The Nord-Trøndelag Health Study 1995-97 (HUNT 2): Objectives, contents, methods and participation

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ABSTRACT

The second Nord-Trøndelag Health Study in 1995-97 (HUNT 2) was partly a follow-up study of HUNT 1, conducted in 1984-86. HUNT 2 comprised, however, a larger scientific program. The large amount of information collected from each participant, and the large number of participants in a wide age range covering an entire county population, make HUNT one of the largest health studies ever performed. This paper describes the survey covering persons aged 20 years and older. In total, 66.7% of men (n=30,860) and 75.5% of women (n=35,280) participated, the highest participation was in age group 60-69 and the lowest among the young and the elderly. Data collected from several questionnaires and with blood and urine samples and various clinical measurements, some of them in sub-samples of the study population, comprise a huge database for research. All data for each person are linked, and data are also linked to various health registries; all data handling being supervised by The Data Inspectorate and The Regional Ethical Committee. Procedures for data access are established, and more than 100 researchers are currently working on HUNT data. A large number of scientific papers in various disciplines are published, among them 15 doctoral theses (June 2003). The research potential of the HUNT biobank is still not fully exploited, but initiatives are taken. In line with other population based studies both in Norway and abroad, there was a decline in participation rate from HUNT 1 to HUNT 2 (16.9%). This has raised concern about the validity of future population based health studies. However, the good local and national network and the support from the population, make up a good platform also for future health studies in Nord-Trøndelag.

Key words: Health survey, methods, participation, epidemiology, cardiovascular disease, hypertension, diabetes, lung disease, osteoporosis, depression, anxiety, hemochromatosis, hearing loss, headache, migraine, prostate, women's health

INTRODUCTION

The first large health survey in Nord-Trøndelag County, Norway (later called the HUNT 1 study) was conducted during 1984-86. It was primarily designed to cover four sub-studies, i.e. on hypertension, diabetes, lung diseases and quality of life. The main objectives were to determine the prevalence of hypertension, diabetes and undiagnosed tuberculosis, and to evaluate the quality of health care provided to hypertensive patients, persons with diabetes, and persons with tuberculosis. Blood pressure, body height, and weight were measured and a miniature chest x-ray was taken. Each participant completed at least two questionnaires. Additionally, non-fasting blood glucose was measured in participants 40 years and older. Persons whose blood test could indicate diabetes were, along with a control group, offered a clinical evaluation. All participants with clinical findings indicating pathology were advised to see their family doctor, who also received clinical results from the health study itself. Venous blood samples were not taken, except in known and newly detected persons with diabetes and in a control group. In total, 74,599 persons aged 20 and older participated (88.1%). The methods applied in HUNT 1 are described in detail elsewhere[1], and so is a comprehensive non-responder study[2,3]. Several studies based on HUNT 1 are published, among these are studies on cardiovascular disease[4-17], diabetes[6,18-23], quality of life[24-29], cancer[30-34] and other topics[35-40].

HUNT 2 (1995-97): OBJECTIVES

The main objectives in HUNT 2 were aimed at the large public health issues like cardiovascular disease, diabetes, obstructive lung disease, osteoporosis and mental health, in concordance with current priorities of the health authorities. Several researchers and research groups presented a wide range of additional scientific questions, some of which were included in the final protocol. The result was a comprehensive health study covering a wide range of topics. The Young-HUNT Study aimed at age group 13-19 was organized separately and is described elsewhere[41,42]. This paper gives

an overview of the population, the contents, the methods applied and the participation in the HUNT 2 study for those aged 20 years and older.

STUDY AREA AND POPULATION

Nord-Trøndelag County is located in the middle of Norway at a latitude of 64 degrees north, and is divided into 24 administrative areas, i.e. municipalities (Figure 1). The county is mostly rural and sparsely populated; the largest of six small towns has a population of 21,000. The average income, the prevalence of higher education, and the prevalence of current smokers are a little lower than the average of Norway. In most respects, however, Nord-Trøndelag County is fairly representative of Norway, for example regarding geography, economy, industry, and sources of income, age distribution, morbidity and mortality.

Due to the Gulf Stream the climate is milder than in other areas of the same latitude. The coastal climate has precipitation as rain in fall, spring, and summer, and snow or rain in winter, but some inland areas have cold, dry winters. During mid-summer there is daylight all night, but days during mid-winter are as short as 5-6 hours, and there may be frost from November through March. Some basic data about Nord-Trøndelag County is given in Table 1.

The population in Nord-Trøndelag County (127,000 residents) is stable, with a net out migration of 0.3% per year (1996-2000), and homogenous (less than 3% non-Caucasian), making it suitable for epidemiological studies.

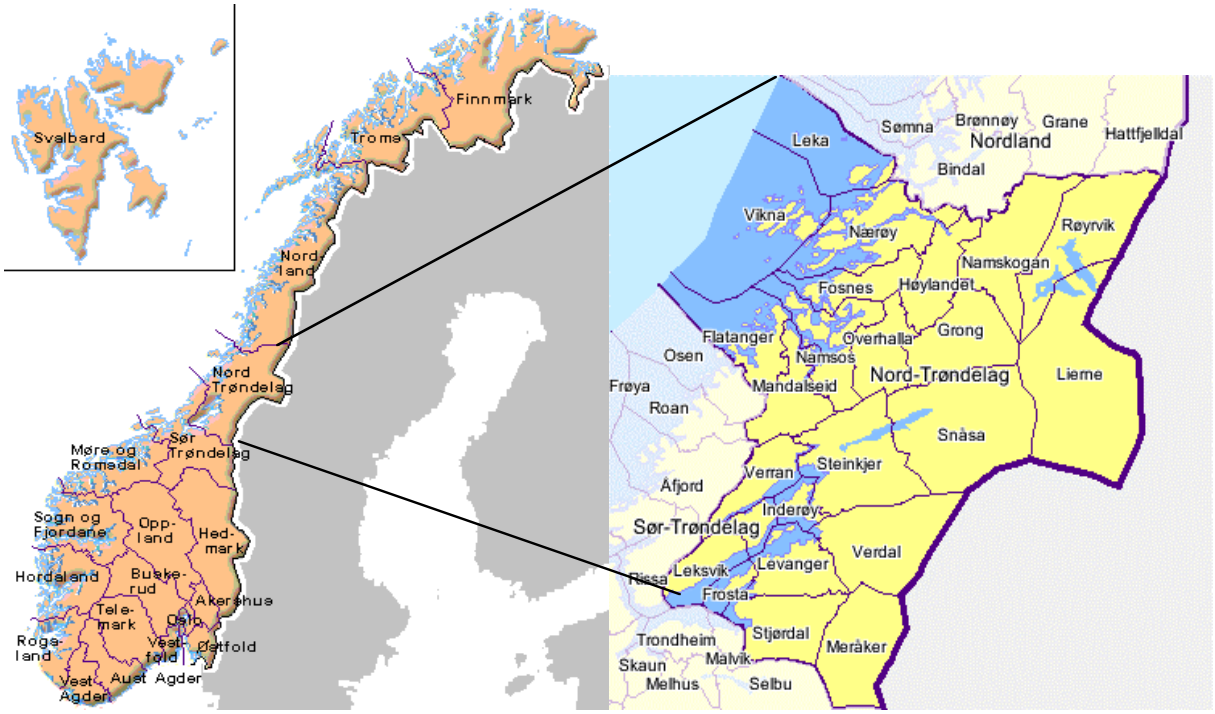
As in HUNT 1 (1984-1986) every individual residing in the county at the age of 20 and older was invited to participate in the HUNT 2 study. Several sub-studies in HUNT 2 were aimed at the elderly, and there was no upper age limit. Some additional sub-studies used other population samples, such as randomized samples, certain age groups, sex-specific samples or samples restricted to certain municipalities.

METHODS

Invitation letter and questionnaires

All residents of Nord-Trøndelag County, aged 20 years (reaching 20 years during the year of the screening in their municipality) and older were invited to the health survey in the two-year period from August 1995 to June 1997. The invitation file was created from periodically updated census data from Statistics Norway. The invitation letter was sent by mail attached to a three-page questionnaire (questionnaire 1) and an information folder. The questionnaire was to be completed prior to the screening and returned at attendance to the screening site. A second questionnaire (questionnaire 2) was handed out at the screening site and should be completed and returned by mail free of cost for the participant. A wide range of topics was addressed in questionnaire 1 and 2:

Figure 1. Norway and Nord-Trøndelag County.



- Health: Subjective health, diabetes[18,20,23], lung diseases[43-45], cardiovascular diseases, thyroid diseases[46-49], muscle- and skeletal diseases[50,51], mental diseases (especially anxiety and depression)[48,51-55], quality of life measures, migraine and other headaches[49,55-65], and physical and mental dysfunction, prostate complaints[66,67], quality of life, urine incontinence[68-72], and female reproductive data i.e. on menarche, pregnancies, hormone use, and gynecological diseases.
- Personal environment: Residence, size of household, education, occupation[73-77], in-house environment, neighborhood, friends, and sense of humor.
- Personal habits, like food intake, use of drugs, use of alcohol and tobacco[70,78,79], and physical activities.
- Family medical histories and health services consumption.

Additional questionnaires were used in sub-samples, and are described elsewhere, i.e. questionnaires on lung diseases[42], diabetes[18,42], hypertension[42], hearing disorders[80-84], and vision[85]. Some selected groups were invited to a more detailed examination as part of a phase 2 examination, i.e. participants in studies on diabetes[18], prostate[66,67], headache[57-62,86], lung function[43-45] and bone densitometry[78,79] (Figure 2).

Table 1. Selected statistical data on Nord-Trøndelag and Norway (From the Norwegian Meteorological Institute and Statistics Norway).

	Nord-Trøndelag (Verdal, Reppe)	Oslo (Blindern)	Tromsø
Climate *(Normal)*			
Mean air temperature (centigrades)	4.4	5.7	2.5
Precipitation (mm/year)	910	763	1,031
		Nord-Trøndelag	Whole country
Geography			
Total area (km^2)		22,463	323,877 (*)
Population *(2000)*			
Total population		127,108	4 478,497
Population density/km^2		6	15 (*)
Population (%)			
- in sparsely populated areas		44	23
- in densely populated areas < 2000 inhabitants		20	11
- in densely populated areas ≥ 2000 inhabitants		36	66
Financial situation (1996) Assessed mean income (brto) NOK			
Males		189,100	227,600
Females		116,900	132,300
Infant mortality (1996)			
Deaths under 1 year of age/1000 live births		5.0	4.1
Induced legal abortions (1996)			
(Per 1000 women 15-49 year)		11.5	13.4
Kindergartens (2002)			
Children in kindergartens *(Per cent 1-5 years)*		68.6	65.9
Education (2001) *(Per cent)*			
Below upper secondary level[1]		22.1	21.2
Upper secondary education[2]		60.5	56.6
Tertiary education, short[3]		14.8	17.5
Tertiary education, long[4]		2.7	4.8
Mortality *(Standardized rates. Deaths /100,000 population, average 1996-2000)*			
Deaths, all causes			
Males		1,032	1,086
Females		640	651
Diseases of the circulatory system (I00-I99)			
Males		475	459
Females		277	261
Malignant neoplasm (C00-C97)			
Males		249	282
Females		168	177

(*) Main land, i.e. Spitzbergen excluded.

[1] Not including persons with unknown or no completed education.

[2] Including the level 'Intermediate level' which comprises education based on completed upper secondary level, but which are not accredited as tertiary education.

[3] Tertiary education, short comprises higher education 4 years or shorter.

[4] Tertiary education, long comprises higher education more than 4 years.

Clinical measurements

*S*creening sessions were performed by the two teams (see Appendix) visiting each municipality of the county, with ordinary opening hours between 10 a.m. and 6 p.m. (occasionally from 8 a.m. to 7 p.m.). All clinical examinations were performed indoors at comfortable room temperature. The team surveying the five largest municipalities used more extensive standard office facilities; the other team working in the 19 smaller municipalities used a large, well-equipped trailer with efficient temperature regulation and other modern facilities.

Blood pressure and heart rate were measured by specially trained nurses or technicians using a Dinamap 845XT (Critikon) based on oscillometry. Cuff size was adjusted after measuring the arm circumference. The Dinamap was started after the participant had been seated for two minutes with the cuff on the arm, and the arm resting on a table. Blood pressure and heart rate were measured automatically three times at one-minute intervals. Blood pressures reported in most papers is the mean of the second and third systolic and diastolic blood pressures. Blood pressures measured with the Dinamap device are slightly lower than those measured with a sphygmomanometer, especially for diastolic blood pressure[87].

Height and weight were measured with the participants wearing light clothes without shoes; height to the nearest 1.0 cm and weight to the nearest 0.5 kg.

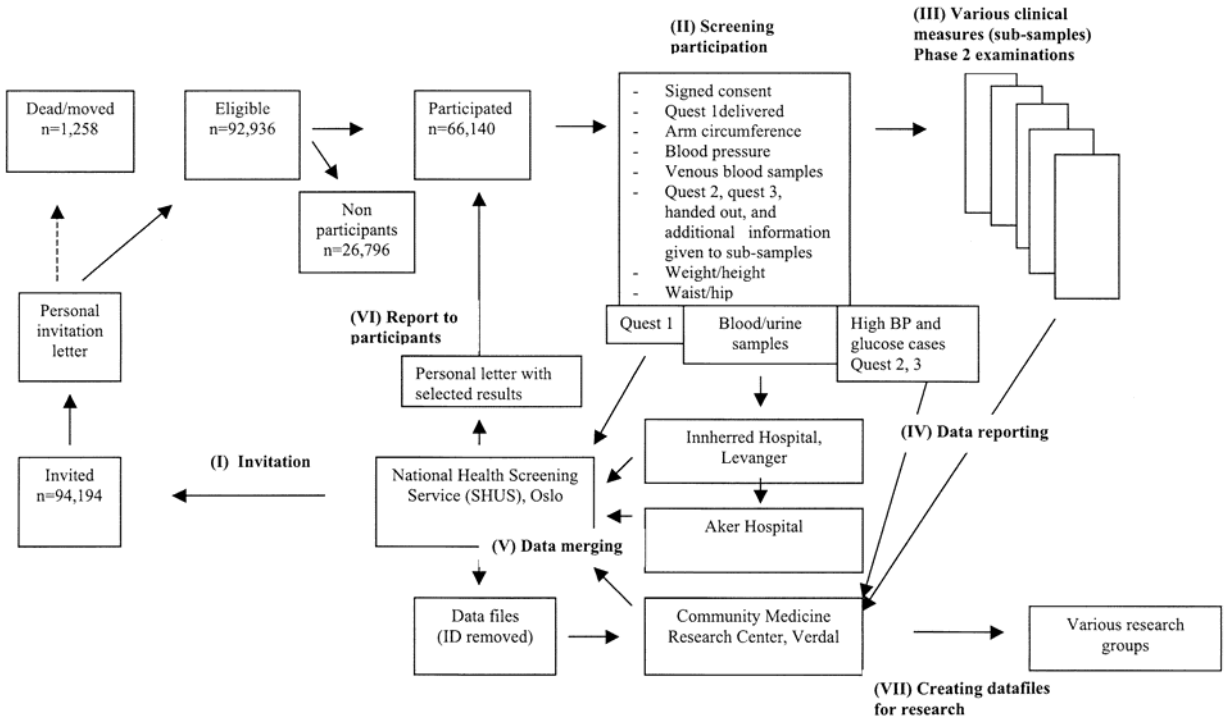


Figure 2. Procedures for invitation, screening, data reporting and creating of research data files. HUNT 2 (1995-97).

Step I: Invitation. National Health Screening Service (SHUS) created invitation letters based on data files from Statistics Norway, including all residents in Nord-Trøndelag County aged 20 years and older. Invitations were mailed a few weeks before the time of screening in the resident's community. The invitation file was regularly up-dated from Statistics Norway.

Step II: Screening participation. All participants went through procedures described in the box.

Step III: Various clinical measures. Phase 2. Participants were selected to various additional clinical measures: bone densitometry, spirometry, hearing, vision. A number of sub-samples were also invited to phase 2 clinical examination: Hemochromatosis, prostate, headache, spirometry, microalbuminuria, hypothyreosis, depression.

Step IV: Data reporting. Questionnaire 1 was sent to SHUS, and blood and urine samples to Innherred Hospital, witch forwarded selected samples to Aker Hospital. Extremely high BP and glucose readings were reported immediately to the Community Medicine Research Center, Verdal, who also received questionnaires 2, 3, and various data sets from additional clinical measurement.

Step V: Data merging. All data were sent to SHUS, where data files were merged.

Step VI: Reports to participants. Based on merged data files from questionnaires, clinical measurements and serum analyses, each participant was mailed a personal report with selected results.

Step VII: Creating data files for research. Data files with removed ID were sent to Community Medicine Research Center (Now: HUNT Research Center), Verdal, where appropriate research files are created and distributed to various research groups based on accepted protocols.

Waist and hip circumferences were measured with a steel band to the nearest 1.0 cm with the participant standing and with the arms hanging 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.

Additional clinical measurements were performed in sub-samples, and are described more in detail elsewhere: Lung function[43,44], bone densitometry[78,79], hearing[80-84], vision[85], headache/migraine[49,55-62,64,65], ankle blood pressure (Doppler technique)[88] and sensibility in the foot[18]. In addition some studies and clinical follow-up procedures will be described in papers in progress.

Blood sampling

Blood sampling was done whenever subjects attended, i.e. in non-fasting or "random" state. In the period from August 1995 to June 1996 7.5 ml whole blood was drawn, serum was separated by centrifuging at the screening site and immediately placed in a refrigerator. The samples were sent in a cooler to the Central Laboratory at Levanger Hospital, Levanger, the same day or within two to three days (for example in weekends). Serum analyses were performed in fresh blood samples, and the remaining serum and clot stored in the biobank at minus 70 °C. From August 1996 to June 1997 routines were changed: An additional 5 ml of blood was drawn in an EDTA tube. This EDTA whole blood was stored in the biobank instead of the clot. The content of the HUNT biobank is described in Table 2.

Table 2. The HUNT 2 biobank, contributed by participants 20 years and older at HUNT 2, 1995-97. Stored at minus 70°C. DNA extraction is ongoing (Status per June, 2003).

	N	Volume ml (approx)	Extracted DNA N
Serum	65,291	1.5[1]	
Whole blood			
- EDTA	29,875	3-4	7,633[2]
- Clots	32,789	3-5	1,810
DNA samples, total	62,664		9,443[3]

[1] All serum in one tube. Serum is already used for analyses in a few studies, i.e. the volume is smaller in some population samples.

[2] After DNA extraction, left whole blood is stored in separate tubes for CONOR (0.4 ml x 4) and HUNT (0.4 ml x 4)

[3] Extracted DNA is stored in two separate tubes.

Laboratory procedures

Serum samples were analyzed at the Central Laboratory at Levanger Hospital, on an Hitachi 911 Autoanalyzer (Hitachi, Mito, Japan), applying reagents from Boehringer Mannheim (Mannhein, Germany). Glucose was measured by using an enzymatic hexokinase method, total cholesterol and HDL cholesterol applying an enzymatic colorimetric cholesterolesterase method, and HDL cholesterol was measured after precipitation with phosphortungsten and magnesium ions. Triglycerides were also measured with an enzymatic colorimetric method, and serum creatinine by Jaffè method. The day-to-day coefficients of variation were 1.3-2.0% for glucose, 1.3-1.9% for cholesterol, 2.4% for HDL cholesterol, 0.7-1.3% for triglycerides and 3.5% for creatinine[18].

In those who confirmed to have diabetes in questionnaire 1 an extra tube of whole blood was drawn in a 5 ml EDTA Vacutainer tube for analyses of HbA1c at Levanger Hospital. Those confirming diabetes were also re-invited to another blood sampling in the fasting state. Additional information was recorded by the nurses performing the sampling (year of diagnosis, type of treatment, state of insulin treatment, name of their GP). Fasting glucose was measured at the site applying a Hemocue. C-peptide and anti-GAD were measured in the fasting state and analyzed at Aker Hospital, Oslo. C-peptide was measured with a radioimmunoassay method (Diagnostic System Laboratories, Webster, TX), anti-GAD was measured via immunoprecipitation by using [^{3}H] leucine translation-labeled GAD65 as an indicator. Reagents were supplied by Novo Nordisk Pharma AS (Bagsvaerd, Denmark). The results of the C-peptide and anti-GAD analyses were mailed to the HUNT Research Center in Verdal, and forwarded to the GP after comments were attached. Additional analyses performed are described in detail elsewhere: Thyroid function[46,47], ferritin[61,89-94], and urine analyses for microalbuminuria[95-97].

Reporting of test results

Some individuals with extremely high blood pressures (DBP≥125 mmHg) were recommended to visit their GP for re-check the same day or within a few days. The HUNT Research Center was informed, and ascertained that follow-up took place. Likewise, non-fasting blood glucose readings ≥11.1 mmol/l were reported to the HUNT Research Center, who immediately informed the screened person by letter, with a copy to the GP.

About three weeks after the health examination each participant received a letter reporting some selected test results from the screening, like blood pressure, glucose, total cholesterol, height, weight, self reported physical activity, ferritin (part of the hemochromatosis screening). Included were also some advice regarding healthy food, smoking and physical exercise. If the above mentioned tests or the screening for anxiety and/or depression disclosed possible pathology, the participant was advised to see his/her doctor for re-check.

PERSONAL PROTECTION AND ETHICS

Both the core study and each sub-study were approved by the Data Inspectorate of Norway and recommended by the Regional Committee for Medical Research

Ethics, and all information from HUNT is treated according to the guidelines of the Data Inspectorate.

Participation in the HUNT study was voluntary, and each participant signed a written consent regarding the screening, subsequent control and follow-up, and to the use of data and blood samples for research purposes. They also consented to linking their data to other registers (subject to approval of the Data Inspectorate). When the data files have been prepared for research purposes, all names and personal ID numbers have been removed.

In Norway, every individual has a unique 11-digit personal identification number given at birth, and HUNT data are linked to the identification number, allowing cross reference of individuals in both HUNT databases and other regional and national health registries. Such linkage has been performed (for specific sub-studies and after appropriate approvals) to insurance statistics from the National Insurance Administration, to the Cancer Registry, the Medical Birth Registry, Census Data of Norway, the Family Registry and to the Cause-of-Death Registry.

At the time of HUNT 2, no study involving genetic DNA-based research was included. Therefore, an extensive information campaign about functional genomic research was performed in 2002, addressing the entire population of the county. Each surviving adult HUNT 2 participant (n=61,426) received an information folder and a personal letter asking for re-consent to include genetic research. Information was also given by mass media and by a specially designed web-site. In total, 1,185 (1.9%) persons withdrew their consent[98]. The re-consent project was also approved by the Data Inspectorate of Norway and recommended by the Regional Committee for Medical Research Ethics.

PARTICIPATION

In total, 94,194 individuals aged 20 years and older were invited to the HUNT 2 study based on a data file from Statistics Norway. The file was updated at regular intervals before invitations were sent out. Despite these routines, 1,258 were dead or had moved out of the county when the screening team arrived, making a total of 92,936 eligible for participation (Figure 2). Out of these 66,140 participated (71.2%) (Table 3). In all age groups under 70, more women than men participated (75.5% versus 66.7%). The participation was strongly age dependent, with the highest participation in the age group 60-69 for both sexes (84.3% in men and 87.0% in women), and gradually lower participation rate in younger and older age groups. Men aged 20-29 had the lowest participation (42.5%).

As the health survey included several stages, from filling in questionnaire 1 to a number of additional clinical tests and interviews (Figure 2), the term participation could have different meanings. In Table 3 participation is defined as having at least filled in questionnaire 1. In all, 807 individuals who filled in questionnaire 1 did not attend the health examination, and some did not attend all parts of the program. Additionally, some people did not fill inn all questions in the various questionnaires, resulting in different numbers of valid responses in different parts of the database. An overview is shown in Figure 2 (flow chart). For details, see the HUNT website[42] or papers in the reference list. An overview of the program in different population groups is demonstrated in Table 4.

Compared to HUNT 1 the participation in HUNT 2 had decreased by 16.9% (Table 5), most pronounced in men and in both sexes in young age groups (Figure 3).

Table 3. Participants at HUNT 2 by age and gender.

	Men				
	Invited	Dead/ moved	Could have participated	Participated	
Age	n	n	n	n	%
20-29	9,522	94	9,428	4,009	42.5
30-39	8,820	65	8,755	5,417	61.9
40-49	9,096	42	9,054	6,511	71.9
50-59	7,066	34	7,032	5,418	77.0
60-69	5,212	31	5,181	4,366	84.3
70-79	4,803	78	4,725	3,776	79.9
80-89	2,075	253	1,822	1,242	68.2
90+	288	58	230	121	52.6
Total	46,882	656	46,226	30,860	66.7
	Women				
	Invited	Dead/ moved	Could have participated	Participated	
Age	n	n	n	n	%
20-29	8,670	73	8,597	4,819	56.0
30-39	8,176	35	8,141	6,133	75.3
40-49	8,595	13	8,582	7,058	82.2
50-59	6,765	12	6,753	5,787	85.7
60-69	5,443	13	5,430	4,723	87.0
70-79	5,707	32	5,675	4,534	79.9
80-89	3,338	308	3,030	1,960	64.7
90+	618	117	501	266	52.8
Total	47,312	603	46,709	35,280	75.5
	Both genders combined				
	Invited	Dead/ moved	Could have participated	Participated	
Age	n	n	n	n	%
20-29	18,192	167	18,025	8,828	49.0
30-39	16,996	100	16,896	11,550	68.3
40-49	17,691	55	17,636	13,569	77.0
50-59	13,831	46	13,785	11,205	81.2
60-69	10,655	44	10,611	9,089	85.6
70-79	10,510	109	10,401	8,310	79.9
80-89	5,413	562	4,851	3,202	66.0
90+	906	175	731	387	52.9
Total	94,194	1258	92,936	66,140	71.2

Non-participation study

Shortly after completing the field work in 1997, a 2.5% random sample of non-attendants was selected (n=685) for a non-participation study[43]. The aim was to investigate the reasons why they did not attend. Of the 226 individuals we reached by telephone, 173 (76.5%) responded positively to being interviewed. A

Table 4. HUNT 2 (1995-97): Summary of screening programme. Number of valid cases may differ from number of participants due to missing values.

	Age and sex groups					Other selected groups (*)			
	1 13-19 M/F	2 20-69 F	3 20-69 M	4 70+ F	5 70+ M	6 5% rs	7 Resp. probl.	8 Hyper- tension	9 Diabe- tes
Number of participants	9,139	28,520	25,721	6,760	5,139	2,792	12,955	8,937	2,102
Questionnaire for adolescents	x								
Questionnaire 1 (same for all groups)		x	x	x	x	x	x	x	x
Questionnaire 2 (age and sex specific)		x	x	x	x	x	x	x	x
Questionnaire 3 – lung							x		
Questionnaire 3 – hypertension								x	
Questionnaire 3 – diabetes									x
Questionnaire – hearing		x	x	x	x	x	x	x	x
Heigth/weight	x	x	x	x	x	x	x	x	x
Sitting height	x					x	x		
Hip/waist	x	x	x	x	x	x	x	x	x
Blood pressure/heart rate	x	x	x	x	x	x	x	x	x
Bone mass (radial)						x	x		
Spirometry	x					x	x		
Hearing test		x	x	x	x	x	x	x	x
Vision		(x)	(x)						
NO (Nitrogen Oxide) expiration test	(x)						(x)		
Stored blood sample (biobank)		x	x	x	x	x	x	x	x
Total cholesterol		x	x	x	x	x	x	x	x
HDL cholesterol		x	x	x	x	x	x	x	x
Triglycerides		x	x	x	x	x	x	x	x
Glucose		x	x	x	x	x	x	x	x
Creatinine		x	x	x	x	x	x	x	x
Se-ferritine		x	x	x	x	x	x	x	x
TSH (Thyroidea Stimulating Hormone)		>40 yrs	50%>50 yrs	x	x	x			x
Microalbuminuria						x		x	x

(*) Group 6: 5% random sample (rs) of participants 20 years and older
Group 7: Reporting respiratory problems
Group 8: Taking antihypertensive drugs
Group 9: Reporting to have diabetes (included are also some participants recruited in the sub-study for the elderly)

(x) indicates sub-samples

Table 5. Participation at HUNT 1 (1984-86) by age and gender[1].

	Men			Women			Both sexes		
	Eligible	Participated		Eligible	Participated		Eligible	Participated	
Age	n	n	%	n	n	%	n	n	%
20-29	7,580	5,513	72.7	6,750	5,481	81.2	14,330	10,994	76.7
30-39	9,199	7,956	86.5	8,570	7,987	93.2	17,769	15,943	89.7
40-49	6,762	6,093	90.1	6,482	6,160	95.0	13,244	12,253	92.5
50-59	6,009	5,557	92.5	5,868	5,595	95.3	11,877	11,152	93.9
60-69	6,595	6,164	93.5	6,699	6,302	94.1	13,294	12,466	93.8
70-79	4,474	4,016	89.8	5,363	4,753	88.6	9,837	8,769	89.1
80-89	1,708	1,306	76.5	2,454	1,775	72.3	4,162	3,081	74.0
90+	205	119	58.0	382	200	52.4	587	319	54.3
Total	42,532	36,724	86.3	42,568	38,253	89.9	85,100	74,977	88.1

letter with a short questionnaire was sent to those not reached by phone (n=459). The reasons for not reaching them by telephone were: 335 did not have a telephone, 61 were not at home, 25 had moved out of the county, 33 were dead, and 5 gave no reason. In all, 153 (33%) answered the questionnaire, leaving a total of 326 individuals (47.6%) to be included in the analyses.

In age group 20-44 the main reasons for not attending the health survey were lack of time or having moved out of the county (54%). In age group 45-69

the main reason was busy in job or they had forgotten the invitation or had no reason. In age group 70+ many reported to have regular follow-up by a doctor or hospital and therefore did not need to attend the health survey (Table 6). Some people (9.6%) could not attend because they were immobilized due to disease, and some (4.1%) refused due to long waiting time at the screening site. A few (8.6%) reported that the health survey was unnecessary or that they were unwilling to participate[43].

DISCUSSION

Compared to other population studies HUNT has several special features: It covers a total population within a geographical area, it has a wide age range, it covers an extensive range of topics (nearly 3000 variables), and it has a high participation rate. HUNT 2 was a follow-up of HUNT 1 with identical or similar questions and assessments on hypertension, diabetes and quality of life. HUNT 2 was, however, much more comprehensive, with a wider age range (13 years old and over) and included more data on each participant. Even if the participation rate in HUNT in general was fairly high compared to most other studies in Norway and abroad[99-102], there is always a potential selection problem. In HUNT 2 data from young age groups, especially in men, should be analyzed with some caution. However, a comprehensive non-participation study after HUNT 1 could not find evidence of selection in health measures in young age groups[2,3]. Old non-participants, however, had significantly more health problems than participants of the same age.

The concerted action from research groups, authorities and the population has resulted in a huge database and has initiated extensive research activities. HUNT is part of CONOR (Cohort Norway)[101], which is a network of Norwegian health studies and biobanks with identical core variables, enabling linkage of databases to achieve a larger and an even more representative population with increased statistical strength. Through several years HUNT has initiated collaboration with various research groups in other European countries and in the USA. Procedures for data access are established, and more than 100 researchers in Norway and abroad are currently working on HUNT data covering studies within a wide range of medical topics. Up to now, HUNT has been the basis for about 150

Figure 3. Participation at HUNT 1 and Hunt 2 by age in men (M) and women (F).

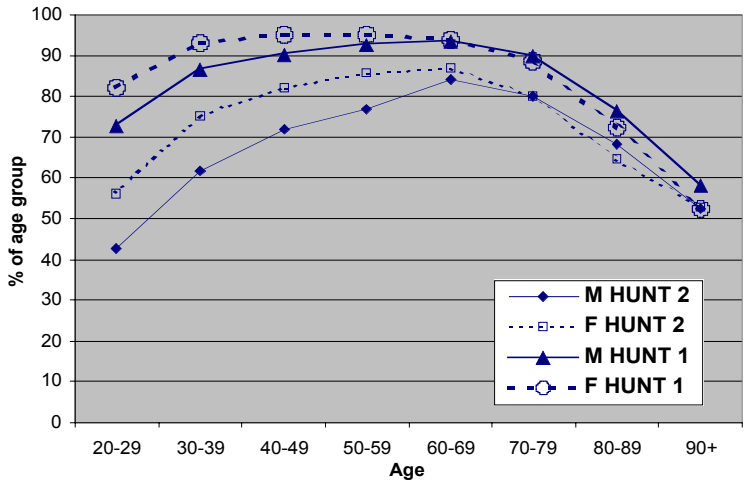


Table 6. Reasons for non-participation in HUNT 2 [43]

	20-44 years		45-69 years		70+ years		Total	
Reasons for non-participation	n	%	n	%	n	%	n	%
Follow-up by physician/hospital	11	5.8	10	13.7	8	28.6	29	10.0
Long waiting hours at screening site	8	4.2	4	5.5	0	0	12	4.1
Busy in job	42	22.1	18	24.7	2	7.1	62	21.3
Immobilised by disease	16	8.4	6	8.2	6	21.4	28	9.6
Moved, or long time absent	59	31.1	10	13.7	6	21.4	75	25.8
Forgot/no reason/other	36	18.9	21	28.8	3	10.7	60	20.6
Unnecessary/unwilling	18	9.5	4	5.5	3	10.7	25	8.6
Total	190	100.0	73	100.0	28	99.9	291	100.0

scientific papers, 15 Ph.D. theses and a large number of reports created for regional and state authorities for use in preventive health care and health planning.

A fundamental premise for population studies is high confidence and legitimacy in the study population. The strategy to achieve and withhold this confidence in the population of Nord-Trøndelag has been successful, and resulted in high participation rates and even enthusiastic public and political support for HUNT and the HUNT Research Center, which is located in the middle of the study population. The decline in participation from HUNT 1 to HUNT 2 has raised some concern, as this probably is part of an international trend. In HUNT 2 the decline was most prominent under the age of 60 (Figure 3). Today, more people are seeing their physician and are having regular medical check-ups[18], and many young people are busy with job and children. The logistics in the screening itself might also play an important role. Due to a larger screening program the time spent at the screening site was longer at HUNT 2 compared to HUNT 1, making it difficult for people who needed to leave their job. In addition, distances to the screening site increased, as the team had to operate from only one location within each municipality (Se Appendix). Due to the larger screening program people also had an appointment hour instead of an appointment day at HUNT 1, making participation less convenient. In addition, there seemed to be less interest in public health and preventive medicine than some decades earlier. Even primary physicians seemed less engaged in public health issues than they used to be in the 1980s. All these factors might have contributed in making health surveys less attractive. Future surveys must take into account that modern people are busy and expect a smooth and efficient screening system with no waste of time. However, the non-participation study performed after HUNT 2 gave no evidence that people had negative attitudes to the study itself (Table 6).

A main challenge for the HUNT study has been to initiate research using the biobank, especially functional genomics. Initiatives are taken in collaboration with the FUGE project[103]. As the genomic era develops the re-consent project including the information campaign about functional genomics was an important experience. This result also confirmed our impression that the HUNT study has a high confidence and legitimacy, and the population is in general strongly supportive[98]. Another main challenge is the planning and realization of a third HUNT study (HUNT 3). The confidence and supportive attitude from the population should be a good platform for conducting future population studies with high participation rates in the Nord-Trøndelag County.

APPENDIX: ORGANIZATION AND FUNDING OF HUNT 2

The HUNT database is a result of tight collaboration and joint actions between local, regional, national and international partners through the last 20 years. The study has involved a large number of individuals and organizations.

The National Health Screening Service (SHUS)(*) was responsible for the technical performance of the basic screening among all persons 20 years and older, and for setting up one field team of five persons to participate in the collection of data in Nord-Trøndelag during the two year period. This “mobile team” had a fully equipped trailer with office facilities where the health screening took place. The mobile team was responsible for the screening in the 19 smaller municipalities. They needed, however, adjacent localities for some of the examinations, for instance the audiometry. In the “stationary team” SHUS provided the leading nurse and the operator for the various technical devices during the first five "run in" months, and also provided technical equipment. SHUS was responsible for the invitations and provided the various sub-studies with necessary addresses, name tags etc. that were used for invitations, reminders etc. Questionnaire 1 and the results of the blood tests were sent to SHUS where the primary statistical analyses were done and appropriate response letters were sent back to the participants. SHUS had the license for storing and linkage of the main files including the national identification number, and prepared research files for statistical analyses.

The National Institute of Public Health (*), Oslo, and Community Medicine Research Center (*), Verdal. The Community Medicine Research Center in Verdal administered the other field team (“the stationary team”), consisting of 12 persons responsible for the screening in the five larger municipalities. Various sub-studies were also organized by the Community Medicine Research Center. The sub-studies included diabetes mellitus, high blood pressure and coronary heart disease, in addition to the Young-HUNT study[41,104-106], and the Bronchial Obstruction in Nord-Trøndelag (BONT) study[43,44]. The Young-HUNT, i.e. the screening of all persons between 13 and 19 years old, was fully organized by the Research Center in Verdal through an established group consisting of the primary investigator, secretary and field workers; seven persons in total. The BONT study, which also included bone mass measurements, was run from the Research Center. The executive group consisted of a primary investigator and field workers, totally six positions covered by 22 different persons. Altogether, the Research Center in Verdal administered approximately 50 collaborators, and was responsible for administrative and practical work ranging from contract negotiations concerning locations and recruiting personnel, to sending out reminders to participants. The National Institute of Public Health, Oslo, Section for Epidemiology, was responsible for the

hearing study in HUNT[80-84]. Their team consisted of a coordinating audiometrist and four field workers (audiometrists and assistants).

Innherred Hospital, Levanger(*). The Central Laboratory at Innherred Hospital, Levanger, was responsible for all routine blood and urine analyses that were part of HUNT. Some specific samples were sent from the laboratory to Aker hospital in Oslo for thyroid status analyses, and to the National Institute of Public Health for immune status. Results from these analyses were transferred to the HUNT database at SHUS, Oslo, to form the basis for response letters to the participants. Innherred Hospital also provided facilities for the biobank, i.e. localities for freezers containing whole blood and serum samples at minus 70°C.

The Faculty of Medicine, NTNU. Scientists at the Faculty of Medicine had a central position in projects on osteoporosis, urinary problems in men, baldness in men, vision impairment, sense of humor and migraine/headache.

NOVA (Norwegian Social Research). A separate sub-study was aimed at residents in nursery homes and other institutions for elderly, organized by NOVA. The field team consisted of two nurses who visited institutions for interviews and clinical measurements.

In addition to the institutions mentioned above, general practitioners and district nurses in the whole county, the 24 municipalities and county authorities, a number of private regional and national organizations, and a number of other national institutions and universities, The Norwegian Research Council, and The Ministry of Health, actively supported the study. HUNT is also part of the nation-wide CONOR (Cohort Norway) collaboration, constituting a network of national health databases and biobanks, in which HUNT is the largest single unit[101].

FUNDING

HUNT 2 was funded by joint efforts of a large number of partners. Main contributions came from The Ministry of Health, through The National Institute of Public Health and The National Health Screening Service (SHUS). The Nord-Trøndelag County Council, The Norwegian University of Science and Technology and The Norwegian Research Council also provided essential funding. Sub-studies were supported by The Norwegian Research Council or a number of private organizations, like The Diabetes Association, The Norwegian Association of Asthma and Allergy and The Norwegian Women's Public Health Association (Norske Kvinners Sanitetsforening). The Hearing Study was funded by the National Institutes of Health (NIH), USA, and some sub-studies were supported by pharmaceutical industry: AstraZeneca (the BONT Study), GlaxoSmithKline (the diabetes study) and MSD (the prostate study). In total, the core study had a cost of about NOK 21 mill., and the sub-studies additionally NOK 10 mill.; infrastructure resources made available by the institutions not included.

(*) Reorganizations have taken place in several collaborating institutions after the field work was finished: The Community Medicine Research Center (now HUNT Research Center, Verdal) was previously part of The National Institute of Public Health. From 2001 the center is part of the Department of Community Medicine and General Practice, Faculty of Medicine, Norwegian University of Science and Technology (NTNU). Innherred Hopsital, Levanger, and Namdal Hospitals, Namsos, were previously owned by The Nord-Trøndelag County Council. From 2001 they are owned by the Ministry of Health and administered by The Regional Hospital Administration (Helse Midt-Norge) and are named Levanger Hospital and Namsos Hospital. From 2002 The National Institute of Public Health (Folkehelsa) and The National Health Screening Service (SHUS) are merged into the Norwegian Institute of Public Health, Oslo.

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