## COHORT PROFILE Cohort Profile: The HUNT Study, Norway

## S Krokstad,<sup>1,2</sup>\* A Langhammer,<sup>1</sup> K Hveem,<sup>1</sup> TL Holmen,<sup>1</sup> K Midthjell,<sup>1</sup> TR Stene,<sup>1</sup> G Bratberg,<sup>1,2</sup> J Heggland<sup>1</sup> and J Holmen<sup>1</sup>

<sup>1</sup>HUNT Research Centre, Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), <sup>2</sup>Levanger Hospital, Nord-Trøndelag Health Authority, Norway

\*Corresponding author. HUNT Research Centre, Department of Public Health and General Practice, Faculty of Medicine NTNU, Forskningsveien 2, 7600 Levanger, Norway. E-mail: steinar.krokstad@ntnu.no

#### Accepted 21 May 2012

The HUNT Study includes large total population-based cohorts from the 1980ies, covering 125 000 Norwegian participants; HUNT1 (1984-86), HUNT2 (1995-97) and HUNT3 (2006-08). The study was primarily set up to address arterial hypertension, diabetes, screening of tuberculosis, and quality of life. However, the scope has expanded over time. In the latest survey a state of the art biobank was established, with availability of biomaterial for decades ahead. The three population based surveys now contribute to important knowledge regarding health related lifestyle, prevalence and incidence of somatic and mental illness and disease, health determinants, and associations between disease phenotypes and genotypes.

Every citizen of Nord-Trøndelag County in Norway being 20 years or older, have been invited to all the surveys for adults. Participants may be linked in families and followed up longitudinally between the surveys and in several national health- and other registers covering the total population.

The HUNT Study includes data from questionnaires, interviews, clinical measurements and biological samples (blood and urine). The questionnaires included questions on socioeconomic conditions, health related behaviours, symptoms, illnesses and diseases.

Data from the HUNT Study are available for researchers who satisfy some basic requirements (www.ntnu.edu/hunt), whether affiliated in Norway or abroad.

### Why was the cohort set up?

The HUNT Study (an acronym for the Norwegian name: **H**else**u**ndersøkelsen i **N**ord-**T**røndelag) constitutes a large population database for medical and healthrelated research. So far three health surveys of the general adult population in the Nord-Trøndelag County, Norway (Figure 1) have been completed, HUNT1 in 1984–86,<sup>1</sup> HUNT2 in 1995–97,<sup>2</sup> and HUNT3 in 2006– 08. At the time of HUNT2 and HUNT3, adolescents aged 13–19 years were invited to the Young-HUNT Study, which has a partly overlapping scientific programme, but this study will be presented in a separate publication in preparation (TL Holmen, personal communication, 18 May 2012).

HUNT1 was primarily designed to address arterial hypertension, diabetes, chest X-ray screening of tuberculosis and quality of life. The scope of the HUNT Study has expanded over time and contributed to important knowledge regarding health-related lifestyle, prevalence and incidence of illness and disease, health determinants and associations between disease phenotypes and genotypes.

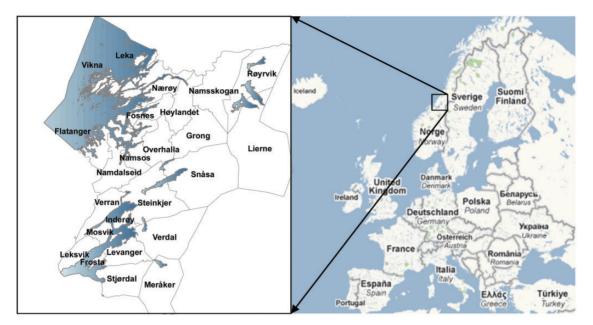


Figure 1 The HUNT Study area, the 24 municipalities in Nord-Trøndelag County, Norway

The surveys have been set up by the HUNT Research Centre organized under the Norwegian Institute of Public Health until 2000, and thereafter the Norwegian University of Science and Technology (NTNU).

HUNT has largely been publicly funded. HUNT3 was mainly funded by the Norwegian Ministry of Health, NTNU, the Norwegian Research Council (the FUGE programme), Central Norway Regional Health Authority, the Nord-Trøndelag County Council and the Norwegian Institute of Public Health. Funding also has been given by commercial enterprises such as Statoil, Sparebank1 Midt-Norge, Nord-Trøndelag Elektrisitetsverk, Gjensidigestiftelsen, AstraZeneca and GlaxoSmithKline. Several other contributors supported sub-studies. In total, the core HUNT3 study had a cost of ~120 million NOK (16 million Euro).

### Who is in the cohort?

#### Setting

Norway is a Northern European country characterized as a social democratic welfare state, with generous universal public health insurance coverage, and predominately public health services.<sup>3</sup> The average life expectancy (2009) is 83 years in women and 79 in men. Nord-Trøndelag constitutes one of 19 counties, geographically situated in the central part of the country. The population size was relatively stable between HUNT1 (125 835 in 1981) and HUNT3 (128 694 in 2006), and except for young adults, the in- and out-migration has been low. In all the HUNT surveys, the data were collected in each of the 24 municipalities in the county by using temporarily located health examination sites staffed by certified fieldwork teams (Figure 1). This article presents the adult part of HUNT, mainly focusing on the HUNT3 Survey (Table 1). The HUNT1 and HUNT2 surveys have been described in detail previously.<sup>1,2</sup>

## The HUNT1 cohort aged 20+ (established 1984–86)

In 1984–86 every citizen of Nord-Trøndelag County aged 20 years or older (or turning 20 years during the year of survey) were invited. A total of 77 212 persons participated (89.4% of those invited) (Figure 2). Questionnaires and clinical measurements (listed in Table 1) were applied. Participants with findings indicating pathology were advised to see their family doctor.<sup>1</sup> The design applied in HUNT1 was largely repeated in HUNT2 and HUNT3.

## The HUNT2 cohort aged 20+ years (established 1995–97)

HUNT2 constituted both a new cross-sectional survey and a follow-up of HUNT1.<sup>2</sup> The scientific programme was extended to include several large public health issues in accordance with current national health priorities. These were cardiovascular disease (CVD), diabetes, obstructive lung disease, osteoporosis, headache, mental health, chronic musculoskeletal pain and urinary incontinence. In addition to questionnaires, interviews and clinical examinations, the participants contributed with blood samples for instant analysis and storage. A total of 65 237 participated in HUNT2 (69.5% of those invited).

Table 1	The	HUNT	Study.	Main	surveys	and	measurements	for	adults
---------	-----	------	--------	------	---------	-----	--------------	-----	--------

Survey	Measurements					
HUNT1 (1984–86)	<ul> <li>Questionnaires (four) with self-reported health, quality of life, illness, diseases (CVD, diabetes), major behavioural risk factors and socio-economic position. Disease-specific questionnaires for hypertension, diabetes and quality of life</li> <li>Anthropometric measures: weight, height</li> <li>Blood pressure and heart rate</li> <li>Chest-X-ray</li> <li>Capillary non-fasting blood glucose (participants 40 years and older and all with known diabetes)</li> <li>Venous blood samples analysed for total HbA1 in persons reporting known diabetes</li> </ul>					
HUNT2 (1995–97)	<ul> <li>Questionnaires (eight) with self-reported health, quality of life, illness, diseases (several), major behavioural risk factors and socio-economic position. Disease-specific questionnaires for hypertension, diabetes and lung diseases</li> <li>Anthropometric measures: weight, height, waist and hip circumference</li> <li>Blood pressure and heart rate</li> <li>For sub-groups: spirometry, forearm bone mineral density (BMD), vision</li> <li>Venous blood samples, analysed cholesterol (total and HDL), triglycerides, glucose, Se-Fe, transferrir and creatinine. Sub-groups: thyroid-stimulationg hormone (TSH), calcium, parathyroid hormone (PTH) and stored (serum aliquots stored at -80°C), DNA extracted</li> <li>Urine: microalbumine and creatinine (sub-groups)</li> </ul>					
HUNT3 (2006–08)						
HUNT1 (1 Invited (aged Participated (8 HUNT1 - 2 coh Participants: HUNT1 - 2 - 3 Participants:	20+) 86 404 9.4%) 77 212 ort <sup>a</sup> 47 316 47 316 Participants: 47 316					

**Figure 2** Flow chart showing the number of invited and the number of participants in the different cohorts in the HUNT Study. The total county population 20+ years in Nord-Trøndelag County Norway have been invited to all the surveys. <sup>a</sup>Participated in both HUNT1 and HUNT2. <sup>b</sup>Paricipated in HUNT1, HUNT2 and HUNT3. <sup>c</sup>Participated in both HUNT2 and HUNT3

Moved to other county:

Dead, emigrated, disappeared: 8545

4357

## The HUNT3 cohort aged 20+ (established 2006–08)

In HUNT3, a total of 93 860 residents were invited in the period from October 2006 to June 2008. The scientific programme of HUNT3 included several main public health issues as in HUNT2, but included also topics like culture participation and religious affiliation. Optimal handling and storage of blood and urine samples were given high priority, as part of the establishment of a new up-to-date biobank. The

Dead, emigrated, disappeared or

moved to other county: 17 389

extensive biobank initiative in HUNT3, including detailed description of methods and procedures, will be presented in a separate publication in preparation (K Hveem, personal communication, 18 May 2012).

## Invitation procedure and information to participants

Invitation files for the HUNT surveys were created from monthly updated national census data. The

	Men			Women			Total		
Age (years)	Invited	Attended <sup>a</sup>	%	Invited	Attended	%	Invited	Attended	%
20–29 <sup>b</sup>	7293	1873	25.7	6991	2645	37.8	14 284	4518	31.6
30–39	7914	2862	36.2	7832	4019	51.3	15 746	6881	43.7
40-49	9212	4557	49.5	8524	5447	63.9	17736	10004	56.4
50–59	8898	5418	60.9	8415	5991	71.2	17313	11409	65.9
60–69	6909	4674	67.7	6892	5137	74.5	13 801	9811	71.1
70–79	4011	2664	66.4	4583	3080	67.2	8594	5744	66.8
80–89	2102	952	45.3	3394	1335	39.3	5496	2287	41.6
90+	228	49	21.5	662	104	15.7	890	153	17.2
Total	46 567	23 049	49.5	47 293	27 758	58.7	93 860	50807	54.1

**Table 2** Participants in the HUNT3 Survey (2006–08) by sex and age at invitation. The total county population aged 20 years or more was invited ( $N = 93\,860$ )

<sup>a</sup>Attended by returning an answered Q1.

<sup>b</sup>A few participants attending at age 19, but turning 20 years during the year of participation, were included in the 20–29 age group.

invitation letter was sent by post and included the first questionnaire (Q1) and an information pamphlet. The information pamphlets (for HUNT2 and HUNT3) were elaborated in co-operation with the Data Inspectorate of Norway, the Health Directorate and the Regional Committee for Medical and Health Research Ethics. The participants delivered Q1 and the written consent when they attended the health examination sites.

#### **Participation in HUNT3**

As the health surveys include several study parts, from filling in Q1 to a number of additional clinical tests and interviews, the response and non-response associated with each study part may differ depending on the invitation criteria that were used. In Table 2, participation in HUNT3 is defined as having at least filled in Q1. Despite the use of monthly updated national census data, 2239 of the 96 099 citizens were dead or had moved out of the county when the fieldwork team arrived, making a total of 93 860 adults eligible for participation. Out of these 50 807 participated (54.1%).

The participation rate declined from HUNT1 to HUNT3 as in most other population-based studies.<sup>4</sup> In all three surveys, more women than men participated, and the highest participation was in the middle aged and the elderly (50–79) with lower participation in the oldest (80+) and in age groups under 40. In HUNT3 the highest participation rate was in age group 60–69, 74.5% for women and 67.7% for men. Men aged 20–29 had the lowest participation rate (25.7%).

# How often have the population been followed up?

The HUNT surveys have been completed at 11-year intervals, enabling cross-sectional and trend studies as well as cohort and other longitudinal study designs (Figure 2).<sup>5</sup> In several sub-studies, selected

participants have been invited for follow-up studies between the main waves, e.g. the lung study, diabetes study, osteoporosis study and chronic pain studies.

#### Linkage to registers covering all participants

Data from all HUNT participants may be linked to several local, regional or national registers through the unique Norwegian 11-digit personal identification number. Linking data is carried out in each project and not centralized to the HUNT Research Centre. Health registers (e.g on forearm and hip fractures, myocardial infarction, stroke, dementia) have been established based on hospital or nursing home files within the region, whereas the national registers cover the total Norwegian population.

The most important registers are the Medical Birth Register of Norway,<sup>6</sup> the Cancer Register of Norway,<sup>7</sup> the Cause of Death Register,<sup>8–11</sup> Norwegian Prescription Database,<sup>12</sup> Statistics Norway's events database (FD-Trygd) covering all types of social security benefits,<sup>13</sup> the National Education Database,<sup>14</sup> Income statistics for persons and families,<sup>15</sup> the Family Register linking participants in families<sup>16</sup> and local hospital disease registers.<sup>17,18</sup>

#### Loss to follow-up between the HUNT surveys

Regarding attrition between the HUNT2 and HUNT3 surveys, the participation rate in HUNT3 decreased by 15.4 percentage points. The decrease was most pronounced in men and younger adults. Among 65 237 participants in HUNT2, 10 507 (16.1%) had died at the time of HUNT3, 240 had emigrated and 1 had disappeared. Out of all HUNT2 participants, 72% of women and 69% of men also participated in HUNT3. People aged 50–59 years in HUNT2 were most compliant in that 74.1% participated in HUNT3. Among HUNT2 participants aged 20–29 years, 46.4% participated in HUNT3, whereas 21.1% had moved out of the county. (Table 3).

**Table 3** Compliance and attrition between the HUNT2 (asbaseline in 1995–97) and the HUNT3 surveys (as follow-upin 2006–08)

Age (years) at participation in HUNT2 (1995–97)	Statu	15 in HU 2006–08)			
· · · ·	Attandad	Not attended	Not	Marradb	Total
$\frac{\text{Age}}{20-29^{\text{c}}}$	Attenueu	attended	IIIvited	Moveu	10141
	4229	2002	20	1024	0115
N	4228	2883	80	1924	9115
%	46.4	31.6	0.9	21.1	100.0
30–39					
Ν	7696	3042	110	784	11 632
%	66.2	26.2	0.9	6.7	100.0
40-49					
Ν	10019	2651	337	597	13 604
%	73.6	19.5	2.5	4.4	100.0
50–59					
Ν	8195	1881	643	341	11 060
%	74.1	17.0	5.8	3.1	100.0
60–69					
Ν	5049	2072	1610	318	9049
%	55.8	22.9	17.8	3.5	100.0
70–79					
Ν	1800	2353	3534	307	7994
%	22.5	29.4	44.2	3.8	100.0
80-89					
Ν	84	378	2074	85	2621
%	3.2	14.4	79.1	3.2	100.0
90+					
Ν	0	4	157	1	162
%	0	2.5	96.9	0.6	100.0
Total					
Ν	37 071	15264	8545	4357	65 237
%	56.8	23.4	13.1	6.7	100.0

<sup>a</sup>Dead, emigrated or disappeared.

<sup>b</sup>Moved out of the county, but still living in Norway.

<sup>c</sup>Includes a total of 214 aged 10-19 years.

#### Non-participation studies

A comprehensive non-responder study was completed after HUNT1.<sup>1</sup> In HUNT2, shortly after completing the fieldwork, a 2.5% random sample of non-attendants was selected (n = 685) for a non-participation study.<sup>2</sup> These studies showed that the main reasons for non-attendance for people aged 20–44 years was lack of time and staying outside the county. In the age group 45–69, the main reasons were being very busy, forgetting the invitation or not being interested. For people aged 70+, the main reasons were having regular follow-up in the health services or being

immobilized due to disease. For the HUNT3 Survey, different non-participation analyses have been completed. These will soon be presented in an article in preparation (A Langhammer, personal communication, 18 May 2012). A comparison between participants answering Q1 and respondents only answering a non-participation questionnaire distributed to all non-participants, a comparison between participants and non-participants in national registers and a comparison of respondents with data from randomly selected general practices. The analyses showed that among non-participants, the prevalences of CVDs, diabetes mellitus and psychiatric disorders were higher both in non-participant data and data extracted from general practice, compared with that reported by participants. According to the register data, the non-participants had lower socio-economic status and a higher mortality than participants. Thus, depending on the question under research, possible selection bias should be taken into consideration.

### What has been measured?

#### Questionnaires in HUNT3 (Table 4)

Q1 was a self-report questionnaire filled in at home before the respondents attended the basic health examination. After the clinical examination, a second questionnaire (Q2) with a common major part and a specific sex and age (20-29, 30-69, 70+ years) part was handed out to everyone. Further, a third category of questionnaires (Q3) was given to individuals with selected diseases or other sub-groups according to particular responses given in Q1 (Table 4). Up to three different Q3s were handed out to each participant. Q2 and Q3 were to be completed at home and returned by mail in a pre-paid envelope. About 80% of the participants returned Q2/Q3. These questionnaires included questions about socio-economic conditions, health-related behaviours, symptoms, illnesses and diseases.

#### Interviews

All participants answered an interview at the health examination sites. Employed people were asked for occupational titles, business sectors and exposures to occupational hazards. Additionally, women were interviewed about menstruation, pregnancies and breastfeeding.

#### **Clinical measurements**

Blood pressure and heart rate were measured using a Dinamap 845XT (Critikon) based on oscillometry.<sup>19</sup> Height and weight were measured with the participants wearing light clothes without shoes: height to the nearest centimetre and weight to the nearest half kilogram. Waist and hip circumferences were measured with a band to the nearest centimetre, with the participant standing and with the arms hanging

Questionnaire (Q) <sup>a</sup>	Inclusion criteria <sup>b</sup>	Contents
Q1	All participants	Global health measures, diseases, symptom and function measures, health-related behaviours, childhood experiences, diseases in the family, health services utilization
Q2 (6 versions)	All participants, stratified by gender and three age groups; 20–29, 30–69, 70+ years	Psychosocial family, occupational and neigh- bourhood conditions, health-related behav- iours including culture and religious affiliation, symptoms of diseases, anxiety and depression, personality traits
Q3 diabetes	Self-reported diabetes in Q1	Treatment, disease-related symptoms
Q3 cardiovascular	Self-reported CVD in Q1	Treatment, disease-related symptoms
Q3 cancer prostate	Self-reported prostate cancer reported at health examination	Psychosocial factors, symptoms and problems
Q3 cancer colon	Self-reported colon cancer reported at health examination	Psychosocial factors, symptoms and problems
Q3 cancer breast	Self-reported breast cancer reported at health examination	Psychosocial factors, symptoms and problems
Q3 psoriasis	Self-reported psoriasis in Q1	Treatment, disease-related symptoms and problems
Q3 hand eczema	Self-reported hand eczema in Q1	Treatment, disease-related symptoms and problems
Q3 health services	Self-reported hospitalization last year in Q1+ 10% random sample	Health services experiences and evaluations
Q3 complementary and alternative medicine (CAM)	Self-reported use of complementary and alter- native medicine in Q1	Alternative medicine utilization, motivation and experiences
Q3 carnivores	Participants in Lierne (case) and Namdalseid (control) municipalities	Experiences of living in an area where large carnivores are common, for health, quality of life, recreation and business

Table 4 Questionnaires in the HUNT3 Survey (2006–08), inclusion and exclusion criteria, contents

<sup>a</sup>http://www.ntnu.edu/hunt/data/que.

<sup>b</sup>No participant was requested to fill in more than three different Q3s. Priority was given to Q3s for diabetes, CVD and cancer; thus a few participants with several diseases were excluded from the other Q3s.

relaxed. The waist circumference was measured horizontally at the height of the umbilicus, and the hip circumference was measured likewise at the thickest part of the hip.

#### Blood and urine sampling, biobanking

Biological material was collected at the health examination stations and transported daily by courier to the biobank. Blood sampling followed a strict quality protocol, collecting serum, plasma, buffy coat, immortalized cells for cell line production, specialized tubes for trace metal/elements analysis and RNA tubes. Urine was collected when possible, and frozen immediately. Procedures have been established for (i) blood fractionation and distribution into 2-D bar coded cryo tubes, (ii) DNA isolation and normalization and (iii) storage and retrieval of 1 million DNA samples operating at  $-20^{\circ}$ C. Samples are also stored at  $-80^{\circ}$ C in manual ultra-freezers and in the vapour phase of liquid nitrogen. Details will be described in a separate paper (K Hveem, personal communication, 18 May 2012).

#### Sub-studies collecting clinical data

In several sub-studies (Table 5), selected participants were invited for additional examinations, like certain age groups, disease- and sex-specific groups or participants restricted to certain municipalities,<sup>20–23</sup> whereas in some sub-studies randomized samples were invited. Data from these sub-studies, which were run and funded separately, are integrated in the HUNT databank and made available for researchers after a 4–5 years protection period of exclusive rights for the researchers responsible for each of the sub-studies.

# What has it found? Key findings and publications

About 600 scientific papers and 78 PhDs based on the data from HUNT, covering a wide range of scientific disciplines, have been published up to May 2012. Data from HUNT1 showed either population-based screening for detecting hypertension<sup>24</sup> or lung X-ray

Table 5	Sub-studies	in the	HUNT3	Survey	(2006–08)
---------	-------------	--------	-------	--------	-----------

Project	Inclusion/exclusion criteria	Sample size <sup>a</sup>	
Phase 1 <sup>b</sup>			
Echocardiography	No heart/lung disease	1278	
Maximum oxygen uptake rate and blood vessel test	No cancer, heart disease, pregnancy, blindness or other medical contraindication to fast walk	5111	
Urine sampling for microalbuminuria examination	Follow-up of a HUNT2 cohort	5861	
Spirometry test and lung interview	Asthma, asthma-related symptoms and 10% random sample	12 128	
Bone densitometry forearm, hips and lumbar spine	As for spirometry and a female cohort having participated in the osteoporosis study in HUNT2	17336	
Phase 2 <sup>c</sup>			
Diabetes or high risk for diabetes type 2, diagnostics and intervention <sup>d</sup>	High Finnish Diabetes Risk Score (FINDRISC), known diabetes	5428	
Oral health examination	Random in specific age cohorts	600	
Headache and alcohol validation interviews, polysomnography	Samples reporting headache in Q1+ control group	297	
Chronic pain, 5-year follow-up (questionnaires)	Reported chronic pain in Q1 in two municipalities	4782	
Neck/low back pain, 1-year follow-up (questionnaires)	Reporting acute pain in neck/low back in two municipalities	220	
Cognitive tests	Selected municipalities, sample without known CNS disease	120	
Psoriasis and hand eczema clinical examination	Self-reported skin diseases and controls	544	
Cerebral magnetic resonance imaging (MRI)	Selected municipalities, sample without known CNS disease	986	

<sup>a</sup>Sample size for the clinical tests.

<sup>b</sup>Phase 1 in HUNT3, at the initial attendance at the health examination sites.

<sup>c</sup>Phase 2 in HUNT3, at a later date.

<sup>d</sup>Co-operation with other European centres in the EU-funded DE-PLAN project.

screening for detecting tuberculosis to be cost effective (data not published). Further, in healthy individuals, quality of life was not affected by receiving the message that they had hypertension.<sup>25</sup>

A number of HUNT studies have been published in high impact journals. Both data and biological material have been used in international collaborative projects revealing previously unknown genetic susceptibility for common diseases such as cancers<sup>26,27</sup> and type 2 diabetes.<sup>28</sup> The risk of urinary incontinence was shown to be higher among women who have had caesarean sections than among nulliparous women, and even higher among women who have had vaginal deliveries.<sup>6</sup>

HUNT publications have raised important questions about the applicability of international guidelines for prevention of CVDs.<sup>29</sup> If guideline recommendations were meticulously applied, as many as 84% of all adults in Norway could exhibit two or more CVDs or risk factors and thus be considered in need of individual clinical attention, raising several practical as well as ethical questions.<sup>30</sup>

Data from HUNT1 and HUNT2 showed a significant increase of obesity and diabetes in the population.<sup>31</sup> More surprisingly, data from HUNT2 showed no association between hypothyroidism and depression and anxiety<sup>32</sup> and that high blood pressure was not associated with headache.33 Moreover, despite the belief in healthy effects of cod liver oil intake, there was a negative dose-response effect between childhood intake and adult bone density.34 HUNT data have also questioned seasonal variation of insomnia symptoms<sup>35</sup> as well as gender differences in prevalence of depression.<sup>36</sup> Data have showed that commonly used prediction equations for spirometry underestimate normal lung function<sup>3</sup> and that use of inhaled corticosteroids for obstructive lung disease was associated with increased bone loss at the forearm, but should nevertheless not give any clinical concerns as to unwanted effects on bone.38

Social epidemiological studies have shown that socio-economic inequalities in health in the HUNT population are comparable with those of other Northern European populations,<sup>39</sup> and have disentangled mechanisms behind socio-economic inequalities in mortality<sup>15</sup> and the high impact of social factors on work-related disability.<sup>13</sup> The HUNT Study has also contributed to important ethical discussions regarding population based epidemiological studies.<sup>40,41</sup> A complete list of publications can be found on HUNT website (www.ntnu.edu/hunt).

# What are the main strengths and weaknesses?

The HUNT Study has several strengths: It covers a total population aged 20-100 years within a specific geographical area, including coastal and inland municipalities with different characteristics. HUNT has a wide age range, thereby covering groups of people with different cohort exposures. Data in each survey have been collected over a 2-year period, enabling studies of seasonal variations in health.35 HUNT databank includes data on an extensive range of topics (>5000 variables). Another obvious strength is that all data are linked to the unique personal identification number enabling linkage of data for each individual, and linkage to a number of local, regional and national health registers, with nearly complete follow-up data. The participation rate was exceptionally high in HUNT1 and very good or acceptable in most age groups in HUNT2 and HUNT3. HUNT3 was a 22-year follow-up of HUNT1 and 11-year follow-up of HUNT2 with a carefully considered combination of identical or similar questions and assessments and new topics.

In HUNT3, a state-of-the-art biobank was established, with storage facilities that ensure availability of the biomaterial for research decades ahead. The inclusion of adolescents aged 13–19 years (Young-HUNT) since 1995, as well as the linkage to the Family Register, makes it possible to establish family trees including three generations for a large number of participants.

About 10% of the participants in the HUNT3 Survey were recommended a clinical check-up with their family doctor. Presumably, most of the participants benefited from this health intervention. On the other hand, health examinations might contribute to dilemmas associated with screening, such as risk focusing, false positive/negative identification and medicalization.<sup>42</sup> However, the Regional Committee for Medical and Health Research Ethics agreed with the HUNT3 management group that the benefits and opportunities in the HUNT Study far exceeded the potential disadvantages for some individual participants.

Epidemiological observational studies are a minor ethical challenge compared with human experiments. During the 27 years of HUNT follow-up management, there has been no report of threats to personal protection or privacy regarding the HUNT Study. Nevertheless, the Norwegian legislation and the case considerations by the public authorities have been constantly changing, complicated and time-consuming for researchers.<sup>43</sup> A new Norwegian Health Research Law that became operative on 1 July, 2009 simplified the use of (strictly defined) health registers, making only one public authority, the Regional Committee for Medical and Health Research Ethics, responsible for project approvals. However, when researchers need to link data to non-health public registers, like registers for social security benefits, family linkage, income and education, the approval procedures are still complicated.

Over the past 27 years, 153 545 subjects (including adolescents) have been invited to the HUNT surveys. Data are available from 126159 participants (82%) with a total of over 5000 variables. HUNT3, adding a large amount of new data to the database, rendered new data storage facilities necessary. A relational database has been developed where data and meta-data are integrated, facilitating consistency, integrity and improved quality assurance. During this process, old and new data have been quality assured, and variable-specific information stored in metadata. Further, all variables have been given names consisting of a prefix, which consists of question and measurement abbreviations, and a suffix indicating the source of data (as HUNT Study, study part, type of data question/interview/measurement/administrative) and whether the data were original or constructed. The metadata include information about previous use of the variable, pivotal references and whether what is part of validated questionnaires or specifications of equipment used. The quality assurance of data and inclusion of metadata will continue in the coming years.

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

Data from the HUNT Study are available for researchers who satisfy some basic requirements (www.ntnu.edu/ hunt) whether affiliated in Norway or abroad. To provide the researcher or research group exclusive rights, the HUNT Research Centre signs a contract with the research institution in charge. The exclusive rights are connected to a specific publication plan based on an application form, a scientific protocol, an ethical approval, other necessary approvals (if any) and a variable specification list.

More details about the contents of the questionnaires and clinical measurements can be found on our website (www.ntnu.edu/hunt).

Conflict of interest: None declared.

#### **KEY MESSAGES**

Among a range of outcomes, the HUNT Study has found the following

- A strong increase of obesity and diabetes has been observed in the Norwegian population since the 1980s. Previously unknown genetic susceptibility not only for diabetes but also for cancers and other common diseases has been revealed.
- HUNT data have showed that lung X-ray screening for detecting tuberculosis is as ineffective and that commonly used prediction equations for spirometry underestimate normal lung function.
- Population-based screening for detecting hypertension was found to be ineffective in the 1980s. Publications have also raised important questions about the applicability of international guidelines for prevention of CVDs and contributed to important ethical discussions regarding population-based epidemiological studies.
- HUNT data have shown the great impact of social factors on health and work-related disability and that the socio-economic inequalities in health in the HUNT population are comparable with those of other Northern European populations.
- Up to May 2012, ~600 scientific papers and 78 PhDs based on data from the HUNT Study have been published, covering a wide range of scientific disciplines.

### References

- <sup>1</sup> Holmen J, Midthjell K, Forsen L, Skjerve K, Gorseth M, Oseland A. [A health survey in Nord-Trøndelag 1984-86. Participation and comparison of attendants and non-attendants]. *Tidsskr Nor Laegeforen* 1990;**110**:1973–77.
- <sup>2</sup> Holmen J, Midthjell K, Krüger Ø et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. Norsk Epidemiologi 2003;13:19–32. http://www.ntnu.no/ojs/ index.php/norepid/article/view/305 (26 June 2012, date last accessed).
- <sup>3</sup> Esping-Andersen G. *The Three Worlds of Welfare Capitalism*. Cambridge: Polity Press & Princeton: Princeton University Press, 1990.
- <sup>4</sup> Galea S, Tracy M. Participation rates in epidemiologic studies. Ann Epidemiol 2007;**17**:643–53.
- <sup>5</sup> Bjelland I, Krokstad S, Mykletun A, Dahl AA, Tell GS, Tambs K. Does a higher educational level protect against anxiety and depression? The HUNT study. *Soc Sci Med* 2008;**66**:1334–45.
- <sup>6</sup> Rørtveit G, Daltveit AK, Hannestad YS, Hunskaar S. Urinary incontinence after vaginal delivery or cesarean section. *N Engl J Med* 2003;**348**:900–7.
- <sup>7</sup> Sjødahl K, Jia C, Vatten L, Nilsen T, Hveem K, Lagergren J. Body mass and physical activity and risk of gastric cancer in a population-based cohort study in Norway. *Cancer Epidemiol Biomarkers Prev* 2008;17: 135–40.
- <sup>8</sup> Dale AC, Nilsen TI, Vatten L, Midthjell K, Wiseth R. Diabetes mellitus and risk of fatal ischaemic heart disease by gender: 18 years follow-up of 74,914 individuals in the HUNT 1 Study. *Eur Heart J* 2007;**28**:2924–29.
- <sup>9</sup> Drøyvold WB, Lund Nilsen TI, Lydersen S *et al.* Weight change and mortality: the Nord-Trøndelag Health Study. *J Intern Med* 2005;**257:**338–45.
- <sup>10</sup> Svebak S, Romundstad S, Holmen J. A 7-year prospective study of sense of humor and mortality in an adult county population: the HUNT-2 study. *Int J Psychiatry Med* 2010; **40**:125–46.
- <sup>11</sup> Vatten LJ, Holmen J, Krüger Ø, Forsen L, Tverdal A. Low blood pressure and mortality in the elderly: a 6-year

follow-up of 18,022 Norwegian men and women age 65 years and older. *Epidemiology* 1995;**6**:70–73.

- <sup>12</sup> Hagen K, Stovner LJ, Skorpen F, Pettersen E, Zwart JA. COMT genotypes and use of antipsychotic medication: linking population-based prescription database to the HUNT study. *Pharmacoepidemiol Drug Saf* 2008;17: 372–77.
- <sup>13</sup> Krokstad S, Johnsen R, Westin S. Social determinants of disability pension: a 10-year follow-up of 62 000 people in a Norwegian county population. *Int J Epidemiol* 2002;**31**: 1183–91.
- <sup>14</sup> Ernstsen L, Bjerkeset O, Krokstad S. Educational inequalities in ischaemic heart disease mortality in 44 000 Norwegian women and men: the influence of psychosocial and behavioural factors. The HUNT Study. *Scand J Public Health* 2010;**38**:678–85.
- <sup>15</sup> Skalicka V, van Lenthe F, Bambra C, Krokstad S, Mackenbach J. Material, psychosocial, behavioural and biomedical factors in the explanation of relative socio-economic inequalities in mortality: evidence from the HUNT study. *Int J Epidemiol* 2009;**38**:1272–84.
- <sup>16</sup> Nilsen SM, Krokstad S, Holmen TL, Westin S. Adolescents' health-related dietary patterns by parental socio-economic position, the Nord-Trøndelag Health Study (HUNT). Eur J Public Health 2010;**20**:299–305.
- <sup>17</sup> Ellekjær H, Holmen J, Ellekjær E, Vatten L. Physical activity and stroke mortality in women. Ten-year follow-up of the Nord-Trøndelag health survey, 1984-1986. *Stroke* 2000;**31**:14–18.
- <sup>18</sup> Næss IA, Christiansen SC, Romundstad P, Cannegieter SC, Rosendaal FR, Hammerstrom J. Incidence and mortality of venous thrombosis: a population-based study. *J Thromb Haemost* 2007;**5**:692–99.
- <sup>19</sup> Lund-Larsen PG. Blood pressure measured with a sphygmomanometer and with Dinamap under field conditions a comparison. *Nor J Epidemiol* 1997;7: 235–41. http://www.ntnu.no/ojs/index.php/norepid/article/view/413 (26 June 2012, date last accessed).
- <sup>20</sup> Dalen H, Thorstensen A, Romundstad PR, Aase SA, Støylen A, Vatten LJ. Cardiovascular risk factors and systolic and diastolic cardiac function: a tissue doppler and

speckle tracking echocardiographic study. *J Am Soc Echocardiogr* 2011;**24**:322–32.

- <sup>21</sup> Hagen K, Zwart JA, Aamodt AH *et al.* The validity of questionnaire-based diagnoses: the third Nord-Trøndelag Health Study 2006-2008. *J Headache Pain* 2010;**11**:67–73.
- <sup>22</sup> Holst D, Schuller A, Dahl KE. [Better dental health care for all?]. Nor Tannlegeforen Tid 2007;117:804–11.
- <sup>23</sup> Pettersen E, Skorpen F, Kvaloy K, Midthjell K, Grill V. Genetic heterogeneity in latent autoimmune diabetes is linked to various degrees of autoimmune activity: results from the Nord-Trøndelag Health Study. *Diabetes* 2010;**59**: 302–10.
- <sup>24</sup> Holmen J, Forsen L, Hjort PF, Midthjell K, Waaler HT, Bjorndal A. Detecting hypertension: screening versus case finding in Norway. *BMJ* 1991;**302**:219–22.
- <sup>25</sup> Moum T, Sørensen T, Næss S, Holmen J. [Does diagnosed hypertension change quality of life? Results from a medical population study in Nord-Trøndelag]. *Tidsskr Nor Laegeforen* 1992;**112**:18–23.
- <sup>26</sup> Hung RJ, McKay JD, Gaborieau V *et al.* A susceptibility locus for lung cancer maps to nicotinic acetylcholine receptor subunit genes on 15q25. *Nature* 2008;452: 633–37.
- <sup>27</sup> Purdue MP, Johansson M, Zelenika D *et al*. Genome-wide association study of renal cell carcinoma identifies two susceptibility loci on 2p21 and 11q13.3. *Nat Genet* 2011; 43:60–65.
- <sup>28</sup> Voight BF, Scott LJ, Steinthorsdottir V *et al*. Twelve type 2 diabetes susceptibility loci identified through large-scale association analysis. *Nat Genet* 2010;**42**:579–89.
- <sup>29</sup> Westin S, Heath I. Thresholds for normal blood pressure and serum cholesterol. *BMJ* 2005;**330**:1461–62.
- <sup>30</sup> Petursson H, Getz L, Sigurdsson JA, Hetlevik I. Can individuals with a significant risk for cardiovascular disease be adequately identified by combination of several risk factors? Modelling study based on the Norwegian HUNT 2 population. *J Eval Clin Pract* 2009; 15:103–9.
- <sup>31</sup> Midthjell K, Krüger Ø, Holmen J *et al.* Rapid changes in the prevalence of obesity and known diabetes in an adult Norwegian population. The Nord-Trøndelag Health Surveys: 1984-1986 and 1995-1997. *Diabetes Care* 1999; 22:1813–20.

- <sup>32</sup> Engum A, Bjøro T, Mykletun A, Dahl AA. Thyroid autoimmunity, depression and anxiety; are there any connections? An epidemiological study of a large population. J Psychosom Res 2005;59:263–68.
- <sup>33</sup> Hagen K, Stovner LJ, Vatten L, Holmen J, Zwart JA, Bovim G. Blood pressure and risk of headache: a prospective study of 22 685 adults in Norway. J Neurol Neurosurg Psychiatry 2002;72:463–66.
- <sup>34</sup> Forsmo S, Fjeldbo SK, Langhammer A. Childhood cod liver oil consumption and bone mineral density in a population-based cohort of peri- and postmenopausal women: the Nord-Trøndelag Health Study. *Am J Epidemiol* 2008;**167:**406–11.
- <sup>35</sup> Sivertsen B, Øverland S, Krokstad S, Mykletun A. Seasonal variations in sleep problems at latitude 63<sup>o</sup>-65<sup>o</sup> in Norway: the Nord-Trøndelag Health Study, 1995-1997. Am J Epidemiol 2011;**174:**147–53.
- <sup>36</sup> Stordal E, Bjartveit KM, Dahl NH, Krüger Ø, Mykletun A, Dahl AA. Depression in relation to age and gender in the general population: the Nord-Trøndelag Health Study (HUNT). *Acta Psychiatr Scand* 2001;**104**:210–16.
- <sup>37</sup> Langhammer A, Johnsen R, Gulsvik A, Holmen TL, Bjermer L. Forced spirometry reference values for Norwegian adults: the Bronchial Obstruction in Nord-Trøndelag Study. *Eur Respir J* 2001;**18**:770–79.
- <sup>38</sup> Langhammer A, Forsmo S, Lilleeng S, Johnsen R, Bjermer L. Effect of inhaled corticosteroids on forearm bone mineral density: the HUNT study, Norway. *Respir Med* 2007;**101**:1744–52.
- <sup>39</sup> Krokstad S, Kunst AE, Westin S. Trends in health inequalities by educational level in a Norwegian total population study. *J Epidemiol Community Health* 2002;**56**: 375–80.
- <sup>40</sup> Ursin LØ. Biobank research and the right to privacy. *Theor Med Bioeth* 2008;**29:**267–85.
- <sup>41</sup> Ursin LØ. Personal autonomy and informed consent. *Med Health Care Philos* 2009;**12**:17–24.
- <sup>42</sup> Skolbekken JA. The risk epidemic in medical journals. Soc Sci Med 1995;40:291–305.
- <sup>43</sup> Skolbekken JA, Ursin K, Solberg B, Christensen E, Ytterhus B. Not worth the paper it's written on? – Informed consent and biobank research in a Norwegian context. *Crit Public Health* 2005;**15**:335–47.