COHORT PROFILE

Cohort Profile: Cohort of Norway (CONOR)

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How did the study come about?

A number of large population-based cardiovascular surveys have been conducted in Norway since the beginning of the 1970s. The surveys were carried out by the National Health Screening Service in cooperation with the universities and local health authorities. All surveys comprised a common set of questions, standardized anthropometric and blood pressure measurements and non-fasting blood samples that were analysed for serum lipids at the Ullevaal Hospital Laboratory. These surveys provided considerable experience in conducting large-scale population-based surveys, thus an important background for the Cohort of Norway (CONOR). In the late 1980s the Research Council of Norway established a programme in epidemiology. This also gave stimulus to the idea of establishing a cohort including both core survey data and stored blood samples. In the early 1990s, all universities, the National Health Screening Service, The National Institute of Public Health and the Cancer Registry discussed the possibility of a national screening service in cooperation with the universities and local health authorities. All surveys comprised a common set of questions, standardized anthropometric and blood pressure measurements and non-fasting blood samples that were analysed for serum lipids at the Ullevaal Hospital Laboratory. These surveys provided considerable experience in conducting large-scale population-based surveys, thus an important background for the Cohort of Norway (CONOR). In the late 1980s the Research Council of Norway established a programme in epidemiology. This also gave stimulus to the idea of establishing a cohort including both core survey data and stored blood samples. In the early 1990s, all universities, the National Health Screening Service, The National Institute of Public Health and the Cancer Registry discussed the possibility of a national representative cohort. The issue of storing blood samples for future analyses raised some concern and it was discussed in the parliament. In 1994, the Ministry of Health appointed the Steering Committee for the CONOR collaboration. In 1994–95, the fourth round of the Tromsø Study was conducted, and became the first survey to provide data and blood samples for CONOR. During the years 1994–2003, a number of health surveys that were carried out in other counties and cities also provided similar data for the network. So far, 10 different surveys have provided data and blood samples for CONOR (Figure 1). The administrative responsibility for CONOR was given to the Norwegian Institute of Public Health (NIPH) in 2002. The CONOR collaboration is currently a research collaboration between the NIPH and the Universities of Bergen, Oslo, Tromsø and Trondheim.

The purpose of CONOR

The CONOR cohort has not been established on the basis of any single hypothesis but is rather a multipurpose study. The ambition was to set up a sufficiently large enough cohort to study aetiological factors for a wide range of diseases. Additionally, this cohort should make it possible to describe Norwegian men and women in terms of distribution of socio-economic factors.

In 2002, CONOR and the Norwegian Mother and Child study (MoBa),7 received a 5-year grant from the Norwegian Research Council to build a technology platform under the Functional Genomics programme (FUGE), called the Biobanks for Health in Norway (Biohealth) platform.3 The overall aim was to investigate separate and combined effects of genes and environment on the risk of disease.

Who is in the sample?

Altogether 309 742 individuals were invited to the 10 surveys based on the 11-digit personal identifier and addresses from the Population Registry of Norway.2 The goal is to include 200 000 participants. We defined those who attended the survey and/or answered at least one questionnaire and signed a written informed consent as participants. The numbers in Table 1 include individuals who participated and had given their written consent for research and linkage to health registries. A total of 7309 persons participated in two CONOR surveys, and one person participated in three. Thus, the total number of...
individuals in the CONOR cohort is 173,236. The distribution of age at the first examination and the number of deaths during follow-up through 2003 is given in Table 2. The individual surveys may have published papers with slightly different total numbers. Sampling procedures differed somewhat between the individual studies. The website for each study contains more detailed information (Table 1).

**What has been measured?**

In all the CONOR surveys, the data collection followed a standard procedure. Letters of invitation were mailed about 2 weeks before the time of appointment and included a questionnaire and a brochure with the aims of the study and information about the examinations and procedures. At the screening, this initial questionnaire was collected from the attendees, participants underwent a physical examination and a non-fasting blood sample was drawn. In most studies, the participants were given one or two supplementary questionnaires, which they were instructed to fill in at home and return by mail in pre-addressed stamped envelopes.

About 4 weeks after attending the examination, a letter with selected results from the examination and blood tests was sent to all participants. Those with the highest scores of cardiovascular risk (a modified Framingham risk score based on multiplying the relative risks attributable to the subject’s gender, serum cholesterol, systolic blood pressure the number of cigarettes currently smoked per day and family history of

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**Table 1**

| Name of the study                  | Year of survey | Number invited | Invited age-groups in years | Number of participants* | Web address |
|-----------------------------------|---------------|----------------|----------------------------|-------------------------|-------------|
| Tromsø IV (The fourth Tromsø Study) | 1994–1995     | 37,558         | 25+                        | 12,797 14,128 26,925   | http://uit.no/tromsoundersokelsen/tromso4/2 |
| HUNT II (The second North-Tromsø Study) | 1995–1997     | 94,196         | 20+                        | 30,441 34,576 65,017   | http://www.hunt.ntnu.no/ |
| HUSK (The Hordaland Health Study) | 1997–1999     | 38,587         | 40–44, 46–47, 70–72        | 11,678 13,851 25,529   | http://www.uib.no/isf/husk/ |
| Oslo II (The second Oslo Study)   | 2000          | 14,209         | 48–77                      | 6919 6919               | http://www.fhi.no/artikler/?id=54685 |
| HUBRO (The Oslo Health Study)     | 2000–2001     | 58,660         | 30, 31, 40, 45, 46, 59/60, 75/76 | 9,509 11,852 21,361   | http://www.fhi.no/artikler/?id=54464 |
| OPPHED (The Oppland and Hedmark Health Study) | 2000–2001     | 22,327         | 30, 40, 45, 60, 75         | 5,602 6,661 12,263     | http://www.fhi.no/artikler/?id=28233 |
| Tromsø V (The fifth Tromsø Study) | 2001          | 10,353         | 30+                        | 3,440 4,457 7,897      | http://uit.no/tromsoundersokelsen/tromso5/2 |
| I-HUBRO (The Oslo Immigrant Health Study) | 2002          | 12,088         | 20–60                      | 1,877 1,737 3,614      | http://www.fhi.no/artikler/?id=28217 |
| TROFINN (The Troms and Finnmark Health Study) | 2002          | 16,229         | 30–77                      | 4,196 4,836 9,032      | http://www.fhi.no/artikler/?id=28261 |
| MoRo II (The second part of the Romsås in Motion Study) | 2003          | 5,555          | 34–70                      | 896 1,093 1,989        | http://www.fhi.no/artikler/?id=28254 |
| CONOR (Cohort Norway)*            | 1994–2003     | 309,742        | 20–103                     | 87,335 93,191 180,546  | http://www.fhi.no/artikler/?id=28138 |

*Number of participants equals those who attended the survey and agreed that information from the CONOR survey and blood samples can be linked to other registers and used in research. A total of 7310 individuals participated in more than one survey. Thus, the total number of individuals equals 173,236.
coronary heart disease) were advised to visit their own general practitioner, and in some cases offered a follow-up examination at the local hospital.³

Measures
Only a restricted core set of measurements and questionnaire responses constitute the CONOR data. Most individual studies that contribute to CONOR have more detailed measurements and questionnaire data. In the following section we describe the key core measurements that all studies contribute to CONOR; at the end we briefly describe some of the additional measurements that are in some of the contributing individual studies. All surveys were carried out in collaboration with the National Health Screening Service, Oslo (now the NIPH). Experienced and trained personnel conducted all procedures. Non-fasting serum total- and HDL-cholesterol, glucose and triglycerides were measured directly by an enzymatic method (Boehringer 148393, Boehringer-Mannheim, Federal Republic of Germany—from 2000 Hitachi 917 auto analyzer, Roche Diagnostic, Switzerland).

The Department of Clinical Chemistry, Ullevål University Hospital, Oslo, performed all laboratory assessments except for HUNT II (The second North-Trøndelag Study) where the analyses were performed at the Department of Clinical Chemistry, Levanger Hospital, Levanger. In Tromsø IV and V, cholesterol and triglycerides were measured at the Department of Clinical Chemistry, University Hospital North-Norway, Tromsø. Calibration procedures were carried out between these laboratories in connection with the surveys (Dr P.G. Lund-Larsen, National Health Screening Service, personal communication). An acceptable stability of the laboratory analyses over time in the population surveys has been reported.⁶

Heart rate, systolic and diastolic blood pressures were measured by an automatic device (DINAMAP, Criticon, Tampa, FL, USA). After 2 min of seated resting, three recordings were made at 1-min intervals. Mean values of the second and third systolic blood pressure measurements were used in calculating the cardiovascular risk score (CVD risk score) (Tverdal, 1989 5/1d). The stability of the blood pressure measures has been evaluated and deemed acceptable.⁵

Body weight (in kilograms, one decimal) and height (in centimetres, one decimal) was measured according to a standard protocol with the participants wearing light clothing without shoes (manually recorded until 2000 and after that with an electronic Height and Weight Scale). Body mass index (BMI) was calculated as kilograms per square metre. Waist circumference was measured at the umbilicus to the nearest centimetre and with the subject standing and breathing normally. In obese individuals, waist circumference was defined as the midpoint between the iliac crest and lower margin of ribs. Hip circumference was measured as the maximum circumference around the buttocks. Both waist and hip were measured with a measuring tape of steel—which was emphasized to be placed horizontally. The waist–hip circumferences were used to calculate the waist–hip ratio.

Most individual studies that contribute to CONOR have several additional measurements—for example, extra samples of blood, ECG and ultrasonographic examination of carotid artery and abdominal aorta. Four of the study sites measured bone mineral density (DEXA and/or SXA) and have established a research group called Norwegian Epidemiologic Osteoporosis Studies (NOREPOS).⁸ Altogether, around 28 000 individuals have had their bone mineral density measured and currently a number of collaborative studies are carried out.

The CONOR questions
All surveys used about 50 core CONOR questions agreed upon before the first CONOR survey in Tromsø in 1994. The exact wording of the questions is available at the CONOR website (http://www.fhi.no/dav/CA11310499.doc). Some questions have been slightly modified over the years.

The CONOR questions cover the following main topics: self-reported health and diseases such as diabetes, asthma, coronary heart disease, stroke and mental distress, musculo-skeletal pains, family history of disease, risk factors and lifestyle, social network and social support, education, work and housing, some types of occupation, use of medications and reproductive history (women).

Several of the questions have been evaluated or validated and deemed acceptable.⁹–¹⁸ The Population Registry of Norway that was used to identify eligible subjects, contains information about gender, date of birth, marital status, address and country of birth.

Blood samples
Blood samples were drawn from the CONOR participants. EDTA blood for CONOR and the other sub-surveys have normally been collected in 7 or 5 ml vacutainers. These vacutainers were made by different manufacturers but were normally made of polypropylene. DNA has been extracted from more than 90 000 specimens to medio 2007, and Biohealth intends to extract DNA from all samples by Spring 2008. The extracted DNA and an additional sample of 1.25 ml EDTA-blood will be stored at a national biobank storage site at HUNT/NTNU biobank in Levanger (Mid-Norway).

What has been found?
Although a number of analyses from each participating study have been conducted, the CONOR file has only recently been compiled and made available for research. The first CONOR project was anchored in NOREPOS describing urban–rural differences in forearm fractures.¹⁹ Other methodological and validation studies have been completed as described above.

What are the main strengths and weaknesses?
The CONOR database has several strengths: it is population based including populations from various parts of Norway, both rural and urban. The 11-digit personal identification number makes it possible to link cohort participants to national health registries. At present, several large linkages to other registers have been or are in the process of being conducted. These include linkages with census-based data for the whole population and the Medical Birth Registry of Norway, Disability Registry, Cancer Registry of Norway. Tables 2 and 3 present number of deaths and new cases of cancer in CONOR since date of examination by linkage to the death and cancer registries. Other large linkages include data from the Norwegian Drug Prescription Database and information from
Can I get hold of the data? Where can I find out more?

Guidelines have been developed for projects using data from CONOR (www.fhi.no). These shall ensure that projects will have a high scientific quality, facilitate quick publication of results from CONOR and make the data accessible for research. Research groups may apply for access. A project leader must be appointed. Researchers not residing in Norway are advised to seek contact with Norwegian counterparts. The study objectives should be within the broader aims of CONOR. Further details of these guidelines are provided at the CONOR website.

Applications and enquiries can be sent electronically to the Norwegian Public Health Insitute (email: conor@fhi.no). Applications will be evaluated by the CONOR Steering Committee.

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