity, physical fitness:**
  Spirometry, 7-d accelerometry, ergometry, hand grip, musculoskeletal exams

- **Cognitive function:** ....

- **Sense organ functions:**
  Audiometry, Sniffing sticks

The German National Cohort – Sources of secondary data

- **Health Insurances**

  Health care utilisation and compliance; GP & specialist visits; hospitalisations; Medication adherence

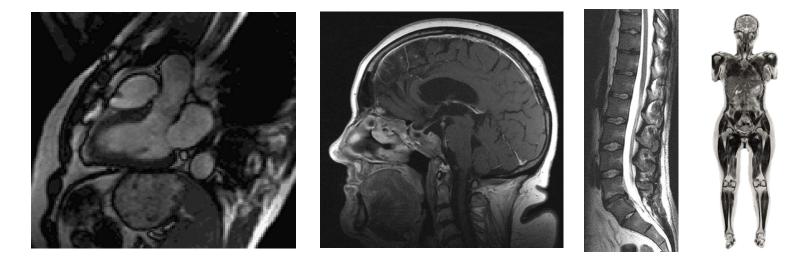- **IAB ("Institut für Arbeit und Beruf")**

  Occupational history, retirement

- **Geotagging** (Job & Home addresses)

  Environmental Exposures

Magnetic resonance imaging (MRI)

Research Areas:
• Neurodegenerative diseases
• Cardiovascular diseases
• Muscular-skeletal diseases
• Diabetes
• Oncologic diseases

Instrument / content	Duration
- Whole body MRI - Heart MRI - Brain MRI	
Overall	**< 60 min**

Collection of bio-specimens

Material	Volume	Material after preparation	Storage -80°C/-180°C
Blood with clotting activator	2x10 ml	**Serum**	30 x 0.19 ml
EDTA blood	2,0 ml	**EDTA blood** - Haematology	local clin. lab.; transport < 6 h
	3x10 ml	**EDTA plasma**	48 x 0.19
		Washed erythrocytes (from EDTA tube)	6 x 0.19
		EDTA blood for (later) DNA extraction	1 x 9 ml
Blood + RNAse inhibitors	2.5 ml	**RNA tubes** (Tempus/PAXgene)	1 x 2.5 ml

The German National Cohort – Collection of bio-specimens (2)

Material	Volume	Material after preparation	Storage -80°C/-180°C
Spot urine (supernatant)	100 ml	After centrifugation	12 x 0.19 ml
		(Aliquots of larger volume for bio-monitoring)	5x10 ml
Urine sediment		(from urine with RNAlater)	
Saliva (spitted)	2 ml	After centrifugation	2 aliquots
Swab (nasal)	1 swab	No preparation; subject to feasibility study	1 swab tip
Faeces			2 aliquots

Prospective ascertainment of vital status and disease occurrences

Vital status:

- Regular follow-up questionnaires (**"active" follow-up**)
- Queries at municipal registries in case of non-response
- For cases of death → obtention of death certificates

Cancer:

- Active follow-up (regular self-reports + verification against clinical records)
- Record linkage to cancer registries

Other chronic disease:

- Active follow-up (regular self-reports)
- Systematic verification of self-reports against clinical records

The German National Cohort – Expected cumulative incidence of cancer (Level 1)

Disease	Average follow-up duration (years + calendar date)		
	5 yrs (2022)	10 yrs (2027)	15 yrs (2032)
Breast	780	1,800	2,900
Prostate	720	1,900	3,200
Colon, Rectum	670	1,800	3,100
Lung	560	1,400	2,400
Bladder	260	710	1,200
Kidney	190	500	850
non-Hodgkin L.	140	340	580
Pancreas	120	330	580
Corpus Uteri	120	320	540
Brain+CNS	90	200	330
Ovary	110	260	440

The German National Cohort – Expected cumulative incidence of non-malignant diseases

Disease	Average follow-up duration (years + calendar date)			
	5 yrs (2022)	10 yrs (2027)	15 yrs (2032)	20 yrs (2037)
MI	1,700	4,400	7,300	10,000
Stroke	1,600	4,300	7,500	11,000
Diabetes	5,800	13,000	21,000	28,000
Rheum. arthritis	250	590	940	1,300
COPD	2,300	5,800	9,700	13,000
Heart failure	1,600	4,600	8,200	12,000
Mortality	4,600	14,000	26,000	47,000

The National Cohort – History & Milestones

- **April 2008:**
  Evaluation basic Study Concept –start-up funding (Helmholtz)

- **2009:**
  Establishment of an enlarged national steering group; Selection of recruitment centers & participating institutions

- **2011-2012:**
  1st and 2nd phase feasibility studies (BMBF funding)

- **April 2011 / April 2012 / Oct 2012:**
  International evaluations of full study proposal and MRT program

- **Sep 2012 – Feb 2013:**
  Foundation of "Nationale Kohorte" e.V.

- **Oct 2013:** Start of recruitment

Collaboration between Constances and the German National Cohort

- **Meetings of German National Cohort and Constances**: Paris (October 2009), Heidelberg (December 2009), Munich (March 2010)

- **4th French-German Forum for cooperation in research** (Berlin October 2011)

- Topics for collaboration between both cohorts
  - **Methods**
    - Harmonization of data
    - Harmonization of biobanks
  - **Specific scientific themes (pooled or comparative analyses):**
    - Diabetes; Cardiovascular Diseases; Cancer; Cognition / Neurodegenerative Diseases
    - Occupational Health; Social Health Inequalities; Health Care, Drugs

Thank you for your attention