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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 FEMTENDE NORSKE EPIDEMIOLOGIKONFERANSEN

VOKSENÅSEN HOTELL, OSLO,

21.-23. NOVEMBER 2007

Den 15. norske epidemiologikonferansen Oslo 22.-23. november 2007, med kurs 21. november

Årets NOFE-konferanse arrangeres i Oslo, av Kreftregisteret, Nasjonalt folkehelseinstitutt og Institutt for allmenn- og samfunnsmedisin ved UiO. Konferansen er lagt til Voksenåsen, høyt hevet over byen – "et sted for vidsyn, vilje og visjoner".

Onsdag 21. november innledes konferansen med et forkurs – "Molekylær epidemiologi i kreftsammenheng". Kurset holdes av professor Anne-Lise Børresen-Dale sammen med flere av hennes kollegaer ved Avdeling for genetikk ved Radiumhospitalet. Kurset holdes i lokalene til Det Norske Medicinske Selskab, i Drammensveien 44.

Konferansen har i år mange aktuelle tema, og vi håper alle finner noe som fanger interessen. Konferansens første dag åpnes av professor Isabel dos Santos Silva, fra London School of Hygiene and Tropical Medicine, som er invitert til å holde foredrag om livsløpsepidemiologi. Etter lunsj vil professor Henrik Møller, leder for the Thames Cancer Registry, holde et foredrag om vitamin D og dets potensielle effekt på utvikling av kreftsykdom. Før siste parallellsesjon vil NOFE utnevne et nytt æresmedlem, som selv vil holde en presentasjon. NOFE vil også dele ut prisen for "beste artikkel 2007", som vil presenteres av den aktuelle forfatteren. NOFEs årsmøte er siste post på det faglige programmet denne dagen. Fredagen innledes av Elena Kvan fra Institutt for farmakoterapi (UiO), med foredraget "Gjelder resultatene fra de store kardiovaskulære legemiddel-studiene både for kvinner og menn?". Preben Aavitsland, avdelingsdirektør for Avdeling for infeksjonsovervåkning ved Nasjonalt folkehelseinstitutt, er invitert til å holde et oversiktsforedrag om infeksjonsepidemiologi. Ut over disse nevnte foredragene vil vi få høre mange andre spennende innlegg basert på innsendte abstracts. Vi har lagt opp til to parallelle sesjoner slik at alle som har sendt inn sine bidrag skal få holde en muntlig presentasjon.

Vi ønsker dere alle hjertelig velkommen til den 15. norske epidemiologikonferansen. Vi håper på et lærerikt kurs og en innholdsrik konferanse, og at alle får noen hyggelige dager i Oslo. Vi ønsker også alle velkommen til festmiddag på Voksenåsen torsdag kveld, hvor vi i tillegg til god mat og drikke kan by på kulturelle og verbale innslag.

Vi vil også benytte anledningen til å takke Kreftregisteret, Nasjonalt folkehelseinstitutt og Institutt for allmenn- og samfunnsmedisin for økonomisk støtte til årets NOFE-konferanse.

Med hilsen fra arrangementkomiteen for NOFE-konferansen 2007

Trude Eid Robsahm, leder (Kreftregisteret), Anette Hjartåker (Kreftregisteret),
Unn E. Hestvik (Kreftregisteret), Steinar Tretli (Kreftregisteret),
Lars Christian Stene (Nasjonalt folkehelseinstitutt), Heidi Lyshol (Nasjonalt folkehelseinstitutt),
Per Nafstad (Institutt for allmenn- og samfunnsmedisin, UiO)

Den 15. norske epidemiologikonferansen Oslo 22.-23. november 2007, med kurs 21. november Program

Onsdag 21. november

Kurs: Molekylær epidemiologi i kreftsammenheng
Kursansvarlig: Professor Anne-Lise Børresen-Dale med flere, Avdeling for genetikk, Radiumhospitalet (RR-HF)
Sted: Det Norske Medicinske Selskab, Drammensveien 44, Oslo

10:00-10:30	Registrering (Kaffe)
10:30-10:35	Velkommen
10:35-11:00	Genomet. DNA-RNA-Protein regulering. Normale celler og normale molekylære prosesser. *Espen Enerly (PhD, Postdok.)*
11:00-11:25	Hva er kreft? Sporadisk og hereditær kreft. Onkogener, tumorsuppressor gener, DNA reparasjonsgener. Påvisning av genforandringer – enkeltgener (DNA). *Anita Langerød (PhD, Postdok.)*
11:25-11:35	**Pause**
11:35-12:00	Påvisning av genforandringer – helgenomisk (DNA) *Lars Baumbusch (PhD, Postdok.)*
12:00-12:25	Påvisning av endret genuttrykk – helgenomisk (RNA). Molekylære subtyper av kreft. Skreddersydd behandling? Betydning for epidemiologiske og kliniske studier. *Therese Sørlie (PhD, Forsker)*
12:25-13:00	**Lunsj**
13:00-13:30	Påvisning av genetiske risikofaktorer for kreft – enkeltnukleotid-variasjon (DNA). *Vessela Kristensen (PhD, Professor)*
13:30-14:00	"Systembiologi" og brystkreft. NOWAC studien. Samarbeid mellom ulike fagområder. *Anne-Lise Børresen-Dale (PhD, Professor)*

Torsdag 22. november

Den 15. norske epidemiologikonferansen
Voksenåsen, Holmenkollen, Oslo

Plenumssesjon

09:30-10:15		Registrering og kaffe
10:15-10:20	T.E. Robsahm	Åpning
10:20-11:05	Isabel dos Santos Silva (Professor, London School of Hygiene and Tropical Medicine, University of London)	*Methodological and practical issues in the study of a selective disease process*

Parallellsesjon A1-A5

Tema: Metode, Ordstyrer: Tor Haldorsen, Kreftregisteret

11:15-11:30	A1	N. Gunnes	Estimation of the mean response in longitudinal studies
11:30-11:45	A2	M. Abdelnoor	Eksplanatorisk versus pragmatisk strategi i klinisk epidemiologisk forskning
11:45-12:00	A3	B. Kulle	Accounting for haplotype phase uncertainty in LD estimation
12:00-12:15	A4	B. Straume	Observer variability in gastroscopy
12:15-12:30	A5	E. Glattre	Fractal epidemiology

Parallellsesjon B1-B5

Tema: Samfunnsmedisin, Ordstyrer: Pål Romundstad, ISM, NTNU

11:15-11:30	B1	P. Kristensen	Har clusterutredninger noen verdi? Eksempelet kreftsaken ved Rosenborg, NTNU
11:30-11:45	B2	A. Syse	Cancer's impact on employment and earnings in Norway
11:45-12:00	B3	I.S. Mehlum	Are occupational factors important determinants for socio-economic inequalities in musculoskeletal pain?
12:00-12:15	B4	P. Kristensen	Tilrettelegging av arbeidet og sykefravær midt i svangerskapet i Den norske mor og barn-undersøkelsen (MoBa)
12:15-12:30	B5	H.M. Gravseth	Intellectual performance and disability pension

12:30-13:30 **Lunsj**

Plenumssesjon

13:30-14:15 Henrik Møller (Professor, Thames Cancer Registry, London) *The vitamin D hypothesis of cancer*

Parallellsesjon A6-A9

Tema: Kreftepidemiologi, Ordstyrer: Kjersti Bakken, ISM, UiT

14:30-14:45	A6	T. Grotmol	Estrogen receptor β – an independent prognostic marker in estrogen receptor α- and progesterone receptor-positive breast cancer?
14:45-15:00	A7	G. Albrektsen	Twin births and maternal risk of endometrial cancer: a cohort study in Norway
15:00-15:15	A8	H. Langseth	Perineal use of talc and risk of ovarian cancer – a review study
15:15-15:30	A9	T.I. Lund Nilsen	Recreational physical activity and cancer risk in subsites of the colon (the HUNT Study)

Parallellsesjon B6-B9

Tema: Hjerte/kar, Ordstyrer: Randi Selmer, Nasjonalt folkehelseinstitutt

14:30-14:45	B6	M. Nordsveen	Co-prescribing of warfarin and NSAIDs/aspirin – frequency and problems
14:45-15:00	B7	S. Narum	Blødninger knyttet til warfarinbruk: rapporter fra bivirkningsregisteret i 2003-2006
15:00-15:15	B8	F.E. Skjeldestad	Genetic and clinical risk factors for venous thrombosis in pregnancy
15:15-15:30	B9	R. Selmer	Statinforskriving etter utdanningsnivå

15:30-15:45 **Kaffepause (med noe å bite i)**

Plenumssesjon

15:45-16:10 Æresmedlem i NOFE, utnevnelse og foredrag

Parallellsesjon A10-A13

Tema: Ulike tema, Ordstyrer: Svetlana Skurtveit, Nasjonalt folkehelseinstitutt

16:15-16:30	A10	S. Graff-Iversen	Health examination surveys (HES) in Europe: recruitment strategies and experiences
16:30-16:45	A11	R. Gislefoss	Janus serumbank – effekt av langtidslagring på serumstabilitet
16:45-17:00	A12	M. Waaseth	Plasmanivå av kjønnshormoner relatert til hormonbruk og menopausestatus – Kvinner og kreft studien
17:00-17:15	A13	N.H. Krog	Tinnitus og psykisk helse: resultater fra HUNT 2

Parallellsesjon B10-B13

Tema: Kosthold, **Ordstyrer: Bjarne Koster Jacobsen, ISM, UiT**

16:15-16:30	B10	S. Forsmo	Childhood cod liver oil consumption is negatively associated with bone density in peri- and postmenopausal women. The HUNT study
16:30-16:45	B11	D. Engeset	Fish consumption and colon cancer risk, with focus on lean fish. The Norwegian Woman and Cancer study (NOWAC)
16:45-17:00	B12	C. Tørris	Breastfeeding, diet and waist circumference
17:00-17:15	B13	A. Hjartåker	The obesity and diabetes epidemics and the risk of cancer: An overview

Plenumssesjon

17:20-17:40	**Beste artikkel 2007**
17:40-18:15	**Årsmøte i NOFE**
20:00-	**Festmiddag**

Fredag 23. november

Den 15. norske epidemiologikonferansen
Voksenåsen, Holmenkollen, Oslo

Plenumssesjon

09:00-09:30	Elena Kvan (PhD, Institutt for farmakoterapi, UiO)	*Gjelder resultatene fra de store kardiovaskulære legemiddelstudier både for kvinner og menn?*

Parallellsesjon A14-A18

Tema: Farmakoepidemiologi, Ordstyrer: Åsmund Reikvam, Institutt for farmakoterapi, UiO

09:30-09:45	A14	A.E. Eggen	Den sjette Tromsøundersøkelsen 2007-2008
09:45-10:00	A15	D. Berild	Trender i antibiotikabruk og antibiotikaresistens i Norge
10:00-10:15	A16	S.R. Kjosavik	Forskrivning av psykofarmaka i Norge i 2005
10:15-10:30	A17	A.K. Eek	Benzodiazepine use and drug-related problems in hospitalised patients with lung diseases
10:30-10:45	A18	S. Skurtveit	Traffic accident risks associated with the prescription of medicinal drugs: a registry-based cohort study

Parallellsesjon B14-B18

Tema: Luftveissykdommer, Ordstyrer: Per Nafstad, IASAM, UiO

09:30-09:45	B14	W. Nystad	Baby swimming and respiratory health
09:45-10:00	B15	S.E. Håberg	Maternal prepregnancy obesity and respiratory illness in early childhood
10:00-10:15	B16	B. Oftedal	Long-term outdoor air pollution at home address and asthma in schoolchildren in Oslo
10:15-10:30	B17	C. Madsen	Associations between environmental exposures and serum Clara cell protein
10:30-10:45	B18	T. Haugan	Forskrivningspraksis av medikamenter på blå resept for pasienter med obstruktiv lungesykdom

10:45-11:15 **Kaffepause (med noe å bite i)**

Plenumssesjon

11:15-11:45	Preben Aavitsland (MD, Nasjonalt folkehelseinstitutt)	*Infeksjonsepidemiologi: noen tanker om smittsom epidemiologi*

Parallellsesjon A19-A23

Tema: Infeksjonsepidemiologi, Ordstyrer: Preben Aavitsland, Nasjonalt folkehelseinstitutt

12:00-12:15	A19	Ø. Næss	Kristian Feyer Andvord's studies on the epidemiology of tuberculosis and the origin of generation cohort analysis in Norway
12:15-12:30	A20	S. Rørtveit	Impetigo in epidemic and non-epidemic phases: An incidence study over 4 ½ years in a general population
12:30-12:45	A21	J.M. Gran	Estimating excess mortality from influenza in Norway
12:45-13:00	A22	B.F. de Blasio	Modeling the impacts of HPV (Human Papilloma Virus) type 16/18 vaccination on the incidence of cervical cancer in Norway
13:00-13:15	A23	O.O. Aalen	Mathematical modelling of infectious disease

Parallellsesjon B19-B23

Tema: Hjerte/kar / diabetes type I / kreft, Ordstyrer: Inger Cappelen, Nasjonalt folkehelseinstitutt

12:00-12:15	B19	I. Ellingsen	Consumption of fruit and berries is inversely associated with carotid atherosclerosis in elderly men
12:15-12:30	B20	I. Eidem	Validiteten av diabetes mellitus-diagnosen i Medisinsk fødselsregister
12:30-12:45	B21	L.C. Stene	Patterns in development of islet autoantibodies at 3, 6, 9 and 12 months of age in children from the general population carrying the type 1 diabetes high-risk HLA genotype – The MIDIA study
12:45-13:00	B22	H. Stensheim	Cause-specific death in women diagnosed with cancer during pregnancy or lactation
13:00-13:15	B23	T.E. Robsahm	Serum vitamin D (calcidiol) and the prognosis of prostate cancer

13:30-15:00 **Lunsj – Vel hjem!**

A1

Estimation of the mean response in longitudinal studies

Nina Gunnes and Odd O. Aalen

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Purpose: In longitudinal studies the subjects are observed at certain observation times; so-called study waves. At each study wave a response, or score value, is measured. A severe problem arises when the data are subjected to censoring, for instance as a consequence of study participants dropping out of the study. We often wish to estimate the mean response in a hypothetical drop-out-free population. There are several methods that serve this purpose: the 'dynamic expected linear increments' (DELI) approach, the 'inverse probability weighting' (IPW) approach and the Aalen-Johansen approach. Our object is to compare the performance of these estimators with regards to both bias and variability.

Material and methods: The DELI-method aims at estimating the expected increments of the response process by using a linear regression model, while the IPW-method weights the subjects still under follow-up by the inverse of their respective probabilities of being observed. We have used both simulated and real-life data in our analyses. The simulation studies are based on a multistage model with a Markov structure, where each stage corresponds to a certain score value. The mean response is estimated for 1000 different simulations of the movement pattern, and the results are finally averaged over all the simulations together with calculation of the empirical variance of the estimators. The methods are also applied on a data set of subjects with severe head damage (work in progress).

Results: Results from the simulation studies show that all three estimators mentioned above perform well in estimating the mean response. The IPW-estimator has the largest empirical variance compared to the other estimators we explore.

Conclusion: The Aalen-Johansen-estimator, the DELI-estimator and the IPW-estimator are all approximately unbiased estimators. However, the variability of the latter estimator seems considerably larger than that of the two former estimators.

A2

Eksplanatorisk versus pragmatisk strategi i klinisk epidemiologisk forskning

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Introduksjon: Epidemiologisk forskning tar sikte på å beskrive helsetilstanden i en populasjon, årsak til sykdom, predikere og forebygge sykdom. Dette innebærer forskning med ulik strategisk tilnærming. Oftest står valget mellom en forklarende eller etiologisk problemstilling og en pragmatisk eller prognostisk problemstilling. Valg av strategi har betydning for hvilken utgangspopulasjon (source population) en velger, utforming av studien og valg av analysemetoder. Disse synspunktene ble introdusert av D. Schwartz allerede i 1971 og videreutviklet de senere år av Poccok og Hennekens.

Formål: Gi en oversikt over metodologiske betraktninger i forhold til valg av strategi i klinisk epidemiologisk forskning.

Resultat: Den *forklarende strategi* fokuserer på å forstå mekanismer i en sykelig prosess ved å peke på etiologiske eller kausale risikofaktorer. I denne strategi er det derfor assosiasjonen mellom eksponering (E) og endepunkt (D) som er hovedhypotesen. Alle andre variabler er bare interessante i den grad de påvirker denne assosiasjonen som en confounder eller effektmodifikator. Den *pragmatiske strategi* er orientert mot risikofaktorer som predikerer sykdom slik at profylaktiske forholdsregler kan tas. Ved denne strategi er hensikten å finne de variabler som predikerer endepunktet (D) og identifisere undergrupper av pasienter med høy risiko for et endepunkt. Begge strategier krever at våre resultater kan generaliseres. Dette innebærer at utvalgspopulasjonen må være godt definert og selektert i den forklarende strategi, og nær den kliniske virkelighet i den pragmatiske strategi. Begge strategier har forskjellig utforming i observasjonelle studier og eksperimentell klinisk forskning.

Konklusjon: Både den eksplanatoriske og pragmatiske strategi er fundamentale i klinisk forskning. Den første fokuserer på å forstå mekanismene i en sykelig prosess ved å peke på etiologiske eller kausale risikofaktorer. Den andre er orientert mot risikofaktorer som predikerer endepunktene og som kan føre til preventive forholdsregler og tiltak.

A3

Accounting for haplotype phase uncertainty in LD estimation

B. Kulle[1,2], A. Frigessi[1], H. Edvardsen[3,4], V. Kristensen[3,4] and L. Wojnowski[5]

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2) Department of Mathematics, University of Oslo, Norway
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4) Medical Faculty, University of Oslo, Oslo, Norway
5) Department of Pharmacology, Johannes Gutenberg University Mainz, Germany

The characterization of linkage disequilibrium (LD) is applied in a variety of studies including the identification of molecular determinants of the local recombination rate, the migration and population history of populations, and the role of positive selection in adaptation. LD suffers from the phase uncertainty of the haplotypes used in its calculation, which reflects limitations of the algorithms used for haplotype estimation. We introduce a LD calculation method, which deals with phase uncertainty by weighting all possible haplotype pairs according to their estimated probabilities as evaluated by PHASE. In contrast to the EM algorithm as implemented in the HAPLOVIEW and GENETICS packages, our method considers haplotypes based on the entire genetic information available for the candidate region. We tested the method using simulated and real genotyping data. The results show that, for all practical purposes, the new method is advantageous in comparison with algorithms that calculate LD using only the most probable haplotype or bilocus haplotypes based on the EM algorithm. The new method deals especially well with low LD regions, which contribute strongly to phase uncertainty. Altogether, the method is an attractive alternative to standard LD calculation procedures, including those based on the EM algorithm. We implemented the method in the software suite R, together with an interface to the popular haplotype calculation package PHASE.

Genetic Epidemiology (Article online in advance of print), doi: 10.1002/gepi.20273

A4

Observer variability in gastroscopy

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Aims: Endoscopy is an observer-dependent diagnostic method, where, until recently, thorough guidelines for the written report have been lacking. There is a growing demand for improvement of the endoscopy record, which may necessitate the supplementation of image documentation. The aim of this study was to estimate inter-observer as well as intra-observer variability in the assessment of images from gastroscopy.

Materials and methods: We designed an Internet interface presenting endoscopy images, accompanied by a multiple choice questionnaire for assessing pathology in the images. 10 images from the distal oesophagus and 10 images from the pyloric antrum were chosen. The images were obtained in a population based gastroscopy study. They were selected to ensure their technical quality and to reflect a broad spectrum of pathology common to most endoscopists. The oesophageal images were followed by 3 questions; presence of oesophagitis according to the LA classification (No / A / B / C / D), suspicion of metaplasia (yes / no), presence of hiatus hernia (yes / no / uncertain). The pyloric antrum images were followed by 5 questions (each with the option of answering yes or no); normal mucosa, oedematous mucosa, erythematous mucosa, erosion(s), ulcer. There were few images of normal mucosa or severe pathology. Physicians with varying endoscopy experience ("moderately experienced" with 200-1000 examinations and "highly experienced" with > 1000 examinations) were invited to answer the questionnaire in order to study inter-observer variability. They were given the opportunity to identify themselves, and those who did were re-invited five months later to assess the same images again, this time in order to study intra-observer variability. Kappa statistics were used for analysis of agreement.

Results: *Inter-observer variability:* Thirteen out of 20 invited physicians (65%) responded. In the assessment of images from oesophagus, there was full agreement on 3 out of 30 questions; one on the presence of hiatus hernia and two on the presence of metaplastic changes. None of the images of oesophagitis were assessed with full agreement between all respondents. On the contrary, 3 images were assessed using all five available categories of grading. In the assessment of images from the pyloric antrum, all 13 respondents agreed fully on 13 out of 50 questions. For one antral image the respondents agreed fully on all 5 questions. Inter-observer agreement varied between κ=0.18 (poor) and κ =0.50 (moderate). When divided into groups of experience, we found that higher experience was not followed by a higher level of agreement. Actually, the "highly experienced" endoscopists held poor agreement on two questions, and less agreement than expected by chance in the question on erythema in the gastric mucosa. *Intra-observer variability:* 11 respondents identified themselves and 10 of these accepted to assess the same images again. Intra-observer agreement varied between κ=0.46 (moderate) and κ=0.70 (good). When divided into groups based on experience, we found that on two questions, the 5 "moderately experienced" endoscopists held excellent agreement, and not lower than moderate agreement in any other question. The 5 "highly experienced" endoscopists did not obtain excellent agreement in any question. On the contrary, responses to the two questions regarding oesophagitis and gastric erythema, held only fair agreement.

Conclusion: Interpretation of endoscopy images is not an exact procedure, and the variability is large. Higher level of experience implies neither better inter-observer nor better intra-observer agreement. Image documentation is important to reveal the ambiguity of gastroscopy. Without image documentation, the written endoscopy record stands alone, with conclusions that may be more definite than are justified. We therefore believe that systematic inclusion of a set of images into endoscopy reports will improve their quality.

A5

Fractal epidemiology

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These days we terminate the writing of a manuscript presenting the mathematical-statistical basics of what we call fractal epidemiology. Its scientific platform is the axiomatic statement that follow-up studies must be described and analysed as dynamic events taking place in space-time. After a couple of years of hard work we believe the mathematical models have finally found their form. We appreciate this opportunity to inform members of NOFE about some features of fractal epidemiology and introduce some of the new concepts and methods and applications. As an example we discuss biocomplexity and non-linearity linked to causes and effects, time-slicing and the falsification-strong DCBA-method by means of which we have already found interesting results contributing to the understanding of assumed exposure-response associations.

A6

Estrogen receptor β – an independent prognostic marker in estrogen receptor α- and progesterone receptor-positive breast cancer?

Tom Grotmol[1], Bjørn O. Mæhle[2], Karin Collett[2], Lars A. Akslen[2] and Steinar Tretli[1]

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Introduction: Females with screen-detected breast cancers have a better outcome than their clinically detected counterparts, adjusted for established prognostic factors. Little is known about the biological mechanisms underlying this difference. Estrogen receptor (ER) β could possibly be involved, given its growth inhibitory signalling properties.

Material and methods: To gain insight into the clinical importance of ERβ in breast cancer, 145 archival primary breast cancers were examined histochemically for ERβ, and quantified with respect to ERα and progesterone receptor (PR) content.

Results: For patients with a positive ERα and PR status, there was a significantly reduced risk of fatal outcome by increasing tumour ERβ level in a multivariate analysis [P(trend) = 0.03 (Cox regression model)]. The risk was 28% and 22% for medium and high ERβ level, respectively, compared with low ERβ level, adjusting for prognostic factors, such as mean nuclear area, tumour diameter, lymph node status, patient age at operation, and body weight. For tumours with negative ERα and PR status, however, there was no association between outcome and ERβ level.

Conclusion: Our findings indicate that ERβ provides independent prognostic information for breast cancers with ERα/PR positive status, a typical feature among screen-detected breast cancers. The role of ERβ needs to be further evaluated in this group of breast cancers.

A7

Twin births and maternal risk of endometrial cancer: a cohort study in Norway

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Aims: Most established risk factors for endometrial cancer have been linked to exposure to unopposed estrogen. Pregnancies involving twins have been found to be associated with higher maternal estrogen levels than singleton pregnancies, possibly affecting cancer risk. In the present study we examine whether twin mothers have a different risk of endometrial cancer than women with singletons only.

Material and methods: Information on reproductive history and cancer diagnoses was assessed through the Norwegian Population register and the Cancer Registry of Norway, respectively. Linking of data from the different national registers was performed at Statistics Norway. Among 1.1 million parous women at risk at ages 30-74 years, a total of 3356 women were diagnosed with endometrial cancer; 101 of these women were twin mothers. The mean follow-up time was 19.5 years (range 1 month to 44 years). Incidence rate ratios (IRR) with 95 percent confidence intervals (95% CI) were calculated in log-linear Poisson regression analyses of person-years at risk.

Results: Twin mothers had a higher risk of endometrial cancer than women with singleton births only (IRR=1.26, 95% CI=1.03-1.53). The overall association was restricted to women with twin boys (IRR=1.57, 95% CI=1.15-2.14); for women with twin girls an elevated risk was observed only before age 55 years (IRR=1.92, 95% CI=1.27-2.89). No significant association was found with sex-nonconcordant twins.

Conclusion: The elevated risk of endometrial cancer in women with twin boys support to the hypothesis that androgens play a role in endometrial cancer carcinogenesis, possibly by influencing the level of estrogens and progesterones during the pregnancy, or by modifying a potential effect of these pregnancy hormones. The increased risk of early age endometrial cancer in women with twin girls may reflect an adverse effect of estrogens.

A8

Perineal use of talc and risk of ovarian cancer – a review study

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Introduction and aims: Ovarian cancer is one of the most common gynaecological neoplasms, especially in industrialized countries. The etiology of the disease is not well understood, except that inherited mutations in the breast cancer genes BRCA-1 and BRCA-2 account for up to ten percent of all cases, and child-bearing, oral contraceptive use, and breast-feeding reduces the risk. Some environmental exposures, such as talc has been suspected as an ovarian carcinogen. Talc refers to both mineral talc and industrial products that contain mineral talc. Mineral talc are used for cosmetic and hygiene products including baby powders and feminine hygiene products. Perineal use of cosmetic talc is a common practise in the United Kingdom, North America, Australia, and some other countries[1]. From pathological studies it is known that particles and fibres that enter the body can migrate to distant organs. Following perineal application, talc particles can migrate from the vagina to the peritoneal cavity and ovaries. A majority of women experience retrograde menstruation, this suggests a mechanism by which talc particles can travel through the female reproductive tract to the ovaries. The carcinogenicity of non-asbestiform talc was assessed by a monograph working group at International Agency for Research on Cancer (IARC) in 2006[2]. After considering biases and possible confounding factors, the IARC working group concluded that the epidemiological studies provided limited evidence for the carcinogenicity of perineal use of talc-based body powder, and classified this use as possibly carcinogenic to human beings (ie, group 2B)[3]. The aim of the present review was to put focus on the importance of this issue as a future research agenda.

Results: The association between talc use in the perineal region and ovarian cancer has been investigated in one cohort study and 20 case-control studies. In the cohort study, there was no association between cosmetic talc use and risk of all subtypes of ovarian cancer combined. The various case-control studies provided indications of either a significant excess risk (ten studies) or, non-significant excess risk or null (ten studies), with odds ratios (ORs) ranging from 1.0 to 3.9. None of the studies reported relative risks below 1.0. The population based case-control studies included studies with 112 to 824 ovarian cancer cases, and had odds ratios ranging from 1.1 to 3.9. The hospital based case control studies included studies with 77 to 462 cases, and reported odds ratios between 1.0 and 2.5. Meta odds ratios were 1.40, 1.12 and 1.35 for population-based, hospital-based and all case control studies combined, respectively.

Conclusion: In conclusion, the epidemiological evidence suggests that use of cosmetic talc in the perineal area may be associated with ovarian cancer risk. However, a causal association is not established. Future studies should focus on seeking evidence in talc exposed female populations worldwide, collect reliable information on age at initial use of body powder, exposure assessments and dose response relationships.

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A9

Recreational physical activity and cancer risk in subsites of the colon (the HUNT Study)

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Background: Physical activity may reduce colon cancer risk, but the underlying mechanisms remain unclear. Relating physical activity to cancer risk in anatomical segments of the colon may advance our understanding of possible mechanisms.

Methods: We conducted a prospective study of 59,369 Norwegian men and women who were followed-up for cancer incidence and mortality. Cox proportional hazards models were used to estimate multi-variably adjusted hazard ratios and 95% confidence intervals (CIs). All statistical tests were two-sided.

Results: During 17 years of follow-up, 736 colon cancers and 294 rectal cancers were diagnosed. Overall, we found an inverse association between recreational physical activity and colon cancer risk, but subsite analyses showed that the association was confined to cancer in the transverse and sigmoid colon. The adjusted hazard ratio, comparing people who reported high versus no physical activity, was 0.44 (95% CI, 0.25-0.78) for cancer in the transverse and 0.48 (95% CI, 0.31-0.78) for cancer in the sigmoid colon. The corresponding hazard ratios for cancer mortality were 0.33 (95% CI, 0.14-0.76) for the transverse and 0.29 (95% CI, 0.15-0.56) for the sigmoid colon. For rectal cancer, there was no association with physical activity in these data.

Conclusion: The inverse association of recreational physical activity with cancer risk and mortality in the transverse and sigmoid segments of the colon may point at increased colon motility and reduced fecal transit time as possible underlying mechanisms.

A10

Health Examination Surveys (HES) in Europe: Recruitment strategies and experiences

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Background: The participation rate has decreased in population surveys in most European countries during the last decades. According to information collected as part of the European Union funded project "Feasibility of Health Examination Surveys" (FEHES) 2006-2008 (http://www.ktl.fi/fehes/), the participation rates, in previous HESs conducted in 12 European countries between 1994 and 2003, varied from 25% to 85%. To obtain more information on recruitment strategies, we approached FEHES contact persons in 32 Member States, EFTA/EEA countries and applicant countries.

Methods: A short e-mailed questionnaire was used. Contact persons were asked to answer for their most recent national or regional HES, or a recent Health Interview Survey (HIS) if no HES was conducted. The contact persons provided information from 26 countries with finished or ongoing surveys during 1990-2008. Here, one survey is included for each country: a HESs in 17 and a HISs in 9 countries.

Results: In most countries (23/26) the first contact to the selected persons or households was a mailed letter, often not including the survey questionnaire. Re-contact to non-responders was made in most countries (23/26). Phone calls as part of the strategy were used in 18 countries, including 13 of 17 countries with HES. Home visits were used by 16 countries, including 10/17 with HES. The numbers of re-contact attempts were in most countries between 1 and 3, and in 6 countries more than 3 re-contact attempts were made. In one country the recruitment effort included: "Invitation letter and next 3 phone calls (after until 25 attempts to get somebody) and a last phone call from the physician". Reimbursement of travel expenses or a small gift for participants was offered by 10/26. Of the 26 contact persons, 13 first mentioned *repeated contact or personal approach* by phone, home visit or letter, when asked which were the *most effective strategies* to increase participation (8/17 countries with HES plus 5/9 with HIS). Other strategies mentioned as the first fell into the categories "participant service" (5/17 for HES and 1/9 for HIS) or "civil duty" (none for HES, 3/9 for HIS). *"Participant service"* strategies included flexible opening hours or offering home visit, professionally skilled/personally interested/ polite field personnel, mass communication, involving local partners, gifts to participants, reimbursement of travel expense, high quality of the invitation letter and pointing at "gain for own health". *"Civil duty"* strategies included mandatory participation, invitation letter signed by Director General Health, highlighting the authority of the National Public Health Institute, a physician making the first phone contact to non-responders, appeal to doing a civil duty and pointing at gain for the community. Several countries named more than one effective strategy, for example a civil duty appeal after first mentioning repeated contact. In all 4 contact persons did not answer. Of those, one told that their HES had been performed in 1990 by means of family physicians, and no information was collected on recruitment. Another contact person told that their ethical committee did not allow them to try alternative strategies. Reasons for non-participation were collected in 12/26 countries. Answers were such as "no interest, no time, health problems, feeling healthy, recently undergone analyses, working elsewhere" or refusal for confidentiality reasons. Some contact persons told that it was not considered ethical to ask for reasons.

Conclusion: For HES, a majority of countries include phone calls or home visits in their recruitment strategy. Repeated, often personal, contact to invited persons was mentioned as the most effective effort by half of the national contact persons.

A11

Janus Serumbank – effekt av langtidslagring på serumstabilitet

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Bakgrunn: Biobankmateriale blir ofte brukt i epidemiologiske studier. Langtidslagring av serum ved –25 °C, som i Janusbanken, kan redusere kvaliteten til prøvene. Janus Serumbank ble etablert i 1973 og er populasjonsbasert. Ca. 90% av prøvene kommer fra personer i 40-årene som har vært med i hjerte/kar helseundersøkelser i Norge. Resten av prøvene kommer fra blodgivere i Oslo og omegn. Etter 33 år med prøveinnsamling har biobanken nå ca. 455 500 prøver fra 333 700 donorer (2007). I dag inneholder Janusdatabasen mer enn 41.000 invasive krefttilfeller. Det er publisert 59 vitenskapelige artikler basert på materiale fra banken. Publikasjonene dekker en mengde ulike biomarkører og kreftformer.

Metode: Vårt mål var å undersøke langtidsstabilitet av prøver lagret ved –25 °C. Vi sammenlignet prøver lagret i 25 år, 2 år og fersktappede prøver, og etablerte referanseområde for en del biokjemiske komponenter. Prøver fra 130 blodgivere fra hver gruppe ble plukket ut. Donorene var 40-49 år på tappetidspunkt og menn ble valgt på grunn av mindre individuell biologisk variasjon i fertilitets-hormonene. Prøvene ble analysert for 22 ulike komponenter i serum inkludert elektrolytter, enzymer, vitaminer, lipider, hormoner, mineraler, vannløselige molekyler og proteiner.

Resultater: Komponentene viste ulikt stabilitetsmønster:
- Komponenter stabile gjennom 25 års lagring: ASAT, kreatinin, jern, IgG ogFSH
- Komponenter med høyere nivå etter 2 år men så stabil: kalium og kalsium
- Komponenter med lite men statistisk signifikant endret nivå etter 25 år: albumin, insulin C-peptide, cystatin-C, kolesterol, natrium, transferrin, SHBG, urinsyre, ferritin, prolaktin, vitamin B12 og testosteron
- Komponenter med betydelig redusert nivå etter 25 år: ALAT, CK, folat og bilirubin

A12

Plasmanivå av kjønnshormoner relatert til hormonbruk og menopausestatus – Kvinner og kreft studien

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Formål: Beskrive plasmanivå av kjønnshormoner relatert til hormonbruk, BMI (kg/m^2) og menopausestatus. Validere selvrapportert menopausestatus og hormonbruk.

Materiale og metoder: Tverrsnittsstudie blant 445 kvinner, 48-62 år, som svarte på et 8-siders spørreskjema høsten 2004, og leverte blodprøve med et 2-siders spørreskjema våren 2005. Plasmanivå av østradiol, progesteron, FSH og SHBG ved bruk av ulike typer hormontilskudd og for ulike BMI-kategorier ble analysert vha. ANCOVA. Forholdet mellom BMI (kontinuerlig variabel) og hormonnivå ble analysert ved hjelp av multippel lineær regresjon. Plasmanivå av FSH og E2 ble brukt som gullstandard i valideringen av selvrapportert menopausestatus.

Resultater: 80% av kvinnene var postmenopausale, 20% av disse brukte hormontilskudd. Østradiol-nivået steg og FSH-nivået sank med stigende østradioldose. SHBG økte hovedsakelig blant de som brukte peroralt hormontilskudd. Vaginalbehandling med østradiol påvirket ikke hormonnivåene. Det var ingen forskjell i BMI mellom hormonbrukere og ikke-brukere. Blant ikke-brukerne var høyere BMI assosiert med høyere østradiol- og lavere FSH- og SHBG-nivåer. Klassifisering av menopausestatus i henhold til 2-siders spørreskjema viste 92% sensitivitet og 73% spesifisitet, mens 8-sidersskjemaet viste 88% sensitivitet og 87% spesifisitet. Hormonbruk viste 100% spesifisitet, og 88% av hormonbrukerne hadde østradiolnivåer over 95% KI for ikke-brukere.

Konklusjon: Bruk av ulike typer hormontilskudd gir ulike plasmanivåer av kjønnshormoner og SHBG. Perorale preparater gir hormonnivåer som ligner nivåene hos fertile kvinner. BMI har innflytelse på hormonnivåer blant kvinner som ikke bruker hormontilskudd. Spørreskjema fra Kvinner og kreft undersøkelsen gir valid informasjon om hormonbruk og menopausestatus blant norske kvinner i overgangsalderen.

A13

Tinnitus og psykisk helse: resultater fra HUNT 2

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Øresus, eller tinnitus, er en fornemmelse av lyd uten ytre lydkilde. Om lag 15% av befolkningen over 20 år i Nord-Trøndelag oppgir at de er plaget av øresus. For pasienter med nedsatt hørsel oppfattes tinnitus ofte som et like stort problem som selve hørselsnedsettelsen. Vanlige følgeplager er søvnproblemer, konsentrasjonsvansker, generell irritasjon og plage av lyden, redusert taleoppfattelse, og ulike typer av psykosomatiske problemer. I mindre kliniske studier er det funnet en til dels meget sterk sammenheng mellom tinnitus og mange psykologiske faktorer slik som angst og depresjon. Epidemiologiske undersøkelser som viser sammenhengen mellom tinnitus og psykisk helse i en generell befolkning mangler imidlertid. Formålet med denne studien er å undersøke sammenhengen mellom tinnitus og symptomer på angst, depresjon, selvfølelse og subjektivt velvære i et generelt befolkningsutvalg.

Hørselsundersøkelsen i Nord-Trøndelag, som ble gjennomført som en del av Helseundersøkelsen i Nord-Trøndelag (HUNT 2) i 1995-97, omfatter audiometriske hørselsprøver og store mengder spørreskjemaopplysninger fra 51 975 personer. Opplysninger om sosial bakgrunn er hentet fra offentlige registre. I tillegg til hørselsmålingene finnes detaljert selvrapportert informasjon om tinnitus, hørselstap, og selvrapporterte symptomer på angst og depresjon, selvfølelse og livskvalitet.

Multivariate analyser (ANOVA) ble gjennomført for å undersøke sammenhengen mellom tinnitus og symptomer på angst, depresjon, selvfølelse og subjektivt velvære. Symptomer på angst og depresjon ble målt ved en forkortet versjon av SCL-25 med 10 spørsmål (4 for angst, 6 for depresjon). Det ble også benyttet en forkortet utgave av Rosenbergs skala for selvfølelse. Livskvalitet ble målt ved ett spørsmål med 7 kategorier fra ”svært misfornøyd” med tilværelsen til ”svært fornøyd”. En additiv indeks ble dannet av et spørsmål om hvor ofte du har øresus (”månedlig”, ”ukentlig”, ”daglig”, eller ”nesten alltid”) og et spørsmål om hvor lenge periodene med øresus vanligvis varer (”få minutter”, ”10 min-1time”, eller ”mer enn 1 time”). De som ikke hadde øresus ble inkludert som 0-kategori. I tillegg ble en variabel inkludert som mål på ”kontrollerbarhet” av symptomene, dvs. når de vanligvis får øresus: ”Etter sterke lyder og/eller når det er stille” (”en viss kontroll”, kodet 1), eller ”vet aldri når” (”ukontrollerbart”, kodet 2). I de innledende analysene som presenteres her ble det kontrollert for effekten av hørselstap og demografiske variabler (kjønn, alder, utdanning, sivilstatus).

Det ble funnet en ikke-lineær sammenheng mellom tinnitus symptomintensitet og alle indikatorene på psykisk helse. De med lavest tinnitusintensitet scoret høyere på angst og depresjon, og lavere på selvfølelse og subjektivt velvære enn både de som ikke hadde tinnitus og de med høyere symptomintensitet. De med minst kontroll over tinnitussymptomene (indikert ved ”vet aldri når” får øresus) scoret høyere enn de øvrige på angst og depresjon, og lavest på selvfølelse og subjektivt velvære. Effektene var imidlertid moderate.

Analysen viser en sammenheng mellom tinnitus og psykisk helse, men av mer moderat karakter enn det som fremgår av kliniske studier. Dette viser betydningen av epidemiologiske studier av et generelt befolkningsutvalg for en bedre vurdering av effektstørrelser. Siden dette er en tverrsnittsstudie, er det ikke mulig å si noe om det er slik at tinnitus fører til nedsatt psykisk helse, eller om nedsatt psykisk helse, selvfølelse, og velvære snarere er sårbarhetsfaktorer for utvikling av tinnitus. Mange faktorer kan påvirke psykisk helse, selvfølelse, og velvære. I videre analyser vil det bl.a. kontrolleres for annen fysisk funksjonsnedsettelse.

A14

Den sjette Tromsøundersøkelsen 2007-2008

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Tromsøundersøkelsen er en forskerinitiert epidemiologisk studie med primært formål å utforske kroniske sykdommer og plager, behandling av sykdommer og plager, bruk av helsetjenester og hvordan kronisk sykdommer og plager påvirker livskvalitet.

Tromsøundersøkelsen har pågått siden 1974, og 38 000 personer har deltatt; 1800 personer har deltatt ved alle fem undersøkelser, og over 12 000 har deltatt tre eller flere ganger.

Tromsøundersøkelsen har høy frammøteprosent, repeterte målinger, nedfrosne blodprøver, og longitudinelle data over befolkningens psykiske og fysiske helse, legemiddelbruk, forbruk av helsetjenester og trygdeytelser, sosiale forhold og livsstil. Det er derfor mulig å studere endringer av ulike helseforhold gjennom livet – faktorer som er relevante for flere sentrale forskningsområder. Kombinasjonen av spørreskjema, blodprøver og kliniske undersøkelser gir mulighet til å studere samspillet mellom genetisk variasjon, livsstil og miljøpåvirkning. Tromsøundersøkelsen deltar i internasjonale genetiske forskningsprosjekter innen hjerte- og karsykdom, osteoporose, kreft og diabetes.

Tromsø 6 gjennomføres med to spørreskjemaer, innsamling av biologisk materiale (blod, urin, hår), mikrobiologisk prøve, målinger (høyde,vekt,midje/hoftemål, blodtrykk), intervju og kliniske undersøkelser. 18 000 deltakere inviteres til screening (fase 1, hovedundersøkelsen) fase 1, og omkring 9000 av de frammøtte inviteres til en utvidet undersøkelse (fase 2, spesialundersøkelsen) noen uker seinere. Utvalget vil være i alderen 25 til 87 år. Invitasjonene tar utgangspunkt i deltakerne i spesialundersøkelsen i Tromsø 4. I tillegg er det invitert nye fødselskohorter (20-100% utvalg).

Oppstarten er 1.oktober 2007 med avslutning ved årsskiftet 2008/9. Kliniske undersøkelser i fase 1 er måling av beintetthet og smerteølsomhet. Kliniske undersøkelser i spesialundersøkelsen er ultralyd av halspulsåre og hjerte, lungefunksjon, /beintetthet i hofte rygg samt kroppssammensetning(DEXA), kognitiv funksjon, øyebunnsfotografering og EKG.

Det er meldt omlag 50 delprosjekter til Tromsø 6, hvorav en del er oppfølgende studier og basert på deltakere i hovedundersøkelsen. En del av deltakerne vil bli invitert til nye undersøkelser i etterkant eller vil bli tilsendt et nytt spørreskjema. Tromsø 6 samler forskere fra UiT, NTNU, UiO, UiB, UNN, Ullevål sykehus og Radium-Rikshospitalet.

Tromsø 6 kan beskrives som en paraply over flere forskningsprosjekter og forskningsgrupper, som har til felles at det benyttes ulike data fra spørreskjemaene, biologisk materiale og fra de kliniske undersøkelsene som basis for forskningen. Prosjektene er i stor grad vitenskapelig samarbeid i skjæringspunktet mellom epidemiologi og klinisk forskning. En ønsker å studere spesielle sykdommer/helseproblemer som hjerte- og karsykdommer, osteoporose, diabetes, KOLS, kronisk smerte, kreft, og mer sykdomsovergripende tema som miljøgifter og sosial ulikhet, arbeidstilknytning, trivsel og helse.

Alle data fra tidligere runder av Tromsøundersøkelsen er nå samlet i databasen EUTRO (Epidemiologiske Undersøkelser i TROmsø). De fleste data fra Tromsø 6 vil legges inn i EUTRO fortløpende under undersøkelsesperioden. Tromsø 6 har egen nettside www.tromso6.no. En oversikt over tidligere innsamlede data i Tromsøundersøkelsen er tilgjengelig via dataverktøyet NESSTAR og presenteres på nettsiden www.tromsoundersokelsen.no.

Tromsø 6 vil gi muligheter for tverrsnittstudier, nye oppfølginger, longitudinelle studier og koblinger til sentrale og lokale helseregistre. Tromsøundersøkelsens nettsider gir informasjon om hvordan forskere kan få tilgang til data for vitenskapelige analyser.

A15

Trender i antibiotikabruk og antibiotikaresistens i Norge

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Antibiotika er vår viktigste legemiddelgruppe, men pga overforbruk og feil bruk har vi nå en verdensomspennende pandemi med antibiotikaresistens som i siste ende truer fremtidig nytte av antibiotika. I Norge har vi hittil hatt få resistensproblemer, men de siste 30 årene har totalforbruket økt med 30%, og de siste 10 årene er bruken av bredspektrede antibiotika doblet. Dette har nå begynt å gjenspeile seg i en trend mot mere resistente bakterier som igjen fører til ytterligere bruk av bredspektrede midler. Foreløpig er situasjonen under kontroll, men hvis det ikke tas et nasjonalt krafttak for å redusere den totale bruken av antibiotika og spesielt bruken av bredpektrede midler, kommer vi snart i samme situasjon som i USA og syd-Europa hvor antibiotika som er førstehåndsmidler i Norge ikke kan brukes lenger. Noen tall for antibiotikabruk og resistens i Norge vil bli presentert.

A16

Forskrivning av psykofarmaka i Norge i 2005

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Formål: Legemidler utgjør en viktig del av behandlingen av psykiske lidelser. Hensikten med denne studien var å analysere forskrivningen av psykofarmaka til den generelle befolkningen i Norge i 2005.

Materiale og metode: En farmakoepidemiologisk tverrsnittsstudie basert på koblete data fra Nasjonalt Reseptregister ved Folkehelseinstituttet og Fastlegedatabasen ved Norsk samfunnsvitenskapelig dataservice. Fra Reseptregisteret ble data fra innløste resepter til enkeltpersoner på antipsykotika, anxiolytika, hypnotika og antidepressiva samt informasjon om forskrivernes spesialiteter hentet ut. Dataene omfatter alle slike resepter fra alle apotek i Norge i 2005. Disse ble koblet med data fra Fastlegedatabasen over hvilke forskrivere som var fastleger.

Resultater: I 2005 fikk 705 230 personer (15,3% av totalbefolkningen) forskrevet psykofarmaka minst én gang: 2,4% brukte antipsykotika, 6,2% anxiolytika, 7,9% hypnotika og 6,0% antidepressiva. Andelen personer som brukte psykofarmaka, og gjennomsnittlig legemiddelbruk per person per år, var høyest i aldersgruppen 40-59 år. For hypnotika økte imidlertid forbruket stadig med alderen og var høyest blant pasienter over 80 år. I nesten alle aldersgrupper var det flere kvinner enn menn som brukte psykofarmaka, og forskjellen økte med pasientenes alder. I sum forskrev fastlegene 80% av disse legemidlene, mens spesialister i psykiatri og barnepsykiatri forskrev 6%. Andre spesialister samt leger under spesialisering forskrev de resterende 14%. De ulike spesialisters forskrivningsvolum varierte betydelig med pasientenes alder. Barn og unge under 20 år fikk forskrevet mellom 26% (hypnotika) og 45% (antipsykotika) av medikamentene av henholdsvis spesialister i pediatri og i psykiatri/ barnepsykiatri. Voksne pasienter fikk forskrevet psykofarmaka hovedsakelig av fastlegene, og andelen økte med pasientenes alder. Pasienter 20-39 år gammel fikk forskrevet mellom 55% (antipsykotika) og 78% (hypnotika) av fastleger, og pasienter over 70 år gammel ca 85%.

Konklusjon: Andelen av befolkningen som bruker psykofarmaka øker med alderen. Fastlegene forskriver mesteparten av disse medikamentene, mens psykiaternes andel avtar med pasientenes alder. Fastlegenes kunnskaper og holdninger er derfor avgjørende for kvaliteten av legemiddelbehandlingen som gis til pasienter med psykiske lidelser.

A17

Benzodiazepine use and drug-related problems in hospitalised patients with lung diseases

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Introduction/aims: Benzodiazepines (BZ) have been shown to suppress respiratory function in patients with chronic obstructive lung disease, and if BZ are indicated in these patients, they should be used with care. To which extent BZ are being used in the "real world" lung patients is not well understood. We aimed to investigate the utilization of BZ in hospitalised patients with lung diseases and, furthermore, to examine frequency and type of drug-related problems (DRPs) in these patients.

Methods: Patients from departments of cardiology, geriatrics, respiratory diseases and rheumatology at five general hospitals in Norway were prospectively included from May to December 2002. Data collected included drugs used, demographic data, relevant medical history, laboratory data and clinical/pharmacological risk factors. DRPs – classified in twelve categories – were recorded and assessed at multidisciplinary morning meetings. Lung disease patients (lung group) in this study were those who had respiratory disease diagnoses registered in the medical records (chronic obstructive pulmonary disease 77%, asthma 17% and others 6%) and also used drugs for respiratory diseases (drugs belonging to ATC group R03).

Results: Of the 798 patients included in the study, 169 patients (27%) were lung disease patients, and of these 94 patients (55.6%) used BZ. The lung group and the non-lung group (629 patients) did not differ with regard to age (72.0 y vs 70.4 y) and gender (60.9% vs 58.5% females). The lung group had, compared to the non-lung group, slightly more clinical/pharmacological risk factors (1.9 vs 1.5, $p< 0.001$) and used more drugs on hospital admission (6.3 vs 4.1, $p< 0.001$). Significantly more patients in the lung group used BZ (55.6% vs 41.5%, $p< 0.001$); this pertained to both more regular use on hospital admission (24.9% vs 17.8%, $p=0.04$) and to commencement of more BZ – including regular and as required medication – during the hospital stay (39.6% vs 28.6% of the patients, $p=0.006$). When restricting the analysis of BZ use to only tranquillizers (diazepam, oxazepam and alprazolam) similar differences between lung and non-lung patients were observed (29.6% vs 15.6%, $p< 0.001$). Significantly more DRPs per patient were found in the lung group compared to the non-lung group (3.3 vs 2.4, $p< 0.001$); the most frequent DRPs linked to BZ in the lung group were *non-optimal dose* and *non-optimal drug*.

Conclusion: Hospitalised lung disease patients used BZ extensively and were also frequently prescribed BZ during the hospital stay. This finding, together with the recording of frequently occurring DRPs and the fact that BZ have respiratory depressive effects, indicates that heightened awareness about BZ use in lung patients is warranted.

A18

Traffic accident risks associated with the prescription of medicinal drugs: a registry-based cohort study

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Background: There is limited information about the traffic accident risk associated with the use of medicinal drugs.

Objectives: To examine whether the use of prescribed medicines by drivers increases the risk of traffic accidents.

Methods: Information on prescriptions, road accidents and emigrations/deaths was obtained from population-based registries. All Norwegians aged 18-70 in January 2004 to September 2006 (3.1 million), were included in the study. Data were linked based on the unique 11-digit identification number, assigned to all individuals living in Norway. The incidence of accidents in the exposed person-time was compared with the incidence of accidents in the unexposed person-time by calculation of the standarized incidence ratio (SIR). The SIR was calculated separately for 10 age groups and sexes.

Results: 22,405 road accidents with personal injuries occurred during the study period. The risk of traffic accident was increased for drivers who had received prescriptions for any medicines (SIR for both sexes combined=1.4; 95% CI: 1.3-1.5). The risk was markedly increased in users of natural opium alkaloids (2.0; 1.7-2.4), benzodiazepine tranquillizers (2.9; 2.5-3.5), and benzodiazepine hypnotics (3.3; 2.1-4.7). Receiving a prescription for carisoprodol also resulted in increased traffic accident risk, SIR 4.0 (2.7-5.6) for men and 3.6(2.5-5.0) for women during the first week after the date of dispensing. The SIR for carisoprodol was higher than for diazepam (men: 2.9; 2.1-3.9) (women: 2.6; 1.8-3.8); codeine (men: 1.9; 1.6-2.3) (women: 1.8; 1.4-2.2); and zopiclone (men: 2.5; 1.9-3.1) (women: 2.2; 1.7-2.8). Little or no increased risk was found for selective beta -2-adrenoreceptor agonists (antiasthmatics) (1.5; 1.0-2.0), calcium receptor antagonists (0.9; 0.5-1.5) and penicillin (1.1; 0.8-1.5).

Conclusions: The increased risk of traffic accident for drivers prescribed opiates and benzodiazepines, supported the results from other studies. The increased risk of z-hypnotics-users warrants further investigation. This pharmacoepidemiological model might be useful to identify medicinal drugs of potential traffic safety risk in populations with prescription and accident registries.

A19

Kristian Feyer Andvord's studies on the epidemiology of tuberculosis and the origin of generation cohort analysis in Norway

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Background: Generation cohort analysis has played an important role in epidemiology as a means to describe the experience of disease rates in people born in successive calendar years. This approach provides important clues about the natural history of specific diseases at the individual level as well as the evolution of disease at population level. Kristian Feyer Andvord suggested that primary infection mainly takes place in childhood and that falling mortality rates at the time of observation was a reflection of exposure early in life. Wade Hamilton Frost later in 1939 published a similar idea citing Andvord, and introduced the concept of 'cohort'. This seminal paper by Frost is widely known in epidemiology as it marks the birth of a concept vital to the discipline's self identification. Less attention has been paid to Andvord. We wanted to follow the origin of this method in the work of Andvord and the causal inferences he made in the period he acted within.

Methods: We went through all his 24 scientific articles and essays published in the period l889 to 1935. To get reach of additional literature on Andvord and generation cohort analysis, we did a literature search using the following key words: 'cohort', 'cohort analysis', 'generation', 'Andvord', 'Frost' and 'tuberculosis'.

Results: In contrast to many other countries, tuberculosis mortality in Norway did not start to decline until 1900. In 1930 Andvord was able to describe tuberculosis mortality for successive birth cohort. 40 years of his adult working life, from 1895 to 1935, he spent on the quest to identify the age dependent susceptibility of the disease by means of comparing first geographic pattern and later birth cohorts. This period coincided with major changes in the scientific conceptions of tuberculosis and diseases in general and with political and ideological notions of prevention. This was also reflected in the causal inferences made by Andvord as he moved from miasmatic to genetic explanations for the decline of mortality. He was reluctant to put any emphasis on improved social living conditions.

Conclusions: Although Andvord developed a powerful tool in epidemiology when he described tuberculosis mortality in a period of great changes, he was influenced by changing models of disease aetiology.

A20

Impetigo in epidemic and non-epidemic phases: An incidence study over 4 ½ years in a general population

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Background: Little is known about incidence and natural variation of impetigo in general populations.

Objectives: To investigate the natural course of impetigo in a well-defined population, and to study the resistance pattern of the causal bacteria over time.

Patients/Methods: This is a population–based incidence study in Austevoll, an island community of 4,457 inhabitants in Norway, in the years 2001-2005. Incidence rates are given as events per person-year. Epidemic periods were identified by statistical process-control analyses.

Results: The incidence rate of impetigo for the whole study period was 0.017, corresponding to a total of 334 cases. The incidence rates were 0.009, 0.026, 0.019, 0.016 and 0.009 in years 2001, 2002, 2003, 2004, and 2005, respectively. Three epidemics were identified, starting in August of 2002, 2003, and 2004, lasting for 11, 11, and 5 weeks, respectively. Incidence rates in these epidemic periods were 0.099, 0.045, and 0.074, respectively. In epidemic periods, S aureus was the causal bacterium in 89% (117/132) of cases, while this proportion was 68% (84/123) in non-epidemic periods (P< .01). S aureus was resistant to fusidic acid in 84% (98/117) and 64% (54/84) of impetigo cases in epidemic and non-epidemic periods respectively (P< .01). When investigating all infections caused by S aureus in the study period, the proportion of fusidic resistance in impetigo cases (76%, 152/201) differed significantly from fusidic resistance in other infections (16%, 18/116) (P< 0.01).

Conclusions: Distinctive epidemic outbreaks occurred during the summer of three of the five follow-up years. In outbreaks, S aureus was more frequently the causal agent and the sensitivity to fusidic acid decreased significantly.

A21

Estimating excess mortality from influenza in Norway

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Purpose: Influenza can be a serious and some times deadly disease, especially for certain risk groups. The aim of this work is to study the relationship between the number of reported deaths and clinical influenza activity in Norway, and to estimate the excess mortality due to influenza.

Material and methods: The data consists of the rate of reported influenza-like illness (ILI) in Norway per week per 100,000 population (1975-1998) and per 1,000 consultations (1998-2004). The ILI activity was compared with the total number of all-cause deaths in the same periods. The analysis is done using Poisson regression with regard to the number of deaths, explained by the reported ILI, week and season. An estimator for the excess mortality is suggested as the difference between the observed number of deaths and the predicted mortality, leaving out the influenza contribution in the prediction.

Results: Analysing both the data from 1975 to 98, and the data from 98 to 2004, we find an average estimated excess mortality of about 1100 deaths per season.

Conclusion: In an average season we assume that influenza contributes to approximately 1100 deaths in Norway.

A22

Modeling the impacts of HPV (Human Papilloma Virus) type 16/18 vaccination on the incidence of cervical cancer in Norway

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Background: HPV vaccination is highly efficacious against the development of high risk HPV 16/18 type related infections, the most common cause of cervical cancer. In Norway, a national screening program was implemented in 1995, aiming to screen women aged 25-69 years every 3 years. How effective and cost-effective HPV vaccination alongside screening would be over the long-term remain key issues for decision makers considering program introduction.

Methods: The objective of the present study was to develop a dynamics history model for the spread of HPV infection in Norway, which included sexual mixing. The model outputs on precancerous lesions, cervical cancer incidence and death was subsequently used to estimate the potential cost-effectiveness of implementing an HPV 16/18 type vaccination alongside screening. The model was calibrated against a series of output targets using data from the Norwegian Cancer Registry. We then explored the potential impact of a vaccine given to 12-year-old girls under a base case assumption of 90% efficacy and 90% coverage for a hypothetical time period of 2008−2110.

Results: Introduction of vaccination while maintaining the present day screening program is estimated to yield a reduction in cervical cancer incidence to around 4% (age-adjusted world standard) around year 2100 compared to the current level of around 10%. However, the conclusions are sensitive to the time perspective adopted as well as variations in key model parameters. Some plausible model scenarios will be presented in the talk.

A23

Mathematical modelling of infectious disease

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Traditionally, chronic diseases, like heart disease and cancer, have been major areas of focus in Norway and other Western countries due to their high frequency in the population. However, infectious disease has re-emerged as threats to Western countries and is also gaining more attention due to increased emphasis on Third World medical problems. The SARS epidemics, the threat of avian influenza, the fear of bioterrorism, multi-resistant microbes in hospitals, sexually transmitted diseases, and the continued spread of HIV and resistant tuberculosis, have lead to a new interest in understanding the spreading potential of infectious disease. While there has been a strong tradition for monitoring and controlling the spreading of infectious diseases in Norway, statistical and mathematical modelling has largely been missing. Such modelling has a strong position in other countries, e.g. U.K., USA and Sweden. This makes us less able to utilize the available data and analyse spread of new infectious diseases, like a possible avian flu epidemic. In the U.K. pandemic plan, for instance, there is a constant reference to mathematical modelling.

Modelling infectious disease is very different from modelling non-infectious disease. The classical tools of epidemiology and biostatistics are not valid, since these tools are typically based on the assumption that individuals are independent. Different mathematical and statistical tools are needed, and it is high time that these well-established methods make an inroad into the epidemiological establishment in Norway. The thematic research area BMMS (http://www.med.uio.no/imb/stat/bmms/) have started work in this area and are planning a course and other activities.

A brief overview will be given of the basic concepts in mathematical modelling of infectious disease, with emphasis on the basic reproductive rate, R_0.

B1

Har clusterutredninger noen verdi? Eksemplet kreftsaken ved Rosenborg, NTNU

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Formål: I litteraturen er det ulike meninger om verdien av å utrede sykdomsclustere. Hensikten med vårt bidrag er å belyse nytteverdien ved å bruke en aktuell clusterutredning som eksempel.

Eksemplet: Midt på 1990-tallet ble det oppdaget fire tilfeller av leukemi og lymfom blant tidligere studenter og ansatte ved Botanisk institutt, NTNU. Enda fire tilfeller kom til i de nærmeste årene, og de som var berørt mistenkte et sykdomscluster forårsaket av eksponering (benzen, radionuklider, fikseringsmidler) ved de kjemiske og biologiske laboratoriene på Rosenborg. Flere av de åtte fikk skadeerstatning i årene som fulgte. Saken ble belyst og fulgt opp av regionale media, Saken tok en helt ny vending 4. desember 2006 da VG slo opp saken som "kreftskandalen ved NTNU". Etter 2-3 uker ble det oppnevnt to offentlige utvalg, et juridisk granskingsutvalg og et medisinsk ekspertutvalg. I løpet av få måneder ble det gjennomført en kartlegging av arbeidsmiljøet på kjemiske/biologiske laboratorier ved alle utdanningsinstitusjoner i Norge. Man blåste støvet av forslag til forskning som hadde vært planlagt 8-10 år tidligere, og en utredning av kreftrisiko blant studenter og ansatte ved Rosenborg som hadde blitt initiert i 2004 ble rapportert i løpet av to måneder. VG satte dagsorden. Basert på lister fra NTNU ble insidensen for leukemi og lymfom registrert blant 7189 studenter og ansatte som ble fulgt opp nær 100 000 personår i Kreftregisteret. I alt ble 12 tilfelle identifisert, hvilket var nær forventningsverdien (SIR 1,1, 95% KI 0,6-1,9). Distinkte forskjeller ble funnet mellom undergrupper, med høyeste rate ratioer (RR) for doktorgradsstipendiater (4 tilfeller; RR 4,8, 95% KI 1,1-20,3) og deltakere på grunnkurs i organisk kjemi (8 tilfeller, RR 4,4, 95% KI 1,2-18,8). Den siste kategorien var en av to forhåndsdefinerte grupper fordi det var det eneste kurset hvor NTNU anga at det hadde vært brukt benzen.

Vurdering: Utredningen viste at Rosenborgclusteret ikke var toppen av et isfjell. Et forbehold var at NTNU ikke hadde klart å identifisere studenter og ansatte fra de første årene etter etablering av laboratoriene. Disse er senere identifisert, og analyser av deres kreftinsidens pågår nå. Den høye forekomsten i undergrupper kunne gi støtte til de mistankene som hadde vært reist i saken, men tolkninger om eventuelle kausale sammenhenger blir usikre på grunn av metodiske problemer, blant annet mangel på eksponeringsdata, små tall og utredningens *post-hoc* karakter. De primære målgruppene er de som er direkte berørt som pasienter, pårørende, studenter, ansatte eller arbeidsgivere. Formidling til disse har av flere grunner vært vanskelig. Saken var i stor grad allmennhetens eie hvor media stemplet saken som kreftskandalen, og primærmålgruppene ble lett tilhørere på sidelinjen. Saken ble også spesiell fordi habilitetsspørsmål ble brakt på bane, ikke av de direkte berørte, men av det juridiske granskingsutvalget.

Konklusjon: Rosenborgsaken er eksempel på en clusterutredning som bidrar til å gi svar på spørsmål av allmenn interesse, selv om den hadde begrenset verdi med hensyn til kausale vurderinger. Formidlingen av resultatene ble vanskeliggjort av en betydelig grad av støy fra media og i det offentlige rom.

B2

Cancer's impact on employment and earnings in Norway

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Background: With a growing population of cancer survivors, more attention is being paid to the long-term health and well-being of people living with a history of cancer. Of particular concern is cancer's effect on productivity and work ability, which in turn is important for persons' financial situation, identity, life satisfaction, and social relationships.

Aim: We explored the impact of cancer on employment and gross labor income in entire working age cohorts in Norway. We were particularly interested in possible gender differences, as well as differences related to educational level.

Material and method: With permission from the Norwegian Data Inspectorate, data from three national registries was linked. We thus have reliable data on the entire population with regards to employment, gross labor income, cancer diagnoses, and potential mediating and/or confounding factors. Logistic regression models were used to explore the impact of cancer on employment in 2001. About 567 000 men and 549 300 women 40-59 years old, of whom 34 000 had received a cancer diagnosis, were included. For those employed in 2001, nearly 89%, ordinary least square (OLS) log-linear regression models were used to model the impact of cancer on their gross labor income.

Results: Logistic regression analyses revealed that a cancer diagnosis was strongly associated with *not* being employed in 2001. A reduced likelihood of employment of about 30-40% was seen for both genders ($p < 0.001$). Strongest effects were seen for relatively recent cancer diagnoses. However, certain effects apparently remained even ten years after diagnosis. Non-Hodgkin lymphoma, leukemia, brain, lung, and head-and-neck cancer were most clearly associated with non-employment, for both genders. For those employed, OLS analyses revealed that cancer was associated with a 13% decline in earnings. Reductions up to about 30% were seen for cancers recently diagnosed. Leukemia, brain, lung, colorectal, and head-and-neck cancer were most clearly associated with reductions in earnings (15-50%). Earning declines were strongly associated with educational level, and a difference could thus be inferred to exist between white- and blue-collar workers. Blue-collar workers had a nearly threefold decline in earnings compared to white-collar workers. The effects of cancer appeared relatively similar for men and women. However, certain disparities deserve mentioning. Cancer is more common among working age women, and thus affects a larger proportion, relatively. In addition, income levels are 40% lower among women than men in this study. Percent wise declines in earnings, although fairly similar, may thus impact more strongly on women's financial situation. No differences were observed between married and non-married women.

Conclusion: Cancer negatively affects persons' affiliation to working life and labor earnings. Cancer survivors' lower income is both a result of a greater proportion not being employed, but also a consequence of those continuing working undertaking modifications in their employment that affect their earnings, e.g. working reduced hours or holding jobs providing lower salaries. A particular strong effect was seen for persons with low education. Persons with low education who encounter cancer experience an economic burden and a decline in work relations that may impact on their quality of life, health, and welfare. A broader understanding of cancer survivors' ability to maintain an affiliation to working life and obtain reasonable earnings is warranted in order to accommodate adequate intervention and assistance on the behalf of welfare societies.

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B3

Are occupational factors important determinants for socio-economic inequalities in musculoskeletal pain?

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Background: Socio-economic inequalities in health are well documented, but the impact of different determinants needs to be further explored. The aim of this study was to quantify socio-economic inequalities in low back pain, neck/shoulder pain and arm pain in the general working population in Oslo, and to examine the impact of job characteristics on these inequalities.

Methods: All economically active 30-, 40-, and 45-year-old subjects who attended the Oslo Health Study 2000–2001 and answered questions on physical job demands, job autonomy, and musculoskeletal pain were included (N = 7,293). Occupational class was used as an indicator of socio-economic position. The lower occupational classes were compared to higher grade professionals, and prevalences, prevalence differences (PD), and population attributable fractions (PAF) were calculated.

Results: There were marked socio-economic gradients in musculoskeletal pain, steeper in men than in women. The absolute differences (PD) were largest for low back pain. The prevalence of low back pain in male non-skilled workers was 25 percent points (pp) higher than in higher-grade professionals, compared to a difference of 15 pp in women. For neck/shoulder pain and arm pain the corresponding differences were approximately 15 pp in men and 10 pp in women. Physical job demands and job autonomy explained a substantial proportion of absolute occupational class inequalities in musculoskeletal pain, particularly in low back pain (38% in male skilled and non-skilled workers combined and 47% in females) and in neck/shoulder pain in men (44%). When analysed separately physical job demands explained a larger proportion of occupational class inequalities in low back pain (29% in men and 40% in women), while job autonomy was more important in explaining inequalities in neck/shoulder pain (38% and 24%, respectively). PAF estimates supported the impact of the job characteristics at the working population level, particularly for low back pain.

Conclusions: In this cross-sectional study, physical job demands and job autonomy explained a substantial proportion of occupational class inequalities in self-reported musculoskeletal pain in the working population in Oslo. This indicates that the workplace may be an important arena for preventive efforts to reduce socio-economic inequalities in musculoskeletal pain.

B4

Tilrettelegging av arbeidet og sykefravær midt i svangerskapet i Den norske mor- og barn-undersøkelsen (MoBa)

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Formål: Andelen kvinner i Norge som blir sykmeldt av lege i løpet av graviditeten er ca. 60%, til tross for at dette er en gruppe som vi må forvente er friskere enn gjennomsnittet. Også i andre land er gravides fraværsbehov høyt, selv om graden av inntektssikring ved slikt fravær varierer fra land til land. Muligheten for å bedre forhold i arbeidsmiljøet og gjøre dette tryggere for mor og barn gjennom tilrettelegging av arbeidet har vært vektlagt. Formålet ved studien var for det første å kvantifisere sammenhengen mellom kvaliteter i arbeidsmiljøet og sykefravær midt i svangerskapet, for det andre å undersøke om tilrettelegging i arbeidet er assosiert med redusert fravær.

Materiale og metoder: Studiepopulasjonen besto av gravide kvinner i MoBa. I alt hadde 46 262 deltakere fylt ut spørreskjema både i svangerskapsuke 17 (Q1) og i uke 30 (Q3) mellom 1999 og 2005. Undersøkelsen omfattet de 22 932 gravide som var ansatt i privat eller offentlig virksomhet, som ikke var fraværende fra arbeidet i uke 17, og som i tillegg hadde avgitt data på nøkkelvariablene som ble studert. Utfallet i studien var fravær fra arbeidet mer enn to uker i tiden mellom de to spørreskjemaene (besvart i Q3). Assosiasjonene mellom kvaliteten på fysisk og psykososialt arbeidsmiljø (basert på informasjon i Q1) og 14-ukers risikoen for fravær mer enn to uker ble analysert og estimert som additive risikoforskjeller (RD) i binomialregresjon i Stata. Betydningen av tilrettelegging av arbeidet (tre kategorier: Ikke nødvendig, nødvendig men ikke gjennomført, og nødvendig og gjennomført; basert på informasjon gitt i Q3) for fraværsrisikoen ble også vurdert i binomial regresjon. Alle data i denne kohortstudien var basert på selvrapportering. Analysene ble gjennomført i multivariate modeller, og stabiliteten for RD-estimatene ble rapportert som 95% konfidensintervall (KI).

Resultater: Under oppfølgingen mellom Q1 og Q2 hadde 7072 deltakere hatt fravær av mer enn to ukers varighet fra arbeidet (risiko 0,308). I univariat analyse var fraværsrisikoen klart assosiert med fysisk arbeidsmiljø, psykososialt arbeidsmiljø og arbeidstidsordning. I en modell som inkluderte flere karakteristika ved arbeidet og arbeidsmiljøet var fravær av mer enn to ukers varighet positivt assosiert med svært stressende eller masete arbeid (RD 0,082; 95% KI 0,056 – 0,108), med svært monotont arbeid (RD 0,078; 95% KI 0,053 – 0,102), samt med fysisk tungt arbeid (RD 0,088; 95% KI 0,062 – 0,115). Tilrettelegging av arbeidet (med tilrettelegging nødvendig, men ikke gjennomført som referanse) var assosiert med en reduksjon i fraværsrisiko på 0,107 (95% KI 0,090 – 0,125) i en modell som inkluderte alle karakteristika ved arbeidet som var av betydning. Risikoreduksjonen assosiert med tilrettelegging av arbeidet var særlig markant for gravide med turnus/skift eller arbeid om kvelden eller natten (RD 0,176; 95% KI 0,147 – 0,204).

Vurderinger og konklusjon: Tilrettelegging av arbeidet var assosiert med redusert fravær midt i svangerskapet. Man bør være varsom med tolkninger av funnene fordi deltakelsen i MoBa er lav, i tillegg er alle data i våre analyser basert på selvrapporterte opplysninger. Mens sammenhengen med arbeidsmiljø var basert på data innsamlet før fraværet var dette ikke tilfelle for spørsmål om tilrettelegging som først ble stilt i Q3.

B5

Intellectual performance and disability pension

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Objectives: Reduction of disability pension (DP) and sickness absence represents an important political objective. A special concern is people who are granted a DP during the first years after entering gainful employment. We wanted to examine determinants for such early disability pension with a life course approach. Especially we wanted to focus on the impact of and relation between intellectual performance and educational attainment on DP. We also considered the influence from mental function, BMI and height on DP.

Methods: Through linkage of several national registers containing personal information from birth into adult age we established a longitudinal, population-based cohort. Study participants were all males born in Norway in the period 1967-1976, as registered by the Medical Birth Registry of Norway. Persons who died, emigrated or were granted a DP before age 23 years (when follow-up started) and persons who did not become gainfully employed during the study period (which lasted until the end of 2003) were excluded. "Delayed entry" was used, i.e. persons entered the study in the year of their first income above the level entitling sickness absence compensation after start of follow-up. The main independent variables were intellectual performance (at conscript) and educational attainment at age 23 years; the latter was dichotomized into a low (11 years or less) and high educated group (12 years or more). The study outcome was having been granted a DP. 302 330 persons were included in the study. Adjusted hazard ratios (HR) and the corresponding population attributable risks (PAR) were computed.

Results: 3651 persons (1.2%) were granted a DP. Almost 2/3 of the DPs were due to psychiatric or musculoskeletal disorders. The DP risk was inversely associated with both educational level and intellectual performance. The adjusted PAR values of these two factors were respectively 47% and 35%. For persons with similar intellectual performance, the HR for DP was about 150% higher in the low educated group compared to the high educated group, also when controlled for a wide range of life course factors. The overall DP risk for subjects with low education was about 5 times the risk for high educated persons. Impaired mental function, over- and underweight and short stature were other risk factors, but the effect of these factors were largely reduced after adjusting for educational level and intellectual performance.

Conclusions: DP in young adults was strongly associated with intellectual performance and educational attainment. Achieving an education reduced the DP risk even for people with low intellectual performance and might thus be regarded as a possible preventive measure.

B6

Co-prescribing of warfarin and NSAIDs/aspirin – frequency and problems

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Aims: Use of warfarin carries an inherent risk of bleeding complications. Concomitant use of warfarin and NSAIDs/aspirin is particularly problematic, and these combinations are contraindicated according to guidelines and computer drug interaction programmes. Whether, and to which extent, the combinations are being used in practice has not been elucidated. We aimed to investigate warfarin utilization – along with occurrence of drug-related problems (DRPs) – in hospitalised patients, and with particular emphasis on co-medication with NSAIDs/aspirin.

Methods: Patients were prospectively and consecutively included, by clinical pharmacists, from May to December 2002, from departments of cardiology, geriatrics, respiratory medicine and rheumatology at five general hospitals. The following data was recorded for each patient: age, gender, drugs used on admission, drugs commenced in hospital, the reason for admission, medical history, and relevant laboratory data. Relevant clinical and pharmacological risk factors for the occurrence of DRPs were recorded, for example use of drugs with narrow therapeutic index and reduced renal and liver function. The clinical pharmacists recorded the data based on the patients' notes, the cardex, and participation on the ward multidisciplinary morning meetings.

Results: Of the 827 patients included in the study 15% (128 patients) were on warfarin treatment. The warfarin users were, compared to the non-users, older, 76.2 vs 69.9 years, used more drugs on admission, 5.7 vs 4.4 per patient, and had more clinical/pharmaceutical risk factors, 2.8 vs 1.4 (all: $p < 0.001$). A total of 1694 DRPs (an average of 2.4 DRPs per patient) were registered for the non-warfarin users, while 434 DRPs (an average of 3.4 DRPs per patient) were found among the warfarin users. The most frequent DRPs registered in the warfarin group were drug-drug interactions, need for monitoring, and non-optimal dose, representing 21%, 15% and 13%, respectively, of the total number of DRPs registered for the group. The excess number of DRPs in the warfarin group was solely linked to warfarin itself; after omitting these, 2.5 DRPs per patient were found. Of the 128 patients prescribed warfarin 27 patients (21%) were co-prescribed aspirin or another NSAID; 17 low-dose aspirin, 6 traditional NSAIDs and 4 COX-2 inhibitors. A total of 325 DRPs (an average of 3.2 DRPs per patient) were found in the warfarin-only group. In the warfarin/NSAIDs/aspirin group 109 DRPs (an average of 4.0 DRPs per patient) were found. Despite the high number of DRPs in the latter group the difference was not statistically significant, presumably due to few individuals in the group. The most frequent DRPs registered for the warfarin/NSAID/aspirin group were interactions and monitoring, representing 24% and 17%, respectively, of the total number of DRPs recorded for this group.

Conclusion: As many as 15% of patients hospitalised in departments of internal medicine/rheumatology used warfarin, and a sizeable proportion of these – every fifth patient – were prescribed aspirin/NSAIDs concomitantly; the extensive utilisation of this combination contrasts with general recommendations. Use of warfarin markedly increased the frequency of DRPs, and concomitant use of aspirin/NSAIDs was associated with additionally increased occurrence of DRPs. In the latter group nearly twice as many DRPs were found compared to the numbers of DRPs observed in the non-warfarin users.

B7

Blødninger knyttet til warfarinbruk: rapporter fra bivirkningsregisteret i 2003-2006

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Formål: Warfarin er effektivt når det gjelder å forhindre blodpropp, men er også det legemidlet som forårsaker flest årlige dødsfall meldt til det norske bivirkningsregisteret. Flere studier har vist at risikoen for blødninger er størst i oppstartsfasen med warfarinbehandling. Dette ble også funnet i en tidligere norsk studie basert på analyse av rapporter fra bivirkningsregisteret i perioden 1990-2000. Vårt inntrykk i bivirkningsarbeidet ved Regionalt legemiddelinformasjonssenter Øst (RELIS Øst) er imidlertid at flertallet av blødninger som meldes ved bruk av warfarin, opptrer etter lang tids bruk. Hensikten med vår studie er å beskrive alle blødningsbivirkningene meldt til bivirkningsregisteret ved bruk av K-vitamin-antagonister i perioden 2003-2006.

Metode: Alle spontanrapporterte blødningsbivirkninger innrapportert til det norske bivirkningsregisteret i perioden 2003-2006 ble registrert.

Resultater: Det ble funnet 289 rapporter på blødningsbivirkninger ved samtidig bruk av K-vitamin-antagonister; en melding med dikumarol og 288 meldinger med warfarin. Gjennomsnittsalderen var 75,9 år og 40% var kvinner. Av bivirkningene var 60% cerebrale, 24% gastrointestinale og 16% lokalisert til andre organsystemer. Førtiåtte prosent av blødningene var fatale. I 22% av meldingene var warfarin det eneste rapporterte legemidlet, 48% brukte 2-5 legemidler og 30% brukte mer enn 5 legemidler på blødningstidspunktet. Flertallet av de meldte blødningene (57%) opptrådte etter mer enn ett års bruk av warfarin. Bare 30 blødninger skjedde i løpet av første behandlingsmåned og av disse opptrådte 59% i løpet av de første 5 dagene.

Konklusjon: I perioden 2003-2006 opptrådte majoriteten av blødningene (57%) etter mer enn ett års bruk av warfarin. Dette er i sterk kontrast til en tidligere norsk studie fra bivirkningsregisteret, der flertallet av blødningene opptrådte i løpet av første behandlingsmåned i perioden 1990-2000. Forskjellen i behandlingsvarighet før blødning mellom disse to periodene kan skyldes endret bruk av warfarin og komedikasjon eller endret rapportering fra legene. Vår studie viste også at i flertallet av de rapporterte blødningsmeldingene brukte pasientene ett eller flere andre legemidler i tillegg til warfarin.

B8

Genetic and clinical risk factors for venous thrombosis in pregnancy

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Background: Venous thrombosis **(**VT) is a multicausal disease and pregnancy increases the risk by a ten-fold. The ante- and postnatal period display different risks of VT. The purpose of our study was to assess risks of VT among carriers of factor V Leiden and Prothrombin G20210A mutation in relation to clinical risk factors for ante- and postnatal VT.

Materials and methods: Invited to this study were 615 women with a validated pregnancy related diagnosis of VT and 1230 controls. The controls were selected from the Medical Birth Registry of Norway. After two reminders, 342 women with their first lifetime VT (response rate 59%) and 353 controls (response rate 33%) met for blood sampling and completion of a questionnaire. Non-responding and responding cases and controls did not differ in major demographic or other established risk factors for pregnancy related VT. Data were analysed separately for ante- and postnatal risk of VTE in SPSS with chi-square test and stepwise forward logistic regression.

Results: Disease manifestation was evenly distributed during first, second and third trimester and postnatally among carriers of hetero- and homozygous factor V Leiden and heterozygous Prothrombin G20210A mutation, whereas carriers of the combined heterozygous factor V Leiden and heterozygous prothrombin gene mutation displayed a significant higher risk for disease manifestation during first trimester than later in pregnancy or the puerperium. Immobilisation and assisted reproduction remained strong antenatal risk factors after adjusting for congenital risk factors, as did immobilisation, preeclampsia, haemorrhage and infection as postnatal risk factors.

Conclusion: Factor V Leiden mutation and Prothrombin gene mutation were independent risk factors of both ante- and postnatal VT. We did not discover any interaction between congenital and clinical risk factors indicating that clinical risk factors had no initiating/additive effect on congenital factors in prediction of VT.

B9

Statinforskriving etter utdanningsnivå

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Formål: Studere insidensen av statinforskriving etter utdanningsnivå.

Materiale og metoder: Helseundersøkelsene i Oslo (HUBRO) og i Oppland og Hedmark (OPPHED) 2000-2001 omfattet personer i alder 30, 40, 45, 46, 59-61 og 75-76 år. I alt 19 784 menn og kvinner i alder 40-61 år møtte til undersøkelse. Samlet frammøteprosent i denne aldersgruppen var 54%. Sentrale kardiovaskulære risikofaktorer, inklusive kolesterol, ble registrert. Videre rapporterte deltakerne om utdanningsnivå, sin kardiovaskulære historie og hvorvidt de var på behandling med kolesterolsenkende medisin. Helseundersøkelsene er koblet mot Reseptregisteret 2004-2006 og 12 409 deltagere som aldri hadde brukt kolesterolsenkende medisin og som ikke rapporterte kardiovaskulær historie ved undersøkelsen, inngikk i studien. Justert insidens ratio ble estimert ved poisson-regresjon.

Resultater:

Tabell. Insidens av statinforskriving

	Antall besvart	Insidens (%)	Insidensratio Ujustert	Justert*	95% CI
Alder 40,45,46					
Menn					
Grunnskole	567	8,5	1,00	1,00	
Videregående	1499	7,7	0,91	0,97	(0,71-1,32)
Univ/Høgskole	1628	5,1	0,60	0,78	(0,55-1,09)
Kvinner					
Grunnskole	761	5,7	1,00	1,00	
Videregående	1923	3,1	0,54	0,83	(0,56-1,25)
Univ/Høgskole	2211	2,7	0,47	0,97	(0,63-1,49)
Alder 59-61					
Menn					
Grunnskole	512	18,2	1,00	1,00	Ref
Videregående	541	20,1	1,10	1,04	(0,82-1,31)
Univ/Høgskole	666	15,3	0,84	0,89	(0,69-1,14)
Kvinner					
Grunnskole	792	16,4	1,00	1,00	Ref
Videregående	654	13,5	0,82	0,94	(0,74-1,19)
Univ/Høgskole	655	9,3	0,58	0,78	(0,59-1,04)

* Justert for total kolesterol, systolisk blodtrykk, røyk (ja, nei) og fylke (Oslo vs Hedmark/Oppland)

Det var lavest insidens blant dem med høyest utdanning. Forskjellene i insidens ble klart mindre når det ble justert for de sentrale risikofaktorene.

Konklusjon: Personer med høyere utdanning har lavere sjanse for å bli forskrevet statinbehandling. Dette kan forklares ved forskjeller i kardiovaskulære risikoprofiler.

B10

Childhood cod liver oil consumption is negatively associated with bone density in peri- and postmenopausal women. The HUNT study

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Aim: To study whether recalled childhood cod liver oil intake relates to variations in bone mineral density (BMD) measured at the forearm in middle-aged women.

Material and methods: In 2001, a total of 3,052 women aged 50-70 years (mean age 59.4 years) attended forearm BMD measurement as participants in a sub-study of the population-based Nord-Trøndelag Health Study, (HUNT). Recalled childhood and current cod liver oil intakes were self-reported. Differences in BMD and odds ratio for low BMD (>1 SD below age-specific mean values) was assessed in four categories of childhood cod liver oil intake: no intake, irregular use, regular fall and winter use, and throughout the year.

Results: Women reporting no childhood cod liver oil intake had statistically significantly higher BMD than those with any ingestion of cod liver oil. The odds ratio for low BMD in women reporting cod liver oil throughout the year compared to women with no intake was 2.3 (95% CI 1.4; 3.9), adjusted for body mass index, smoking, menopausal status, oestrogen use and current milk consumption. There were indications of a negative dose-response effect of childhood cod liver oil intake on bone.

Conclusion: In women aged 50-70 years, their childhood cod liver oil intake may be negatively related to forearm BMD, possibly because of the previous high vitamin A concentration in cod liver oil. Further studies should investigate whether cod liver oil intake is associated with the high fracture rates in the Nordic countries.

B11

Fish consumption and colon cancer risk, with focus on lean fish. The Norwegian Woman and Cancer study (NOWAC)

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Introduction: Recent studies have shown a decreased risk of colon cancer with consumption of fish. However, most studies on fish consumption do not distinguish between lean and fatty, or between poached and fried fish. In this study we investigates the association between consumption of fish and colon cancer, with special focus on lean fish, in The Norwegian Women and Cancer (NOWAC) study.

Subjects and methods: We analysed total fish, fatty fish, lean fish and fish products. Lean fish was further divided into poached and fried fish. 63,914 women were included in the analysis, of which 254 colon cancer cases. The participants completed a dietary questionnaire between 1996–99 and were followed up for incidence of colon cancer until December 2004.

Results: There were no association between total fish, fatty fish, lean fish, or fish products and colon cancer. When dividing into fried and poached lean fish, we found no association between fried lean fish and colon cancer. For poached fish we found an increased risk in the third tertile of poached lean fish consumption (RR 1.46, 95% CI 1.04-2.06).

Conclusion: The present study does not support the hypothesis of a protective effect of fish on colon cancer risk. An increased risk was seen for high consumption of poached lean fish. The mechanisms for this are unknown.

B12

Breastfeeding, diet and waist circumference

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Background: Obesity is a major contributor to the global burden of chronic disease and disability, and has reached epidemic proportions globally. Maternal obesity is associated with increased complications throughout pregnancy, and increased health risks to both mother and child. Breastfeeding has been related to increased weight loss among lactating mothers in the postpartum period and recently also to decreased risk of type 2 diabetes. We therefore questioned whether prolonged breastfeeding is a health-promoting behaviour that contributes to decreased risk of obesity.

Methods: A total of 206 women participated in the cross-sectional Norwegian EBBA study (Energy Balance and Breast cancer Aspects-study) during 2000-2002. The study subjects had to meet the following criteria: 25 to 35 years of age; self-reported regular cycles (cycle length, 22-38 days) within the previous 3 months; no use of hormonal contraceptives and no pregnancy or breast-feeding over the previous 6 months; no infertility, gynaecologic or chronic disorders (i.e., diabetes, hypothyroidism/hyperthyroidism). Among the 206 women, 101 women had given birth and thus were included in the present study. Information on marital status, age, education, reproductive history, length of breastfeeding for each child, height and weight at 18 years of age, past and current lifestyle including leisure activity and tobacco use was collected by self-recall and interview. In a validated precoded food diary, developed for the present study population, dietary data were collected on 7 different week days during the menstrual cycle. Women were asked to record the type and the portion size of every food item consumed during 24 hours on day 3-6 and day 21-23 in the menstrual cycle. The average daily intake of energy and nutrients were computed using a food database and software system developed at the Department of Nutrition, University of Oslo, Norway. The women had a clinical examination the first possible day after onset of the menstrual bleeding, day 1-5, that included height, weight, waist and hip measurement. BMI (kg/m^2), waist circumference and waist-hip-ratio were used as measures for relative weight.

Results: In the EBBA cohort, 101 pareous women aged 25-35 years (mean 32.33) reported lifetime duration of lactation; 96% had ever breastfed (range 1-36 months), with a mean breastfeeding length of 10.36 months for each child (median: 10.33). Mean BMI was 25.0, mean weight 70 kg, mean waist circumference 81.8 cm, and mean waist-hip-ratio was 0.78 m. Breastfeeding was positively associated with energy intake ($p < 0.05$) and overall negatively associated with waist-hip-ratio ($p < 0.01$). When dividing the women by median split, women who breastfed < 10 months were compared with women who breastfed ≥ 10 months. The women who breastfed < 10 months differed significantly from women who breastfed for ≥ 10 months in years of education ($p=0.05$), energy intake ($p=0.08$), intake of protein ($p=0.03$) and carbohydrates ($p=0.03$). Women breastfeeding for ≥ 10 months, were in general less overweight. The mean BMI was 25.4 among those who breastfed < 10 months vs. 24.7 ≥ 10 months ($p=0.34$), mean waist circumference was 84.0 cm among those who breastfed < 10 months vs. 80.0 cm ≥ 10 months ($p=0.05$) and mean waist-hip-ratio was 0.80 m among those who breastfed < 10 months vs. 0.77 ≥ 10 months ($p=0.01$).

Conclusion: These results support the hypothesis that prolonged breastfeeding is a health-related behaviour that enhances the women's anthropometric measurements, especially waist and waist-hip-ratio. Breastfeeding is also associated with energy intake and education.

B13

The obesity and diabetes epidemics and the risk of cancer: An overview

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The prevalence of overweight (body mass index, BMI, between 25 and 30 kg/ m^2) and obesity (BMI of 30 kg/m^2 or higher) is increasing rapidly worldwide, especially in developing countries and countries undergoing economic transition to a market economy. One consequence of obesity is an increased risk of developing type II diabetes.

Overall, there is considerable evidence that overweight and obesity are associated with risk for some of the most common cancers. There is convincing evidence of a positive association between overweight/ obesity and risk for adenocarcinoma of the oesophagus and the gastric cardia, colorectal cancer, postmenopausal breast cancer, endometrial cancer and kidney cancer (renal-cell). Premenopausal breast cancer seems to be inversely related to obesity. For all other cancer sites the evidence of an association between overweight/obesity and cancer is inadequate, although there are studies suggesting an increased risk of cancers of the liver, gallbladder, pancreas, thyroid gland and in lymphoid and haematopoietic tissue.

Far less is known about the association between diabetes mellitus type I (also called insulin dependent diabetes mellitus or juvenile diabetes), type II diabetes (called non-insulin dependent diabetes mellitus or adult onset diabetes mellitus) and cancer risk. The most common type of diabetes mellitus, type II, seems to be associated with liver and pancreas cancer, and probably with colorectal cancer. Some studies suggest an association with endometrial and postmenopausal breast cancer. Studies reporting on the association between type I diabetes mellitus, which is relatively rare in most populations, and cancer risk are scanty, but suggest a possible association with endometrial cancer.

Overweight and obesity, as well as type II diabetes mellitus are largely preventable though changes in lifestyle. The fundamental causes of the obesity epidemic – and consequently the diabetes type II epidemic – are societal, resulting from an environment that promotes sedentary lifestyles and over-consumption of energy. The health consequences and economic costs of the overweight, obesity, and type II diabetes epidemics are enormous. Avoiding overweight and obesity, as well as preventing type II diabetes mellitus, is an important purpose to prevent cancer and other diseases. Prevention of obesity and type II diabetes should begin early in life, and be based on the life-long health eating and physical activity patterns. Substantial public investments in preventing overweight, obesity and type II diabetes mellitus are both appropriate and necessary in order to have a major impact on their adverse health effects including cancer.

B14

Baby swimming and respiratory health

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Background: It is hypothesised that there may be a relationship between environmental exposures from baby swimming in indoor pools and infant respiratory health outcomes. However, data are sparse and inconclusive.

Aim: The objective was to estimate the effect of baby swimming the first six months of life on respiratory diseases from 6 to 18 months.

Material and methods: We used data from the Norwegian Mother and Child Cohort Study (MoBa) conducted by the Norwegian Institute of Public Health in children followed from birth to the age of 18 months (n =29887) (www.fhi.no/tema/morogbarn). The main health outcomes were maternal reports of: lower respiratory tract infections (LRTI), otitis media and wheeze between 6 and 18 months of age. Wheeze was defined as an episode of chest congestion or whistling in the chest; lower respiratory tract infections (LRTI) included RS-virus, bronchiolitis, bronchitis or pneumonia, and otitis media, was defined as at least one episode. All outcomes were dichotomized into yes *versus* no. The main exposure was maternal reports of their children's participation in baby swimming at age 6 months. The question was: "Does your child participate in baby swimming?", The children were categorized into baby swimming (yes) *versus* no baby swimming (no). We used logistic regression analysis to estimate the association between baby swimming and LRTI, wheeze and otitis media adjusting for different covariates.

Results: Participation in baby swimming was common, about 25%. The prevalence of baby swimming was also almost similar among children with and without maternal history of atopy (26.7% *versus* 25.4%). The prevalence of lower respiratory tract infections (LRTI), wheeze and otitis media in children from 6 to 18 months was respectively 13.2%, 39.9%, and 30.3%. The history of maternal atopy was 25.6%. Children who took part in baby swimming were not more likely to have LRTI, otitis media, or to wheeze. However, children with atopic mothers who attended baby swimming tended to have an increased risk wheeze, aOR 1.20 (1.07-1.35), whereas they did not have an increased risk of LRTI, aOR 1.06 (95%CI 0.91-1.23), or otitis, 1.04 (0.92-1.17).

Conclusion: The results do not provide much evidence to support the hypothesis that there may be a causal link between baby swimming and infant respiratory diseases up to age 18 months. We underline, however, that there tended to be an effect in children of atopic mothers. Our study investigates only the effect of baby swimming before age 6 months and respiratory disease from 6 months up to age 18 months.

B15

Maternal prepregnancy obesity and respiratory illness in early childhood

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Aim: Maternal obesity is a risk factor for adverse outcomes of pregnancy, and obesity is associated with respiratory and atopic illness in adults and children. The authors aim was to explore possible effects of maternal adiposity during pregnancy on early childhood respiratory health. The authors examined associations between a high maternal prepregnancy body mass index (BMI) and the incidence of lower respiratory tract infections and wheeze up to18 months of age, taking into account the possible influence of pregnancy outcomes and complications in pregnancy.

Methods: The study is based on the Norwegian Mother and Child study (MoBa), a population based cohort study which will include 100,000 pregnant women. The study population consisted of 33,192 children born between 1999 and 2005 with follow-up through 18 months of age. We were interested in exploring direct and indirect effects of maternal BMI on childhood respiratory outcomes, and applied a path analyses, with one path directly from maternal BMI to childhood respiratory outcome, and other paths going via different obstetric problems (complications in pregnancy, low birth weight, premature birth, and caesarean section). All the path equations included the maternal background variables (asthma, age, income, education, marital status, smoking in pregnancy, parity, multiple births) and gender, and the equations including the respiratory outcomes also included postnatal variables, such as postnatal parental smoking, breastfeeding and kindergarden attendance. By including paths for both gestational age and low birth weight, the effects of BMI mediated through these intermediates were estimated and included in the total effects.

Results: Positive associations between maternal obesity (BMI $\geq$ 30) and lower respiratory tract infections and wheeze in offspring up to18 months in crude analysis weakened after adjustment for lifestyle factors. However, a small direct effect of maternal obesity on wheeze (Risk difference (RD) = 0.033, 95% confidence interval: 0.012, 0.053) remained significant after adjustment for lifestyle factors, pregnancy complications and birth outcomes, suggesting that maternal adiposity during pregnancy may have a direct effect on wheeze in early childhood.

Conclusion: Maternal obesity during pregnancy was related to respiratory disease in children up to 18 months in bivariate analyses. However, lifestyle and maternal characteristics associated with high maternal BMI attenuated the associations. For wheeze, a modest association with maternal prepregnancy obesity could not fully be explained by other factors, indicating that obesity in pregnancy might have a small direct effect on childhood wheeze.

B16

Long-term outdoor air pollution at home address and asthma in schoolchildren in Oslo

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Objective: Several studies have demonstrated associations between short-term air pollution exposure and asthma symptoms in children already diagnosed with asthma. Whether long-term exposure to air pollution causes asthma is less clear. Furthermore, to reduce misclassification of exposure, more accurate methods for exposure estimation is needed. The aim is to study the relation between long-term exposure to outdoor air pollution at home address and asthma in 9-10-year-old children in Oslo.

Material and methods: Children from the Oslo Birth Cohort were followed up in 2001-2002. Simultaneously a cross-sectional study of all children born in 1992 and living in Oslo in August 2001 was carried out. Of these children, 3503 children provided information on asthma onset, wheeze and potential confounding variables by a parental questionnaire. Only children who had lived in Oslo since birth were included in our study. Exposure to outdoor air pollution was assessed by the EPISODE model, a dispersion model based on emissions, meteorology, topography, and air pollution concentrations measured at regional background stations in southern part of Norway. The model calculates concentrations for each km^2 and at thousands of geographical points with busy traffic. Exposure was assigned according to each child's home address. Long-term exposure to nitrogen dioxide (NO_2) was calculated as the mean concentration in the first year of life, in time from birth to first asthma and in last year. Cox proportional hazard regression model was used to analyse time to first asthma, adjusting for relevant potential confounders. To analyse current wheeze, multiple logistic regression analysis was used.

Results: The NO_2 concentrations at home address ranged from 1.5 to 84.0 $\mu g/m^3$ for exposure in the first year of life and from 1.4 to 65.1 $\mu g/m^3$ for last year's exposure. Preliminary results indicate no associations between long-term exposure to residential outdoor air pollution and time to first asthma, with similar results for current wheeze.

Conclusion: Moderate levels of long-term exposure to traffic-related air pollution may not have any effect on asthma and wheeze in schoolchildren in Oslo.

B17

Associations between environmental exposures and serum Clara cell protein

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Background: Cardiopulmonary morbidity and mortality has been associated with several environmental exposures. One mechanism behind this association could be pathophysiological changes in the cardiopulmonary system induced by inflammatory responses.

Material and methods: In the present study we explored associations between environmental exposures and serum concentrations of lung Clara cell protein 16 kiloDalton, a biomarker that has recently been used to assess altered lung epithelial permeability.

Results: Serum Clara cell protein concentrations were inversely associated with both numbers of cigarettes smoked per day and numbers of pack-years of smoking. No associations were found between long-term exposure to ambient air pollutants and serum concentrations of serum Clara cell protein. Still, short-term variations in both ambient air pollution and temperature were associated with increases in serum Clara cell concentrations. All findings were robust when other factors were adjusted for.

Conclusions: These findings suggest both chronic and acute associations between environmental exposures and the epithelial barrier permeability in the lungs of elderly men.

B18

Forskrivningspraksis av medikamenter på blå resept for pasienter med obstruktiv lungesykdom

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Formål: Kartlegge primærlegenes forskrivningspraksis av medikamenter på blå resept for pasienter med obstruktiv lungesykdom i perioden 1995-2004.

Materiale og metode: Data ble innsamlet direkte fra elektroniske pasientjournaler hos 8 legesenter i Sør- og Nord-Trøndelag. Vi identifiserte alle pasienter, 7 år og eldre, med diagnosene astma og/eller KOLS i perioden 1995-2004. Opplysninger om forskrivninger av refusjonsberettigete medikamenter var basert på journalførte medikamentnavn, koder basert på Anatomisk Terapeutisk Kjemisk legemiddelregister (ATC-koder) og refusjonspunkt, § 9.2 ("Asthma bronchiale og obstruktive kroniske lungesykdommer"). Analysene i studien er basert på det totale antall pasienter registrert med allmennlegekontakt hvor de aktuelle diagnosene er registrert innenfor hvert kalenderår. Resultatene er gitt i andelen pasienter som fikk forskrevet medikamenter på blå resept samme kalenderår som diagnosen var brukt i allmennpraksis. I tillegg ble det utført analyser på undergruppene inhalasjonssteroider (ATC-kode R03BA) og kombinasjonspreparater av inhalasjonssteroider og langtidsvirkende beta2-agonist (ATC-kode R03AK).

Resultater: I alt 4486 pasienter inngikk i analysematerialet. Andelen pasienter som fikk forskrevet medikamenter på blå resept var høy gjennom hele studieperioden for både KOLS- og astmapasienter, selv om en liten nedgang ble observert fra 1995 til 2004. Andelen sank fra 81% til 76% for KOLS-pasienter og 85% til 77% for astmapasienter. Utviklingen i forskrivningsmønstret viste en markant endring fra inhalasjonssteroider til kombinasjonspreparater. Andelen KOLS-pasienter registrert med forskrivning av inhalasjonssteroider gikk ned fra 62% i 1995 til 13% i 2004, og for astmapasienter fra 64% til 24%. I takt med nedgangen av forskrivninger på inhalasjonssteroider økte andelen kombinasjonspreparater, i 2004 fikk 50% av KOLS-pasientene og 45% av astmapasienter forskrevet kombinasjonspreparater. Den samlede andelen KOLS-pasienter som fikk forskrevet rene inhalasjonssteroider eller/og kombinasjonspreparater var derimot uendret gjennom hele studieperioden (64% i 1995 mot 63% i 2004). For astmapasienter fant vi en liten økning i den samlede bruken av inhalasjonssteroider og kombinasjonspreparater i studieperioden (64% i 1995 mot 69% i 2004).

Konklusjon: Det ble i perioden 1995-2004 observert en overgang i forskrivningsmønstret fra inhalasjonssteroider til kombinasjonspreparater for både astma- og KOLS-pasienter. I henhold til norske forskrivningsregler er inhalasjonssteroider og kombinasjonspreparater forhåndsgodkjent for refusjon ved astma. Ved KOLS har ikke inhalasjonssteroider godkjent medisinsk indikasjon, mens kombinasjonspreparatene har godkjent medisinsk bruksområde for alvorlig KOLS med hyppige forverringer. Forskrivningsmønsteret som framkom i vår studie fra tiden før refusjonsendringene trådte i kraft i juli 2006, tyder på at oppsplittingen av tidligere refusjonspunkt § 9.2 kan komme til å virke etter hensikten ved at et overforbruk av kombinasjonspreparater til KOLS-pasienter med mild og moderat KOLS opphører. Krav til individuell søknad for refusjon av kombinasjonspreparater ved KOLS, har bidratt til at KOLS-pasienter har sluttet med slik medisin, men det kan bidra til manglende bruk der slik egentlig er indisert, samtidig som leger kan la seg friste til å bruke astmadiagnose for å unngå papirarbeid. En ny kartlegging av primærlegenes forskrivningspraksis, med data fra både før og etter endringer i refusjonssystemet, vil derfor være et viktig bidrag i arbeidet med å oppnå korrekte behandlingstiltak for astma- og KOLS-pasienter.

B19

Consumption of fruit and berries is inversely associated with carotid atherosclerosis in elderly men[1]

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Epidemiologic data suggest that fruit and vegetable consumption is associated with a lowered risk of cardiovascular disease. We assessed the association between the intima-media thickness (IMT) of the carotid artery and dietary intake of vegetables, fruit and berries in elderly men with a high risk of cardiovascular disease. Subjects (mean age 70 ± 5 years) were survivors from a cohort of 1 232 men that participated in the Oslo Diet and Antismoking Study in 1972-3. Measurements of the carotid IMT by high resolution B-mode ultrasound, risk factor assessment and dietary data based on a food frequency questionnaire were collected in 1997-9. Complete dietary and ultrasound data were available for 547 subjects. The carotid intima media thickness in the highest quartile of dietary intake of fruit and berries was 0.89 ± 0.18 mm compared to 0.96 ± 0.25 in the lowest quartile giving a mean difference of 0.075 mm (SE 0.027; P=0.033). In multivariate regression analysis increased intake of fruit and berries remained inversely associated with intima media thickness after adjustment for age, cigarette smoking, dietary cholesterol and saturated fat, consumption of milk, cream and ice cream and energy intake (multivariate regression coefficient = 0.257; R^2=0.066, SE = 0.209, P<0.001). The difference of 348 g of fruit and berries/day between the lowest and highest quartile of intake was associated with a 5.5% adjusted difference in mean IMT. These findings suggest that consumption of fruit and berries may be protective against carotid atherosclerosis in elderly men at high risk of cardiovascular disease.

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B20

Validiteten av diabetes mellitus-diagnosen i Medisinsk fødselsregister

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Gravide kvinner med type 1 diabetes har økt risiko for komplikasjoner i svangerskapet, medfødte misdannelser og dødfødsel. Data fra medisinsk fødselsregister (MFR) har vært grunnlag for viktige publikasjoner om risiko for komplikasjoner hos gravide kvinner med diabetes. Vi presenterer data om validiteten til diabetesdiagnosen i MFR. Av fødsler til og med 1998 med kjent type 1 diabetes før svangerskapet basert på opplysninger fra Norsk diabetesregister (NDR), ble 97% registrert som diabetes før svangerskapet i MFR (gammelt registreringsskjema). For fødsler 1999-2004, ble 94% kodet som pre-gestasjonell (type 1- eller type 2-) diabetes. Ved sammenligning med sykehusjournalen til kvinner identifisert i MFR med diabetesdiagnose før svangerskapet (fødsler i 1998) ble diabetes før svangerskapet ifølge MFR, bekreftet i journalen i 80% av tilfellene. Av fødsler kodet med svangerskapsdiabetes ble 89% bekreftet i journalen. Vi konkluderer med at sensitiviteten for pre-gestasjonell diabetes er meget god, spesielt for fødsler før 1999, men MFR kan for den perioden ikke brukes til å klassifisere pre-gestasjonell diabetes hos mor som type 1- eller type 2 diabetes. For fødsler fra og med 1999 kan type diabetes spesifiseres, men prediktiv verdi for disse diagnosene er ikke undersøkt. Prediktiv verdi for diagnosen pre-gestasjonell diabetes i MFR for fødsler i 1998 er ikke optimal, men akseptabel for et rutineregister som ikke har diabetes som hovedfokus.

B21

Patterns in development of islet autoantibodies at 3, 6, 9 and 12 months of age in children from the general population carrying the type 1 diabetes high-risk HLA genotype – The MIDIA study

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Aims: Norway is among the countries in the world with highest incidence of childhood-onset type 1 diabetes, with a cumulative incidence by age 15 of about 0.4%. The disease results from destruction of the insulin producing beta-cells in the pancreas, and clinical disease is preceded by preclinical period of variable length where so-called islet autoantibodies can be detected in the circulation. There are several susceptibility genes for type 1 diabetes, but well established combinations of susceptibility alleles in the HLA complex are by far the quantitatively most important, and these are most frequently used for identification of high-risk individuals for prospective studies. Limited published data are available on the dynamic pattern of islet autoantibody development at 3, 6, 9 and 12 months of age. We present islet autoantibody data from the 526 first enrolled children in the MIDIA study, who all carry the type 1 diabetes high-risk *HLA* genotype *DRB1*0401-DQA1*03-DQB1*0302/DRB1*03-01-DQA1*05-DQB1*02 ("DR4-DQ8/DR3-DQ2")*, identified after screening about 25,000 newborns from the general Norwegian population.

Materials and methods: Autoantibodies to insulin (IAA), glutamic acid decarboxylase65 (anti-GAD) and the protein phosphatase related molecule IA2 (anti-IA2) were measured with radiobinding assays in blood samples collected when the children were aged 3, 6, 9 and 12 months, and then annually.

Results: Among 526 children tested for islet autoantibodies at least once (range 1-14 samples from each child, median 4), the median follow-up time from birth was 12 months (range 2.9 months to 5.3 years), and a total of 2104 samples were tested. One-hundred and seven children were positive for at lease one islet autoantibody at least once. Excluding maternal (auto)antibodies, 14 children were positive in at least two consecutive samples, 12 of which were positive for ≥2 islet autoantibodies at least once. In addition, 2 children were positive for multiple autoantibodies in their most recent sample. Five children developed type 1 diabetes (at median age 1.3 years) during the current follow-up.

Conclusion: Development of persistent islet autoantibodies associated with increased risk of type 1 diabetes is not uncommon in children from the general population carrying the high-risk HLA genotype aged under 12 months, may develop as early as at six or nine months of age.

B22

Cause-specific death in women diagnosed with cancer during pregnancy or lactation

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Background: Cancer diagnosed during pregnancy or lactation may be associated with increased risk of cause-specific death.

Materials and methods: In this population-based cohort study with data from the Cancer Registry and the Medical Birth Registry of Norway, 45 511 women, aged 16-49 years, diagnosed with their first malignancy from 1967-2004, were allocated to one of 4 groups:

Group 1: No pregnancies after cancer (reference group)
Group 2: Cancer diagnosed during pregnancy
Group 3: Cancer diagnosed during lactation; until 6 months post-partum
Group 4: Pregnant after cancer

A Cox proportional hazards model with time-dependent covariates assessed cause-specific survival for all cancer types combined and for the most frequent cancer types in young women. The common cancer types for these women are breast cancer, cervical cancer, malignant melanoma, ovarian cancer, lymphoma and leukaemia, brain tumours and thyroid cancer. The most frequent malignant diseases during pregnancy and lactation are breast cancer and malignant melanoma. The groups 1-3 were followed from the date of diagnosis, group 4 from date of first delivery after cancer. All groups were followed to date of death, date of emigration, to the age of 60 years or until Dec 31, 2004. The multivariate analyses were adjusted for age at diagnosis, initially extent of disease and diagnostic periods.

Results: For all cancer types combined, the risk of cause-specific death was decreased for group 4, (HR 0.5, 95% CI 0.4-0.6) with no difference between the other groups. Breast cancer patients diagnosed during lactation were the only group which displayed a significantly increased risk of dying from their cancer, HR 1.9, 95% CI 1.3-2.7. Women with malignant melanoma had no significantly increased risk of cause-specific death, but women diagnosed during pregnancy had a slightly elevated risk. The risk of cause-specific death decreased during the three diagnostic periods (1967-1984, 1985-1994 and 1995-2004).

Conclusion: The diagnosis of most cancer types during pregnancy or lactation does not increase the risk of cause-specific death. Breast cancer diagnosed during lactation represents an exception with increased cancer-specific death. The normal changes in the breast tissue due to pregnancy and breastfeeding might lead to delay in diagnosis of a malignant tumour. “The healthy mother effect” in women pregnant after cancer was confirmed for all cancer types combined. The same pattern with decreased cancer-specific death was seen for breast cancer and malignant melanoma when analysed singularly, although this was not significant.

B23

Serum vitamin D (calcidiol) and prognosis of prostate cancer

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Background: Based on repeated observations that cancer mortality and incidence vary according to climate and sun exposure, vitamin D were proposed to influence the cancer process. For several cancer forms, an adequate level of vitamin D may inhibit the progression of the cancer disease. Mainly the previous studies are ecological, with no information about individual vitamin D levels.

Objective: The present study aim to investigate whether the individual serum level of calcidiol, at the time of diagnosis, is a prognostic factor in patient with prostate cancer.

Material and method: The study group includes 160 patients with prostate cancer, all histologically verified and registered at the Cancer Registry of Norway in the period 1984-2004. All cases have a serum sample in JANUS serum bank, collected at the entering at the Radium hospital, which were the treating hospital. For 123 of the patients, the blood samples were taken before any treatment was given, while 37 of the patients have had hormone therapy prior to the blood test. Before any statistical analyses, the serum level of calcidiol was classified as low (< 50nmol/l), medium (50-80nmol/l) and high (> 80nmol/l). Detailed information about clinical characteristics (stage of disease, PSA, Hb, Creatin) at the time of diagnosis as well as treatment information was extracted from the patient journals. A Cox proportional hazard regression model was used to assess the role of calcidiol level as a prognostic factor.

Results: During the time of follow-up, 58 deaths occurred of whom 42 died from prostate cancer. The median time of follow-up was 2.7 years (range 1.2-141.3 months). Serum level of calcidiol above 50 nmol/ was shown to have a protective effect (RR 0.41 95% CI 0.17-0.95), compared to serum levels below 50nmol/l. However, no additional effect was observed for serum levels above 80 nmol/l. When analyzing the 37 patients on hormone therapy only, the effect of holding a serum level of calcidiol above 50 nmol/l was even stronger (70%). Analyses only including the 127 patients with blood samples taken before any therapy, gave no significant results. However, this might be due to the very few deaths in the group during follow-up (n=12).

Conclusion: The serum level of calcidiol, at the time of diagnosis seems to be a strong prognostic factor in patients with prostate cancer. Serum levels above 50 nmol/l, might be enough to influence cancer prognosis in a beneficial way.

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