Cardiovascular disease and diabetes mellitus in Norway during 1994-2009

CVDNOR – a nationwide research project

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ABSTRACT

Background: Although having a long tradition in cardiovascular epidemiologic research, nationwide data on cardiovascular disease (CVD) incidence and morbidity has not been available in Norway.
Objectives: The main objectives of The Cardiovascular Disease in Norway (CVDNOR) project are 1) to study trends in CVD incidence, prevalence, survival and mortality and 2) providing CVD endpoints for national and regional health surveys and clinical studies.
Methods: CVDNOR includes information from all hospital stays with a CVD, including congenital heart defects, or diabetes mellitus (DM) primary or secondary diagnosis code during 1994-2009. Information was retrieved from the electronic Patient Administrative Systems (PAS) from all Norwegian somatic hospitals. Data include age, gender, municipality of residence, hospitalization and discharge dates, main and secondary diagnoses and CVD-related procedure codes. All deaths due to CVD or DM are also included, as well as sociodemographic information and linkage to Cohort Norway (CONOR). In sub-projects we have also linked CVDNOR to the Medical Birth Registry of Norway and to the Cancer Registry.
Results: During 1994-2009, 1.3 million patients (4.3 mill hospitalizations) had a CVD diagnosis or procedure code, or DM. Of these, 470895 (35.8%) died during 1994-2010. In addition, 68523 men and women died from CVD without being hospitalized for CVD or DM during the same period. Among 173243 CONOR participants, 9075 (5%) died after participating in the health survey and through 2010. A total of 44118 (25.5%) CONOR participants had a CVD and 7575 (4.4%) had a DM related hospitalization after participating in CONOR, through 2009. In CVDNOR, 53039 (4%) had congenital heart defect codes.
Conclusions: CVDNOR will be a valuable source of information supporting future epidemiologic research, with important implications for prevention and treatment strategies.

INTRODUCTION

During the last decades, cardiovascular disease mortality has decreased substantially in Norway [1,2] as in other Scandinavian and western European countries [3-5]. The changes have not been uniform across all sex and age groups [1]. While mortality trends are known in Norway, there is lack of information on trends in incidence and survival. Norway did not have, until 2012, a national register on cardiovascular disease (CVD). This has hampered studies of incidence and survival as well as aetiologic research nationwide.

The Norwegian Patient Register, containing information on all patients hospitalized at Norwegian hospitals since 1990, has the potential to overestimate the true number of hospitalizations and cannot provide information on incidence, due to the lack of person-identifiable information until 2008. Several regional studies have published important information on risk factors [6-8] and occurrence of CVD [9-12]. Nevertheless, as shown by the WHO MONICA project, there is a non-negligible difference in occurrence and risk factors for CVD between and even within countries [13,14]. Therefore, findings from regional studies may not be generalizable to the general Norwegian population. To fill this gap of knowledge on one of the most important sources of morbidity and mortality in the Norwegian population and elsewhere, the CVDNOR project was planned.

CVDNOR – A PROJECT OFFERING NEW RESEARCH OPPORTUNITIES

The Cardiovascular Disease in Norway (CVDNOR) project began as a collaborative research project between the University of Bergen and the Norwegian Knowledge Centre for the Health Services. It is a population study with major focus on CVD and DM. The two main objectives are:

Table 1. Diagnoses and procedures in CVDNOR 1994-2009.

Diagnoses included in CVDNOR	**ICD9** (1994-1998)	**ICD10** (1999-2009)
Diseases of the circulatory system	390-459	I00-I99
Oedema, proteinuria and hypertensive complications during pregnancy and childbirth	642	O10-O16
Diabetes mellitus during pregnancy	648.0	O24
Transient cerebral ischemic attacks and related syndromes	435	G 45
Diabetes mellitus	250	E10-E14
Non-diabetic hypoglycaemic coma	251.0	E15
Sudden, unexpected death	798.1	R96
Congenital malformations of the circulatory system	745-747	Q20-Q28
Main diagnostic and treatment procedures	**SIF95** ±	**NCMP**┼ **and NCSP** ¶
Interventions in the heart and great vessels	3000-3299	FA-FY
Coronary angiography/left-sided catheterization	3291, *3235**, *3238**	FYDB,TFC10, XF911, XF912, XF914
Right-sided catheterization	3290	TFC00
Electrophysiologic study/intervention of the heart	3292	FPA, FPB, FPFE
Transthoracic/transesophageal echocardiogram	3293	FYDE
Percutaneous coronary intervention (PCI)	3294, *3236**, *3239**	FNG
Coronary artery bypass grafting (CABG)	3112-3129	FNA-FNF
Pacemaker/defibrillator implantation procedures	3200-3209	FPE, FPF, FPG
Interventions on peripheral blood vessels and lymphatic system	8800-8899	PA-PY

* Local codes used by University hospitals Haukeland and Stavanger.
± Norwegian classification of medical procedures; 3rd edition, 1995.
┼ Norwegian classification of medical procedures.
¶ The NOMESCO classification of surgical procedures; NCMP and NCSP were brought together in 2006 [20].

1. to study trends in CVD incident and recurrent events, short and long term prognosis (survival) and associated factors in the total Norwegian population,
2. to provide CVD and DM endpoints for national and regional health surveys conducted during the last decades in Norway, as well as for clinical studies. CVDNOR will facilitate studies of the impact of several known and potential risk factors (alone and in combination, as well as of changes in risk factors) in CVD occurrence.

Data collection and quality control

Hospital data

Hospital stays with a CVD (ICD9: 390-459, ICD10: I00-I99, G45), DM (ICD9: 250, ICD10: E10-E14) or congenital malformations of the circulatory system (ICD9: 745-747, ICD10: Q20-Q28) as either primary or secondary diagnosis, as well as all related procedures, were retrieved from the electronic Patient Administrative Systems (PAS) in all Norwegian somatic hospitals from 1994 (the year from which all hospitals adopted an electronic PAS) through 2009. A list of hospitals providing data can be found at www.cvdnor.no. An overview of the main diagnostic and procedural codes eligible for inclusion in CVDNOR is given in Table 1. For hospitalizations containing at least one eligible diagnosis or procedure code, all other diagnosis codes and procedure codes for that stay were also extracted.

A system called FS (Forskning i Sykehus = Research in hospitals) developed by Tomislav Dimoski at the Norwegian Knowledge Centre for the Health Services was used to extract the data retrospectively. The FS-system has been used in studies of other disease entities [15]. It can semi-automatically collect standardized data on patient stays. Patients are identified by use of the Norwegian personal identification number (ID). Transfers between wards, departments or hospitals for the same or different conditions in a patient can therefore be accounted for. A quality control compared FS system-extracted data with patients' hospital records and found that 99% of the data were correct with regard to date and time of admission and main diagnosis [16].

CVDNOR includes a unique ID-number for each patient and a unique code for each hospitalization. In addition, age at hospitalization, gender, municipality of residence, time and dates of hospitalization and discharge (including transfers between wards and departments within the hospital), hospital, department and ward codes, main and secondary diagnoses (up to 20), medical procedure codes (up to 30) performed during the hospital stay, and information about type of hospitalization (acute or elective). Hospitalizations less than 24 hours apart are merged and considered as one.

A more detailed report on CVDNOR data and quality issues will be published shortly at www.cvdnor.no.

Cause of Death Register (www.ssb.no/dodsarsak_en)

For all patients identified with a CVD or DM hospitalization and who later died, information about date of death, underlying and contributing cause(s) of death has been retrieved from the Cause of Death Registry.

In addition, information on individuals who died from CVD or DM but had no previous hospitalizations for CVD or DM was also obtained. Thus, CVDNOR contains data on all CVD or DM related deaths during the study period.

Linkage of hospital data and cause of death data with other sources of information
To increase the information obtained and broaden the field of potential research, a series of important linkages have been made to other data sources including national registries.

Statistics Norway, Population Register (www.ssb.no/english)
Sociodemographic information includes marital status, personal and family income, country of birth, own education, education of spouse, and municipality.

COhort of NORway (CONOR) (www.fhi.no/conor)
Since the 1970's, large regional health surveys with a focus on CVD and DM risk factors have been conducted throughout Norway. These surveys were the starting point for the national research collaboration COhort of NORway (CONOR) [17], in which all Norwegian medical faculties (Tromsø, Trondheim, Bergen and Oslo), and the Norwegian Institute of Public Health participated. For the period 1992-2003, the number of participants in CONOR was 173 243, of whom 7460 participated twice.

The linkage of CONOR with CVDNOR provides the opportunity to study the impact of risk factors (e.g. health behaviours, anthropometry, health status) on CVD morbidity and mortality. In addition, changes in risk factors (in those individuals participating twice) and their impact on CVD occurrence may be examined. CONOR data have so far not been used for studies of CVD incidence due to the lack of nationwide morbidity data.

Other health surveys and clinical trials
CVDNOR data will also be used as endpoints in several other health surveys including the Norwegian Counties Studies (www.fhi.no) and the Hordaland Health Studies (http://husk.b.uib.no). In addition, CVDNOR data will be used for extended follow-up of the randomized clinical trials NORVIT [18] and WENBIT [19].

Congenital malformations of the circulatory system, a CVDNOR substudy
The hospital data also include information on congenital malformations of the circulatory system during the same time period. Epidemiologic studies of congenital malformations of the circulatory system have never been undertaken on a national level in Norway due to lack of data. This CVDNOR project will describe the epidemiology of congenital heart defects, such as examining national time trends, risk factors, and mortality of congenital heart defects in Norway. The project also ascertains information on congenital heart defects from the Medical Birth Registry of Norway and from the clinical database on congenital heart defects (Berte) at Oslo University Hospital.

CVDCancer, a CVDNOR substudy
The purpose of this project is to examine CVD occurrence in cancer survivors. It is known that patients who have been treated for cancer have an excess risk of developing CVD, compared to the population at large. In this project we link CVDNOR to the Norwegian Cancer Registry to study the incidence of CVD in cancer patients compared to the general population. Through linkage to CONOR, risk factors for CVD among CONOR participants with and without cancer will be compared.

Norwegian Prescription Database (www.norpd.no)
There are plans to link to the Norwegian Prescription Database (NorPD), although this has not been done yet (as of March 2013). The NorPD contains data about dispensed drugs in Norway, and this linkage will provide the opportunity to examine use of specific medications in relation to incidence and prognosis of CVD and DM. It will also be used to better define disease entities, by exploring the medication use (such as diabetes medication to identify individuals with DM not hospitalized).

Summary of data sources linked to CVDNOR

Linkages between CVDNOR and other data sources will facilitate longitudinal epidemiologic studies of research questions otherwise not possible to answer. The linked datasets will provide the opportunity for future research projects, and will be a valuable resource for epidemiologic studies.

Data security

Data from different sources are linked by Statistics Norway. The personal identification number (unique for each Norwegian resident) is replaced by a project specific and unique identification number (ID) before data files are forwarded to the University of Bergen. Data from the different sources are stored as separate datasets on a secure Windows server at the University of Bergen. The unique ID makes it possible to link the different data files. Researchers with given privileges may log on to the server via a 'Remote Desktop' solution. The Statistical packages SAS, SPSS, STATA and R are installed on the server in addition to standard software such as Microsoft Office. Data processing is usually done on the server.

Researchers are permitted access only to those data sources that are needed for each specific project.

Ethical considerations and approvals

The CVDNOR project, including the sub-project on congenital heart defects, was first approved by the Regional Committee for Medical and Health Research Ethics, Health Region West (036/09). Subsequently, the sub-study on CVDCancer has been approved (REK

Table 2. An overview of CVDNOR hospitalizations and deaths 1994-2009.

	Men	Women	Total
Number of patients, *n (%)*	640325 (48.7)	674692 (51.3)	1315057
Age at time of hospitalization, *mean (sd)*	64.0 (19.0)	66.0 (21.3)	64.9 (20.2)
Hospitalizations*, *n (row %)*			
CVDNOR**	2270535 (53.2)	1996173 (46.8)	4266751
CVD	1677554 (54.1)	1421295 (45.9)	3098849
CHD	750031 (61.1)	477909 (38.9)	1227940
AMI	157230 (61.3)	99272 (38.7)	256502
PCI	59781 (74.7)	20291 (25.3)	80072
Cerebrovascular disease	259102 (52.8)	231591 (47.2)	490693
Diabetes mellitus	340537 (53.4)	297208 (46.6)	637745
AF	346490 (55.0)	282955 (45.0)	629445
Congenital malformations of the circulatory system	27054 (51.0)	25985 (49.0)	53039
Deaths			
Deaths among CVDNOR hospitalized patients, *n (% of patients)*	234059 (36.6)	236836 (35.1)	470895 (35.8)
CVD deaths among CVDNOR hospitalized patients, n *(% of patients)*	104157 (16.3)	111090 (16.5)	215247 (16.4)
CVD deaths among persons not hospitalized in CVDNOR, 1994-2009	31192	37331	68523

* Hospitalizations less than 24 hours apart are merged.

**Hospitalizations fulfilling the inclusion criteria described in Table 1.

CVD – cardiovascular disease; CHD – coronary heart disease (ICD9: 410-414, ICD10: I20-25); AMI – acute myocardial infarction (ICD9: 410, ICD10: I21,I22); PCI – percutaneous coronary interventions; AF – atrial fibrillation (ICD9: 427.3, ICD10: I48).

Table 3. Hospitalizations and deaths due to cardiovascular disease or diabetes mellitus among CONOR participants (1994-2003). A CVDNOR project 1994-2009.

CONOR participants	Men	Women	Total
Number of CONOR participants	84156	89087	173243
Participants who died due to CVD, *n (%)*	5139 (5.9)	3918 (4.2)	9057 (5.0)
Participants hospitalized with a CVD diagnosis after the CONOR survey, *n (%)*	24698 (29.0)	19421 (21.8)	44118 (25.5)
Participants hospitalized with a DM diagnosis after the CONOR survey, *n (%)*	4313 (5.1)	3262 (3.7)	7575 (4.4)

CONOR – Cohort of NORway; CVD – cardiovascular disease; DM – diabetes mellitus.

2009/861-19), as has linkages to the Hordaland Health Studies (REK 2009/825), the Norwegian Counties studies 1974-88 (REK 2012/827), and the clinical trials NORVIT-WENBIT (REK 2010/1880).

PRELIMINARY RESULTS

During the study period 1994-2009, 1315057 persons (51.3% women) contributing with 4266751 hospitalizations (46.8% among women) fulfilled the inclusion criteria listed in Table 1.

A total of 68523 patients died from CVD without being hospitalized during the same period (Table 2). Mean (SD) age for hospitalized patients was 64.9 (20.2) years. Women were older than men at the time of hospitalization. A coronary heart disease (CHD) diagnosis code was found in 1/3 of the hospitalizations as main or secondary diagnosis. A DM diagnosis code was found in 15% and a cerebrovascular disease diagnosis code in 10% of all hospitalizations, and an atrial fibrillation diagnosis code was found in 14.8%. During the study period, 35.8% of patients who had a CVDNOR hospitalization died. Of these, 45.7% had a CVD related code as the underlying cause of death and 63.2% had a CVD related code mentioned on the death certificate. In CVDNOR, 53039 (4%) patients were registered with a congenital heart defect code.

Table 3 summarizes the events (hospitalizations and deaths) for CONOR participants after participation in the health survey. Among all CONOR participants, 25.5% had at least one CVD hospitalization and 5% died due to CVD. During follow up, 4.4% of CONOR participants had a hospitalization during which DM was coded as main or secondary diagnosis.

Additional information regarding marital status, residence, country of birth and education for patients 30 years and older included in CVDNOR at their first hospitalization is given in Table 4. Those individuals who did not match with the Population Registry (28357 individuals; 16226 men and 12091 women) are excluded from the table.

Almost half of the patients were married and 52% lived in the South-East region, versus 10% in the North region. The majority of patients (92.4%) were born in Norway. Only 1.3% was born in another Nordic country and the remainder (6.3%) elsewhere. Some

Table 4. Socio-demographic data for patients 30 years and older at first hospitalization registered in CVDNOR and with match to the Population Registry: a CVDNOR project 1994-2009.

Patients with a CVDNOR diagnosis or procedure	Men	Women	Total
Number of patients, *n (%)*	570 428	585 171	1 155 599
Marital status*, *n (%)*			
Married	369 111(64.7)	263 507 (45.0)	632 618 (54.7)
Widow(er)	52 897 (9.3)	191 791 (32.8)	244 688 (21.2)
Divorced/separated	66 502 (11.7)	64 949 (11.1)	131 451 (11.4)
Unmarried	78 987 (13.9)	62 636 (10.7)	141 623 (12.3)
Missing	2931 (0.5)	2 288 (0.4)	5219 (0.5)
Residence by health region *n (%)*			
South-East	312249 (54.7)	324409 (55.4)	636658 (55.1)
West	110609 (19.4)	113482 (19.4)	224091 (19.4)
Mid	81248 (14.2)	82365 (14.1)	163613 (13.5)
North	63382 (11.1)	62621 (10.7)	137919 (14.2)
Missing	2940 (0.5)	2294 (0.4)	5234 (0.5)
Country of birth *n (%)*			
Norway	540 853 (94.8)	553 666 (94.6)	1 094 519 (94.7)
Nordic countries outside Norway	7 502 (1.3)	8 083 (1.4)	15585 (1.4)
Europe outside Nordic countries	9 958 (1.8)	9 933 (1.7)	19891 (1.7)
Outside Europe	12 053 (2.1)	13 406 (2.3)	25459 (2.2)
Missing	62 (0.0)	83 (0.0)	145 (0.0)
Education *n (%)***			
Basic or no education	210 063 (36.8)	271 051 (46.3)	481 114 (41.6)
Upper secondary education	254 005 (44.5)	220 243 (37.6)	474 248 (41.0)
Tertiary education, short	60 663 (10.6)	67 832 (11.6)	128 495 (11.1)
Tertiary education, long	29 644 (5.2)	10 070 (1.7)	39714 (3.4)
Missing	16 053 (2.8)	15 975 (2.7)	32 028 (2.8)

* Marital status the year of the first hospitalization or the year before if missing.
** Maximum achieved education the year before the first hospitalization.

75.7% had upper secondary education or less.

Figure 1 presents trends in hospitalizations with a CVD or DM related diagnosis or CVD procedure during the study period. Hospitalization rates per 100000 inhabitants are age-standardized using the Nordic population in the year 2000 as standard population. Both the number of hospitalizations and age adjusted rates increased from 1994 to 2006 and levelled off or even decreased thereafter.

The CVDNOR data became available for analysis around mid-2012. Our first objective was to investigate trends of acute myocardial infarction (AMI) incidence rates, by sex and age groups (Sulo et al, submitted; abstract presented at EuroPrevent, Rome, April 2013). Overall, age standardized incidence rates decreased during 2001-2009. However, among younger adults (<45 years), rates of hospitalization for incident AMI increased over time. Other on-going analyses include trends in survival after AMI, trends in AMI event rates and recurrences and association between education level and survival after AMI (two abstracts accepted to ESC 2013, Amsterdam).

How can CVDNOR data be accessed?

Information on how to apply for access to CVDNOR data can be found on the study website www.cvdnor.no.

Strength and weaknesses

CVDNOR is a large dataset covering the whole population of Norway. As such it is not influenced by selection bias. However, as in other registry-based information, details on risk factors, severity of the disease, medication use and other clinical information is missing. Because patients with less severe forms of CVD or DM are not always hospitalised (or die), the estimates based on CVDNOR data will underestimate the true occurrence of these conditions. However, by linkages to the prescription registry, information on the true incidence of medically treated diseases like DM will likely be obtained.

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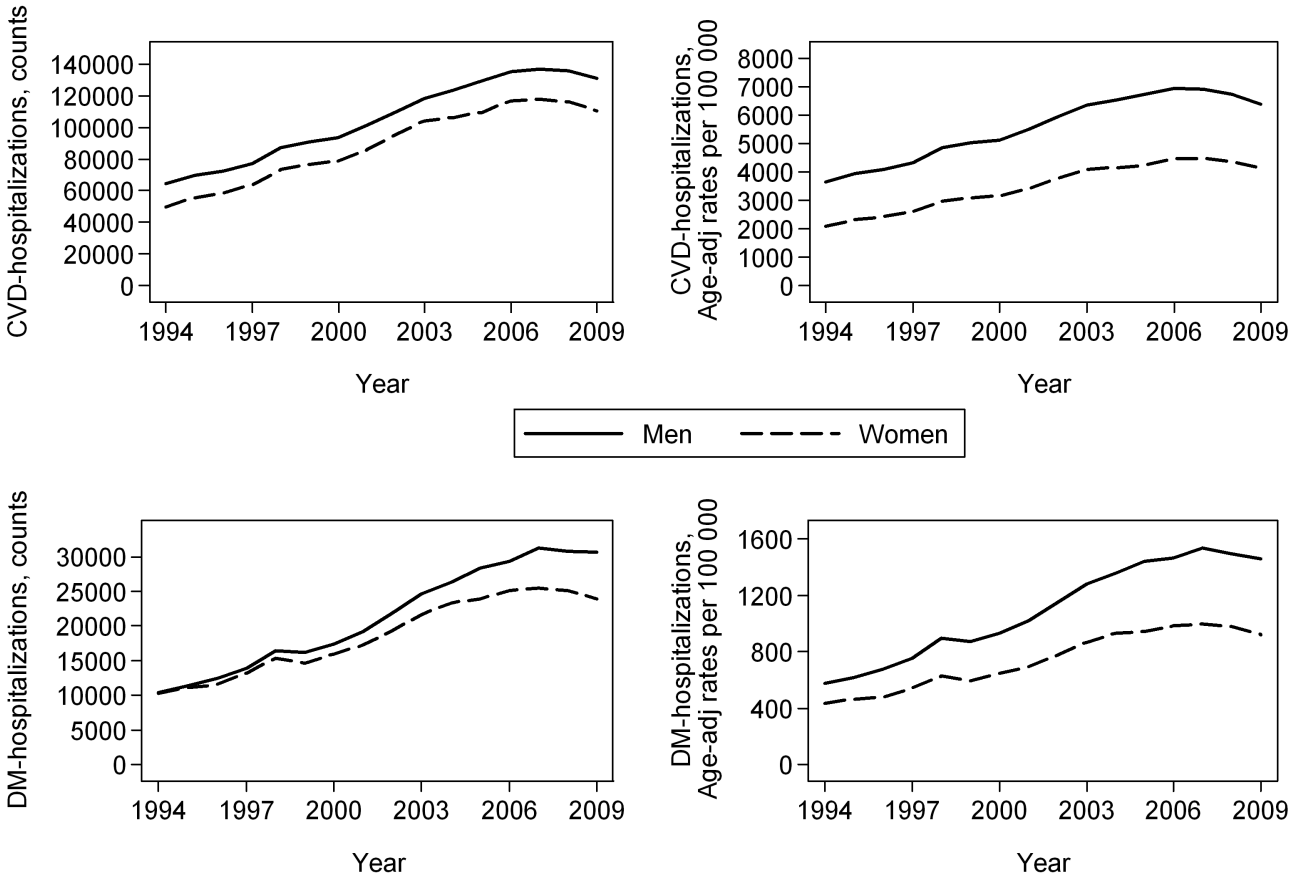

Figure 1. Trends in hospitalizations with a cardiovascular (CVD) or diabetes mellitus (DM) related diagnosis or CVD procedure, 1994-2009.

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