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Utgis vanligvis med to regulære nummer pr. år. I tillegg kommer supplement med sammendrag fra Norsk forening for epidemiologis årlige konferanse.

DEN ATTENDE NORSKE EPIDEMIOLOGIKONFERANSEN

STIKLESTAD,

4.-5. NOVEMBER 2010

Den 18. norske epidemiologikonferansen
Stiklestad 4.-5. november 2010

Årets NOFE-konferanse arrangeres ved Stiklestad Nasjonale Kultursenter i Verdal i regi av HUNT forskningssenter og Institutt for samfunnsmedisin, NTNU. Verdal var arnestedet for Helseundersøkelsen i Nord-Trøndelag som i dag representerer en omfattende og viktig database for populasjonsbaserte studier av internasjonalt format. I dag er forskningssentret med den nye biobanken imidlertid lokalisert 10 km lenger sør i Levanger.

Konferansen har i år som tidligere et bredt spekter av aktuelle tema, som sikkert vil treffe mangfoldet av norske epidemiologer. Genetisk epidemiologi er et forskningsfelt det satses tungt på både nasjonalt og internasjonalt i vår tid, og vi ser fram til å høre dr. *Paul Brennan* fra International Agency for Research on Cancer (IARC) i Frankrike foredra om hel-genom assosiasjonsstudier. Den sosiale epidemiologien har på den annen side alltid vært relevant for å forstå utviklingen i helsetilstanden i befolkninger. Professor *John Gunnar Mæland* fra Universitetet i Bergen, hovedredaktør for den nye boka om Sosial epidemiologi utgitt i 2009, holder sitt foredrag fredag 5. november. Den siste inviterte foredragsholderen i år er dr. *Philippe Autier*, fra International Prevention Research Institute (iPRI) i Frankrike. Han tar for seg det høyaktuelle temaet kreftscreening med tanke på debatten om effekten av mammascreening som fortsatt pågår for fullt.

Til sist på torsdag blir det kåring av årets epidemiologiske artikkel. NOFEs årsmøte er som vanlig også på programmet. Om kvelden blir det den tradisjonsrike NOFE-middagen, som i år avholdes på historisk grunn der Olav den hellige falt i 1030.

Vi ønsker dere alle hjertelig velkommen til den 18. norske epidemiologikonferansen. Vi vet det blir en innholdsrik konferanse, og håper dere alle får to hyggelige dager på Stiklestad.

Med hilsen fra arrangementkomiteen for NOFE-konferansen 2010

Steinar Krokstad og Arnulf Langhammer (HUNT forskningssenter), Pål Romundstad, Johan Håkon Bjørngård og Lars Vatten (Institutt for samfunnsmedisin) og Tom Ivar Lund Nilsen (Institutt for bevegelsevitenskap NTNU og styreleder i NOFE)

Den 18. norske epidemiologikonferansen
Stiklestad 4.-5. november 2010

Oversiktsprogram

Thursday, November 4th

10:00-10:55	Registration/coffee
10:55-11:00	Welcome
11:00-12:00	***"Screening for cancer"*** Invited speaker: **Dr. Philippe Autier**, International Prevention Research Institute (iPRI), France
12:00-13:15	Oral presentations of submitted abstracts (parallel sessions, **A1-5** and **B1-5**)
13:15-14:30	Lunch
14:30-15:30	***"Genome-wide association studies – present status and future perspective"*** Invited speaker: **Dr. Paul Brennan**, International Agency for Research on Cancer (IARC), France
15:30-16:45	Oral presentations of submitted abstracts (parallel sessions, **A6-10** and **B6-9**)
16:45-17:00	Coffee break
17:00-17:45	Oral presentations of submitted abstracts (parallel sessions, **A11-13** and **B10-12**)
17:45-18:15	"The publication of the year" award
18:15-18:45	NOFE's annual meeting
20:00-	Conference dinner

Friday, November 5th

09:00-10:00	***"Social epidemiology"*** Invited speaker: **Prof. John G Mæland**, University of Bergen
10:00-11:00	Oral presentations of submitted abstracts (parallel sessions, **A14-17** and **B13-16**)
11:00-11:15	Coffee break
11:15-12:15	Oral presentations of submitted abstracts (plenary session, **A18-21**)
12:15-12:30	Concluding remarks
12:30-13:30	Lunch
13:30-	Buss departure to Værnes (Arrive approximately 14:45)

Den 18. norske epidemiologikonferansen
Stiklestad nasjonale kultursenter, 4.-5. november 2010

Detaljert program

TORSDAG 4. NOVEMBER

10:00-10:55			Registrering/kaffe
Plenumssesjon			
10:55-11:00		Steinar Krokstad	Velkommen
11:00-12:00		**Philippe Autier**	***Screening for cancer***
Parallellsesjon A1-A5			
Tema: Kreftepidemiologi			
12:00-12:15	A1	Tom Grotmol	Age-period-cohort (APC) analysis of primary bone cancer incidence rates in the United States (1976-2005)
12:15-12:30	A2	Kristine E. Andreassen	Bilateral testikkelkreft: redusert risiko etter introduksjon av cisplatin-basert kjemoterapi?
12:30-12:45	A3	Jo Stenehjem	Kjemisk eksponering og kreftforekomst blant ansatte i norsk offshoreindustri
12:45-13:00	A4	Ida Laake	A prospective study of body mass index, weight change and risk of cancer in the proximal and distal colon
13:00-13:15	A5	Signe Opdahl	Breast cancer risk factors among parous and nulliparous women
Parallellsesjon B1-B5			
Tema: Fysisk aktivtet/kroppsmasse			
12:00-12:15	B1	Koenraad Cuypers	Body weight misperception and perceived slimming pressure in normal weight adolescents is associated with development of overweight and obesity in young adulthood. The Young-HUNT study, Norway
12:15-12:30	B2	Kristin B. Borch	Physical activity and overall mortality in the Norwegian Women and Cancer study
12:30-12:45	B3	Børge Moe	Type 2 diabetes og glykemisk kontroll hos menn. Er styrketrening like effektivt som utholdenhetstrening?
12:45-13:00	B4	Linda Leivseth	Respiratory symptoms and lung function associated with self-rated physical and psychological health: The Nord-Trøndelag Health Study
13:00-13:15	B5	Aina Emaus	Comparison of self-report and objectively measured physical activity: Do we follow the guidelines? Results from the Tromsø Study
13:15-14:30		**Lunsj**	
Plenumssesjon			
14:30-15:30		**Paul Brennan**	***Genome-wide association studies – present status and future perspective***

Parallellsesjon A6-A10
Tema: Genetisk epidemiologi

15:30-15:45	A6	Hege M. Bøvelstad	Blood gene expression variation in postmenopausal women exposed to hormonal treatment – The NOWAC Postgenome Study
15:45-16:00	A7	Sarah Sæther	Postmenopausal hormonal therapy and gene expression signature in blood
16:00-16:15	A8	Marissa LeBlanc	Genome-wide study identifies *PTPRO* and *WDR72* and *FOXQ1-SUMO1P1* interaction associated with neurocognitive function
16:15-16:30	A9	Anita Iversen	Single Nucleotide Polymorphisms (SNPs) in *CYP17A1* and daily 17-β estradiol among young healthy women. The EBBA-I study
16:30-16:45	A10	Ernst I.S. Thomassen	Detection of human microRNAs in whole blood and plasma samples from the Norwegian woman and cancer study (NOWAC)

Parallellsesjon B6-B9
Tema: Metode

15:30-15:45	B6	Inger Johanne Bakken	Norsk pasientregister i epidemiologisk forskning – Fra opphold til pasient med personidentifiserbare data
15:45-16:00	B7	Lise Lund Håheim	Development of national quality indicators for cardiovascular disease: Theoretical framework and formalized consensus process
16:00-16:15	B8	Arnulf Langhammer	Utvikling av HUNT databank
16:15-16:30	B9	Arnulf Langhammer	Ikke-møtt spørreskjemabasert studie i Helseundersøkelsen i Nord-Trøndelag 2006-08 (HUNT 3)
16:45-17:00		**Kaffepause**	

Parallellsesjon A11-A13
Tema: Metode- og teoriutvikling

17:00-17:15	A11	Eiliv Lund	A novel approach to carcinogenesis – exposure driven functional model
17:15-17:30	A12	Alena Bartonova	Complex radiochemical environment and carcinogenesis: new approach in data interpretation and an assessment of knowledge
17:30-17:45	A13	Kathrine Frey Frøslie	Bruk av funksjonell data-analyse på glukosebelastningsdata

Parallellsesjon B10-B12
Tema: Klinisk epidemiologi

17:00-17:15	B10	Fred Andersen	The effect of stimulation therapy and donepezil on cognitive function in Alzheimer's disease. A community based randomised controlled trial
17:15-17:30	B11	Pål E. Martinussen	Prescription of benzodiazepines and z-hypnotics in psychiatric institutions: Evidence from Norway
17:30-17:45	B12	Linda Leivseth	Natural course of musculoskeletal pain – a prospective cohort study

Plenumssesjon

17:45-18:15	**Årets artikkel 2010, utnevning og foredrag**
18:15-18:45	**Årsmøte i NOFE**
20:00-	**Festmiddag**

FREDAG 5. NOVEMBER

Plenumssesjon

09:00-10:00		**John G. Mæland**	***Sosialepidemiologi***

Parallellsesjon A14-A17
Tema: Sosialepidemiologi

10:00-10:15	A14	Linda Ernstsen	Socioeconomic inequalities in prevalence of smoking in the Nord-Trøndelag Health Study (HUNT) 1995-2008
10:15-10:30	A15	Kristine Pape	Påvirker psykisk uhelse i ungdomsårene mottak av langtids trygdeytelser som ung voksen?
10:30-10:45	A16	Sara Marie Nilsen	Educational inequalities in disability pension: The impact of illness, occupational, psychosocial and behavioural factors
10:45-11:00	A17	Audhild Løhre	Who are we to believe – the child, teacher, or parent? Reports on victimization from different informants, and associations with children's health complaints

Parallellsesjon B13-B16
Tema: Miljø og demografi

10:00-10:15	B13	Cecilie Dahl	pH variations in Norwegian drinking water and the effect on bone health. The NOREPOS Study
10:15-10:30	B14	Alena Bartonova	Exposure scenario approach to environmental health problems: two case studies
10:30-10:45	B15	Anita Øren	Endringer i den norske befolkningens pengespillvaner etter spilleautomatforbudet
10:45-11:00	B16	Aileen Yang	Impact of socio-demographic factors on time-use
11:00-11:15		**Kaffepause**	

Plenumssesjon A18-A21
Tema: Hjertekar-epidemiologi

11:15-11:30	A18	Torgeir Sørensen	The relationship between religious attendance and blood pressure: the HUNT study, Norway
11:30-11:45	A19	Bjørn Mørkedal	Informativeness of indices of blood pressure, obesity and serum lipids in relation to ischaemic heart disease mortality in a prospective population study (HUNT II)
11:45-12:00	A20	Marie S. Sandvei	Forekomst, dødelighet og risikofaktorer for subaraknoidalblødning
12:00-12:15	A21	Jannicke Igland	Relativ betydning av etablerte risikofaktorer for hjerte- og karsykdom – Helseundersøkelsene i Hordaland
12:15-12:30		**Avslutning**	
12:30-13:30		**Lunsj**	
13:30-		**Buss til Værnes (ankomst ca. 14:45)**	

A1

Age-period-cohort (APC) analysis of primary bone cancer incidence rates in the United States (1976-2005)

Kristin P. Anfinsen[1], Freddie I. Bray[2], Rebecca Troisi[3], Thora J. Jonasdottir[1], Oyvind S. Bruland[4], Susan S. Devesa[3] and Tom Grotmol[1,2]

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Background: Primary bone cancer comprises three major histological subtypes: osteosarcoma (OS), Ewing sarcoma (ES) and chondrosarcoma (CS). The most frequent subtype, OS, primarily occurs in adolescence, but has a second peak at the oldest ages, usually attributed to late effects of radiotherapy and chemotherapy, and Paget's disease. The adolescent age distribution of ES resembles that of OS, suggesting a link between the onset of puberty and these subtypes of bone cancer. CS is rare in childhood, and incidence rates, unlike those of OS and ES, increase fairly uniformly with age.

Given the limited knowledge about the etiology of primary bone cancer, and the unusual age-incidence distribution for OS and ES, we undertook an APC analysis to determine whether incidence varied by birth cohort or calendar period. For other cancers, such as testis and breast, the identification of cohort patterns has generated new hypotheses regarding environmental risk factors.

Method: We fit an APC model to incidence data among U.S. whites for OS, ES and CS obtained from nine registries of the Surveillance, Epidemiology, and End Results (SEER) program, which covers about 10% of the U.S. population, 1976-2005. The purpose was to examine the temporal development of each bone cancer subtype, with an aim to providing etiologic clues as to the role of birth cohort-related changes.

Results: Incidence of OS decreased between 1976 and 2005 among those 60 years and older, and rates declined among cohorts born 1905-34. The risk of CS doubled among females 20-69 years, with rates increasing among consecutive birth cohorts born 1925-54, whereas those of males were unaltered. For both sexes, ES incidence rates tended to be stable.

Conclusion: The risk reduction in OS at older ages was most likely due to improved radiotherapy and more effective chemotherapy. The CS risk increase in females corresponds to birth cohorts who were increasingly exposed to estrogens, both in terms of contraceptives (from 1960 onwards), and hormone therapy (from 1950 onwards). In support of our hypothesis that estrogens are involved in the increase in CS among women over time, *in vitro* studies show that the estrogen signaling pathway stimulates proliferation of both normal and malignant chondrocytes. Further studies are warranted to pursue the possible etiological significance of estrogen exposure in CS risk.

A2

Bilateral testikkelkreft: Redusert risiko etter introduksjon av cisplatin-basert kjemoterapi?

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Formål: Undersøke risikoen for at pasienter behandlet for unilateral germinalcelle tumor i testikkelen (TGCT) skal utvikle kontralateral TCGT, og sammenligne denne risikoen for pasienter behandlet før og etter 1980 (cisplatin-basert kjemoterapi ble tilgjengelig pasienter med testikkelkreft i Norge på slutten av 1970-tallet). Vår hypotese var at risikoen ville være lavere for pasienter diagnostisert etter 1980, pga en mulig beskyttende effekt av cisplatin-basert kjemoterapi. Etter 1980 har så å si alle pasienter med metastatisk sykdom blitt behandlet med cisplatin, i motsetning til bare 20-25 % av de med lokalisert sykdom.

Materiale og metode: Vi inkluderte 7102 menn med unilateral TGCT (3921 hadde seminom og 3181 non-seminom), registrert i Kreftregisterets database og diagnostisert i perioden 1953-2007. 10- og 20-års kumulativ insidens for kontralateral TGCT og justert hazard ratio (HR) ble beregnet for forskjellige subgrupper, og de diagnostiske periodene 1953-1979 (I) og 1980-2007 (II). Det ble tatt hensyn til competing risk (død) i analysene. Vi beregnet også standardisert insidensratio (SIR) for de samme undergruppene.

Resultat: 175 menn ble diagnostisert med kontralateral TGCT. Periode I: 38 tilfeller, 10- og 20- års kum.ins. 1,3 % (95% CI=0,9-1,9) og 1,9 % (95% CI=1,4-2,6). Periode II: 137 tilfeller, 10- og 20- års kum.ins. 2,7 % (95% CI=2,2-3,2) og 3,9 % (95% CI=3,3-4,7). SIR i periode I var 14,6 (95% CI=9,6-21,2) og 25,3 (95% CI=12,1-46,5) for pasienter med henholdsvis lokalisert and metastatisk sykdom. I periode II var de korresponderende tallene 19,0 (95% CI=15,6-22,9) og 9,8 (95% CI=6,4-14,5).

		1953-1979				**1980-2007**			
		10-års kum.ins.		Comp.risk reg.		10-års kum.ins.		Comp.risk reg.	
Første TGCT:		%	95% CI	HR	95% CI	%	95% CI	HR	95% CI
Alder	< 30 yrs	2,7	1,6-4,2	ref		3,7	2,8-4,7	ref	
	>=30 yrs	0,7	0,4-1,3	**0,18**	**0,08-0,39**	2,0	1,5-2,6	**0,48**	**0,34-0,66**
Hist.	Sem.	1,2	0,7-2,0	ref		1,5	0,8-2,6	ref	
	Non-sem.	2,8	2,2-3,6	0,86	0,42-1,78	2,5	1,9-3,3	0,87	0,63-1,21
Sykdoms utbredelse	Lok.	1,3	0,8-2,1	ref		3,2	2,6-4,0	ref	
	Met.	1,4	0,7-2,6	0,70	0,34-1,47	1,6	1,0-2,4	**0,5**	**0,33-0,77**

Konklusjon: Det har vært en fordobling av insidensen av både unilateral og bilateral TGCT i periode II, sammenlignet med periode I. Alder over 30 år gir økt risiko i begge perioder. I periode II, er risikoen halvert for pasienter med metastatisk, sammenlignet med lokalisert sykdom. Funnene støtter vår hypotese om at introduksjonen av cisplatin i 1980 har redusert risikoen for kontralateral TGCT, i alle fall for pasienter med metastatisk sykdom.

A3

Kjemisk eksponering og kreftforekomst blant ansatte i norsk offshoreindustri

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Formål: Oljeproduksjon har spilt en viktig rolle i det norske samfunnet de siste 40 årene, og er i dag en av Norges største industrier med over 200 000 ansatte. Flere studier har funnet sammenhenger mellom eksponeringer i oljerelatert industri og ulike kreftformer, men få av disse er gjort på ansatte i norsk offshoreindustri. Med bakgrunn i dette, er det overordnete målet med det foreliggende prosjektet å kartlegge kjemisk eksponering og kreftforekomst blant norske offshoreansatte.

Materiale og metoder: Prosjektet inkluderer 28 000 offshorearbeidere som i 1998-99 via spørreskjema ga detaljert informasjon om utdanning, arbeidshistorikk, arbeidsmiljø, levevaner og kosthold. Prosjektet er delt inn i tre delstudier:

1. En kohortstudie som tar sikte på å følge opp personene for utvikling av kreft frem til juni 2011.
2. En kasus-kohortstudie som har full yrkeshistorikk og dermed mer presis eksponeringsinformasjon for alle kasus og et utvalg av hovedkohorten, dette utvalget vil brukes som kontrollgruppe til ulike kreftkasus.
3. En valideringsstudie som med sterkt avidentifiserte data vil beskrive kompletthet/overlapp i Kreftregisterets kohort sammenlignet med offshoreansatte registrert i Arbeidsgiver-/ arbeidstakerregisteret. Videre vil valideringsstudien beskrive kreftforekomst i forhold til gruppetilhørighet (deltakere, non-respondere, døde, emigrerte og ikke arbeidet offshore) og kreft diagnostisert før 1998.

Informasjon om kjemisk eksponering kommer fra en jobbeksponeringsmatrise basert på stillingstittel, arbeidssted, startår, varighet og skiftordninger. Det er aktuelt å estimere risiko for følgende kreftformer: Lymfe- og blodkreft, mesoteliom, lunge- og luftveiskreft, non-melanom hudkreft, urinveiskreft, spiserørskreft og malignt melanom. Aldersjustert kreftrisiko blant offshoreansatte i forhold til den norske befolkningen vil estimeres med standardisert insidens ratio (SIR) med 95 % konfidensintervall (KI). Kreftrisiko etter kjemisk eksponering vil estimeres med insidensrate ratio (IRR) med 95 % KI hvor det justeres for potensiell konfunderende effekt fra alder, observasjonsperiode, alkohol, røyking, arbeid før/etter offshore, arbeid i avspaseringsperiodene, utdanning og sivilstatus.

Foreløpige resultater: Offshorekohorten ble i 2007 koblet til Kreftregisterets hoveddatabase for en foreløpig vurdering av kreftforekomsten i perioden 1999-2005 for denne yrkesgruppen sammenlignet med den norske befolkningen for øvrig. For akutt myelogen leukemi og cancer pleura ble det estimert en SIR på henholdsvis 2,0 (95 % KI; 0,97-3,72) og 2,18 (95 % KI; 0,89-4,55). For andre kreftformer var ikke økningen i risiko like betydelig (Aas et al., 2009)*.

Konklusjon: Resultatene fra koblingen i 2007 må tolkes med forsiktighet på grunn av få kasus, kort oppfølgingstid og manglende bruk av eksponeringsinformasjon, men antyder likevel økning i risiko for visse kreftformer blant offshorearbeidere. Koblingen i 2011 forventes å kunne gi mer presise risikoestimater.

*Aas GB, Aagnes B, Strand LÅ, Grimsrud TK. Suggested excess of occupational cancers in Norwegian offshore workers: preliminary results from the Cancer Registry offshore Cohort. *Scand J Work Environ Health.* 2009;35(5):397-399.

A4

A prospective study of body mass index, weight change and risk of cancer in the proximal and distal colon

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Background: Body mass index (BMI) is an established risk factor for colon cancer, but whether the association between BMI and risk is stronger for men than for women is not yet resolved. Also, risk may differ between the proximal and distal colon. Moreover, weight change may influence risk, but studies have been inconclusive. We investigated these issues in the Norwegian Counties study, a large, population-based cohort study.

Material and methods: Between 1974 and 1988 three screening examinations were carried out in Finnmark, Oppland and Sogn og Fjordane. Initially, all residents between 35 and 49 years were invited. At each screening the participants' weight and height were measured. We estimated hazard ratios (HRs) and confidence intervals (CIs) with Cox regression.

Results: We followed 38,822 men and 37,357 women for an average of 23.3 years. During follow-up we identified 450 cases of colon cancer in men, 228 in the proximal colon and 174 in the distal colon, and 419 cases in women, 237 in the proximal colon and 159 in the distal colon In men, the association between BMI and colon cancer risk differed between subsites (P = 0.02). We found no association between BMI and risk in the proximal colon and a strong association in the distal colon, HRs (95% CIs) per 5 kg/m^2 were 1.07 (0.86–1.33) and 1.49 (1.19–1.87), respectively. The association did not differ between subsites in women (P=0.95), HRs (95% CIs) per 5 kg/m^2 were 1.15 (0.99–1.34) and 1.25 (1.05–1.49) for the proximal and distal colon, respectively. Among overweight men (BMI ≥ 25 kg/m^2), those who gained ≥10 kg were at increased risk compared to those who maintained their weight, HR = 2.09 (95% CI, 1.21–3.63), while weight loss was not associated with decreased risk. Weight change was not associated with colon cancer risk in women.

Conclusion: Our results indicate that there is a gender difference in the association between BMI and colon cancer risk and furthermore support the hypothesis of different etiologies for the proximal and distal colon. Weight gains <10 kg did not influence colon cancer risk.

A5

Breast cancer risk factors among parous and nulliparous women

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Background: Pregnancy has been suggested to reduce breast cancer risk through induction of persistent changes to the mammary gland, which in turn would make the breast less susceptible to carcinogenic factors. A characterization of how parity interacts with factors known to increase breast cancer risk could improve our understanding of the mechanisms through which both pregnancy and other factors influence the risk of this malignancy.

Methods: In a cohort of 63,041 Norwegian women followed from 1961 to 2008, we studied whether the risk of postmenopausal breast cancer associated with menstrual and anthropometric factors may interact with parity. Biological interaction, defined as departure from an additive model, was evaluated by calculating hazard ratios for combinations of parity with each of the other exposure variables (age at menarche, age at menopause, height and body mass index), and quantified by the attributable proportion (AP) due to interaction.

Results: Among both nulliparous and parous women, breast cancer risk increased with earlier age at menarche, later age at menopause, taller adult stature and increasing body mass index. There was evidence for synergism between parity and body mass index (AP 0.18, 95 % confidence interval (CI) 0.02 to 0.33), where nulliparous women with a high body mass index had a higher risk of breast cancer than expected in an additive model. For combinations of age at menarche and parity (AP -0.01, 95 % CI -0.17 to 0.15) and for combinations of height and parity (AP 0.02, 95 % CI -0.26 to 0.30), there was no evidence for departure from additivity. Breast cancer risk among parous women with early menopause was lower than expected based on an additive model, however, the departure from additivity was not statistically significant (AP -0.28, 95 % CI -0.73 to 0.16).

Conclusion: Menstrual and anthropometric factors influence breast cancer risk among both parous and nulliparous women. There was no indication for biological interaction between parity and age at menarche or height on breast cancer risk. The results regarding an interaction between age at menopause and parity were not conclusive. However, there was evidence for biological interaction between nulliparity and high body mass index, suggesting a joint effect beyond additivity for the combination of these two factors.

A6

Blood gene expression variation in postmenopausal women exposed to hormonal treatment – The NOWAC Postgenome Study

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The use of peripheral blood to obtain a gene expression signature related to disease and drug response is a novel and promising approach in cancer research. In order for such studies to succeed, knowledge of baseline values of the peripheral blood gene expression of normal women is needed. Also, one need to obtain knowledge about whether different exposures can be observed through altered blood gene expression. So far, various inter-individual (i.e. fasting, BMI) and exposure (i.e. smoking) factors are found to be mirrored in peripheral blood. The increased risk of breast cancer attributable to the use of hormonal therapy (HT) is well established, making HT an interesting candidate for further investigation. Using blood samples from a large data set of postmenopausal women from The Norwegian Women and Cancer (NOWAC) Postgenome Study, we have in this study examined whether there are differences in gene expression pattern of women using HT versus those that do not. In the talk I will present the statistical methodology used for the analysis, and show some preliminary results.

A7

Postmenopausal hormonal therapy and gene expression signature in blood

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Objective: In order to develop a valuable tool for assessing gene signatures that are related to exposure, disease, and response to treatment, it is requisite to consider the normal inter-individual differences in gene expression patterns, based on background information on exposure and lifestyle. Blood samples are easily collected, and there is growing evidence that the transcriptome of peripheral blood cells might reflect biological as well as pathological processes of multiple organs in the human body. In functional genomics, microarray technology and microarray data analysis are useful for deciphering gene expression in a genome-wide scale. With improved techniques and more consistent laboratory procedures, variation seen is more likely due to biological variability than technical noise. With sample sizes large enough, groups can be compared, and we can look for gene expression differences. Here, we will investigate blood samples from women, currently exposed to different categories of systemic drugs for hormonal therapy (HT). Objective is to identify pathways that are influenced, and signatures related to drug exposure.

***Material and methods*:** A random sample of 439 women that originate from the Norwegian Women and Cancer Study (NOWAC), not diagnosed for cancer. After exclusion of pre-/perimenopausal women, 336 postmenopausal women have been grouped into users of estradiol systemic (E2, N=11), estradiol plus progestogen systemic (E2+P, N=33), tibolone (N=12), users of other medication (N=194), and users of neither HT nor other medications (N=115). We have detailed data on medication use, so the group "other medications" can be further divided. RNA extraction, quality control, hybridization and data processing were performed by collaborators at NTNU Genomics Resource Center in Trondheim. Samples were analyzed using Illumina whole-genome expression microarrays type HU-6. We use R (http://cran.r-project.org/) and tools from the Bioconductor project (http://www.bioconductor.org/) for the data analysis. Here will be presented some preliminary results from the technical analysis.

A8

Genome-wide study identifies *PTPRO* and *WDR72* and *FOXQ1-SUMO1P1* interaction associated with neurocognitive function

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Background: Several aspects of neurocognitive function have a high heritability, but the molecular genetic mechanisms underlying the variation in neurocognition is not known. Here we performed a genome-wide association study (GWAS) to identify genes associated with neurocognitive domains.

Methods: A sample of 700 subjects (schizophrenia spectrum disorder, n = 190, bipolar disorder n = 157 and healthy controls n = 353) were tested with an extensive neuropsychological test battery, and genotyped genome-wide using the Affymetrix Genome-Wide Human SNP Array 6.0 (Affymetrix Inc, Santa Clara, CA, USA). After extensive quality control, linear regression analysis of each the 24 cognitive tests on the SNP dosage was performed, including age, gender, education and disease group as covariates. Additionally, 9 SNPs trending towards genome-wide significance were considered for epistatic interactions.

Results: Four SNPs and 2 independent association signals exceeding the levels of statistical significance accepted as "genome-wide" were identified. Three intronic SNPs in protein tyrosine phosphatase, receptor type, O (*PTPRO)* were associated with learning and memory tested with California Verbal Learning Test-II Long Delay Free Recall (rs17222089, $p = 1.55\text{x}10^{-8}$; rs11056571, $p = 1.68\text{x}10^{-8}$; and rs2300290, $p = 1.09\text{x}10^{-8}$), and rs719714 downstream of WD repeat domain 72 (*WDR72)* was associated with executive functioning measured with CW-3: Inhibition component of the Delis – Kaplan Executive Function System Color-Word Interference Test, interference ($p = 4.32\text{x}10^{-8}$). The findings were unrelated to disease status. A highly significant epistatic interaction was found between rs9378605 upstream of Forkhead box Q1(*FOXQ1)* and rs9378605 downstream of SUMO1 pseudogene 1 (*SUMO1P1)* for the Grooved Pegboard test ($p = 7.6\text{x}10^{-14}$).

Conclusions: We identified four novel loci associated with neurocognitive function and one novel epistatic interaction. The findings should be replicated in independent samples, but indicate a role of *PTPRO* in learning and memory, *WDR72* with executive functioning, and an interaction between *FOXQ1* and *SUMO1P1* for motor speed.

A9

Single nucleotide polymorphisms (SNPs) in *CYP17A1* and daily 17-β estradiol among young healthy women. The EBBA-I study

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Objectives: Elevated estrogen levels, measured pre- or postmenopausally, have consistently been associated with increased risk of breast cancer among postmenopausal women. *CYP17A1* encodes cytochrome P450 enzymes involved in the biosynthesis of estrogens but studies of associations of this gene with circulating estrogen levels have had inconsistent results. To study the functional relevance of genetic variability in *CYP17A1*, we assessed the association between eight single nucleotide polymorphisms (SNPs) spanning *CYP17A1* and biologically free salivary 17β-estradiol levels throughout the menstrual cycle in healthy young women, hypothesising that there might be an association between variation in the gene and the salivary level of estradiol.

Material and methods: Among 204 healthy women, aged 25–35 years, who participated in the The Norwegian Energy Balance and Breast cancer Aspects Study (EBBA-I), reproductive characteristics were assessed by questionnaire and interview. Clinical examinations, anthropometry measurements and blood sampling were performed in all women at three different time points during one menstrual cycle. Daily salivary levels of 17β-estradiol were measured throughout one entire menstrual cycle using radioimmunoassay (RIA), performed by the Reproductive Ecology Laboratory at Harvard University, USA. DNA was extracted from whole blood. Eight tagging SNPs (rs1004467, rs743575, rs4919687, rs3781286, rs3824755, rs10786712, rs743572, rs2486758) representing *CYP17A1* variability in the Caucasian population were selected using MAF >5 % and $r^2 = 0.80$. The eight polymorphisms were genotyped at the Molecular Epidemiology Lab, Fred Hutchinson Cancer Research Center, USA. Hormone data were log transformed prior to the multivariable linear regression analyses used to study associations between genotypes and 17β-estradiol levels.

Results: After adjusting for age**,** the rs2486758 polymorphism was significantly associated with overall mean salivary 17β-estradiol levels and women with at least one copy of rs2486758 had 18.5 % higher overall mean salivary 17β-estradiol levels compared to women with the homozygous common allele genotype ($p = 0.026$). There were no differences in age, body composition, reproductive characteristics, hormonal contraceptive use, energy intake, alcohol use, smoking status or physical activity in leisure time between subgroups of women with different rs2486758 genotype.

Conclusion: Estradiol levels in premenopausal women may in part be determined by genes. Interventions to alter estradiol levels to reduce breast cancer risk may need to be tailored according to genotype.

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A10

Detection of human microRNAs in whole blood and plasma samples from the Norwegian woman and cancer study (NOWAC)

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Introduction: microRNAs (miRNAs) are naturally occurring endogenous short non-coding RNAs that post-transcriptionally regulate coding mRNAs either by degrading them or suppressing their translation. Estimations suggest that miRNAs may regulate expression of more than 30 % of all human protein coding genes. miRNAs have important functions in development, cell proliferation, differentiation, signaling pathways, apoptosis, immune responses and metabolism. Emerging evidence suggests a direct link between miRNAs and diseases such as viral infections, genetic disorders, heart failure, and cancers. The expression patterns of miRNAs in human cancers are highly tissue-specific. For instance, cancers of the thyroid, breast, brain, colon, and lung are connected to de-regulated expression of miRNAs. The discovery of miRNAs in blood cells and as stably circulating ncRNAs, has opened up promising approaches for diagnosis and prognosis of human diseases including cancers.

Aim of the study: Our main goal of the study is to find a novel microRNA which can be used as a diagnostic biomarker for an early detection of breast cancer. Using our unique bio-bank of blood and plasma samples from the NOWAC study, the first aim was to find a reliable assay for detection and quantification of microRNAs in these materials. Another aim is to see if the expression levels of microRNAs in blood and plasma samples from cancer patients differ significantly from the same materials of healthy control individuals.

Materials and methods: Normal whole blood and plasma samples from women between 55 and 67 years old stored at -70° C for 1-2 years; total RNA was extracted from these materials using QIAGEN kits; miRCURY LNA microRNA Array Panels were purchased from Exiqon; real time-PCR were run on ABI7900HT from Applied Biosystems.

Results: Recently, we have started to evaluate a microRNA array real-time PCR assay to see how specific, reproducible and sensitive it is. Our prelimenary results reveal that miRNAs are stably expressed and preserved in whole blood and plasma samples from healthy control individuals, where they successfully can be detected using microRNA RT-PCR assay. Although it is difficult to come to any conclusions at this moment, the picture emerging from these initial studies reveal that some microRNAs are equally expressed, whereas others are higher or lower expressed in whole blood compared to plasma. The next step in our study is to see if the expression levels of microRNAs in blood and plasma samples from cancer patients are different from the same materials sampled from healthy individuals.

A11

A novel approach to carcinogenesis – exposure driven functional model

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After many decades of basic research driven by the mutation theory of carcinogenesis and similarly for more than five decades applying mathematical models to incidence data, still nobody has proposed a model for carcinogenesis with a given numbers of mutations, time ordered and with biological meaning. The enormous amount of detailed experimental information without a common interpretation has lead some researchers to state that we are approaching a pre-paradigmatic time in cancer research. As part of such a movement we would like to propose an exposure determined functional model. The main argument for a novel model is the obvious need to incorporate exposures as the driving forces of carcinogenesis in any model. Since it is difficult for technical reasons to incorporate the multitude of exposures in daily life of humans in cell studies and animal experiments, these studies will have a reductionistic approach. On the other side, even exposures are incorporated in most epidemiological studies the common prospective design is not very well suited for analysis of gene expression and epigenetics which is necessary for the functional analyses of pathways as part of a dynamic understanding of the carcinogenic process. This points to the need for a novel design of the next generation of epidemiological studies.

A12

Complex radiochemical environment and carcinogenesis: new approach in data interpretation and an assessment of knowledge

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Objective: To develop a visual aide for understanding complexities in cancer etiology and to assess knowledge regarding environmental determinants of estrogen-mediated cancers.

Materials and methods: In the HENVINET project, we developed a multi-stage method for knowledge assessment. The broad aim is to support the formulation of policy-relevant recommendations for action towards preventive or remediation measures related to environmental determinants of multiple health end points, including estrogen-related cancers. We have developed a graphical/visual presentation of cancer etiology caused by environmental stressors. Selection of cancer types was based on available information and the reported relative risks. In interpretation, the complexity of interaction between xenobiotics was a priority, but the diagrams also include gene/environment interactions. The resulting interactive diagram system with questionnaires provides related information, based on own review, in a hierarchical way. The tool is available for use at the www.henvinet.eu web site.

We invited a group of experts, selected according to their experience in environmental health and/or oncology, to test the diagrams, and to assess the state of the presented knowledge. The questions are formulated as "What is your level of confidence in being able to ", and address most elements of the diagrams. For selected issues, the experts are also asked if in their opinion, the current knowledge warrants precautionary actions.

Results: In general, the 9 independent experts answering the questionnaires have lower confidence in being able to predict the cancer-related effects and environmental stressors for all types of cancer addressed, compared to being able to assess the impact of exposure on risk. For several elements in the diagram, the causal association is subject of controversy. This includes arsenic in drinking water, ionizing radiation or airborne particulate matter and their relationship with e.g. lung cancer. Other relations, with large body of evidence, are by the experts uniformly recognized with high levels of confidence. Regarding measures to be taken (conditional on the current state of knowledge), the experts agreed on the need for precautionary policies for pesticides and ionizing radiation, while there was lower consensus on the need for such policies regarding radiofrequencies and power lines related electromagnetic fields.

Conclusion: The HENVINET cancer causal diagrams are a new experience for experts as they offer a simultaneous overview of xenobotics described in the etiology of selected site specific cancers. The evaluation by the invited experts provided first valuable experience in a self-learning interaction in a science and policy-linking system that expands the idea of complexity. This is an important step both in professional risk management and communication, and in improving tools that may lead to advances in regulatory perspective. We are also confident that such approaches, where complexities are laid out and discussed, will ultimately raise public confidence in science.

A13

Bruk av funksjonell data-analyse på glukosebelastningsdata

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Formål: En oral glukosebelastningstest over to eller tre timer er en klinisk undersøkelse som brukes mye både i praktisk klinisk arbeid og innen forskning. Under en slik test måles individets blodsukker med en serie blodprøver før og etter et kontrollert sukkerinntak. Ofte tas det målinger hver halvtime i to timer. Den informasjonen som brukes videre i klinikk eller statistiske analyser er vanligvis blodsukkernivå før sukkerinntaket (fastende verdi) eller blodsukkernivå to timer etter sukkerinntak. Diagnosen diabetes mellitus fastsettes på bakgrunn av disse to verdiene. Svangerskapsdiabetes er definert som en totimers-verdi mellom 7.8 og 11.1 mmol/l, og diabetes i svangerskapet er definert som en verdi på 11.1 eller høyere. Vi anvender funksjonell data-analyse på slike glukosebelastningsdata. Formålet er å utnytte informasjon fra hele serien med målinger på en bedre måte enn det som er vanlig i dag. Vi ser på sammenhenger mellom glukosemålinger, svangerskapsdiabetes og fødselsvekt.

Materiale og metoder: Rikshospitalets STORK-studie (STORe barn og Komplikasjoner) rekrutterte i 2001-2008 totalt 1031 friske gravide kvinner. Deltakelse i studien innebar en rekke kliniske undersøkelser, deriblant glukosebelastning både tidlig og sent i svangerskapet (hhv uke 14-16 og uke 30-32). Totalt 974 kvinner gjennomførte den første testen, og 924 gjennomførte begge testene. Vi brukte pakken ”fda” i programmet R til å gjøre den funksjonelle dataanalysen. Analysen består av flere deler, blant annet kurvetilpasning ved hjelp av glattede kubiske splines, funksjonell prinsipalkomponent-analyse og funksjonell regresjon. Vi laget modeller basert på enkeltmålinger, prinsipale komponenter og selve kurvene.

Resultater: Vi vil presentere resultater som viser hvordan metoder for funksjonell data-analyse kan brukes på glukosebelastningsdata.

Konklusjon: Disse analysene åpner for nye måter å tenke på slike data på. Både splines-kurvene og prinsipalkomponentkurvene kan tolkes i lys av fysiologiske prosesser og virke både hypotese-genererende og innby til andre måter å måle på. Dermed illustrerer dette analysemetoder som også kan være nyttig i andre kliniske og epidemiologiske problemstillinger.

A14

Socioeconomic inequalities in prevalence of smoking in the Nord-Trøndelag Health Study (HUNT) 1995-2008

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Objective: To examine 13-year trend in smoking by socioeconomic position in The Nord-Trøndelag Health Study (HUNT).

Methods: Two cross sectional surveys were used: HUNT 2 (1995-97) and HUNT 3 (2006-08). Education was used as indicator of socioeconomic position and data was retrieved from Statistics Norway. Educational level was divided into three groups; primary (primary and lower secondary school), secondary (upper secondary and lower secondary school) and tertiary (first and second stage of tertiary education). In each survey the sample was restricted to women and men 40-69 years of age. The prevalence of smoking across educational groups in both women and men, as well as absolute and relative measures of inequality was estimated.

Results: Difference in smoking across educational group was found in both surveys, were those with primary level education were more likely to be smokers than those who completed tertiary level education. Additional, more women than men reported current smoking. In women, age adjusted prevalence difference in smoking (difference between primary and tertiary level education) decreased from 26% in HUNT 2 (1995-97) to 22% in HUNT 3 (2006-08) while Relative Index of Inequality (RII) slightly decreased from 4.38 (3.82-5.03) in HUNT 2 (1995-97) to 3.93 (3.40-4.54) in HUNT 3 (2006-08). In men, the age adjusted prevalence difference decreased from 20% in HUNT 2 (1995-97) to 17% in HUNT 3 (2006-08) and RII remained unchanged from 3.18 (2.76-3.67) in HUNT 2 (1995-97) to 3.02 (2.56-3.57) in HUNT 3 (2006-08).

Conclusions: Both absolute and relative socioeconomic inequalities in smoking were larger among women compared to men in both surveys. Despite a decrease in the age adjusted prevalence difference in smoking from HUNT 2 (1995-97) to HUNT 3 (2006-08), relative inequalities in smoking remain unchanged. It is unlikely that the relative inequalities reflect less knowledge of the consequences of smoking. More work is needed to provide equal opportunities for behavior change, especially among women.

A15

Påvirker psykisk uhelse i ungdomsårene mottak av langtids trygdeytelser som ung voksen?

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Formål: Psykiske plager i ungdomsårene, samt det å vokse opp med psykisk syke foreldre, kan bidra til økt sårbarhet. Slik økt sårbarhet vil kunne vanskeliggjøre inngangen til arbeidslivet og evnen til å stå i jobb på sikt. Vårt mål var å undersøke om psykiske plager i ungdomsårene eller psykisk uhelse hos foreldre påvirket risikoen for å motta langtids (> 6 måneder) trygdeytelser som ung voksen. Videre ønsket vi å undersøke betydningen av familieforhold ved å sammenligne søsken.

Materiale og metoder: I et prospektivt, longitudinelt design fulgte vi ungdomskohorten i UngHUNT 1 1995 – 1997 (8984 ungdom i alderen 13-19 år) med tanke på mottak av langtids trygdeytelser i FD-trygd databasen i perioden 1998 – 2007. Dataene ble koblet til foreldredata fra HUNT1 (84-86) og HUNT2 (95-97) samt Utdanningsregisteret. Informasjon om psykisk helse og konfunderende faktorer var tilgjengelig for 8806 ungdommer (3250 søsken) og 13018 foreldre. Vi benyttet logistisk regresjon og flernivå logistisk regresjon i de multivariable analysene.

Foreløpige resultater: Symptomer på angst og depresjon i tenårene var assosiert med mottak av langtids trygdeytelser i oppfølgingsperioden. Effekten var sterkere for gutter enn jenter, ble redusert etter justering for somatisk helse, bosituasjon og problematferd og forsvant etter justering for foreldrenes psykiske helse. Symptomer på angst og depresjon hos foreldrene var assosiert med mottak av langtids trygdeytelser hos barna, spesielt i forholdet mor-datter.

Konklusjon: Psykisk uhelse, både hos ungdommene selv og deres foreldre, var i vårt materiale assosiert med økt mottak av langtids trygdeytelser som ung voksen.

A16

Educational inequalities in disability pension: The impact of illness, occupational, psychosocial and behavioural factors

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Objectives: The purpose of this study was to examine illness, occupational, psychosocial and behavioural factors in the explanation of educational inequalities in disability pensioning.

Methods: The baseline data consisted of 32,948 participants in the Nord-Trøndelag Health Study 1995-97 (HUNT 2), 25-66 years old, without disability pension and in paid work. We performed additional analyses on 3,716 homemakers and 1,908 unemployed/laid-off persons. Information on the occurrence of disability pension was obtained from the National Insurance Administration database up to 2008. Data analyses were performed using Cox regression and multiple imputation for the multivariable analyses.

Results: The total cumulative incidence of disability pension was higher in women (25-49 years: 9%, 50-66 years: 30%) than men (25-49 years: 5%, 50-66 years: 24%). The age-adjusted educational gradient was steepest among the youngest, and the relative risk of disability was consistently higher in lower education groups. After adjustment for illness, occupational, psychosocial and behavioural factors we still found considerable educational inequalities in disability pension. The medical condition ("longstanding limiting illness") showed the strongest impact on the risk of disability pension, but did not contribute to the explanation of educational inequalities. The largest educational inequalities in the fully adjusted model were found in young men, with a HR of 3.17 (2.30-4.38) for those with primary education and a HR of 2.35 (1.78-3.11) for those with secondary education compared to tertiary education. The corresponding numbers for young women were 2.65 (2.12-3.13) and 1.85 (1.56-2.20). Educational inequalities in homemakers and unemployed/laid off persons were somewhat more pronounced than in the working population.

Conclusion: After adjustment for illness, occupational, psychosocial and behavioural factors there is still considerable educational inequalities in disability pensioning in both women and men.

A17

Who are we to believe – the child, teacher, or parent? Reports on victimization from different informants, and associations with children's health complaints

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Background: Concordance in the reporting of children's health is low to moderate, but evidence related to the consistency of reporting victimization among school children is scarce. Victims of bullying in school experience later health problems, and we therefore assessed concordance in reporting victimization between teacher, parent and children. We also assessed and compared the prevalence of health complaints related to reporting of victimization.

Material and methods: In a cross-sectional study of 419 children in grades 1-10 frequency of victimization was reported by children, teachers and parents, and frequency of health complaints (anxiety, sadness, headache, stomach ache) was reported by the children. Concordance between informants was analysed by cross-tables and Spearman's rho and associations of victimization with health complaints were estimated by logistic regression.

Results: Among children who reported regular victimization, less than half of these cases were confirmed by teachers or parents, and conversely, among children who were reported to be victimized by the adults less than half of the children confirmed victimization. In relation to self-reported victimization among children, there was a strong dose-related effect with self-reported anxiety, sadness, stomach ache and headache. The associations of victimization reported by teachers or parents were generally weaker than the associations of self-reported victimization.

Conclusion: There is low to moderate agreement between children and significant adults in reporting peer victimization, and associations with health complaints will therefore vary, depending on the source of reported victimization.

A18

The relationship between religious attendance and blood pressure: the HUNT study, Norway

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Objective: Research from the USA shows a possible relationship between religious attendance (RA) and blood pressure (BP). The religious context in the USA differs widely from Scandinavia regarding religious expressions, attitudes and frequency of attendance. The aim was therefore to test whether the relationship between RA and BP is specific to the religious culture in the USA or whether a similar relationship exists between RA and BP in a Norwegian context.

Design and method: Data from the Nord-Trøndelag Health Study's third wave, HUNT 3 (2006-08), was used. The associations between RA and diastolic (DBP) and systolic (SBP) blood pressure in women (n=20,218) and men (n=16,065) were investigated in a cross-sectional study using multiple regression analyses.

Results: Mean DBP for women/men was 71.0 mm Hg/76.6 mm Hg. Mean SBP was 128.5 mm Hg/134.0 mm Hg. 39.1%/42.8% of women/men never attended religious services. 3.8%/3.4% attended more than 3x/month. The bivariate associations were statistically significant between RA and SBP in both genders and women's DBP but not men's DBP. After adjustment, inverse associations between RA and DBP/SBP for both genders were found. The RA-DBP relationship ($p<0.001$) demonstrated a gradient in effect for both genders, with increasing RA associated with decreasing DBP, with 1.29/1.69 mm Hg lower in women/men respectively in those attending more than 3x/month, 0.85/1.13 mm Hg lower in those attending 1-3x/month, and 0.51/0.16 mm Hg less in those attending 1-6x/6 months. Differences in RA-SBP ($p<0.05$) were 1.68/1.71 mm Hg, 0.06/0.06 mm Hg, and 0.57/0.74 mm Hg, respectively.

Conclusion: In a large population-based survey in Norway, RA was associated with lower DBP and SBP after adjusting for relevant variables.

A19

Informativeness of indices of blood pressure, obesity and serum lipids in relation to ischaemic heart disease mortality in a prospective population study (HUNT II)

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Background: The informativeness of blood pressure, obesity and serum lipids associated with cardiovascular events may depend on how the indices are expressed, and mid blood pressure, waist-to-hip ratio adjusted for body-mass index (BMI) and the ratio of total to HDL cholesterol may be more informative than other expressions. Our aim was to study the informativeness of indices of blood pressure, obesity and serum lipids associated with ischaemic heart disease mortality in a large, homogeneous population.

Materials and methods: Blood pressure, weight, height, waist and hip circumference, total and HDL cholesterol, and triglycerides were measured at baseline (1995-1997) in 28 158 men and 32 573 women. Information on deaths from ischaemic heart disease (IHD) was obtained from the Causes of Death Registry in Norway from baseline until the end of 2007. Informativeness was analysed using the difference in twice the log-likelihood of a Cox model with and without each index.

Results: During 11 years of follow-up, 597 men and 418 women had died from IHD. Systolic blood pressure in men and pulse pressure in women were the most informative predictors of blood pressure, and waist-to-hip ratio adjusted for BMI was the most informative expression of obesity in both men and women. Among serum lipids, the most informative predictor was the ratio of total cholesterol to HDL cholesterol.

Conclusion: Using more informative expressions of conventional risk factors for ischemic heart disease may improve both the validity and precision of estimates of risk, and may be useful both clinically and for preventive purposes.

A20

Forekomst, dødelighet og risikofaktorer for subaraknoidalblødning

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Formål: Subaraknoidalblødning (SAB) er en hjerneblødning som skyldes at en utposning på en blodåre på hjernens underside sprekker. Siden blødningen er relativt sjelden har det vært vanskelig å påvise risikofaktorer i prospektive studier, men røyking, blodtrykk, høyt alkoholinntak og det å være kvinne er kjent å øke risikoen. Fordi SAB ofte oppstår relativt tidlig i livet og har høy sykelighet og dødelighet, kan de samfunnsmessige konsekvensene sammenlignes med dem av iskemisk hjerneslag, den vanligste typen slag. Formålet med studien er å måle forekomst, dødelighet og risikofaktorer for SAB ved hjelp av Helseundersøkelsen i Nord-Trøndelag (HUNT) og Tromsøundersøkelsen.

Materiale og metoder: Vi registrerte alle som fikk SAB etter deltakelse i HUNT 1 og 2 og Tromsø 3 og 4. Risikofaktoranalysene er basert kun på HUNT 2 og Tromsø 4. Vi estimerte forekomst, dødelighet og risikofaktorer ved hjelp av Cox og Poisson regresjonsanalyser.

Resultater: Forekomsten av SAB var 9,8 per 100.000 personår, 12,5 hos kvinner og 6,9 hos menn (hazard ratio (HR) 1.7, 95 % konfidensintervall (KI) 1.1 til 2.5). Letaliteten etter 2 og 30 dager og 6 måneder var 18.3%, 36.2% og 40.8% og økte med alder. Røykere hadde bedre overlevelse enn aldri-røykere. Systolisk og diastolisk blodtrykk var positivt assosiert med risiko for SAB (p for trend <0.001), og sammenlignet med aldri-røykere hadde nåværende røykere høyere risiko (HR 5.6, 95 % KI 3.5 til 9.2). Overvekt (BMI 25-29.9) var negativt assosiert med risiko for SAB (HR 0.6, 95% KI 0.4 til 1.0). Det var ingen sammenheng mellom totalkolesterol, HDL-kolesterol eller triglyserider og risiko for SAB i totalpopulasjonen, men hos deltakere under 50 år var HDL-kolesterol negativt assosiert med risiko (HR per standardavvik økning 0.6, 95% CI 0.4 til 0.9).

Konklusjon: Forekomsten av SAB var 9,8 per 100.000 personår og høyere hos kvinner enn menn. Letaliteten er høy og øker med alder, og røykere har bedre overlevelse enn aldri-røykere. Systolisk og diastolisk blodtrykk samt røyking var assosiert med økt risiko for SAB, mens overvekt var assosiert med lavere risiko. Ingen blodlipider var assosiert med risiko, unntatt HDL-kolesterol hos deltakere under 50 år, som var negativt assosiert med risiko.

A21

Relativ betydning av etablerte risikofaktorer for hjerte- og karsykdom – Helseundersøkelsene i Hordaland

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Formål: Formålet med studien var å rangere etablerte risikofaktorer for hjerte- og karsykdom etter relativ betydning for å finne de sterkeste prediktorene for insidens og dødelighet. Spesielt ønsket vi å undersøke om rangeringen av risikofaktorene var ulik for menn og kvinner og for ulike aldersgrupper.

Materiale og metoder: Homocysteinstudien i Hordaland i 1992-93 er en populasjonsbasert kohortstudie som rekrutterte 18 044 menn og kvinner født i perioden 1925-1952. Deltagerne ble fulgt til 31.12.2006 og datamaterialet ble koblet mot de pasientadministrative systemene ved sykehusene i Helse Vest (det regionale HKS-registeret) og mot Dødsårsaksregisteret for å kunne bruke både insidens og mortalitet som endepunkt. I denne sub-studien valgte vi å bruke deltagere i to aldersgrupper; 39-43 år og 64-69 år ved baseline. Deltagere som brukte blodtrykksmedisin eller hadde etablert hjerte- og karsykdom eller diabetes ved baseline ble ekskludert fordi vi ønsket å sammenligne risikofaktorer i en frisk befolkning. Studiepopulasjonen bestod av 15 515 menn og kvinner. Den relative betydningen av de ulike risikofaktorene ble sammenlignet med Cox-regresjon. For å kunne sammenligne hazard ratio (HR) for de ulike risikofaktorene mot hverandre var det nødvendig å måle risikofaktorene på samme skala. Dette ble løst ved å rangtransformere risikofaktorene og skalere de nye variablene fra 0 til 5 før estimering. Etter denne transformeringen kan HR tolkes som HR per kvintils økning i risikofaktor for alle risikofaktorene og HR for de enkelte risikofaktorene kan derfor sammenlignes direkte mot hverandre. Størrelsen på HR kan brukes til å rangere risikofaktorene etter betydning. I tillegg til modeller for de to aldersgruppene justert for kjønn, gjorde vi også analyser separat for menn og kvinner.

Resultater: Kolesterol og triglycerider var svært viktige risikofaktorer for kardiovaskulær død blant for unge menn og kvinner, men ikke for eldre menn og kvinner. I den eldste gruppen var sigarettrøyking (pack-years) og totalt plasma homocystein viktige risikofaktorer både for menn og kvinner. I tillegg var systolisk blodtrykk og aleneboer-status viktig for menn og fysisk inaktivitet viktig for kvinner. De tre viktigste risikofaktorene for akutt hjerteinfarkt (sykehusinnleggelse eller død) blant de yngste mennene var kolesterol, triglycerider og røyking. De yngste kvinnene fulgte omtrent samme mønster, men lav utdannelse var like viktig som røyking. For den eldste gruppen var røyking den viktigste risikofaktoren både for menn og kvinner, mens systolisk blodtrykk kun hadde signifikant effekt hos kvinner.

Konklusjon: Vi fant ulik rangering av risikofaktorer mellom menn og kvinner og mellom de to aldersgruppene. Generelt slo alle risikofaktorene sterkere ut blant de unge enn blant de gamle. Den mest konsistente risikofaktoren for akutt hjerteinfarkt for begge kjønn og begge aldersgrupper var sigarettrøyking.

B1

Body weight misperception and perceived slimming pressure in normal weight adolescents is associated with development of overweight and obesity in young adulthood. The Young-HUNT study, Norway

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Objectives: To explore if body weight misperception and perceived slimming pressure in normal weight adolescents influence their weight status in young adulthood.

Methods: A longitudinal study of 1255 normal weight adolescents (12-20 yrs) who participated in Young-HUNT 1 (1995-97) followed up ten years later in HUNT 3 (2006-08). At both times comprehensive self administered questionnaires, including lifestyle and health-issues, were completed with a clinical examination including standardized measurements of height, weight, and waist circumference.

Results: Both female and male normal weight adolescents who misperceived themselves as overweight or experienced slimming pressure had a higher risk for becoming overweight or obese in young adulthood compared to adolescents who perceived themselves as having normal weight or no need for slimming. The odds ratio (OR) of becoming overweight was 3.47 (CI: 2.35-5.11) in girls and 2.50 (CI: 1.20-5.21) in boys. The corresponding odds ratios for obesity were 3.22 (CI: 1.82-5.72) for girls and OR 2.94 (CI: 1.26-6.82) for boys. Perceived slimming pressure revealed almost equivalent associations.

Conclusions: This study suggests that misperception of weight and perceived slimming pressure during adolescence may be a risk factor for overweight/ obesity in young adulthood. Public health interventions may benefit from addressing issues related to body weight perception and slimming behaviour.

B2

Physical activity and overall mortality in the Norwegian Women and Cancer study

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Objective: Physical activity and its relationship with mortality has been studied in several studies were evidence suggests a strong and consistent inverse association. The aim of this study was to prospectively investigate the association between self-reported level of total physical activity, including all domains of free-living activity, and mortality in women participating in the prospective Norwegian Women and Cancer study (NOWAC).

Material and methods: The NOWAC study is a population-based prospective cohort study initiated in 1991. A random sample of 179 387 women aged 30-70 selected from the National Central Person Register were invited to participate by answering a questionnaire; the initial recruitment was done between 1991 and 1997. For the analysis presented here, we included women answering in 1996/1997 and in addition a second questionnaire as well, mailed in 1998; in total 84864 women. After exclusions due to lack of information on physical activity level at baseline and information on vital status at end of follow up (2008) the study population included 76674 women eligible for analysis. Information about physical activity was obtained through a self-administered questionnaire at enrolment using a scale from 1 (low level) to 10 (very high level). Cox proportional hazards regression with years of follow-up as the time scale was used to estimate adjusted hazard ratios with corresponding 95% confidence intervals (CIs). The hazard ratios were interpreted as estimates of relative risks (RRs) of all cause mortality, and specified in mortality of cardiovascular disease and cancer.

Results (preliminary): At baseline 71.6% of the cohort reported their physical activity level 5 or higher, and 28.4% reported their physical activity level as 4 or less. Mean follow-up time was 10.7 years. Moderate to high physical activity levels (i.e. level 5 or higher) were associated with a decrease in risk of overall mortality, with evidence of a dose-response effect.

Conclusion: These preliminary results indicate that physical activity decreases overall mortality in a dose-response manner among Norwegian women.

B3

Type 2 diabetes og glykemisk kontroll hos menn. Er styrketrening like effektivt som utholdenhetstrening?

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Formål: Forskningsresultater viser at den sterke økningen av type 2 diabetes assosieres med økningen av inaktivitet og overvekt. I motsetning til den relativt velkjente positive effekten av utholdenhetstrening finnes det kun begrenset informasjon om effekten av styrketrening på type 2 diabetes. Hensikten med studiet var å sammenligne effekten av utholdenhetstrening og styrketrening på glykemisk kontroll hos menn med type 2 diabetes.

Materiale og metoder: Vi gjennomførte en randomisert klinisk studie hvor 26 menn (gjennomsnittelig alder = 57 ± SD 7.94) med type 2 diabetes ble tilfeldig fordelt til en utholdenhetstreningsgruppe eller en styrketreningsgruppe. Subjektene trente tre ganger per uke i 12 uker. Metabolske faktorer (hemoglobin A_{1C} (HbA_{1C}); fastende glukose og C-peptid; total, LDL, og HDL kolesterol; triglyserider; blodtrykk), kroppssammensetning, VO_2max og muskelstyrke ble målt før og etter intervensjonen. Gjennomsnittelige forskjeller i endring mellom gruppene ble analysert ved hjelp av en linear mixed effects model for repeterte målinger over tid hvor det ble justert for baseline verdier av alder, kroppsmasseindeks og HbA_{1C}.

Resultater: Begge gruppene hadde signifikant forbedring i HbA_{1C} (utholdenhetstreningsgruppen hadde en nedgang fra 7.10 ± SD 0.97 til 6.55 ± SD 0.74 (p-verdi = 0.015) og styrketreningsgruppen fra 7.21 ± SD 1.8 til 6.85 ± SD 0.66 (p-verdi = 0.002). Begge treningsgruppene hadde signifikante forbedringer i både systolisk og diastolisk blodtrykk (p-verdier < 0.05) og i flere av variablene som målte kroppssammensetning (p-verdier < 0.05). I de andre målte metabolske faktorene var det ingen signifikante forskjeller i endring mellom de to treningsgruppene.

Konklusjon: Både utholdenhetstreningsgruppen og styrketreningsgruppen hadde liknende forbedringer i glykemisk kontroll. Forbedringene samsvarer med hva tidligere studier har rapportert. Det kan derfor tyde på at både utholdenhetstrening og styrketrening har gunstig effekt for menn med type 2 diabetes.

B4

Respiratory symptoms and lung function associated with self-rated physical and psychological health: The Nord-Trøndelag Health Study

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Objective: Although common among people with chronic obstructive lung diseases, it is not known to what extent impaired physical and psychological health is associated with respiratory symptoms or reduced lung function. We aimed to study the associations of respiratory symptoms and reduced lung function, with poor health, anxiety, depression, and satisfaction with life.

Methods: We analysed data from 5700 women and 5119 men participating in the lung sub-study of the population based Nord-Trøndelag Health Study 1995-97. In a cross-sectional design we used logistic regression to calculate odds ratios (ORs) with 95% confidence intervals (CIs) for poor health, anxiety, depression, and dissatisfaction with life associated with respiratory symptoms (dyspnoea, cough, and wheeze) and categories of forced expiratory volume in one second in per cent of predicted (FEV_1 % predicted). In sex specific analyses, we adjusted for age, body mass index, smoking, education, co-morbidity, and in the first analyses also FEV_1 % predicted.

Results: Increasing grade of dyspnoea was associated with poor health, anxiety, depression (among men only), and dissatisfaction with life [all $p_{trend}<0.002$]. Decreasing level of daily activities due to dyspnoea was associated with poor health, anxiety, depression, and dissatisfaction with life (among women only) [all $p_{trend}<0.03$]. Being wakened by dyspnoea was associated with poor health, anxiety, depression (among women only), and dissatisfaction with life (among men only). Chronic cough was associated with poor health, anxiety, depression (among men only), and dissatisfaction with life (among women only). Having experienced wheeze or dyspnoea last year was associated with poor health, anxiety, depression, and dissatisfaction with life. Lower FEV_1 % predicted was associated with poor health (all $p_{trend}<0.002$) and depression (among women only) [$p_{trend}=0.033$].

Conclusions: Most respiratory symptoms were associated with poor health, anxiety, depression, and dissatisfaction with life. Reduced lung function was associated with only poor health and depression among women.

B5

Comparison of self-report and objectively measured physical activity: Do we follow the guidelines? Results from the Tromsø Study

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Aims: Regular physical activity (PA) is a key element in healthy lifestyle. National recommendations for PA are i.e. 10000 step counts/day or at least 30 minutes/day of moderate-to-vigorous intensities PA (MVPA). Additionally, there are different methods for measuring PA. The aims of this study was therefore 1) to study the level of physical activity in a healthy population aged 40-44 years and 2) to study whether variation in self-reported physical activity reflects the variation in objectively measured physical activity.
Methods: During 2007-8, 5017 men and 5607 women aged 30-69 years attended the sixth survey of the Tromsø study. Self-reported PA during leisure-time and work were assessed through a questionnaire. In a sub-study, the Activity Study, physical activity (Actigraph L.L.C, GT1M-Activity Monitor, Pensacola, Florida) and physical fitness (VO_2max treadmill test) were objectively measured, among 313 healthy men and women aged 40-44 years. Statistical analyses were performed.
Results: Among those participating in the Activity study, 87% of men and 84% of women reported that they met the physical activity recommendation by being in physical activity more than 4 hours/week. Objectively measurements using Actigraph showed that the proportion of accumulating at least 30 min/day or more of MVPA in either one continuous bout or several shorter bouts lasting 10 minutes was 30% for women and 22% for men. 27% of women met the recommended level of more than 10000 steps/day and among men this percentage was 22%. Self-reported leisure PA was significantly correlated with VO_{2max} (ml/kg/min) (women spearman correlation coefficient r=0.40, P<0.001, men, r=0.44 P<0.001) and objectively measured moderate-to-vigorous PA (>2000 counts/min) (women, r=0.28, P <0.01, men, r=0.25, P <0.01).

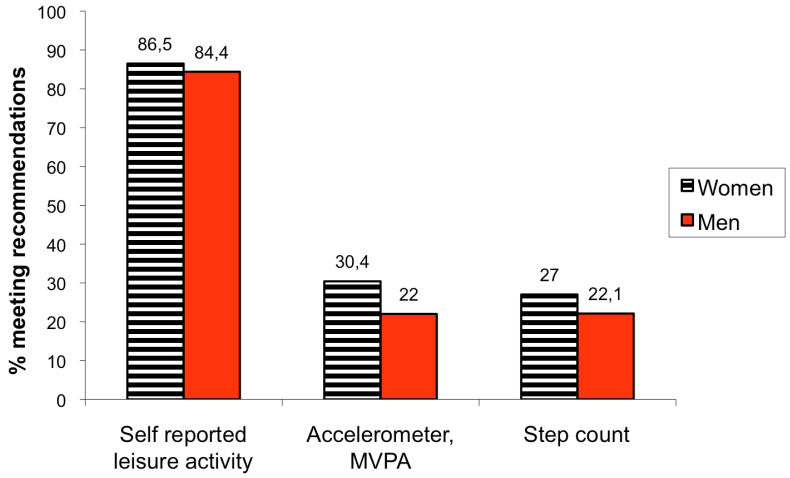

Figure I. Percentage of adults meeting physical activity guidelines. *Self-reported leisure time activity;* at least 4 hours a week of physical activity. *Accelerometer;* accumulation 30 min/day or more of moderate to vigorous physical activity (MVPA), in either one continuous bout, or several shorter bouts lasting i.e.10 minutes *Step count*: Minimum 10 000 steps per day. The Tromsø Activity Study, n=270.

Conclusion: About one third of the study population met the recommendations for objectively measured PA, which are in accordance with comparable studies in other countries. However, the proportion of subjects following guidelines was much higher when based on self-report than on objectively measured PA.

B6

Norsk pasientregister i epidemiologisk forskning – Fra opphold til pasient med personidentifiserbare data

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Norsk pasientregister (NPR) omfatter informasjon om alle pasienter som mottar behandling i spesialist-helsetjenesten og har dermed en sentral plass blant de norske helseregistrene. Fra 2008 har registeret personidentifiserbare data (Nye NPR). Kryptert fødselsnummer i NPR er unikt for hver pasient og kan dekrypteres ved behov. Gjennom dette innlegget ønsker vi å presentere noen av de mange mulighetene Nye NPR gir innen epidemiologisk forskning.

Telling av pasienter: NPR inneholdt tidligere et pasientnummer som var unikt for hver pasient innenfor hver institusjon og kalenderår. Pasientene kunne dermed ikke følges over institusjoner og det var med få unntak ikke mulig å få gode estimater for antallet pasienter. Med personidentifiserbare data kan man oppnå tall for antall pasienter totalt eller antall pasienter innenfor ulike diagnosegrupper. Dataene kan fordeles på en rekke ulike bakgrunnsvariable, som kjønn, alder og bosted.

Kobling mellom ulike datasett i NPR: Pasientforløp kan undersøkes ved først å definere en aktuell studiepopulasjon ved hjelp av gitte kriterier (for eksempel tilstands- og/eller prosedyrekoder). Deretter hentes alle opphold for studiepopulasjonen ut fra NPRs totale filer. På denne måten kan man for eksempel få informasjon om ø-hjelps innleggelser etter kirurgi, senere innleggelser med samme tilstand, eller senere innleggelser med en antatt følgetilstand. Det er også mulig å koble data fra ulike sektorer, slik at man kan oppnå informasjon om for eksempel somatiske innleggelser for pasienter i psykisk helsevern eller oppfølging i psykisk helsevern av pasienter med somatisk sykdom.

Kobling til utenforliggende register: Gjennom kobling til utenforliggende registre øker forskningsmulighetene ytterligere. Det gjennomføres for tiden et samarbeidsprosjekt mellom Kreftregisteret og NPR hvor data fra de to registrene kobles. Det arbeides videre med en løsning for inklusjon av data fra Folkeregisteret til NPR (for eksempel data for død). Dette er data som vi antar også vil ha interesse for mange forskningsmiljøer.

Ekstern bruk av data: Data kan bestilles fra NPR enten som statistikk, anonyme opplysninger eller personidentifiserbare data. Det er etablert en egen utleveringsgruppe som håndterer alle databestillinger. Forskningsmiljøene bør på forhånd vurdere om de behovene de har kan dekkes gjennom data i tabell-form. Slike utleveringer har kort saksbehandlingstid og krever ikke konsesjon. Anonyme utleveringer er ofte problematiske da anonymiseringsprosessen vanligvis krever at sentrale opplysninger må fjernes. Personidentifiserbare utleveringer krever behandling hos REK eller Datatilsynet, har lengre saks-behandlingstid i NPR, og er ut fra et personvernperspektiv uheldige når NPR kan utarbeide tabeller på bestilling fra forskningsmiljøene. Vi vil oppfordre forskningsmiljøene til økt bruk av data fra NPR.

B7

Development of national quality indicators for cardiovascular disease: Theoretical framework and formalized consensus process

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Objective: To describe a structured methodological approach for the development of a set of national quality indicators (QI) for the domain of cardiovascular disease (CVD).

Material and methods: The Norwegian Knowledge Centre for the Health Services recently proposed a framework for national QI development. The framework delineates the theoretical basis underlying a national QI system and presents recommendations on how health services can be measured with transparent procedures and appropriate methodology. Specifically, it is recommended that consensus processes are to be used for relevant stages of the selection and evaluation processes of QI sets, to ensure the scientific and professional aspects, as well as health policy and value-related dimensions of indicator selection and development.

To be applicable, the various recommendations of the framework need further operationalization, and to be adapted to specific domains, such as CVD. In this work, a specific procedure for the selection and empirical testing of a set of national QIs for cardiovascular disease is presented.

This study is part of the CVDNOR-project, and it will explore the development of national health service QI using patient administrative data collected by the Norwegian Knowledge Centre for the Health Service from hospitals for the period 1994 to 2010. Empirical testing will include data quality, longitudinal analysis to test the change /stability of the indicators over time, and assessment of risk adjustment. The proposed panel of indicators will be rated in two stages according to an established formalized consensus process (The Rand/UCLA Appropriateness Method).

Results: Sources for potential indicators of structure, process and result indicators to be explored are: A) Internationally established QIs developed by projects initiated by the Nordic Council of Ministers, OECD and WHO, B) QI based on published systematic reviews of effect of treatment procedures, C) Norwegian expert panel suggestions.

Conclusions: The criteria for prioritizing and selection of individual QIs for CVD will be based on the suggested method described in the Framework report.

B8

Utvikling av HUNT databank

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Helseundersøkelsen i Nord-Trøndelag har gjennomført omfattende datainnsamling av alle innbyggere over 19 år i 1984-86, 1995-97 og 2006-2008, og av ungdom i alderen 13-19 år i 1995-97, 2001 og 2006-2008, i tillegg til en rekke oppfølgingsprosjekt. Data har tidligere vært lagret i mange ulike SPSS-filer, hvorav noen har vært avidentifisert og koblet til ulike registerdata. Den store mengden data økte behovet for en mer rasjonell, oversiktlig og kvalitetssikret lagring og håndtering.

Forut for HUNT3 startet derfor arbeidet med oppbygging av en databaseløsning for HUNT-data. Data ble lagret i en relasjonsdatabase utviklet i Dataphor og Orakel. Det er utviklet en ny struktur for variabelnavn basert på engelsk forkortelse av spørsmål eller målemetode (prefiks) og kode for studiedel (suffiks). Foreløpig er det inkludert 5.700 variabler i databasen, men det gjenstår import av variabler fra mange tilleggsundersøkelser i HUNT 1-3. Det legges inn metadata på variabler og instrument som forklarer eventuelle endringer ved kvalitetssikring, kilder for spørsmål, måleutstyr med feilmarginer, copyright for ulike skjema og utvalg for ulike studiedeler. Spørsmål- og svaralternativer er både på norsk og engelsk; utover dette er all informasjon i databasen på engelsk. Ved datautlevering får forskere data på prosjektspesifikk identifikasjon, og eksport av tilleggsvariabler er langt enklere og sikrere enn tidligere. Ved kobling til eksterne registre sender HUNT forskningssenter datafil til forsker, mens bro mellom fødselsnummer og prosjektspesifikke id-nummer sendes til registereiere. Sistenevnte kobler på data, fjerner fødselsnummer og sender datafil til forskere.

Konklusjon: Utvikling av ny databasestruktur i HUNT databank muliggjør betydelig forbedring av datahåndtering, dokumentasjon, kvalitetssikring, import og eksportprosedyrer for data. Database-løsningen forenkler også harmonisering til andre databasers grensesnitt. Mye arbeid gjenstår, spesielt gjelder dette inklusjon data fra de mange oppfølgingsprosjekt, men også metadata for variabler generelt. Undersøkelser som strekker seg over såpass store tidsrom er i stor grad avhengig av prosjektkunnskap som de ulike forskere og merkantilt personell har. Samling av prosjektinformasjon i databanken letter informasjonsoverføring til framtidige forskere og blir langt mindre personavhengig.

Handtering og forvaltning av så store datamengder er en fortsatt meget ressurskrevende, men jobben kan med den nye databanken gjøres sikrere og leveringstiden av data blir kortere.

B9

Ikke-møtt spørreskjemabasert studie i Helseundersøkelsen i Nord-Trøndelag 2006-08 (HUNT 3)

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Bakgrunn: Nord-Trøndelag har vært egnet for helseundersøkelser pga. homogen befolkning, lite migrasjon, sykdomsbilde og forekomst av risikofaktorer på linje med nasjonale data og tidligere stort oppmøte. Oppmøtet har imidlertid vist synkende tendens med 88,5, 71,2 og 54,0 % for henholdsvis HUNT 1, 2 og 3. Dette kan true generaliserbarhet av forskningsresultatene.

Metode: I 2009 sendte man et forenklet 2-siders skjema med sentrale spørsmål angående livsstil, sykdommer og årsak til de personer som ikke møtte til HUNT 3 (n=46.440), hvorav 6.922 svarte (=MiniHUNT).

Resultat: Sammenlignet med deltagere i HUNT rapporterte flere deltagere i Mini-HUNT sykehus-innleggelser, dårlig helse og mye nervøsitet, angst, depresjon. Forekomsten av hjerteinfarkt, angina pectoris, nyresykdom og diabetes var i aldersgruppe 40-90 år nesten 50 % høyere blant deltagerne i Mini-HUNT, og for blodtrykksbehandling var tilsvarende forskjell ca 20 %. Menn i samme alders-gruppe hadde tilsvarende mønster for kols, men ellers var det ikke forskjell mellom gruppene for lunge-symptomer eller astma. I alderen 40-69 år ble muskelskjelettplager av mer enn 3 måneders varighet rapportert av 20 % flere deltagere i HUNT enn i Mini-HUNT og for urininkontinens var tilsvarende forskjell over 50 %. Det var ca 20 % høyere andel dagligrøykere i Mini-HUNT for aldersgruppen over 40 år, og uavhengig av alder rapporterte 30-40 % færre av deltagerne i Mini-HUNT fysisk aktivitet oftere enn 2-3 ganger per uke.

I aldersgruppe 20-39, 40-69 og 70 år eller mer, anga henholdsvis 63, 54 og 24 % at de ikke hadde tid til å møte på invitasjonstidspunktet, mens henholdsvis 14, 8 og 10% at de ikke hadde fått invitasjon. Blant de eldste anga 16 % at de var for syk til å møte, mens dette var årsak for færre enn 2 % av de yngre.

Konklusjon: Undersøkelsen viste relativt store forskjeller i plager, sykdom og livsstil mellom de som møtte til HUNT 3 og deltok i Mini-HUNT. For en del sykdommer gjenspeiles nok en underrepresenta-sjon av de syke i HUNT 3, mens for en del mer plagsomme symptomer som muskelskjelettsmerter og urininkontinens var forholdet motsatt. For assosiasjonsstudier kan problemet med oppmøteskjevhet først og fremst gi fortynning av eventuell effekt, men for insidens og prevalensstudier vil generaliser-barheten fortsatt være usikker uten korreksjon for kunnskap om større andeler av ikke-møtte. Selv etter overnevnte studie av ikke-møtte mangler informasjon om nesten 35 % av befolkningen. Bildet kan nyanseres ytterligere med data fra SSB, via Reseptregisteret eller diagnosestatistikk fra utvalg av fylkets fastleger for å få tryggere estimat av sykdomsprevalens.

B10

The effect of stimulation therapy and donepezil on cognitive function in Alzheimer's disease. A community based randomised controlled trial

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Background: The progressive neurodegeneration in Alzheimer's disease (AD) induces irreversible cognitive impairment. Treatment options include cholinesterase inhibitors and a variety of stimulation therapies, but lack of consensus hampers the development of evidence based therapeutic guidelines. This trial was designed to study the effect of stimulation therapy and the additional effect of donepezil on cognitive function.

Method: Patients with mild and moderate AD were recruited from nine rural municipalities in Northern Norway to receive stimulation therapy (5 areas) or standard care (4 areas). All patients were randomised to donepezil or placebo in a double blinded fashion, making a two-by-two factorial design. They were all tested with three different cognitive tests four times during the one year study period.

Results: 187 patients were included in the study and 146 completed one year follow-up. Patients receiving stimulation therapy retained cognitive abilities during the study period. Donepezil had no additional effect but significant more adverse reactions (p=0.008) compared to placebo. The control groups also preserved cognitive function. No time trend differences between groups were found. The results were consistent for three independent cognitive tests and confirmed by subgroup analyses.

Conclusion: Postponement of cognitive deterioration by one year confirms the existence of a therapeutic window in AD for symptomatic treatment. Donepezil had no additional effect on cognitive function in patients receiving stimulation therapy. Frequent follow-ups during study participation could act as stimulation therapy itself and contribute to the observed effect among the controls.

B11

Prescription of benzodiazepines and z-hypnotics in psychiatric institutions: Evidence from Norway

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Purpose: With this paper we investigate the use of benzodiazepines and z-hypnotics in Norwegian psychiatric hospitals. Benzodiazepines and benzodiazepine-like drugs are commonly prescribed for persons with severe mental health illness. With low toxicity and alleged lack of dependence, these medications are used for reducing anxiety, agitation, sleeplessness, muscle tensions and convulsions, as well as for relieving side-effects of traditional antipsychotics, among others. However, benzodiazepines carry the risk of drug abuse, dependence and the development of tolerance, and can cause cognitive and psychomotor impairment and have residual effects on the day following intake. Little is known about the use of benzodiazepines among patients treated in mental health institutions, and their use in the context of co-occurring substance use disorders is particularly controversial since benzodiazepines may exacerbate existing substance use disorders or become abused substances.

Data and methods: The analysis builds on a cross-sectional registration of the Norwegian adult in-patient population in psychiatric care in 2007. Using a logistic regression model we are able to analyse the effects of socio-demographic characteristics, type of drug abuse and diagnosis of the patients on the likelihood of being prescribed benzodiazepines or z-hypnotics. The patient characteristics incorporated in the model are age, gender, education, marital status, main source of income, drug abuse and diagnosis. In addition, we also control for institution type and possible geographic variations.

Results: The likelihood of being prescribed benzodiazepines or z-hypnotika decreases if being male, and increases with age, while workforce participation implies a greater likelihood of treatment with z-hypnotika and lesser likelihood of treatment with benzodiazepines. Alcohol abuse is associated with a higher probability of z-hypnotics, but not when controlled for diagnosis. Abuse of LSD, ecstasy, solvents, methylated spirits, etc. implies higher likelihood of both benzodiazepine and z-hypnotics prescription. As for diagnoses, both benzodiazepines and z-hypnotics are prescribed for neurotic disorders and personality disorders, and also for affective disorders for the latter. Z-hypnotics are also used more often in District Psychiatric Centres than hospitals.

Conclusion: The high share of patients with co-occurring disorders being prescribed benzodiazepines is surprising, given the many warnings about the use of benzodiazepines in cases of comorbidity. There is no documented therapeutic effect of benzodiazepines to persons with substance use, and benzodiazepines also tend to aggravate addiction problems for substance users and imply reduced psychomotoric and cognitive functions. Our findings thereby differ from other international studies documenting that patients with co-occurring disorders are less inclined to be prescribed benzodiazepines than patients without such illnesses. Furthermore, our finding that it is among those with personality disorders we find the highest share of prescribed benzodiazepines is also unexpected, since for instance the Norwegian Board of Health Supervision's guide for prescription of addictive drugs emphasises that great deal of precaution need to be taken in cases of benzodiazepines for persons with personality disorders.

B12

Natural course of musculoskeletal pain – a prospective cohort study

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Purpose: Musculoskeletal pain is a major cause of morbidity, disability, sick leave, and health care costs. The purpose of this study was to investigate the natural course of musculoskeletal pain in the neck/shoulders and/or the lower back. We hypothesised that the pain would gradually decrease over time, and that whether having pain one or both sites at baseline would influence the natural course of pain.

Method: In a prospective cohort design we analysed data from 219 persons participating in the Natural Course of Musculoskeletal Pain (NaCoMP) study. This was a sub-study of the comprehensive population-based Nord-Trøndelag Health Study 2006-2008 (HUNT 3). We used multilevel models for repeated measures with measurements at level 1 and persons at level 2. We adjusted for age, sex, number of other pain sites, and use of any medication or treatment. The analyses included measurements at baseline, and one, two, and five months post baseline.

Results: The effect of time was different among those with pain at only one site compared to pain at both sites at baseline. From baseline to month five, the pain gradually decreased for those with pain at one site at baseline, while it increased slightly for those with pain at both sites at baseline.

Conclusion: Compared with having pain at only one site at baseline, having pain at both sites was associated with a poorer prognosis. It is important that health professionals treating patients with musculoskeletal pain is aware of this.

B13

pH variations in Norwegian drinking water and the effect on bone health. The NOREPOS study

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Introduction: Osteoporosis is a major health concern in Norway, but we have insufficient knowledge about the causes. Acid pollution is a problem in parts of the country, and intake of acid polluted water could over time contribute to metabolic acidosis, which in turn could cause excretion of calcium and magnesium from the body by stimulating bone resorption. Acidified water also contains a higher concentration of heavy metals known to be harmful to the skeleton. The relationship between pH in Norwegian drinking water and bone health has not previously been studied.

Methods: In a preliminary analysis we looked at whether spatial clustering of forearm and hip fractures coincided with areas of low pH in drinking water. We used SaTScan (version 8.2), to identify clusters based on COhort of NORway (CONOR), a national collaborative population study including 180,000 participants and with 22,830 forearm- and 2,650 hip fractures. Data on drinking water were obtained from Norwegian waterworks. Maps of clusters of fractures and pH in drinking water were compared.

Results: Raw drinking water across the regions of Southern, Eastern and Western Norway was generally more acidic (pH<7) than in the regions of Northern-Norway. Significant clusters of fractures were found in the East and the West (p=0.001 to p=0.046). The geographic locations of the clusters stratified into age and sex groups differed somewhat between fracture sites.

Discussion: There could be a negative relationship between the pH of raw drinking water and the prevalence of fractures in the Norwegian population, and acidified water entering the waterworks might be an indicator of a higher chemical availability of pollutants potentially harmful to bone-health. Further results based on the linkage between waterworks and CONOR will be presented, with focus on the association of individual measurements of bone mineral density (BMD) (n=35 000), pH and toxic compounds in the different types of drinking water.

Conclusion: Clustering of self-reported fracture prevalence across Norway is mainly found in regions where drinking water is shown to be more acidic. Analyses of individual measurements of BMD and water quality may further elucidate this finding.

B14

Exposure scenario approach to environmental health problems: two case studies

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Objective: To develop environmental exposure scenarios for two environmentally contaminated areas, the Michalovce area (SK) with high long-term exposure to PCBs originating from their production (banned in 1984), and the Ostrava region (CZ) with high industrial pollution related to PAH. In both regions, a multitude of health effects related to the pollution levels has been documented.

Materials and methods: The aim is to develop concepts that would ultimately allow assessment of population health risks, in this case, in areas with known long-term environmental burdens and large populations (between 0,5 and 1 million inhabitants). The exposure scenarios are developed within an integrated environmental health impact assessment framework. This framework describes the integration of several processes in developing and tracking environmental health policies. The assessment can serve three purposes: 1) determine the existence and magnitude of the risk faced by society, 2) to predict what possible interventions may be done to reduce that risk (if perceived to be necessary to reduce), and 3) to provide a means of follow-up to assess the effectiveness of policies. For health risk or impact assessment, the scenarios usually model the exposures that would lead to some potential effect on health. This exposure assessment can be useful for policy-making and evaluation purposes, but for a health impact assessment, the resulting exposure and/or dose levels would be used with the results of an appropriate dose-response assessment to produce an estimate of risk. The health assessment provides information that decision-makers can use to develop policies that would address the issues of concern. The exposure scenario considers the pollutant at question, associated health effects, exposure metric used in health assessment, relevant time periods and resolution of the data, geographical scale and relevant population. A causal diagram, following the concept of the DPSEEA chain used by WHO, then enables identification of the necessary information to be gathered. Exposure assessment protocol then follows this causal diagram.

Results: Two protocols for PAH and two protocols for PCB exposures were developed, and assessed.

Conclusion: This method of assessing population exposures related to environmental problems is an expansion of the exposure scenarios in regulatory risk assessment. In environmental problems, population and not an individual need to be considered, and population risks assessed. This leads to a new set of issues to be solved, not least, the need for additional data regarding population habits (food consumption, time activity). Such data are however often lacking, but can be compensated by using suitable statistical modeling.

B15

Endringer i den norske befolkningens pengespillvaner etter spilleautomatforbudet

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Formål: SINTEF utførte én befolkningsstudie om pengespillvaner og problemer før spilleautomatene forsvant sommeren 2007, og én i 2008 som da var en automatfri periode. Det ble ikke observert noen signifikant endring i andel av nåværende spilleavhengige fra 2007 til 2008, til tross for spilleautomatforbudet. Målet med studien var å finne eventuelle endringer av spillevaner i den norske befolkningen fra 2007 og 2008, til 2009. I tillegg ble det fokusert på hva som skjedde med de tidligere spilleautomatspillerne – spilte de mer eller mindre etter spilleautomatforbudet?

Materiale og metoder: Studien omfatter én kvantitativ oppfølgningsstudie bestående av en spørreskjemaundersøkelse, og én kvalitativ del bestående av dybdeintervju via telefon. Studien omfatter både personer med og uten spilleproblemer. Spørreskjema ble sendt ut til 3 803 personer i 2009, hvor svarprosenten ble 67 prosent. Instrumentet NODS ble brukt for kartlegging av spilleproblemer. Telefonintervju ble gjennomført med 16 personer uten spilleproblemer, tre personer i risikosonen for å utvikle et spilleproblem og 29 personer med et selvdefinert spilleproblem. I tillegg ble fem pårørende intervjuet.

Resultater: Andelen personer som hadde spilt pengespill i løpet av det siste året (nåværende spillere) var uendret fra 2007 til 2009, mens det var noen færre nåværende spillere i 2009 enn i 2008. Personene som deltok i spørreundersøkelsene i 2007 og 2008, spilte ikke nødvendigvis de samme spillene i 2009. Deltakelse i forskjellige pengespill var stort sett lik, eller noe redusert, fra 2007 og 2008, til 2009, bortsett fra en liten økning i lottospill. Rundt to av tre risikospillere hadde endret NODS skåre fra 2007 og 2008 til 2009, hovedsakelig til normalspillere. Det var flere som fikk redusert grad av spilleproblemer, enn økt. Omtrent halvparten av de som tidligere hadde spilt på spilleautomater én til flere ganger ukentlig, oppga at spilleautomatforbudet hadde ført til en reduksjon i spillingen deres. Også den kvalitative undersøkelsen viste at omtrent halvparten sluttet, eller reduserte spillingen betraktelig, etter forbudet. Den andre halvparten spilte like mye eller mer på andre spillarenaer. Personer med spilleproblemer etterspør et bedre behandlingstilbud og en plass hvor de kan henvende seg for økonomisk veiledning.

Konklusjon: Oppfølgningsstudien viste at spillevaner endrer seg hos enkeltpersoner i løpet av et par, tre år. Spilleautomatforbudet førte til at omtrent halvparten av de som tidligere spilte hyppig på spilleautomater, sluttet eller reduserte spillingen.

B16

Impact of socio-demographic factors on time-use

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Background: Human time-activity patterns and their relationship to environmental factors are an important part of exposure assessment for environmental contaminants. In Europe, a database of time-use patterns developed for social science research, the Multinational Time Use Survey (MTUS), provides data that can potentially be used for exposure studies and covers a wide range of countries.

Methods: MTUS provides aggregated daily diary data for 41 activity categories which were reclassified into the microenvironments (MEs) home, work (includes school), travel, outdoor and other (unspecified locations which might occur both indoors and outdoors). The population was stratified into 8 subgroups, distinguishing between gender, age groups (<15, 15-64, >64), and employment status for the middle age group. For each country, descriptive statistics for time spent in the MEs per day were calculated using diaries from 1990 to 2005. Linear regression was used to assess the impact of a set of socio-demographic and environmental factors on time spent at home, work and travel.

Results: Among employed persons per country, men spent on average 56%-61% of their daily time at home and women 63%-68%. The average daily time spent at work is 14%-19% and 19%-28%, for women and men respectively. On average, time spent on travel is slightly higher for men (3%-7%) than women (2%-6%). Based on the regression analysis, variables like higher education level, weekends, living in rural areas, being female reduces the average time spent at work for all countries.

Conclusion: The findings indicate that though the average time spent in each ME does not vary greatly between countries, there seemed to be a significant variability in the effect of the socio-demographic factors on time-use.

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