Cohort of Norway (CONOR): Materials and methods

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CONOR (COhort NORway) is a large collaborative project between epidemiological centres at the University of Tromsø, the Norwegian University of Science and Technology in Trondheim, the University of Bergen, the University of Oslo, and the Norwegian Institute of Public Health.

Data from 10 regional studies

In CONOR, regional data from 10 different epidemiological studies have been merged into a national database, which is more representative of the Norwegian population than each of the individual sites.

The database consists of information obtained from questionnaires, a simple physical examination, analyses of blood samples, and frozen stored blood and/or DNA. The main purpose of CONOR is to study the aetiology of rare diseases by testing environmental, inheritable, cultural and social factors in order to describe the dispersion of diseases and risk factors by time, place and socio-demographic factors.

CONOR is particularly suitable for studying gene-environment interactions and for linkages to various national registers (eg. cancer-, cause of death-, hospital- and medical birth registers).

Invitation and procedures

Altogether 309,742 individuals were invited in the 10 studies based on addresses from the Population registry of Norway (Hammer, 2002). Some of the individual studies invited all subjects above a specific age (for example all above 19 years in HUNT II), whereas others invited all subjects in selected age groups (for example all 30-, 40-, 45-, 60 and 75 years in OPPHED and TROFINN). The web site for each study contains more detailed information (see Table 1).

In all 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 booklet with the aims of the study and information about the examinations and procedures. At the screening, the main questionnaire was collected from the attendees, they went through a physical examination and a non-fasting blood sample was drawn for analyses in fresh serum. Another sample was stored at minus 80 degrees. In most studies, the participants were given one or two supplementary questionnaires, which they were instructed to fill in at home and to return by mail in pre-addressed envelopes.

About four weeks after attending the examination, a letter with some results from the examination and blood tests was sent to all participants. Those with the highest scores of cardiovascular risk were offered a new clinical examination at the regional University Hospital - or, in some of the studies, were asked to visit their own general practitioner.

Measures

All surveys have been carried out in collaboration with the National Health Screening Service, Oslo (now Norwegian Institute of Public Health). 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 where the analyses were performed at the Department of Clinical Chemistry, Innherad Hospital, Levanger. Comparisons of blood-samples were performed between the laboratories, and small differences were found (Tverdal A et al 1997). Calibration procedures were carried out between these laboratories in connection with the surveys (Dr. Lund-Larsen PG, National Health Screening Service, personal communication). An acceptable stability of the laboratory analyses over time in the population surveys has been reported (Foss & Urdal, 2003).

Heart rate, systolic and diastolic blood pressures were measured by an automatic device (DINAMAP, Criticon, Tampa, USA), which measured the blood pressure in

mm Hg automatically by an oscillometric method. After 2 minutes of preceding rest, three recordings were made at one-minute intervals. Mean values of the second and third systolic blood pressure measurements were used in calculating the cardiovascular risk score (CVD risk score) (Tverdal et al., 1989). The stability of the blood-pressure measures have been evaluated and deemed acceptable (Lund-Larsen, 1997).

Body weight (in kilograms, one decimal) and height (in cm, 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 kg/m^2. Waist circumference was measured at the umbilicus to the nearest cm 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 horizontal. Waist and hip circumference were used to calculate the waist-hip ratio using the formula waist (cm)/ hip circumference (cm).

Most of the studies consist of a central core and several supplementary projects – for example extra samples of blood, ECG, ultrasonographic examination of carotid artery and abdominal aorta, and bone mineral densitometry (BMD). The web site for each study contains more detailed information (see Table 1). Only a limited and mutual core of each study constitutes CONOR. Most of the studies have published reference papers with more detailed information about their own study (Table 2).

The CONOR-questions
All surveys used 50 common CONOR-questions agreed upon before the first CONOR survey in Tromsø in 1994. The exact wording of the questions is available at the CONOR web site (http://www.fhi.no/dav/CA11310499.doc). Some of these questions were placed on the second questionnaire handed out at the screening station – and thus have lower response rate.

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, environment while growing up, social network and social support, education, work and housing, some types of occupation, use of medications and reproductive history (women).

Several of these questions have been evaluated or validated previously and were deemed acceptable (Tretli et al., 1982; Jacobsen & Thelle, 1987; Løchen & Rasmussen, 1992; Thune et al., 1997, Joakimsen et al., 1998; Saltin & Grimsby, 1968; Derogatis et al., 1974; Ainsworth et al., 1996; Brugha et al., 1985; Strand et al., 2003; Søgaard et al 2003). The Population registry of Norway, which was used for invitation, contains information about gender, birth date, marital status, address and country of birth.

Participation in the CONOR studies

Altogether 181,891 subjects accepted to participate and provided a declaration of consent – 7,460 of these participated in more than one survey. The age distributing of these 174 430 participants is shown in table 3. The participation rate varied among the surveys. The participation was slightly reduced throughout the study-period 1994-2003 - and was higher in rural as compared to urban areas.

Ethics and approvals

All participants of the studies included in CONOR, have given their written consent. The participant's names and personal ID numbers are omitted when data are used for research purposes. The Norwegian Data Inspectorate has approved - and the Regional Committees for Medical Research Ethics has evaluated each individual study. The studies have been conducted in full accordance with the World Medical Association Declaration of Helsinki.

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TABLE 1. Number of invited and participating subjects in Cohort Norway (CONOR) 1994-2003.

Name of the study	Year of survey	Number invited[†]	Invited age-groups in years[‡]	Number of participants[*]			
				Men	Women	Total	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-Trøndelag Health Study)	1995-1997	94,196	20 +	30,442	34,576	65,018	http://www.hunt.ntnu.no/
HUSK (The Hordaland Health Study)	1997-1999	38,587	40-44, 46-47, 70-72	11,678	13,852	25,530	http://www.uib.no/isf/husk/
Oslo II (The second Oslo Study)	2000	14,209[§]	48-77	6,919		6,919	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	9,751	12,264	22,015	http://www.fhi.no/artikler/?id=54464
OPPHED (The Oppland and Hedmark Health Study)	2000-2001	22,327	30, 40, 45, 60, 75	5,650	6,752	12,402	http://www.fhi.no/artikler/?id=28233
Tromsø V (The fifth Tromsø Study)	2001	10,353	30 +	3,491	4,586	8,077[**]	http://uit.no/tromsoundersokelsen/tromso5/2
I-HUBRO (The Oslo Immigrant Health Study)	2002	12,088[††]	20-60	1,915	1,768	3,683	http://www.fhi.no/artikler/?id=28217
TROFINN (The Troms and Finnmark Health Study) [‡‡]	2002	16,229	30-77	4,318	5,009	9,327	http://www.fhi.no/artikler/?id=28261
MoRo II (The second part of the Romsås in Motion Study)	2003	5,535	34-70	899	1,096	1,995	http://www.fhi.no/artikler/?id=28254
CONOR (Cohort Norway)	1994-2003	309,742	20-103	87,157	92,928	181,891[*]	http://www.fhi.no/artikler/?id=28138

* Number of participants equals those who attended the survey and/or answered at least one questionnaire and signed a written consent. 7,460 persons participated in a second CONOR survey and 1 person participated in a third. Thus, the total numbers of participants with consent were 174,430.

† The numbers include all individuals invited. The individual surveys could have published papers with slightly different total numbers.

‡ HUSK: All 40-44 years and those participating in a study in 1992-93 born 1950-51 and 1925-27; Oslo II: All those invited to the Oslo Study 1972-73, except those invited to HUBRO and MoRo I (Invited in 1972/73: all men born 1923-32 and 7% random sample of those born 1933-52); Tromsø V: All 30, 40, 45, 60, 75 years and all those participating in phase II in Tromsø IV - which included: all born 1920-1939, 5-10% sample of other age groups attending phase I, all women born 1940-44; I-HUBRO: 30% random sample of people born in Pakistan, all born in Turkey, Sri Lanka, Iran, Vietnam - except those invited to HUBRO; MoRo II: All those participating in a study in 2 local districts in Oslo in 2000 (MoRo

I) born 1933-1969 – except those participating in HUBRO; TROFINN: All 30, 40, 45, 60, 75 years and all those participating in three Finnmark studies in the period 1974-1988 – which included: All born 1925-1947, all born 1948-1968 invited to Finnmark I, II or III.

§ 2,515 more men who belonged to the Oslo II cohort, also belonged to the HUBRO cohort, and were only invited to HUBRO. Of these 1,320 men participated. They are only counted as invited to HUBRO. 50 more men belonged to the MoRo-cohort, and are only counted as invited there.

Include 17,308 invitees (31 and 46 years – additional cohorts) who were not reminded. The attendance-rate of these was low.

** 7,166 of these participated also in Tromsø IV.

†† Include 4,116 persons (20-30 years – additional cohort) who were not reminded. The attendance-rate of these was very low.

‡‡ Include 18 of 25 municipalities in Troms and 10 of 19 municipalities in Finnmark. The other municipalities participated in Tromsø V and in SAMINOR, i.e. a health survey in communities with Sámi and Norwegian population, at the same time.

Table 2. Reference papers to the 10 participating CONOR studies.

Tromsø IV: Wilsgard T. Longitudinal analyses of cardiovascular risk factors. The Tromsø study 1974-1995. ISM skriftserie nr. 65. Tromsø, Norway: Institute of Community Medicine, University of Tromsø, 2002.

HUNT II: Holmen J, Midthjell K, Krüger Ø, Langhammer A, Lingaas Holmen T, Bratberg GH, Vatten L, Lund-Larsen PG. The Nord-Trøndelag Health Study 1995-97 (HUNT 2): Objectives, contents, methods and participation. Nor J Epidemiol 2003; 13: 19-32.

HUSK: Bjelland I, Tell GS, Vollset SE, Refsum H, Ueland PM. Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. Arch Gen Psychiatry 2003 Jun;60(6):618-26 - and

Sanne B, Mykletun A, Dahl AA, Moen BE, Tell GS; Hordaland Health Study. Occupational differences in levels of anxiety and depression: the Hordaland Health Study. J Occup Environ Med 2003;45:628-38.

Oslo II: Lund Håheim L, Holme I, Hjermann I, Søgaard AJ, Lund-Larsen PG, Leren P. Resultater fra Oslo-undersøkelser blant de samme menn i 1972/3 og i år 2000. Endring i risikofaktorer for hjerte- og karsykdom. Tidskr Nor Laegefor (Cond accepted)

HUBRO: Søgaard AJ, Selmer R, Bjertness E, Thelle D. The Oslo Health Study. The impact of self-selection in a large, population-based survey. Int J Equity Health 2004:3: 1-24. Online: http://www.equityhealthj.com/content/3/1/3

OPPHED: Only web-site - http://www.fhi.no/artikler/?id=28233

Tromsø V: Johnsen SH, Fosse E, Joakimsen O, Mathiesen EB, Stensland-Bugge E, Njølstad I, Arnesen E. Monocyte count is a predictor of novel plaque formation: a 7-year follow-up study of 2610 persons without carotid plaque at baseline the Tromso Study. Stroke. 2005;36(4):715-9.

I-HUBRO: Holvik K, Meyer HE, Haug E, Brunvand L.Prevalence and predictors of vitamin D deficiency in five immigrant groups living in Oslo, Norway: the Oslo Immigrant Health Study. Eur J Clin Nutr. 2005;59:57-63.

TROFINN: Only web-site - http://www.fhi.no/artikler/?id=28260

MoRo II: Jenum AK,. Anderssen SA, Birkeland KI, Holme I, Graff-Iversen S, Lorentzen C, Ommundsen Y, Raastad T, Ødegaard AK, Bahr R. Promoting physical activity in a low-income multi-ethnic district: behavioural, psychological and biological effects of a pseudo-experimental community intervention study to reduce risk factors for diabetes and cardiovascular disease (submitted)

CONOR: Engeland A, Søgaard AJ. CONOR (Cohort NORway) – en oversikt over en unik forskningsdatabank. Nor J Epidemiol 2003;13:73-7 - and Magnus P, Arnesen E, Holmen J, Stoltenberg C, Søgaard AJ, Tell GS. CONOR (Cohort NORway): historie, formål og potensiale. Nor J Epidemiol 2003;13:79-82.

Table 3 Number of participants in Cohort Norway (1994-2003) according to gender and age-groups (at the time they attended the screening station). If participating in more than one study, only the last one is counted.

Age	Men N	Women N	Total N
<20	116	148	264
20-29	5 884	7 236	13 120
30-39	13 322	15 547	28 869
40-49	27 969	32 148	60 117
50-59	10 517	10 176	20 693
60-69	12 229	10 373	22 602
70-79	13 119	11 883	25 002
80+	1 460	2 303	3 763
Total	84 616	89 814	174 430