CARDIOVASCULAR DISEASE IN NORWAY (CVDNOR), 1994-2014 PROJECT:

AN OVERVIEW OF DATA USE AND PUBLICATIONS

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In Norway, medical research has a long tradition, advantaged among other things by its well-structured society where each resident has a unique personal identification number. Many health surveys carried out throughout the country have contributed with knowledge on several health conditions and risk factors in the general population (1-4).

Cardiovascular disease (CVD) represents the largest cause of death worldwide (5) with the number of deaths projected to increase throughout 2040 (6). Data from The Cause of Death Registry (7) point to a clear and continuous decline in CVD mortality in Norway during the last four decades. Information on incidence, prevalence of and survival following a CVD event has been provided from regional studies (8-10), but cannot be generalized due to potential geographical gradients (11), known to characterize CVD occurrence. The Norwegian Patient Registry (12) does not have information on disease incidence and recurrence on an individual level until 2009. The Norwegian Cardiovascular Disease Registry (13) was established in 2012.

CVDNOR - data collection, structure and content

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 (now part of the Norwegian Institute of Public Health). The main objectives were to analyze incidence, recurrence and survival following various CVD sub-entities and to provide CVD endpoints for various national and regional health surveys as well as clinical studies and databases in order to explore various etiological hypotheses. CVDNOR has two core components; hospital data and death data.

CVD hospital data 1994-2014

In 2010, information on all hospital stays with at least one of the diagnostic and procedural codes listed in Table 1, were retrieved from the electronic Patient Administrative Systems of all somatic hospitals from 1994 (the year from which all hospitals adopted an electronic Patient Administrative Systems) through 2009. Data were retrieved retrospectively using a semi-automatic, standardized program called 'FS' ('Forskning i Sykehus') developed by Tomislav Dimoski at the Norwegian Knowledge Centre for the Health Services. Later, similar data were obtained from the Norwegian Patient Registry for the period 2009-2014. Besides the CVD or diabetes-related diagnostic codes, all other diagnosis codes and procedures during that particular hospital stay were also extracted. Each patient was assigned an encrypted ID based on his/her Norwegian personal identification number. Transfers between wards, depart-

ments or hospitals for the same or different conditions in a patient can therefore be accounted for.

Core information includes patient's age at hospitalization, sex, 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).

Death data

Information on date, underlying and contributing cause(s) of death for all individuals registered with an eligible hospitalization during 1994-2014 was retrieved from The Cause of Death Registry. In addition, we retrieved information on all deaths with at least one of the diagnostic codes listed in Table 1 on the death certificate among persons who were not registered in the hospital data. These data allowed for follow up studies of survival after CVD and identifying deaths among persons without prior CVD hospitalizations.

Data structure and main definitions

Detailed information on definitions used and data quality in CVDNOR is published previously (14). Here, we will illustrate some of the methodological challenges and definitions used when working with the data. These issues also apply when using data from the Norwegian Patient Registry and the Norwegian Cardiovascular Disease Registry.

Table 1. Diagnoses and procedures in CVDNOR 1994-2014

Diagnoses included in CVDNOR	ICD-9 (1994-1998)	ICD-10 (1999-2014)
Diseases of the circulatory system	390-459	I00-I99
Oedema 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].*

Defining hospitalizations

Hospitalization data in CVDNOR were delivered as one record per hospitalization, generated by first combining ward stays to department stays and then department stays to a hospital stay. The main diagnosis for the hospitalization was set to be equal to the main diagnosis (according to the DRG-system) from the first ward stay. All other diagnoses were set to be secondary diagnoses. The original hospitalization data include transfers between hospitals, re-hospitalizations even shortly after a previous hospitalization and sometimes overlapping hospitalizations for the same individual. If a new hospitalization started <24 hours from discharge of the previous one, the two were merged, regardless of whether both hospitalizations occurred at the same hospital or not. If a new hospitalization started >24 hours from discharge of the previous hospitalization it was defined as a new hospitalization.

Readmissions and new events

When analyzing data, it is important to distinguish between a new event and a readmission. This is a difficult task as there are no clear guidelines for all CVD sub-entities. However, in the case of acute myocardial infarction (AMI), a new hospitalization >28 days following discharge from the previous AMI hospitalization is considered a new event whereas hospitalizations ≤28 days from discharge are considered to be complications of the previous event.

Identifying the first (incident) event in register data

Ideally, information on an individual's lifelong medical history is the best way to identify an incident event. However, such information is usually not available in register-based studies using data from the Patient Administrative Systems. To overcome this, a simple method is often used. Any time an event is identified in the data set, a retrospective search for previous hospitalizations for the same individual with the same diagnosis is performed within the same register data. If no previous hospitalizations are found, the identified event is defined as incident. The period used to check for previous hospitalizations is called lookback period (LP). In the case of AMI, an 'incident' event is defined as a hospitalization (non-fatal) with AMI as discharge diagnosis or death (fatal) with AMI as underlying cause without any AMI hospitalizations during the last 7 years (15).

Data linkages

Figure 1 depicts the core data in the CVDNOR project and additional linkages to other data sources in different completed and ongoing projects. Data were encrypted by Statistics Norway and linked to information on income, highest attained education,

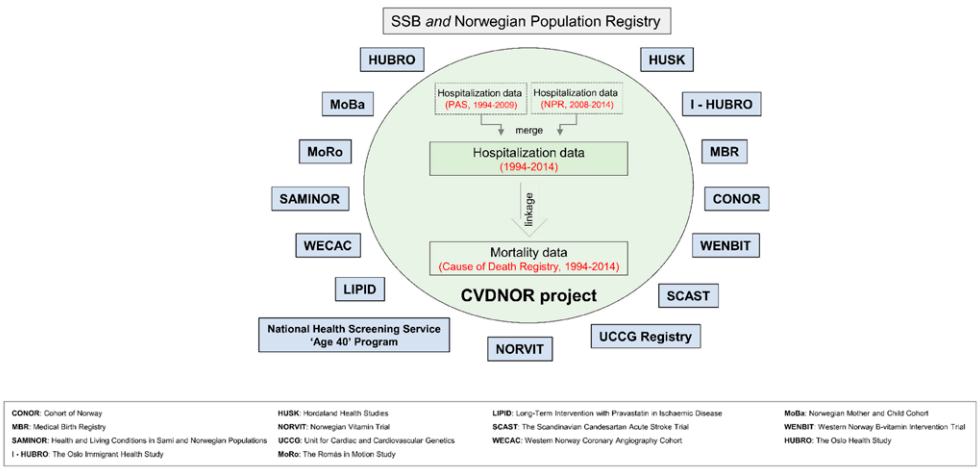

Figure 1. Schematic overview of data structure and linkages in CVDNOR

Table 2. Number of patients and hospitalizations by main disease categories in CVDNOR, 1994-2014

Main disease categories	Total, n (%)		Men, n (%)		Women, n (%)	
	Individuals	Hospitalizations	Individuals	Hospitalizations	Individuals	Hospitalizations
Cardiovascular disease (ICD-9: 390-459; ICD-10: I00-I99)	1 235 284 (100)	4 278 545 (100)	631 330 (51.1)	2 318 783 (53.0)	603 959 (48.9)	1 959 762 (47.0)
Coronary heart disease (ICD-9: 410-414 ; ICD-10: I20-I25)	478 075 (100)	1 592 667 (100)	283 400 (59.3)	984 176 (61.8)	194 678 (40.7)	608 491 (38.2)
Acute myocardial infarction (ICD-9: 410; ICD-10: I21, I22)	248 840 (100)	336 883 (100)	152 863 (61.4)	206 672 (61.4)	95 978 (38.6)	130 211 (38.6)
Cerebrovascular disease (ICD-9: 430-438; ICD-10: I21, I22)	315 188 (100)	683 905 (100)	158 645 (50.3)	361 707 (52.9)	156 544 (49.7)	322 198 (47.1)
Diabetes mellitus (ICD-9: 250; ICD-10: E10-E14)	225 455 (100)	890 088 (100)	120 831 (53.6)	485 951 (54.6)	104 625 (46.4)	404 137 (45.4)
Atrial fibrillation (ICD-9: 427; ICD-10: I48)	295 465 (100)	942 558 (100)	160 696 (54.4)	527 201 (55.9)	134 769 (45.6)	415 357 (44.1)
Congenital malformations of the circulatory system (ICD-9: 745-747; ICD-10: Q20-Q28)	33 668 (100)	70 353 (100)	16 800 (49.9)	35 933 (51.1)	16 868 (50.1)	34 420 (48.9)

country of birth and civil and emigration status. Before the data were sent back to the University of Bergen, a unique ID replaced the personal identification number.

Results

Over a 21-year period, 1.235.284 individuals (51.1% men and 48.9% women) were registered with a CVD-related discharge diagnosis in Norway accounting for 4.278.545 unique hospitalizations (53.0% among men and 47.0% among women) and yielding an average of 3.5 hospitalizations per person (3.7 among men and 3.2 among women) (Table 2). Similar information for relevant CVD sub-entities, including coronary heart disease (CHD), AMI, cerebrovascular disease, diabetes mellitus (DM), atrial fibrillation (AF) and congenital malformations of the circulatory system is provided in Table 2.

Of patients hospitalized with a CVD, DM or congenital malformation of the circulatory system diagnosis, 43.5% (42.1% among men and 45.0% among women) died during the year 2014 (Table 3). The proportion dying from a CVD-related underlying cause was 19.8% (18.6% among men and 21.1% among women) while the proportion dying from a non-CVD condition was 23.7% (23.5% among men and 23.7% among women) (Table 3).

As of October 2019, CVDNOR data have been used in 65 publications, some of these are presented in Table 4. Below we present some results grouped thematically.

Trend analyses and disease burden

Many studies have linked CVDNOR to the Population Registry and the Medical Birth Registry of Norway (MBRN) and explored time trends in incidence (16-18), hospitalizations (19), prevalence (20), recurrence (19), treatment (21) and mortality [rates (22-24) of various CVD sub-entities or

Table 3. Numbers and proportions of deaths among individuals with a hospitalization with a cardiovascular disease, diabetes mellitus or congenital malformation of the circulatory system diagnosis

Deaths, n (%)	Total	Men	Women
All deaths	568 808 (43.5)	281 507 (42.1)	287301 (45.0)
CVD* deaths	258 631 (19.8)	124 201 (18.6)	134430 (21.1)
Non-CVD** deaths	310 177 (23.7)	157 306 (23.5)	152871 (23.7)

** ICD-9: 390-459; ICD-10: I00-I99. ** All other codes*

described their recent burden in Norway (25-27).

Overall, these studies demonstrate a continuous decline in AMI incidence (16, 17), event rates (19) and risk of recurrences (19) coupled with a clear improvement in short and long-term survival following an incident event (22, 23), contributed among other things by improved treatment during the acute phase of the disease (21). Another important achievement observed using CVDNOR data was the reduction in out-of-hospital CHD rates (28). Trends in the prevalence of congenital heart defects (especially those severe) also declined in Norway during 2004-2009 (20) as did the one-year mortality following these congenital heart defects (24). Another study observed a substantial increase in the risk of such defects in younger siblings, once the older sibling had experienced one (26).

Socioeconomic and ethnic gradients in disease occurrence and outcomes

Other studies (21, 28-33) have focused on educational and ethnic gradients in disease incidence (29, 31) and complications (32), treatment modalities (21) or mortality (28, 33).

The existence of the welfare state in Norway has so far not been able to eliminate inequalities in health. To illustrate, educational gradients characterized AMI incidence (29) and survival (33), utilization of coronary angiography (21), and complication rates, as measured by development of heart failure (HF) (32) - a serious complication of AMI. Additionally, less educated individuals had a higher risk of dying outside a hospital from CHD compared with those with higher education (28). Another study focused on ethnic differences and reported that some immigrant subgroups had higher AMI and stroke rates compared with ethnic Norwegians (31), pointing to the need of better understanding the risk profile and applying preventive measures among these subgroups.

Excess morbidity and mortality in specific subgroups

One study (34) reported an excess mortality associated with the development of HF among patients hospitalized with an incident AMI. Other studies reported an excess risk of HF and AF (35), stroke and cerebrovascular disease (36) as well as AMI and CHD (37) among patients with familiar hypercholesterolemia as compared with the general Norwegian population. In children with Down syndrome, the co-existence of severe congenital heart defects increased by 4-7 times the five-year mortality compared with children without such comorbidities (27).

Biological markers and other risk factors/etiological studies

Several studies have explored associations between various biomarkers or classical CVD risk factors and CVD-related health conditions in community-dwelling adults and/or patients' subgroups.

Higher glycine (38), kynurenine metabolites (39) and non-fasting triglyceride (40) levels were associated with higher risk of AMI or CHD while higher plasma trimethylamine-N-oxide (41), cotinine (42) and choline/betaine (43) were associated with higher risk of AF. Altered vitamin B-6 homeostasis (44) and cystathionine (45) levels were associated with the risk of stroke.

Other studies have focused on pregnancy disorders and subsequent maternal health. One study reported an increased risk of subsequent major coronary events among mothers with preeclampsia (PE), especially if associated with the child being born small for gestational age (SGA) and/or preterm delivery (46). Similarly, gestational hypertension increased the risk of maternal CVD morbidity (47). Another study reported an increased long-term risk of maternal CVD morbidity among mothers presenting hyperemesis gravidarum (hyperemesis) during pregnancy (48). Another group of studies have focused on offspring (49-53) rather than maternal health. In one of these studies, the periconceptional folic acid supplement use showed no association with severe congenital heart defects. However, an unexpected association with an increased risk of septal defects warrants further investigation (49).

Another study showed an increased risk of having a child with a congenital heart

defect among diabetic women and those with pregestational or gestational diabetes compared with non-diabetic women (52). Early-onset PE was strongly associated with infant risk of severe congenital heart defects (51). A recent study found an increased risk of non-severe congenital heart defects among offspring of mothers consuming higher amounts of sucrose-sweetened soft beverages (50).

Methodology, prediction models, other

CVDNOR data have also been used to i) assess the accuracy in identifying incident events in register-based datasets (15), ii) evaluate the ability of different anthropometric measures in predicting AMI (54), iii) construct a prediction model for stroke and AMI for use in primary prevention guidelines in Norway (55), iv) test the long-term effect of blood pressure-lowering medications in stroke patients (56), v) evaluate the quality of self-reported information on disease history (57), vi) explore interactions between various metabolic markers (58, 59), and vii) quantify the role of traditional risk factors in the observed ethnic gradients of CHD in Norway (60).

Limitations inherent to data collection and structure

Data obtained from the Patient Administrative Systems do not include information on relevant lifestyle factors, anthropometric indicators or history of all diseases, nor medications taken at the hospital or prescribed upon discharge. We do not have information on patients' participation in rehabilitation programs. The Patient Administrative Systems data cover hospitalizations and outpatient contacts (the latter only from 2008 onwards). As such, contacts with primary or other health care facilities are not included. One should keep in mind that some CVD sub-entities may not require immediate hospitalization and can be followed ambulatory for relatively long periods. Therefore, such limitations should be kept in mind when interpreting study findings, especially those exploring disease incidence and/or prevalence.

CVDNOR data are not suitable for conducting stratified analyses on disease subtype (e.g. ST-elevation MI versus non-ST elevation MI) or severity (HF with preserved versus reduced ejection fraction) as such information is not registered. The identification of diseases in CVDNOR is based on ICD-9 and ICD-10 codes only. Therefore, changes in diagnostic criteria or coding procedures may impact the observed trends. In such cases, prior knowledge on these potential changes will facilitate interpretation of findings.

Lastly, an individual is included in CVDNOR only if he/she has at least one CVD or DM-related diagnosis (either as primary or secondary). If a cardiac patient is subsequently hospitalized with no mention of any CVD or DM-related diagnosis, this hospitalization would not be included in CVDNOR. Such limitations may be relevant in studies exploring all-cause readmission rates following a previous CVD-related hospitalization as well as when measuring the burden of comorbidities. Lastly, CVD-related diagnoses retrieved from the Patient Administrative Systems are not validated against patient journals.

Acknowledgement

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Table 4. Published studies using data from the CVDNOR project

Author (Publication Year)	Study Focus Study Focus	Study Population
I. Trend analyses and disease burden		
Sulo G, Igland J, Nygård O, Vollset SE, Ebbing M, Tell GS. (2014)(16)	AMI incidence	Incident (non-fatal and fatal) AMIs, 2001-2009
Sulo G, Igland J, Vollset SE, Ebbing M, Egeland GM, Tell GS. (2018)(17)	AMI incidence	Incident (non-fatal and fatal) AMIs, 2001-2014
Sulo G, Vollset SE, Nygård O, Igland J, Egeland GM, Ebbing M, Tell GS. (2014) (19)	i) AMI event rates and ii) AMI recurrences following an incident AMI	AMI events (incident and recurrences), 1994-2009
Leirgul E, Fomina T, Brodwall K, Greve G, Holmstrom H, Vollset SE, Tell GS, Øyen N. (2014)(20)	Prevalence of congenital heart defects	954 413 births registered in the MBR, 1994-2009
Sulo E, Vollset SE, Nygård O, Sulo G, Igland J, Egeland GM, Ebbing M, Tell GS. (2015)(22)	28-day and one-year mortality following an incident AMI	115 608 patients with an incident AMI, 2001-2009
Jortveit J, Oyen N, Leirgul E, Fomina T, Tell GS, Vollset SE, Eskedal L, Dohlen G, Birkeland S, Holmstrom H. (2016)(24)	Mortality among live-born children with congenital heart defects	954 413 births registered in the MBR, 1994-2009
Sulo E, Vollset SE, Nygård O, Igland J, Sulo G, Ebbing M, Egeland GM, Hawkins NM, Tell GS. (2016)(21)	Utilization of coronary angiography and revascularization procedures in patients with an incident AMI	104 836 patients with an incident AMI, 2001-2009
Sulo E, Nygård O, Vollset SE, Igland J, Ebbing M, Østbye T, Jørgensen T, Sulo G, Tell GS. (2017)(28)	Out-of-hospital coronary deaths	All coronary deaths occurring outside a hospital, 1995-2009.
Sulo G, Igland J, Nygard O, Vollset SE, Ebbing M, Cerqueira C, Egeland GM, Jorgensen T, Tell GS. (2017)(18)	Early and late-onset HF in patients with an incident AMI	69 372 patients with an incident AMI and no prior hospitalization for HF, 2001-2014
Sulo G, Igland J, Sulo E, Overland S, Egeland GM, Vollset SE, Tell GS. (2019) (23)	28-day and one-year mortality following an incident AMI by cause and place of death	144 473 patients with an incident AMI, 2001 - 2014
Sulo G, Igland J, Vollset SE, Nygard O, Ebbing M, Sulo E, Egeland GM, Tell GS. (2016)(25)	Describe patterns and timing of HF as a complication of an incident AMI	86 771 patients with an incident AMI and no prior hospitalization for HF, 2001-2009
Brodwall K, Greve G, Leirgul E, Tell GS, Vollset SE, Øyen N. (2017)(26)	Quantify the risk of congenital heart defects recurrences among twins, full siblings, and half-siblings	902 880 births registered in the MBR, 1999-2009
Brodwall K, Greve G, Leirgul E, Klungsoyr K, Holmstrom H, Vollset SE, Øyen N. (2018)(27)	Describe specific cardiac phenotypes in Down syndrome	953 450 births registered in the MBR, 1999-2009
II. Gradients in disease occurrence		
Igland J, Vollset SE, Nygård O, Sulo G, Ebbing M, Tell GS. (2014)(29)	Educational inequalities in AMI incidence	141 332 patients with an incident (non-fatal and fatal) AMI, 2001-2009
Igland J, Vollset SE, Nygård O, Sulo G, Sulo E, Ebbing M, Naess O, Ariansen I, Tell GS. (2014)(33)	Educational inequalities in 28-day and one-year mortality following an incident AMI	111 993 patients with an incident AMI, 2001-2009
Ariansen I, Mortensen L, Igland J, Tell GS, Tambs K, Graff-Iversen S, Strand BH, Naess O. (2015)(30)	The role of cognitive ability in late adolescence on the observed educational gradients in CHD	57 279 men born during 1949-1959, participating in the National Health Screening Service's Age 40 Program.

Rabanal KS, Selmer RM, Igland J, Tell GS, Meyer HE. (2015)(31)	Compare the burden of AMI and stroke across ethnic groups in Norway	67 683 AMI patients and 43 252 stroke patients, 1994-2009
Sulo E, Vollset SE, Nygård O, Igland J, Sulo G, Ebbing M, Egeland GM, Hawkins NM, Tell GS. (2016)(21)	Educational differences in the utilization of coronary angiography and revascularization procedures in patients with an incident AMI	104 836 patients with an incident AMI, 2001-2009
Sulo G, Nygård O, Vollset SE, Igland J, Ebbing M, Sulo E, Egeland GM, Tell GS, (2016)(32)	Educational differences in the risk of HF among patients with an incident AMI	70 506 patients with an incident AMI and no prior hospitalization for HF, 2001-2014
Sulo E, Nygård O, Vollset SE, Igland J, Ebbing M, Østbye T, Jørgensen T, Sulo G, Tell GS. (2017)(28)	Educational differences in the risk of dying from CHD outside a hospital	All coronary deaths occurring outside a hospital, 1995-2009

III. Excess mortality and special populations		
Sulo G, Igland J, Nygård O, Vollset SE, Ebbing M, Poulter N, Egeland GM, Cerqueira C, Jorgensen T, Tell GS, (2017) (34)	Explore the excess mortality associated with HF as an early or late complication of an incident AMI	69 372 patients with an incident AMI and no prior hospitalization for HF, 2001-2009
Hovland A, Mundal LJ, Igland J, Veierod MB, Holven KB, Bogsrud MP, Tell GS, Leren TP, Retterstol K. (2017)(35)	Compare the risk of heart failure and atrial fibrillation between patients with genetically confirmed familiar hypercholesterolemia and the general Norwegian population	4273 patients included in the UCCG Registry during 2001-2009
Hovland A, Mundal LJ, Igland J, Veierod M B, Holven KB, Bogsrud MP, Tell GS, Leren TP, Retterstol K. (2018)(36)	Compare the risk of ischemic stroke and total cerebrovascular disease between patients with genetically-confirmed familiar hypercholesterolemia and the general Norwegian population	3144 patients included in the UCCG Registry, 2001-2009, without cerebrovascular disease
Mundal LJ, Igland J, Veierod MB, Holven KB, Ose L, Selmer R, Wisloff T, Kristiansen IS, Tell GS, Leren TP, Retterstol K. (2018)(37)	Compare the risk of AMI and CHD between patients with genetically-confirmed familiar hypercholesterolemia and the general Norwegian population	4273 patients included in the UCCG Registry, 2001-2009, without CHD
Brodwall K, Greve G, Leirgul E, Klungsoyr K, Holmstrom H, Vollset SE, Øyen N. (2018)(27)	Impact of congenital heart defects and extracardiac malformations on survival among children with Down syndrome	953 450 births registered in the MBR, 1999-2009
IV. Biological markers and other risk factors		
Ding Y, Svingen GF, Pedersen ER, Gregory JF, Ueland PM, Tell GS, Nygård O. (2015) (38)	Associations between plasma glycine and AMI	4109 patients with SAP undergoing coronary angiography, included in the WECAC
Eussen SJ, Ueland PM, Vollset SE, Nygård, O, Midttun O, Sulo G, Ulvik A, Meyer K, Pedersen ER, Tell GS. (2015) (39)	Associations between kynurenine and its metabolites levels and acute coronary events	3328 community-dwelling adults, age 70-72 years, participating in the HUSK
Egeland GM, Igland J, Sulo G, Nygard O, Ebbing M, Tell GS. (2015)(40)	Associations between non-fasting triglyceride plasma levels and AMI	140 790 individuals, age 18+ years, participating in CONOR

Svingen GFT, Zuo H, Ueland PM, Seifert R. Loland KH, Pedersen ER, Schuster PM, Karlsson T, Tell GS, Schartum-Hansen H, Olset H, Svenningsson M, Strand E, Nilsen DW, Nordrehaug JE, Dhar I, Nygård O. (2018)(41)	Association between plasma trimethylamine-N-oxide levels and AF	3797 patients with SAP included in the WECAC 3143 participants in the HUSK
Zuo H, Nygard O, Vollset SE, Ueland PM, Ulvik A, Midttun O, Meyer K, Igland J, Sulo G, Tell GS. (2018)(42)	Associations between smoking status, plasma cotinine levels and AF	6682 participants in the HUSK
Zuo H, Svingen GFT, Tell GS, Ueland PM, Vollset SE, Pedersen ER, Ulvik A, Meyer K, Nordrehaug JE, Nilsen DWT, Bonaa KH, Nygård O. (2018)(43)	Associations between plasma choline and betaine and AF	6949 participants in the HUSK; 4164 patients with SAP enrolled in the WECAC; 3733 patients with AMI enrolled in the NORVIT
Zuo H, Tell GS, Ueland PM, Nygård O, Vollset SE, Midttun O, Meyer K, Ulvik A. (2018)(44)	Associations between altered vitamin B-6 homeostasis and cerebral stroke	6891 participants in the HUSK
Leirgul E, Gildestad T, Nilsen RM, Fomina, T, Brodwall K, Greve G, Vollset SE, Holmstrom H, Tell GS, Øyen N. (2015)(49)	Associations between periconceptional intake of folic acid supplements and infant risk of congenital heart disease	652 977 births registered in the MBR, 1999-2009
Berge LI, Skogen JC, Sulo G, Igland J, Wilhelmsen I, Vollset SE, Tell GS, Knudsen AK. (2016)(61)	Associations between health anxiety and risk of CHD	7052 individuals, age 40-46 years, participating in the HUSK
Dale MTG, Magnus P, Leirgul E, Holmstrom H, Gjessing HK, Brodwall K, Haugen M, Stoltenberg C, Øyen N. (2019)(50)	Associations between maternal intake of sucrose-sweetened soft beverages in the first trimester and CHD in offspring	88,514 births registered in the MoBa, 2000-2009
Brodwall K, Leirgul E, Greve G, Vollset SE, Holmstrom H, Tell GS, Øyen N. (2016) (51)	Associations between maternal preeclampsia and severe congenital heart disease in offspring	914 703 singleton births registered in the MBR, 1994-2009
Leirgul E, Brodwall K, Greve G, Vollset SE, Holmstrom H, Tell GS, Øyen N. (2016) (52)	Associationss between (i) pre-gestational or gestational diabetes and congenital heart defects in offspring and (ii) low-for-gestational age birth weight and cardiac defects in offspring	914 427 births registered in the MBR, 1994-2009
Fossum S, Naess O, Halvorsen S, Tell GS, Vikanes AV. (2019)(48)	Associations between hyperemesis gravidarum (hyperemesis) and maternal CVD morbidity	989 473 women with singleton births registered in the MBR, 1967-2002
Øyen N, Olsen SF, Basit S, Leirgul E, Strom M, Carstensen L, Granstrom C, Tell GS, Magnus P, Vollset SE, Wohlfahrt J, Melbye M. (2019)(53)	Associations between periconceptional folic acid supplementation and congenital heart defects in offspring	102 985 births registered in the MoBa, 2000-2009
Riise HKR, Sulo G, Tell GS, Igland J, Nygård O, Vollset SE, Iversen AC, Austgulen R, Daltveit AK. (2017)(46)	Associations between PE phenotypes and maternal CHD/CVD	708 614 women, age 16-49 years at childbirth, registered in the MBR, 1980-2009
Dhar I, Svingen GFT, Ueland PM, Lysne V, Svenningsson MM, Tell GS, Nygård O. (2018)(45)	Associations between cystathionine and total and ischemic stroke	2036 patients with SAP undergoing coronary angiography, included in the WECAC who did not take B-vitamins
Riise HKR, Sulo G, Tell GS, Igland J, Nygård O, Iversen AC, Daltveit AK. (2018)(47)	Associations between gestational hypertension and maternal CVD, accounting for the additional role of small-for gestational-age infants, preterm delivery, and parity	678 957 women registered in the MBRN, 1980-2009

Riise HKR, Sulo G, Tell GS, Igland J, Egeland G, Nygard O, Selmer R, Iversen A C, Daltveit AK. (2019) (62)	Associations between hypertensive pregnancy disorders and maternal CVD after adjustment for established CVD risk factors	20 075 women with a first delivery, 1980-2003, participating in the CONOR
Brodwall K, Greve G, Leirgul E, Klungsoyr K, Holmstrom H, Vollset SE, Øyen N. (2018)(27)	Associations between congenital heart defects and extracardiac malformations	953 450 births registered in the MBR, 1999 - 2009

V. Methodology, prediction models, others		
Sulo G, Igland J, Vollset SE, Nygård O, Egeland GM, Ebbing M, Sulo E, Tell GS. (2015)(15)	Assess the potential impact of methods used to identify incident events on their time trends.	All patients, age 25+ years, hospitalized with an AMI in Norway, 1994-2009
Egland GM, Igland J, Vollset SE, Sulo G, Eide GE, Tell GS. (2016)(54)	Asses the ability of various anthropometric measures in predicting AMI	140 790 individuals participating in the CONOR
Eliassen B, Melhus M, Tell GS, Borch KB, Braaten T, Broderstad AR, Graff-Iversen S. (2016)(57)	Asses the quality of questionnaire data as opposed to hospital discharge data by ethnicity, sex, age and education attainment	16 865 individuals, age 30 and 36-79 years, participating in the SAMINOR-1 survey
Selmer R, Igland J, Ariansen I, Tverdal A, Njolstad I, Furu K, Tell GS, Klemsdal TO. (2017)(55)	Developing a new model for the prediction of 10-year risk of incident acute myocardial infarction or cerebral stroke (NORRISK 2)	Model population: 31 445 men and 35 267 women; External validation population: 19 980 men and 19 309 women participating in the CONOR, 1994–1999
Bjørnestad EØ, Borsholm RA, Svingen GFT, Pedersen ER, Seifert R, Midttun Ø, Ueland P M, Tell GS, Bonaa KH, Nygård O, (2017)(59)	Examine the potential modifying effect of Neopterin and C-reactive protein levels in the association between tHcy and AMI among patients with CHD	4164 patients with SAP undergoing coronary angiography, enrolled in the WECAC
Hilvo M, Meikle PJ, Pedersen ER, Tell GS, Dhar I, Brenner H, Schottker B, Laaperi M, Kauhanen D, Koistinen KM, Jylha A, Huynh K, Mellett NA, Tonkin AM, Sullivan DR, Simes J, Nestel P, Koenig W, Rothenbacher D, Nygård O, Laaksonen R. (2019)(58)	Investigate whether the combination of ceramides with phosphatidylcholines would be synergistic in the prediction of CVD	3789 patients with SAP undergoing coronary angiography, enrolled in the WECAC; 5991 patients with a history of AMI or UAP, enrolled in the LIPID
Hornslien A, Sandset EC, Igland J, Terent A, Boysen G, Bath PM, Murray GD, Berge E. (2015)(56)	Assess the long-term benefits of blood pressure lowering treatment with Candesartan	2029 patients with acute stroke and hypertension, enrolled in the SCATS
Rabanal KS, Meyer HE, Tell GS, Igland J, Pylypchuk R, Mehta S, Kumar B, Jenum A K, Selmer R, Jackson R. (2017)(60)	Explore the role of traditional risk factors on the observed CVD ethnic gradients	Participants in three surveys: HUBRO, I-HUBRO and MoRo II

AF: atrial fibrillation; AMI: acute myocardial infarction; CHD: coronary heart disease; CVD: cardiovascular disease; HF: heart failure; UAP: unstable angina pectoris; SAP: stable angina pectoris.
CONOR: Cohort of Norway; HUSK: Hordaland Health Studies; HUBRO: The Oslo Health Study; I-HUBRO: The Oslo Immigrant Health Study; LIPID: Long-Term Intervention with Pravastatin in Ischaemic Disease; MBR: Medical Birth Registry; MoBa: Norwegian Mother and Child Cohort; MoRo: The Romsås in Motion study; NORVIT: Norwegian Vitamin Trial; SAMINOR: Study on Health and Living Conditions in Sami and Norwegian Populations; SCAST: The Scandinavian Candesartan Acute Stroke Trial; UCCG: Unit for Cardiac and Cardiovascular Genetics; WECAC: Western Norway Coronary Angiography Cohort; WENBIT: Western Norway B-vitamin Intervention Trial.

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