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Trond Peder Flaten
Institutt for kjemi,
Norges teknisk-naturvitenskapelige
universitet, 7491 Trondheim

Telefon: 73 59 18 06

Telefax: 73 55 08 77

e-post: trond.flaten@chem.ntnu.no

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THE SEVENTEENTH NORWEGIAN CONFERENCE IN EPIDEMIOLOGY

HURTIGRUTEN,

5-6 NOVEMBER 2009

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The 17th Norwegian Conference in Epidemiology Hurtigruten, November the 5th and 6th, 2009

Welcome to the 17th Norwegian Conference in Epidemiology arranged by the Norwegian Epidemiological Association (NOFE) and Institute of Community Medicine, University of Tromsø.

“Frontiers in Epidemiology” is the theme for this year’s conference. By choosing the Hurtigruten-ship as venue, the frame for the scientific programme should be in harmony with our intention with this meeting: to contribute to a Norwegian epidemiological research environment continuously moving forward.

The scientific programme comprises presentations from four invited keynote speakers and 47 submitted and accepted abstracts. In addition, we have dedicated one afternoon to elaborate on Norwegian biobanks in the seminar “Digging for gold in Norwegian biobanks”.

This conference will be a journey along our beautiful coast, and we have therefore allowed several breaks in the programme for taking delight in the nature and landscape sailing through.

This year the Norwegian Association for Epidemiology has offered travel funds to 16 of the participating PhD-students as part of NOFE’s strategy to invest in younger epidemiological scientists.

This is the first time the annual conference arranged by NOFE has English as the official conference language. Not only the invited speakers, but also the many colleagues from abroad working in Norway will benefit from this. We are also pleased to have participants from all Nordic countries at this conference.

It is a privilege to welcome all of you on board the Hurtigruten ship and to the NOFE-conference 2009. We wish you all a pleasant journey.

The organizing committee for the NOFE-conference 2009

*Eiliv Lund, Tormod Brenn, Solrunn Hansen, Sissel Andersen and Magritt Brustad
Institute of Community Medicine, University of Tromsø*

**The 17th Norwegian Conference in Epidemiology
Hurtigruten, November the 5th and 6th, 2009**

Programme

Thursday, November the 5th

- 07:00 Breakfast
- 09:15 Magritt Brustad – Conference opening remarks
- 09:30 Special lecture – Vilmundur Gudnason: Imaging in modern epidemiology – The AGES Reykjavik Study
- 10:15 Break
- 10:30 Special lecture – Saminda Pathmasiri: Population biobank networking and challenges – what can P3G do?
- 11:15 Coffee break
- 11:45 Special lecture – Kristian Hveem: Commercialization of biobank related activities. Time for a national solution?
- 12:30 Lunch break
- 14:00 Eiliv Lund – Introduction to Digging for gold in Norwegian biobanks
- 14:05 Hilde Langseth – The JANUS biobank
- 14:20 Inger Njølstad – The Tromsø Study
- 14:35 Kristian Hveem – The HUNT biobank
- 14:50 Per Magnus – Mother and child
- 15:05 Vanessa Dumeaux – The NOWAC biobank
- 15:20 Eiliv Lund – Discussions and summary
- 16:00 Coffee break
- 17:00 Parallel session 1, speeches 1-10
- 18:15 NOFE Annual meeting
- 19:00 Programme end
- 20:00 Dinner

Friday, November the 6th

- 07:00 Breakfast
- 09:15 Special lecture – Andy Gilman: Human health research challenges in the Arctic in a time of climate change
- 10:00 Break
- 10:15 Special lecture – Vilmundur Gudnason: Risk assessment for cardiovascular disease
- 11:00 Coffee break
- 11:30 Parallel session 2, speeches 11-22
- 13:00 Lunch break
- 14:15 Parallel session 3, speeches 23-36
- 16:00 Coffee break
- 16:30 Parallel session 4, speeches 37-47
- 18:00 Paper of the year
- 18:30 Next year's conference
- 18:40 Programme end
- 20:00 Conference dinner

**The 17th Norwegian Conference in Epidemiology
Hurtigruten, November the 5th and 6th, 2009**

Parallel session 1 – Thursday, November the 5th 17:00-18:15

Room: Løvstakken

Theme: Methodological aspects

Chair: Marit B. Veierød

Room: Ulriken

Theme: Diet and activities

Chair: Guri Skeie

- | | | | | | | |
|----|----------------------|--|--------------|----|-----------------------------|--|
| 01 | Christine
L. Parr | Recall bias in melanoma risk factors and measurement error effects: a nested case-control study within the Norwegian Women and Cancer Study | 17:00 | 02 | Karina
Standahl
Olsen | Effects of plasma fatty acid ratios on the blood transcriptome |
| 03 | Nanna
Kurtze | Comparison of physical activity questionnaires in the Nord-Trøndelag Health Study (HUNT 1 and 2) and the International Physical Activity Questionnaire | 17:15 | 04 | Randi E.
Gislefoss | Analytical recovery of folate and its degradation products in serum stored at -25°C for up to 29 years |
| 05 | Øystein
Karlstad | The validity of mother-reported asthma and asthma medication use in 7 year old children | 17:30 | 06 | Cecilie
Kyrø | Intake and determinants of intake of whole grain foods in the Scandinavian countries |
| 07 | Mari
Nygård | Evaluation on the biomarkers for progression of the cervical dysplasia: molecular epidemiological study using information from the registries and biobanks | 17:45 | 08 | Koenraad
Cuypers | Receptive and creative cultural activities and health: A cross-sectional HUNT-study |
| 09 | Marit
Waaseth | Sex hormones and gene expression in peripheral blood from postmenopausal women – the NOWAC postgenome study | 18:00 | 10 | Gudrun
Maria
Waalder | Physical activity and activities of daily living (ADL) in the elderly in five counties in Norway |

**The 17th Norwegian Conference in Epidemiology
Hurtigruten, November the 5th and 6th, 2009**

Parallel session 2 – Friday, November the 6th 11:30-13:00

Room: Løvstakken

Theme: Statistics and methods

Chair: Tom Wilsgaard

Room: Ulriken

Theme: Environment

Chair: Erik Anda

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|----|-------------------|---|--------------|----|---------------------|--|
| 11 | Yiting Xue | Estimating the impact of seasonal influenza with relevance for pandemics: Disease burden and economic costs | 11:30 | 12 | Charlotta Rylander | Perfluorinated compounds and blood gene signatures in postmenopausal women – the NOWAC postgenome study |
| 13 | Elja Arjas | Nested case-control data utilized for multiple outcomes: a likelihood approach | 11:45 | 14 | Anna Sofia Veyhe | The Northern Norway Mother and Child Contaminant Cohort Study |
| 15 | Odd O. Aalen | Causal modelling: New statistical methods for epidemiology | 12:00 | 16 | Solrunn Hansen | Levels of organochlorines during pregnancy, delivery and postpartum period in women from northern Norway |
| 17 | Jon Michael Gran | Estimating direct and indirect effects of HIV treatment from cohort data | 12:15 | 18 | Alena Bartonova | Do we know enough? Knowledge evaluation in environmental health: the HENVINET methodology |
| 19 | Tron Anders Moger | A frailty analysis of two-generation melanoma data from the Swedish multi-generation register | 12:30 | 20 | Alena Bartonova | Assessment of health risks from ambient PAH exposure |
| 21 | Petter Kristensen | Dealing with emigration in epidemiology | 12:45 | 22 | Lise Marie Fjellsbø | Relative risk for mortality from long term exposure to PM2.5 in Europe |

**The 17th Norwegian Conference in Epidemiology
Hurtigruten, November the 5th and 6th, 2009**

Parallel session 3 – Friday, November the 6th 14:15-16:00

Room: Løvstakken

Theme: Cancer

Chair: Bo Terving Hansen

Room: Ulriken

Theme: Heart disease/diabetes

Chair: Randi Selmer

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|----|-------------------------|---|--------------|----|----------------------------------|--|
| 23 | Trude Eid
Robsahm | Cancer risk in Norwegian elite athletes performing in the period 1936-2006 | 14:15 | 24 | Lars C.
Stene | Assessing interactions between established susceptibility polymorphisms and putative environmental factors in type 1 diabetes |
| 25 | Guri
Skeie | Cod liver oil, other dietary supplements and survival among cancer patients with solid tumours | 14:30 | 26 | Josepha
Joseph | Incidence of type 2 diabetes in groups stratified according to criteria of metabolic syndrome. The Tromsø Study |
| 27 | Marit B.
Veierød | Ultraviolet exposure in five life decades and risk of cutaneous malignant melanoma | 14:45 | 28 | Laila
Arnesdatter
Hopstock | Seasonal variation in incidence of acute myocardial infarction and all-cause mortality in a subarctic population. The Tromsø Study 1974-2002 |
| 29 | Kjersti
Bakken | Menopausal hormone therapy and breast cancer risk – Impact of different treatments (The EPIC-study) | 15:00 | 30 | Ottar
Nygård | Combined results and long-term follow-up in NORVIT and WENBIT with 6837 coronary artery disease patients: Homocysteine-lowering B-vitamin treatment does not prevent major cardiovascular events |
| 31 | Inger T.
Gram | Smoking and risk of ovarian cancer; results from the EPIC study | 15:15 | 32 | Elisabeth
Strand-
hagen | Cholesteryl ester transfer protein (CETP) TaqIB polymorphism, HDL-cholesterol, alcohol consumption and the risk of coronary heart disease; a case-cohort study (INTERGENE) |
| 33 | Anne
Helene
Olsen | Breast cancer mortality in Norway after the introduction of mammography screening | 15:30 | 34 | Thor
Aspelund | Explaining the massive declines in Coronary Heart Disease Mortality rates in Iceland, 1981–2006 |
| 35 | Per-Henrik
Zahl | Swedish mammography screening trials revisited | 15:45 | 36 | Moira
Strand
Hutchinson | Low serum 25-hydroxyvitamin D levels are associated with increased all-cause and cardiovascular disease mortality risk in a general population. The Tromsø study. |

**The 17th Norwegian Conference in Epidemiology
Hurtigruten, November the 5th and 6th, 2009**

Parallel session 4 – Friday, November the 6th 16:30-18:00

Room: Løvstakken

Theme: Registries

Chair: Stein Atle Lie

Room: Ulriken

Theme: Others

Chair: Tom Nilsen

- | | | | | | | |
|----|----------------------------|---|--------------|----|----------------------------|---|
| 37 | Grethe
Albrektsen | Histological type and grade of breast cancer tumors by time since a childbirth | 16:30 | 38 | Caroline
Fleten | Parental-offspring associations in body mass index in the Norwegian Mother and Child Cohort Study |
| 39 | Inger
Kristin
Larsen | Trends in colorectal cancer incidence in Norway 1962-2006: an interpretation of the temporal patterns by anatomic subsite | 16:45 | 40 | Anne
Tandberg | Trends in incidence and mortality for triplets in Norway 1967-2006. The influence of assisted reproductive technologies |
| 41 | Ingeborg
Hartz | Use of drugs with an abuse potential among disability pensioners in Norway | 17:00 | 42 | Ruhina
Tasmin
Biswas | Noise-annoyance from traffic and plasma cortisol in a population based study |
| 43 | Svetlana
Skurtveit | Nicotine dependence predicts problematic use of prescribed opioids. Prospective population-based cohort study. | 17:15 | 44 | Bente
Ofteidal | Exposure to long-term traffic noise, noise annoyance and blood pressure |
| 45 | Ingvild
Eidem | Congenital anomalies in newborns of women with type 1 diabetes: Nation-wide population based study in Norway 1999-2004 | 17:30 | 46 | Bo
Terning
Hansen | Smokers have an increased risk of developing genital warts |
| 47 | Lise
Lund
Håheim | Calculation of volume of health services that are registered in the Norwegian Patient Registry | 17:45 | | | |

01

Recall bias in melanoma risk factors and measurement error effects: a nested case-control study within the Norwegian Women and Cancer StudyChristine L. Parr¹, Anette Hjartåker², Petter Laake¹, Eiliv Lund³ and Marit B. Veierød¹

1) Institute of Basic Medical Sciences, Department of Biostatistics, University of Oslo

2) Cancer Registry of Norway, Institute of Population-based Cancer Research

3) Institute of Community Medicine, University of Tromsø

Correspondence: Christine L. Parr, e-mail: c.l.parr@medisin.uio.no, telephone: +47 22 85 12 80

Objective: To study recall bias in a number of self-reported melanoma risk factors and the effects on estimated melanoma risk. The evidence implicating pigmentation factors and sun exposure in the etiology of melanoma derives largely from case-control studies that may suffer from recall bias after much public information about the effects of ultraviolet radiation. Recall bias in relation to melanoma has been investigated in only a few studies and for a limited number of risk factors.

Material and methods: A nested case-control study of recall bias was conducted within the Norwegian Women and Cancer Study. In 2004 a regular follow-up questionnaire was sent to 208 melanoma cases and 2,080 controls matched on age and sub-cohort. Responses to questions about pigmentation factors (eye-, and hair color, nevi, and skin color after acute and chronic sun exposure) and ultraviolet exposures (sunburns, sunbathing vacations, and solarium use) were compared to responses collected at enrolment in 1991–1997. Data were analyzed for 162 cases (response, 78%) and 1,242 controls (response, 77%) using measures of agreement stratified on case-control status and conditional logistic regression to estimate melanoma risk based on the prospective and retrospective exposure measurements. The questions about melanoma risk factors were embedded in a larger health- and lifestyle questionnaire with no particular emphasis on melanoma, and the study subjects were not aware that recall bias would be studied.

Results: Significant shifts in responses (toward lower or higher values in the second questionnaire) were observed among both cases and controls, but a shift in cases alone was observed for skin color after chronic sun exposure, and a larger shift in cases was observed for nevi. Weighted kappa was lower for cases (median 0.40, range -0.01–0.89) than for controls (median 0.46, range 0.10–0.87) for most age intervals of sunburn, sunbathing vacations, and solarium use. Differences in odds ratio (OR) estimates of melanoma based on prospective and retrospective measurements indicate measurement error that is difficult to characterize, but the same risk factors were identified: lighter or red hair color, more skin redness after acute sun exposure, less tanning after chronic sun exposure, more nevi, and more sunburns before age 30 years were associated with significantly increased risk ($P_{trend} < 0.01$).

Conclusion: In carefully conducted case-control studies, the effect of recall bias may be relatively small compared to non-differential reporting errors in both cases and controls, but as recall bias is a plausible bias, precautions should be taken in all new case-control studies of melanoma.

02

Effects of plasma fatty acid ratios on the blood transcriptome

Olsen KS¹, Fenton C², Anderssen E³, Frøyland L⁴, Paulssen RH², Dumeaux V¹ and Lund E¹

1) Institute of Community Medicine, University of Tromsø, Norway

2) Microarray Resource Centre Tromsø, Faculty of Medicine, University of Tromsø, Norway

3) Department of Cancer Research and Molecular Medicine, NTNU, Trondheim, Norway

4) National Institute of Nutrition and Seafood Research (NIFES), Bergen, Norway

Correspondence: Karina Standahl Olsen, e-mail: karina.s.olsen@uit.no, telephone: +47 77 64 48 18

Introduction: Nutrition is one of the major modifiable risk factors for atherosclerosis and several cancers. Long-chain fatty acids give rise to more or less inflammatory signaling molecules by acting as precursors for the synthesis of eicosanoids, with omega (n)-6 fatty acids giving rise to more potent inflammatory molecules than omega (n)-3 fatty acids. Their relative amounts may be a more accurate predictor than the absolute amounts, as they compete for the same set of enzymes. Despite the well-known metabolism of fatty acids, the molecular and physiological mechanisms of these dietary risk-modifying factors need further elucidation.

Objective: In the context of a large representative cohort of postmenopausal Norwegian women, we have explored the association between blood gene expression profiles and pro-inflammatory blood lipid profiles. The lipid profiles were defined by combining the ratios of linoleic/ α -linolenic acid (LA/ALA), arachidonic/eicosapentaenoic acid (AA/EPA) and total n-6/n-3.

Material and methods: Samples from 286 women were successfully analyzed for expression profiles in PAXgene-stored whole blood using ABI1700 microarrays, and fatty acid concentrations were measured in citrate-buffered plasma using rapid gas chromatography. Data pre-processing and analysis were carried out using the R software and bioconductor packages.

Results: Differentially expressed genes according to a pro-inflammatory lipid profile were related to several biological processes and pathways, including inflammation, T-cell activation, and lipid metabolism. Several genes of the Fc epsilon receptor 1 signaling pathway were up-regulated in samples with a pro-inflammatory lipid profile.

Conclusion: These preliminary results indicate that dietary fatty acids do have an effect on the blood transcriptome, and that an unfavourable lipid profile may be related to a pro-inflammatory gene expression profile. Further analyses will be conducted to reveal the complex effects of the lipidome on the blood transcriptome.

03

Comparison of physical activity questionnaires in the Nord-Trøndelag Health Study (HUNT 1 and 2) and the International Physical Activity Questionnaire

Nanna Kurtze¹, Vegar Rangul² and Bo-Egil Hustvedt³

1) SINTEF Health Research, Global Health and Welfare, Oslo

2) Faculty of Teaching, Engineering and Nursing, Nord-Trøndelag University College

3) Institute of Basic Medical Sciences, Department of Nutrition, University of Oslo

Correspondence: Nanna Kurtze, e-mail: Nanna.Kurtze@sintef.no, telephone: +47 47035596

Objective: In epidemiological studies several methods have been used to assess physical activity (PA), but the lack of a gold standard has hampered the development. However, the 12-country reliability and validity study has developed an instrument for cross-national monitoring of PA. The purpose of this study is to compare the international physical activity questionnaire (IPAQ, short, 7 days) for the assessment of PA with two differently structured PA questionnaires used in HUNT 1 and HUNT 2.

Material and methods: All three questionnaires were administered twice to a random sample of 108 men aged 20-39 and validity by comparing results with VO_{2max} , and ActiReg, an instrument that measures PA and energy expenditure (EE). ActiReg discriminates between the body positions: stand, sit, bend forward and lie and also registers if there is motion or not in each of them.

Results: In HUNT 1 the intraclass correlation coefficients (ICC) ranged from 0.81 to 0.88, showing very good reliability. In HUNT 2 ICC were 0.08 for light activity and 0.39 for hard PA, showing poor and fair reliability, respectively, while ICC for the IPAQ ranged from a low of 0.30 for moderate activity hours, to a high of 0.80 for sitting hours, showing good reliability with high correlations for sitting hours per day, vigorous hours and days, and moderate for walking days and hours. In all three questionnaires we found moderate, significant correlation between the index based on questionnaire responses and VO_{2max} (HUNT 1 $r=0.48$ ($p\leq 0.01$)) and for hard PA (HUNT 2, $r=0.46$ ($p\leq 0.01$)) and for total vigorous activity IPAQ ($r=0.41$ ($p\leq 0.01$)). In HUNT 1 metabolic equivalent (MET) values of 6 or more estimated from ActiReg and total vigorous activity from IPAQ most strongly correlated with the index $r=0.39$, $r=0.55$, respectively and in HUNT 2 with hard PA $r=0.31$, $r=0.48$ ($p\leq 0.01$) respectively. Associations of other measures obtained from ActiReg with questionnaires measures were weaker for all three questionnaires; only total IPAQ walking was fair correlated with METs 1-3, 3-6 and 6+, respectively ($r=-0.27$, 0.26 and 0.24 ($p\leq 0.05$)). IPAQ METs correlated most strongly with ActiReg METs 3-6 ($r=0.34$ ($p\leq 0.01$)).

Conclusions: Our results indicate that the PA questionnaire in HUNT 1 and the “hard” PA in HUNT 2 is reproducible and provides a useful measure of leisure time PA for men. Both questionnaires are very short and compared favourably with much longer instruments for assessment of more vigorous PA. It should be an appropriate tool for use in further epidemiological studies, particularly when interest is in aspects of PA reflected in fitness or METs greater than 6. The “light” activity question from HUNT 2 had poor reproducibility and did not correlate well with most of the comparison measures. Our results indicate that IPAQ short version for men has acceptable reliability and criterion validity for vigorous activity and sitting. Walking has moderate reliability. Only the IPAQ for walking had a fair correlation with METs 6+. The questions about moderate activity had fair reproducibility and correlated poorly with most comparison measures. HUNT 1 yielded the most significant data on PA behaviour and shows promise as a useful research and evaluation tool.

04

Analytical recovery of folate and its degradation products in serum stored at –25°C for up to 29 years

Randi E. Gislefoss^{4,5,7}, Rita Hannisdal^{1,2,7}, Tom K. Grimsrud⁵, Steinar Hustad^{1,6}, Lars Mørkrid⁴ and Per Magne Ueland^{1,3}

1) Section for Pharmacology, Institute of Medicine, University of Bergen, Norway

2) National Institute of Nutrition and Seafood Research, Bergen, Norway

3) Laboratory of Clinical Biochemistry, Haukeland University Hospital, Bergen, Norway

4) Institute of Clinical Biochemistry, Faculty of Medicine, University of Oslo and Department of Medical Biochemistry, Rikshospitalet-Radiumhospitalet Medical Centre, Norway

5) Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo, Norway

6) Hormone Laboratory, Haukeland University Hospital, Bergen, Norway

7) These authors contributed equally to the work

Correspondence: Rita Hannisdal, e-mail: rita.hannisdal@med.uib.no telephone: +47 97 60 11 05

Objective: Epidemiological studies on folate status and risk of chronic diseases often involve determination of folate in frozen serum samples stored in biorepositories for decades. Instability of folate in serum may attenuate associations in studies based on measurements of folate in archival samples.

Material and methods: Serum specimens stored at –25 °C for 0, 4, 6, 17 and 29 years in the JANUS biobank were retrieved. Folate was determined by three different methods, (1) a LC-MS/MS assay measuring 5-methyltetrahydrofolate (5mTHF), its oxidation product 4-alpha-hydroxy-5-methyltetrahydrofolate (hmTHF) and other folate species; (2) a microbiological assay; and (3) an assay that involves the conversion of folate species to p-aminobenzoylglutamate (pABG), which is then quantified by LC-MS/MS.

Results: There were no differences in total homocysteine (tHcy) or methylmalonic acid (MMA) according to duration of sample storage, indicating no change in folate status across the study period. Concentrations of 5mTHF and microbiological active folate were lower in samples that had been subjected to long-term storage and were consistent with a marked decrease. Substantial amounts of hmTHF were detected in all specimens, but did not accumulate upon long-term storage (> 4 years). Folate measured as pABG declined at a slow rate, and most of the folate was recovered as pABG equivalents after 29 years of storage.

Conclusion: There was a substantial degradation of folate in frozen serum samples stored for decades. Degraded folate was best recovered as pABG equivalents.

05

The validity of mother-reported asthma and asthma medication use in 7 year old children

Kari Furu¹, Øystein Karlstad¹, Svetlana Skurtveit¹, Siri Haaberg¹, Per Nafstad^{1,2}, Stephanie London³ and Wenche Nystad¹

1) Norwegian Institute of Public Health, Division of Epidemiology, Oslo

2) Institute of General Practice and Community Medicine, University of Oslo

3) Epidemiology Branch, Department of Health and Human Services, National Institutes of Health, North Carolina, United States

Correspondence: Øystein Karlstad, e-mail: oystein.karlstad@fhi.no, telephone: +47 21 07 81 27

Objective: Questionnaires have been a central source of information on asthma prevalence and asthma medication use. The validity of parental reporting of pediatric asthma and asthma medication use has been questioned. Aim 1) Examine validity of mother reporting on their children's asthma *medication* use in the Norwegian Mother and Child Cohort (MoBa), by using the Norwegian Prescription Database (NorPD) as reference standard. Aim 2) Examine if mother reporting on their children's asthma *disease* and *diagnosis* in MoBa is consistent with the children's use of asthma medication recorded in NorPD.

Materials and methods: The study population consisted of 2056 children who are part of the first follow-up of 7-8 year old children in MoBa (response rate 61%). Data reported on the MoBa questionnaire by the mother on the child's asthma medication use and asthma disease and diagnosis was compared with data on dispensed asthma medications recorded in NorPD. Asthma medications were inhaled β 2-agonists (ATC code R03AC), inhaled glucocorticoids (R03BA), combination inhaler with β 2-agonists and glucocorticoids (R03AK) and leukotriene receptor antagonists (R03DC) in both MoBa and in NorPD. MoBa question used for aim 1: "Has the child used medications, spray, inhaler or other medications for asthma during the last year?" (Alternatives: No / yes). 264 individuals did not answer this specific question and were excluded from this analysis. MoBa question for aim 2: "Has the child ever had asthma?" (Alternatives: Yes / yes, has current asthma / physician-diagnosed asthma). Responders were divided into 4 groups; current asthma diagnosed by a physician, current asthma but not diagnosed by a physician, asthma but not current, never asthma. For both aims, data from NorPD was extracted for each responder for 365 day period preceding the date of filling in the MoBa questionnaires.

Results: Aim 1: 125 of 137 children who redeemed prescriptions in NorPD were reported to use asthma medication according to the MoBa questionnaire (sensitivity 91%). 1594 of the 1655 children without redeemed prescriptions were not reported to use asthma medications in MoBa (specificity 96%). Aim 2: 98 of 122 (80%) of children with reported current asthma diagnosed by a physician had redeemed prescriptions for asthma medication during the 365 days preceding the date of filling in the MoBa questionnaires. Only 22 of 1805 (1%) of those who reported never asthma were recorded with asthma medication prescriptions during the 365 day period.

Conclusion: Mother reporting on MoBa questionnaire of their children's asthma *medication* use in the last year was highly valid with both sensitivity and specificity over 90%. Mother reporting on their children's asthma *disease* and *diagnosis* was consistent with dispensed asthma medications recorded in NorPD.

06

Intake and determinants of intake of whole grain foods in the Scandinavian countriesCecilie Kyrø^{1,2,3}, Anja Olsen² and Guri Skeie³

1) Department of Human Nutrition, University of Copenhagen, Copenhagen, Denmark

2) Institute of Cancer Epidemiology, The Danish Cancer Society, Strandboulevarden 29, 2100 Copenhagen, Denmark

3) Institute of Community Medicine, University of Tromsø, Tromsø, Norway

Correspondence: Cecilie Kyrø, ceciliek@cancer.dk, telephone: +45 26130905

Background: Intake of whole grain foods has been associated with a lower risk of developing chronic diseases such as type 2 diabetes, cardiovascular disease, obesity and some types of cancer. Furthermore the intake of whole grain foods has been associated with socio-economic factors and a generally healthier lifestyle. Because of the numerous health benefits of whole grain, knowledge about the consumption and the determinants of the intake is needed. Much of the research on the health effects of whole grain foods has been done in the US. In the Scandinavian countries, however, the population consumes much more whole grain and therefore serves as a better basis for research on whole grain foods.

Objective: The objective of this study is to describe the intake of whole grain foods in Norway, Sweden and Denmark. Furthermore the aim is to reveal the socio-economic and dietary determinants of the intake of whole grain foods.

Design: The present study is part of the joint Nordic initiative “HELGA” supported by NordForsk. The HELGA projects aims to evaluate health aspects related to whole grain foods. The established “HELGA cohort” consisting of the following three prospective cohorts was used in this study: The Norwegian Women and Cancer Study of 37,000 women aged 41-56 years, the Northern Sweden Health and Disease Study of 26,000 women and men aged 30, 40, 50 and 60 and the Danish Diet and Cancer cohort of 57,000 women and men aged 50-65 years. Intake of whole grain foods was assessed with country-specific semi-qualitative food frequency questionnaires from the entire HELGA cohort (n 120,000). The intake was quantified into whole grain product/day.

Statistics: The intakes were presented as medians with 5th and 95th percentiles. Differences between countries were evaluated by the ANOVA principle. Multiple linear regression analyses were used for the determinant analyses with intake of whole grain foods as the dependent variable.

Results: The mean intakes of whole grain products were highest in Norway when looking exclusively at women (mean intake of whole grain in g product/day: Norway: 135, Sweden: 91, Denmark: 120, p<0,001). The intake when looking at men was also lowest in Sweden (mean intake of whole grain in g product/day: Denmark: 144, Sweden: 123, p<0,001). In Denmark and Sweden men consumed more whole grain than women (p<0,001). Intake of whole grain was positively associated with longer education, a higher intake of vegetables and a higher intake of cheese. Also it was found that the intake was negatively associated with the intake of white bread and smoking. The associations found were strongest for Sweden.

Conclusions: The intake of whole grain of women in the Nordic countries was highest in Norway and lowest in Sweden. When comparing men in Denmark and Sweden, the intake of whole grain foods was highest in Denmark. Whole grain intake was positively associated with length of education, intake of vegetables and cheese. The intake was negatively associated to the intake of white bread and smoking. These associations were found for all Nordic countries, but the associations were strongest for Sweden.

07

Evaluation on the biomarkers for progression of the cervical dysplasia: molecular epidemiological study using information from the registries and biobanks

Mari Nygård¹, Maria Hagerup-Jenssen¹, Siri Hovland², Hanne Skomedal², Walter Ryd³, Ole Klungsoyr¹ and Bjørn Hagmar¹

1) The Cancer Registry of Norway, Oslo, Norway

2) R&D, NorChip AS, Klokkearstua, Norway

3) Cyt. Dept. Sahlgrenska University Hospital, Göteborg, Sweden

Correspondence: Mari Nygård, e-mail: mari.nygard@kreftregisteret.no, telephone: +4723333949

Objective: Malignant progression of pre-invasive lesions is notoriously difficult to study, since all pre-invasive lesions are subjected to treatment. In rare occasions, the treatment is postponed and the natural development of the lesion remains undisturbed for a limited period of time. Several biomarkers have been evaluated in order to improve diagnostic criteria of preinvasive lesions in cervix uteri, cervical intraepithelial neoplasia (CIN). Ki 67, p16 and expression of E6/E7 mRNA have been proposed also as biomarkers for progression. We have established a model for studying progression by selecting a patient material in relation to pregnancy. The aim of the study was to evaluate whether positivity to HPV mRNA, p16, Ki67 or HPV type DNA was related to grade of CIN and/or progression.

Material and methods: Among all pregnant women in 1996-7 in Norway, those with diagnosed CIN grade I-III during pregnancy were identified from the Cancer Registry of Norway. 149 women with minimum of two serial histology specimens were included into the study. Formalin fixed paraffin embedded (FFPE) tissue blocs were identified from biobanks. Two pathologists independently performed diagnostic adjudication. Real-time NASBA (NorChip AS, Klokkearstua, Norway) was used for E6/E7 mRNA from HPV16,18,31,33,45. For HPV DNA GP5+/6+ was used, followed by reverse line-blot for typing of 39 HPV types individually and 6 rare HPV types as a pool. P16/Ki67 were detected immunohistochemically (Cell Marque, p16, 16P04 and Assey, Filled Disp., CONFIRM Anti-Ki67 K-2, Ventana). Prevalence of biomarkers by dysplasia grade (normal, CINI-III) was estimated. Linear mixed models were used for the longitudinal analyses to accommodate highly unbalanced structure of the data. The outcome was degree of seriousness (CIN grade) in the histology-samples and the different biomarkers served as the time varying covariates.

Results and conclusion: The mean age of subjects (at 1st visit) was 29 years. Prevalence of HPV DNA, mRNA, Ki-67 and p16 increased by increasing grade of CIN lesion. By our criteria, 28 (18) women showed progression. All biomarkers studied (HPV mRNA was excluded from analyses) showed strong association with CIN seriousness in longitudinal analyses except positivity for low risk HPV that showed negative association (albeit not statistically significant). Ki67 and positivity for high risk HPV DNA predicted best the histological severity of cervical lesions, especially for women for whom histological progression was confirmed.

08

Receptive and creative cultural activities and health: A cross-sectional HUNT-study

Koenraad Cuypers¹, Margunn Skjei Knudtsen², Turid Lingaas Holmen¹, Steinar Krokstad¹, Kristian Midthjell¹ and Jostein Holmen¹

1) HUNT Research Centre, Department of Public Health and General Practice, NTNU

2) Department of Public Health, Nord-Trøndelag County Council

Correspondence: Koenraad Cuypers, kjcuype@online.no, telephone: 0047 99254952

Objective: Increasing prevalence of disability and the persisting inequalities in health have initiated a search for new preventing strategies, and culture activities have been introduced both in patient rehabilitation and in public health policy. However, there are still questions whether this might be confounded by socio-economic status or other factors. We wanted therefore to investigate how leisure time participation in cultural activities associates with perceived health, anxiety and depression in a large general population.

Material and methods: In the third Nord-Trøndelag Health Study (HUNT 3, 2006-2008) all citizens of the county aged 13 and older were invited. Questions included receptive cultural activities (been to museum, art exhibition, concert, theatre, movie, church, sport events) and creative cultural activities (participation in associations, music, song, theatre, parish work, out-door activities, dance, physical exercise, sport). Comprehensive questionnaires provided additional data on perceived health, anxiety and depression (measured by Hospital anxiety and depression scale), life satisfaction, psychosocial distress, social capital and life-habits. As indicator of socio-economic status we used Erikson Goldthorpe Portocarero (EGP) social class scheme. Uni- and multivariate logistic regression and general linear models were used for analyses.

Results: A significant association between cultural activities and perceived health and depression was present, even controlled for SES, age, other health related factors, and social capital. A significant association of the creative cultural index (OR: 1.04, CI: 1.03–1.06) with perceived health was found in women. A significant association between perceived health and both the receptive (OR: 1.06, CI: 1.03–1.10) and creative index (OR: 1.06, CI: 1.04–1.08) was seen in men. In men, there was a significant association between depression and both the receptive index (OR: 1.06, CI: 1.02–1.10), and the creative index (OR: 1.05, CI: 1.02–1.07).

Conclusion: Despite that most cultural activities demonstrated a socioeconomic gradient, the overall effect of SES was not great, and could not explain the association between cultural activities and health. Moreover, our study reveals a gender and index wise different association with indicators of mental health. The clinical impact of cultural activities should be evaluated in prospective studies.

09

Sex hormones and gene expression in peripheral blood from postmenopausal women – the NOWAC postgenome study

Marit Waaseth¹, Vanessa Dumeaux¹, Karina Standahl Olsen¹, Charlotta Rylander^{1,2} and Eiliv Lund¹

1) Institute of Community Medicine, University of Tromsø

2) Norwegian Institute for Air Research, the Polar Environmental Centre, Tromsø

Correspondence: Marit Waaseth, e-mail: marit.waaseth@uit.no, telephone: +47 77 64 48 83

Objective: Hormone therapy (HT) with estrogens and/or progestogens is a known risk factor of breast cancer and has influence on endogenous sex hormone concentrations. The aim of the study was to explore potential associations between endogenous and exogenous sex hormones and gene expression in peripheral blood among a random sample of postmenopausal women.

Material and methods: A random sample of 445 postmenopausal women aged 48-62 years donated blood samples in 2005 (74% response rate). After exclusion of pre-/perimenopausal women, full genome scan (mRNA) was performed through ABI microarray analysis of 289 whole blood samples. Each microarray chip contains 32 878 probes representing 29 098 genes. After further exclusions due to poor quality of samples and/or probes, the final expression matrix comprised 285 samples and 16 185 probes for statistical analysis. Questionnaires provided data on HT use and other life style factors. Plasma concentrations of endogenous sex hormones were measured by immunometry. We used R (<http://cran.r-project.org>) and tools from the Bioconductor project (<http://www.bioconductor.org>) for the statistical analyses. Differential gene expression was assessed using gene-by-gene analysis (Limma), global gene expression analysis (GlobalAncova), gene set enrichment analysis (Globaltest) and functional mapping/gene network tools (HEFAlMp (<http://sonorus.princeton.edu/hefalmp/>), GO (<http://www.geneontology.org/>) and DAVID (<http://david.abcc.ncifcrf.gov/>)).

Results: There were no significant associations between endogenous sex hormones and global gene expression. Out of 285 women, 182 were medication users; 52 used HT and 160 used other medications. Some medication categories showed extensive influence on gene expression, and medication users were excluded from most analyses.

Gene-by-gene analysis revealed gene sets differentially expressed between users of some HT types and nonusers. The set of 33 genes found differentially expressed for systemic estradiol therapy was confirmed as an estradiol signature; significantly differentially expressed between samples in the first and fourth quartile of estradiol concentration among nonusers ($p=0.02$). Functional mapping did not reveal functional networks in which these genes participate. Among gene sets curated from literature and based on blood transcriptomics, one gene set from GO comprising estrogen responsive genes were also found to be differentially expressed between high and low estradiol concentration categories ($p=0.03$).

Conclusions: We have identified an estrogen signature and further research may reveal the function of these genes and how they are related to plasma estradiol concentrations. In our study so far, other sex hormones have not shown a profound influence on gene expression in this random sample of postmenopausal women. The variation in hormone concentrations is not large and the gene expression signals may be too subtle. However, the analyses are ongoing.

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Physical activity and activities of daily living (ADL) in the elderly in five counties in Norway

Gudrun Maria Waaler¹, Sidsel Graff-Iversen^{1,2}, Hege Bentzen³, Anne Johanne Sjøgaard^{1,4} and Lisa Forsén¹

1) Norwegian Institute of Public Health, Division of Epidemiology, Oslo

2) Institute of Community Medicine, University of Tromsø

3) Diakonhjemmet Hospital

4) Institute of General Practice and Community Medicine, University of Oslo

Correspondence: Gudrun Maria Waaler, e-mail: gudrun.maria.waaler@fhi.no, telephone: +47 21078186

Background: The future changes in our society's age composition will lead to an increased demand on the health care sector. Studies show that there is a positive association between physical activity (PA) and activities of daily living (ADL) in the elderly. By improving the elderly populations' PA one might postpone the period for when people need help in activities of daily living or need to move to nursing homes.

Aim: The aim of the study is to investigate the association between PA and ADL in 75 year olds in Norway, and to explore whether this association varies between the different genders, socioeconomic classes and geographical areas.

Material: The present cross sectional study is based on three health surveys (HUBRO, OPPHED and TROFINN) performed in 2001-2002, targeting all 75 year old (75 and 76 year old in Oslo) men and women in five counties in Norway (n = 6,627). In the surveys PA was measured in mean hours of activity during a week (none, 1 or less, 1-2, 3 or more), differing between light- and hard physical activity. ADL was measured by assessing whether the respondents were able to move, read and hear, and the extent to how the respondents' health reduced their ability to move in their home, move outside of their home, participate in social unions/ leisure activities, use public transportation and perform daily errands.

Method: Simple cross tables and adjusted prevalence, to e.g. more complex structural equation models (SEM). Discussion: No results are available at the present time. However, we would like to address and discuss among others what variables to include in analyses and how to choose the correct analytical tools.

Conclusion: By carefully choosing reasonable methods, risk factors for inactivity and low ADL might be identified in the elderly population in Norway.

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Estimating the impact of seasonal influenza with relevance for pandemics: Disease burden and economic costs

Yiting Xue and Birgitte Freiesleben de Blasio

Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Norway

Correspondence: Yiting Xue, e-mail: yiting.xue@medisin.uio.no, telephone: +4722851405

Background: The disease burden of influenza is complicated to estimate with the presence of non-specific symptoms. Few studies on the cost of influenza have included influenza-attributable diseases. No population-based study has been performed to estimate the productivity lost from self-reported sick leave.

Objective: Using Norwegian data, we study the impact of influenza, incorporating the influenza-associated morbidity and the self-reported sick leave.

Methods: We estimated excess hospitalizations and doctor-certified sick leave due to influenza using Poisson regression, and developed a simulation model to assess self-reported sick leave and total productivity lost.

Results: We found that during season 98/99 to 05/06, there were on average 2718 excess hospitalizations associated with influenza each season (16% registered as influenza, 51% as pneumonia and 33% as others). These hospitalizations contributed to a direct cost of 23 million 2005/06 USD. Each season there were on average 483 252 working days lost due to influenza and 170 272 people had to take sick leave, resulting in a productivity lost of 140 million USD. This indicates a total cost of 365 to 731 million USD in a pandemic.

Conclusion: Seasonal influenza is a considerable burden to society and the indirect cost is much higher than the direct cost.

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Perfluorinated compounds and blood gene signatures in postmenopausal women – the NOWAC postgenome study

Charlotta Rylander^{1,2}, Vanessa Dumeaux¹, Karina Standal Olsen¹, Marit Waaseth¹, Torkjel Sandanger^{1,2} and Eiliv Lund¹

1) Institute of Community medicine, University of Tromsø, Norway

2) Norwegian institute for Air Research, Tromsø, Norway

Correspondence: Charlotta Rylander, e-mail: charlotta.rylander@uit.no, telephone: +4741643404

Background: As a result of many years of production and use in industry and consumer products, perfluorinated compounds (PFCs) are frequently found in the environment as well as in human blood worldwide. Concerns have been raised since perflurooctane sulphonate (PFOS) and perfluoro-octanoate (PFOA) are potent peroxisome proliferators in rodents and in human hepatocytes and a number of toxicological effects have been observed in PFOS/PFOA exposed rodents. Gene expression signatures of peripheral blood cells have been successfully used to assess the impact of environmental exposures, such as smoking, metal fumes and ionizing radiation in humans. Gene expression changes associated to organic contaminants in human blood samples have not been investigated so far in a large population based study.

Objective: To assess the impact of PFOS, PFOA and perfluorohexane sulphonate (PFHxS) on blood gene signatures in a group of 270 healthy, postmenopausal women.

Material and methods: The women included in the analysis are participants of the Norwegian Women And Cancer (NOWAC) cohort. Detailed information about their life style and diet was available from questionnaires. PFCs were measured in the plasma samples' using liquid-liquid extraction and analysis on HPLC-QTOF-MS. Gene expression profiles in whole blood were investigated using the Applied Biosystems expression array system. After preprocessing of data, 16185 genes remained and were used in the statistical analysis. Gene by gene analysis (limma) as well as gene set enrichment analysis (global test) were performed using the freely available software R, version 2.8.1 and the Bioconductor package. Enrichment of more than 40 different gene sets, curated from previous publications, Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO), all associated with PFC exposure were evaluated.

Results: Gene sets related to the fatty acid metabolism as well as the insulin signaling pathway were differentially expressed between the PFOS high (> 30 ng/ml) and the PFOS low group (<30 ng/ml). None of the tested gene sets were significantly enriched in the PFOA or PFHxS groups.

Discussion and conclusions: To our knowledge this is the first study investigating the impact of PFCs on blood gene signatures in humans. Even though the investigated contaminants were present in the blood from all participants, some effects observed in the blood signatures were consistent with findings from toxicological studies. The presented results are, however, preliminary, and should be interpreted with caution. It is too early to conclude what consequences these findings have on human health.

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Nested case-control data utilized for multiple outcomes: a likelihood approach

Olli Saarela¹, Sangita Kulathinal¹, Elja Arjas^{1,2} and Esa Läärä³

1) National Institute for Health and Welfare, Finland

2) Department of Mathematics and Statistics, University of Helsinki

3) Department of Mathematical Sciences, University of Oulu

Correspondence: Elja Arjas, e-mail: Elja.Arjas@helsinki.fi, telephone: +358-50-5637463

Objective: Suppose a nested case-control design has been applied for collecting covariate data when studying a specific disease. With possible new outcomes of interest it would be sensible to utilize the previously selected control group instead of, or in addition to, a new control selection, given that the same covariate data are relevant and available and that their measurements had adequate stability and quality.

Results: We formulate this problem in the framework of competing risks survival models and then show that the statistical estimation problem can be formulated and carried out in practice in terms of corresponding likelihood inference. The method is compared with other alternatives in a simulation study, demonstrating some of its advantages.

Reference: Saarela O, Kulathinal S, Arjas E, Läärä E (2008): Nested case-control data utilized for multiple outcomes: a likelihood approach and alternatives. *Statistics in Medicine* 27 (28): 5991-6008.

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The Northern Norway Mother and Child Contaminant Cohort Study

Anna Sofia Veyhe¹, Jon Øyvind Odland¹, Solrunn Hansen¹, Evert Nieboer^{1,2} and Torkjel M. Sandanger³

1) Department of Community Medicine, Faculty of Health Science, University of Tromsø, Norway

2) Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada

3) NILU in the Polar Environmental Centre, Tromsø, Norway

Correspondence: Anna Sofia Veyhe, e-mail: anna.sofia.veyhe@uit.no, telephone: +47 776 45773

Introduction: The Northern Norway Mother and Child Contaminant Cohort Study was initiated in 2007 and will continue until the end of 2009. The objective of this presentation is to share the background, objectives and the methods of this comprehensive study.

Background: People living in the arctic and sub-arctic regions are at higher risk of exposure to environmental contaminants, especially those that consume traditional diets. Because organisms are especially sensitive to toxic substances during stages of rapid development, potential health consequences are potentially serious to the foetus and child. The basis for this concern is that many contaminants are transferred from the mother via the placenta to the foetus and by breast milk to the child. The study described is intended to supplement other systematic studies conducted in the circumpolar countries (e.g., Arctic Monitoring Assessment Programme, AMAP)

Objectives and approach: A primary objective is to assess the body burden of the AMAP suite of environmental contaminants of the mother, the foetus and the newborn child. This includes determining a number of organochlorine compounds (PCBs and a group of pesticides), newly “emerging chemicals” (e.g., brominated flame retardants and fluorinated surfactants), and toxic metals (e.g. mercury, lead and cadmium). These will be measured in maternal serum, whole blood, or hair, as well as in breast milk; in cord blood/plasma of the foetus; and in meconium or serum from the new born. In addition to these exposure measures, aspects of their impact or effect will also be explored. Specifically, a selection of hormones in blood plasma will be measured to assess the hormonal status of the mother six weeks postpartum and the potential influence of the contaminants on this. Other effects to be considered are the impact on birth weight, gestational age, apgar score and perhaps sex ratio.

Methods: Well established and validated methods for the contaminants and clinical chemistry variables will be employed. Samples for the organic contaminants will be carried out locally at the Norwegian Institute of Air Research (NILU), metals at Statens Arbeidsmiljøinstitutt (STAMI), and hormones at the University Hospital of Northern Norway (UNN). The completion of a self-administrated questionnaire is timed with the first maternal contact (early pregnancy). The information covers the following topics among others: current and past place of residence, family income, parental ethnicity, lifestyle, past and present diet (including store bought and traditional food). Maternal blood pressure is measured at each of the three visits. In addition, details about the delivery and the baby will be available for entry into the project database. Statistical methods will include univariate analysis, analysis of variance (ANOVA), multiple linear regression, and logistic regression.

Concluding comment: The option of periodic follow-up of the children to age 12 is being considered for a subsequent phase.

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Causal modelling: New statistical methods for epidemiology

Odd O. Aalen

Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo

Correspondence: Odd O. Aalen, e-mail: o.o.aalen@medisin.uio.no, telephone +47 22 85 12 36

Objective: The statistical methods used in epidemiology are undergoing a rapid change. Traditional approaches like logistic and Cox regression are insufficient for many purposes and are gradually being supplemented with approaches that consider much more carefully the causal aspects of the study. Elaborate causal thinking is becoming part of mainstream statistical methodology. This has been going on for many years but is now gaining pace.

One major issue is that of time-dependent confounding which is common and far more complex than ordinary confounding. Another aspect is to understand mediation, or alternatively the concepts of direct and indirect effects. These issues are particularly relevant when observations can be taken frequently over a period of time. Detailed follow-up data over time are becoming increasingly common these days.

A very brief overview of some of these aspects will be given.

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Levels of organochlorines during pregnancy, delivery and postpartum period in women from northern Norway

Solrunn Hansen¹, Jon Øyvind Odland¹, Tom Wilsgaard¹, Evert Nieboer^{1,2}, Anna Sofia Veyhe¹ and Torkjel M. Sandanger³

1) Department of Community Medicine, Faculty of Health Science, University of Tromsø, Norway

2) Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Ontario, Canada

3) NILU in the Polar Environmental Centre, Tromsø, Norway

Correspondence: Solrunn Hansen, e-mail: solrunn.hansen@uit.no, telephone: +47 77 64 48 36

Background and objectives: Persistent organic pollutants in the environment have the ability to bioaccumulate and to endure in the environment for years. Most of these substances potentially have detrimental health and developmental effects. The foetus and the newborn child are especially sensitive to the toxic substances because of their transfer from mother to child via the placenta and umbilical cord. Levels of contaminants in mother's blood and milk are therefore an indication of the potential risk to the growing child. The Northern hemisphere is struggling with long-range transports of organochlorine compounds (OCs). We do not know the exact situation of levels and outcomes in our area. The Northern Norwegian Mother and Child Contaminant Cohort Study was initiated in 2007 and will continue until the end of 2009. The cohort consists of about 500 pregnant women from the counties of Nordland, Troms and Finnmark. Levels of contaminants in biological materials from mother and child will be determined. The primary objective of this study is to see if there is a pattern of change in contaminant levels in maternal blood during pregnancy, delivery and postpartum period.

Material and methods: For a random subset of 51 women, serum samples were collected during the 2nd trimester, day 3 after delivery and 6 weeks postpartum and were analyzed for 12 polychlorinated biphenyl (PCB) congeners and 4 pesticides (p,p'-DDE, HCB, trans-nonachlor and cis-nonachlor). The linear mixed model was used to analyze the data. All concentrations were log-transformed prior to the statistical analysis.

Results: We detected relatively low levels of all compounds, with p,p'-DDE and PCB 153 exhibiting the highest concentrations. Geometric unadjusted mean levels of all compounds peaked at delivery, and continued to decrease significantly during the 6 weeks post partum period. Interestingly, when contaminant concentrations were lipid adjusted, the statistical significant was lost for PCBs, and for p,p'-DDE. However, for the latter a subsequent increase was evident between delivery and 6 weeks postpartum. A slightly different pattern was seen for trans-nonachlor.

Conclusion: Relatively low levels of PCBs and pesticides are reported from the Northern Norway. The results suggest that for PCBs (and perhaps trans-nonachlor) there is no critical collection period, but this may not apply to p,p'-DDE.

Estimating direct and indirect effects of HIV treatment from cohort data

Jon Michael Gran, Kjetil Røysland and Odd O. Aalen

Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo

Correspondence: Jon Michael Gran, e-mail: j.m.gran@medisin.uio.no, telephone +47 22 85 14 54

Objective: When estimating the effect of treatment on HIV using data from observational studies, standard methods may produce biased estimates due to the presence of time dependent confounders. Such confounding can be present when a covariate, affected by past exposure, is both a predictor of the future exposure and the outcome. Examples are HIV-1 RNA and CD4 cell count, serving as markers for disease progression. When analysing direct and indirect effects of treatment we encounter the same problems. The objective is to study direct and indirect effects using a method based on mimicking randomized trials from subsets of the observed data.

Material and methods: The data we use is from the Swiss HIV cohort study, and goes from 1996, when HAART treatment became available in Switzerland, to September 2003. We analyse these data as a sequence of many mimicked randomized trials, to estimate direct and indirect effect using the method of dynamic path analysis. Such methods rely on models describing possible paths from treatment, via other covariates, to the final outcome (in our case AIDS or death) to be defined. We analyse different variants of such models, but with the indirect effect going mainly through CD4 and HIV-1 RNA values.

Results: Our estimates of direct and indirect effects show how parts of the overall treatment effect are mediated through the level of CD4 and HIV-1 RNA. As this paper is still a work in progress, more detailed results will follow.

Conclusion: We show that by considering constructed subsets of the observed data, mimicking randomized trials, datasets such as those from HIV cohort studies can be analysed using dynamic path analysis. Such methods can be important in supporting and understanding treatment and disease dynamics.

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Do we know enough? Knowledge evaluation in environmental health: the HENVINET methodology

Alena Bartonova¹, Hans Keune², Martin Kraye von Kraus³, Hai-Ying Liu¹, Aileen Yang¹ and the HENVINET team⁴

1) NILU Norwegian Institute for Air Research, Kjeller

2) Faculty of Political and Social Sciences, University of Antwerp, Belgium

3) WHO European Centre for Environment and Health Rome/Copenhagen.

4) see www.henvinet.eu or <http://henvinet.nilu.no>

Correspondence: Alena Bartonova, e-mail: alena.bartonova@nilu.no, telephone: +47 63 89 81 52

Objective: Prioritizing research or management needs involves significant input from experts. Only few methods involving systematic knowledge evaluation are widely used. The aim of this study is to design and implement such methodology for a number of environmental health issues based on the priority areas of the Environment and Health Action Plan, in broad categories the asthma and allergies, cancer, neurodevelopmental disorders and endocrine disruption. This is one of the bases for creating a network of environmental health professionals, the main aim of the HENVINET project.

Material and methods: We have designed a methodology that involves a combination of scientific review and expert evaluation. First, an issue is translated into a schematic framework, a causal chain diagram that identifies the links between environmental change and its consequences on health. Based on the diagram, we develop a web questionnaire for experts to assess the diagrams completeness and accuracy, and the state of knowledge in each element and link. Finally, the experts need to analyze agreements and disagreements in their answers, and suggest prioritized actions. Statistical consensus measures are used to summarize the results of the evaluation.

Results: Six diagrams are available for expert evaluation through our web site (brominated flame retardants DecaBDE and HBCD, chlorpyrifos, phthalates, traffic pollution, climate change and respiratory health), and several are being prepared (six types of cancer with environmental determinants, nanoparticles). The diagrams related to individual chemicals are using the framework of formal risk assessment and often include e.g. detailed toxicological considerations. The diagrams related to policy issues use less detailed questions but provide an overall picture. As an example of assessment results, the evaluations for Climate change and respiratory health show that of the possible eight determinants of respiratory health related to climate change (dampness, molds, heat waves, cold exposure, surface ozone, particulate matter, pollen and dust mites), least knowledge exists with regard to particulate matter. Usually, recruitment of experts for the evaluation is difficult: each diagram has been evaluated by between 12 and 25 experts, and about half then attend the final workshop. The final workshop has so far been carried out for three of the six issues open for evaluation.

Conclusion: A methodology for evaluation of knowledge has been designed to allow prioritization of issues within environmental health. It has been successfully implemented for a number of environmental health issues, and serves as one of the bases for networking of environmental health community. The method offers a wide range of applications both in research and its applications for policy making.

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A frailty analysis of two-generation melanoma data from the Swedish multi-generation register

Tron Anders Moger^{1,2}, Marion Haugen, Ben Yip³, Håkon K. Gjessing⁴ and Ørnulf Borgan⁵

1) IMB/Department of Biostatistics, University of Oslo, Oslo

2) Institute of Health Management and Health Economics, University of Oslo, Oslo

3) Genome Research Centre, Department of Psychiatry, University of Hong Kong, Hong Kong

4) Norwegian Institute of Public Health, Division of Epidemiology, Oslo

5) Institute of mathematics, University of Oslo, Oslo

Correspondence: Tron Anders Moger, e-mail: tronmo@medisin.uio.no, telephone: +4747245998

Background: Frailty models offer a useful tool for handling multivariate survival data. In order to handle complex dependence structures, the total frailty component for an individual may be split into several parts, such as common environment, genetics and individual environment. One may then determine the contribution of each to the total frailty variance. Due to the complexity of the models, there have not been that many applications to general family data in the literature.

Objective: One main objective was to develop an alternative to the additive frailty model for multivariate survival data. We present a hierarchical frailty model based on Lévy type distributions, which include most common frailty distributions as special cases.

Methods: The model is applied to a case-cohort sample of age at onset data for melanoma from the Swedish multi-generation register, organized into 126196 nuclear families. We fit a parametric model where all frailty components are gamma distributed, and the baseline hazard follows a Weibull distribution. The covariates are birth cohort and gender.

Results: Without covariates, most of the frailty variance is due to individual environment (97.2%), while only 2% is due to genetics. With covariates, less than 1% of the total frailty variance is due to individual environment, as this is very well explained by birth cohort. Genetics account for 92.8%, while common environment accounts for 6.9%. The relative risk for birth cohort is 1.49 per 10 years (95% CI 1.48-1.50), while gender is borderline significant with a relative risk for males of 0.97 (95% CI 0.94-0.99).

Conclusion: The model gives an improved fit to the data compared to a corresponding additive frailty model. It has some nice properties, such as the total frailty variance being the sum of the variance of each frailty component. This yields simple expressions for the correlation between individuals in a family, and for each component's contribution to the total frailty variance.

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Assessment of health risks from ambient PAH exposureAlena Bartonova¹, Mirek Dostal², Eva Rychlikova³ and Radim Sram²

1) NILU Norwegian Institute for Air Research, Kjeller

2) Institute for Experimental Medicine Czech Academy of Sciences, Prague, Czech Republic

3) Regional Public Health Institute Kolin, Czech Republic

Correspondence: Alena Bartonova, e-mail: alena.bartonova@nilu.no, telephone: +47 63 89 81 52

Objective: In the last 20 years, knowledge was generated about the relationship between levels of selected carcinogenic PAHs and a number of adverse health effects in children and in adults. The aim of this study was to review the evidence with the aim to identify important exposure factors, and to conduct an environmental health risk assessment.

Material and methods: In the Czech Republic, long-term studies were carried out in areas with relatively higher load by particulate matter and associated pollutants. In addition to routine monitoring, monitoring of 12 PAHs in gas and particle phase was performed over a longer period of time daily in 5 winter and every three days in 7 summer months. A birth cohort was recruited consisting of 88% of children born in 1994-1999 in two districts in the Czech Republic, over 7500 subjects. A subset of 1492 mother/infant pairs was recruited into the Immune Biomarker study at which maternal and cord blood samples were obtained at delivery. The cohort and the mother-child pairs were followed up in a series of investigations funded over the subsequent 15 years from different sources. Respiratory health and impact of genetic polymorphism on respiratory morbidity was investigated, as well as intrauterine growth retardation and other health endpoints, leading to dose response functions. In this study, we have reviewed this complex research (about 60 publications), analyzed information about exposure factors, and have carried out an environmental health risk assessment for a heavily exposed population in an industrial district. Both monitoring (B(a)P, PM) and dispersion modeling was available in this district for high geographical resolution of the exposure estimates. The risk assessment combined both own derived dose-response functions and data from other sources.

Results: Populations in the districts of the original investigations and the industrial area have similar characteristics. In the geographic area of the original investigations, the observed annual means of c-PAH during the period 1993 to 2005 were in the range between 5 and 22 ng/m³, PM₁₀ ranged between 17 and 75 µg/m³. In the industrial district (approx. 6500 inhabitants), the levels are similar or higher both for B(a)P and PM₁₀. 100% of the population there lives in exceedance of PM₁₀ limits, 78% in exceedance of B(a)P target limits, for 14% this exceedance is tenfold. Individual cancer risk from B(a)P is estimated in the order of persons per thousand and ten thousand. Further, the pollution levels will with high probability lead to low body weight and intrauterine growth retardation, and to lower respiratory diseases. The industry is the main source of exposure, and as also other pollutants are present, carcinogenic effects of e.g. arsenic and B(a)P would be additive or even multiplicative.

Conclusion: At current levels of PM₁₀ and PAH in the investigated industrial area, a number of adverse health outcomes will occur in children and in adults, with high numbers attributable to the industrial pollution sources.

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Dealing with emigration in epidemiologyPetter Kristensen^{1,2} and Tor Bjerkedal^{1,3}

1) Institute of General Practice and Community Medicine, University of Oslo, Oslo

2) National Institute of Occupational Health, Oslo

3) Norwegian Armed Forces Medical Services, Institute of Epidemiology, Oslo

Correspondence: Petter Kristensen, e-mail: petter.kristensen@stami.no, telephone: +47 23195373

Objective: Emigration causes loss to follow-up and may be a source of bias in epidemiological studies. The aim was to study the influence of the choice of handling migration on estimated mortality and cancer incidence in the population of origin.

Material and Methods: All persons born in Norway between 1967 and 1976 and who were not registered dead before 1992 (N=614 176) were followed up in several national registers. Migration movements were identified in the FD-Trygd events data base, death in the Cause of Death Register, and incident cancer in the Cancer Registry of Norway. The population was followed up starting in 1992 and ending in 2004. Four different follow-up scenarios concerning migration were analysed: First, considering only person-time before emigration; second, considering person-time as national residents both before emigration and after repatriation; third, disregarding whether emigration took place or not; and fourth scenario, excluding all who emigrated during follow-up. Mortality and cancer incidence rates were compared in follow-ups using a Poisson regression model.

Results: A total of 40 366 (6.6%) of the study population had between 1 and 13 migration movements and 5354 deaths and 4447 first cancer cases were recorded during follow-up. Mortality and cancer incidence were only marginally influenced by choice of follow-up scenario. Mortality was higher after repatriation than in the source population, in particular during the first year of follow-up (rate ratio adjusted for age, gender, parental education level, and childhood chronic disease: 2.03; 95% confidence interval 1.02–4.03). This excess had little influence on total population rates. Cancer incidence was not affected by repatriation status.

Conclusions: Mortality rates after repatriation were probably elevated because persons who expected to die shortly were more prone to return to their native country (“salmon bias”). The analytical choice concerning follow-up has little influence on estimated outcome occurrences in populations with rather low migration rates. Theoretically, the second scenario should be superior because all person-time as national residents will count, both before emigration and after repatriation. However, the best solution in practice is apparently to censor out persons at the date of emigration in order to avoid salmon bias. This option is also conceptually and analytically simpler.

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Relative risk for mortality from long term exposure to PM_{2.5} in Europe

Lise Marie Fjellsbø, Maria Dusinska and Alena Bartonova

Norwegian Institute for Air Research (NILU), P.O.Box 100, NO-2027 Kjeller, Norway

Correspondence: Lise M. Fjellsbø, e-mail: lbf@nilu.no, telephone: +47 63 89 80 86

Background: A large number of epidemiological studies have shown an association between mass concentration of ambient particulate matter and an increased human mortality rate. Data indicate that air pollution is directly linked to pulmonary toxicity, lung cancer, cardiovascular morbidity and mortality in the general population. General consensus is that air pollution can trigger an inflammatory response via a reactive oxygen species (ROS) -dependent mechanism and stimulate local inflammatory reaction in the lungs. The ROS and pro-inflammatory cytokines released into the blood stream may cause adverse cardiovascular effect. Several studies indicate that PM_{2.5} particles are more hazardous than larger PM as these particles are the most efficient in penetrating and depositing in the alveolar region of the respiratory system and can be translocated via blood stream.

Objective: Prospective cohort studies investigating long-term exposure are suggested as primary basis for estimating mortality effects related to air pollution. These studies evaluate the health effects in a specific population over a period of years. Compared with time series studies, which provide estimates of health effects due to recent exposure, the prospective cohort studies give a more complete assessment of the impact of air pollution since it includes long-term, cumulative effects. The WHO reports from 2004 and 2006 recommend using the American Cancer Society (ACS) study as reference also in Europe, and most ongoing European studies and projects are following this recommendation. However, there is a need to investigate if the recommended coefficient, based on estimate of a 6% increase in mortality hazard rates per 10µg/m³, must be updated. To be able to do this, we have reviewed the most recent literature and projects and compared them with the results from the ACS study.

Result: The present approach used for the evaluation of the health impact of ambient PM exposure recommended by WHO still rely on the use of only one risk factor and one coefficient (WHO 2006). Obviously more knowledge and mechanistic information is needed to be able to identify dose response effect and to assess the risk. Many critical issues such as background levels of exposure, threshold/non-threshold approach, additional endpoints (such as life years lost, and more specific morbidity and mortality subcategories), vulnerable groups, source specific measurement of pollutant, choice of endpoints including molecular markers and biomarkers of individual susceptibility quantification of uncertainties etc need to be discussed. There may be differences in health outcomes depending on whether PM_{2.5} is present at low, medium or high concentration; whether there is a threshold; or whether it is present in combination with other pollutants. However, our review shows that there is still not enough knowledge to propose a new method for the evaluation of the health impact of air pollution (PM_{2.5}), and therefore the use of the estimated coefficient 6% per 10µg/m³ of PM_{2.5} (based on recent prospective studies) as the primary basis for estimating all cause mortality seems still reasonable. For cardiopulmonary and lung cancer mortality this gives an adjusted relative risk of 9% and 14%, respectively. A more sophisticated molecular/ toxicological-based source specific approach to risk assessment and air quality management is likely to contribute significantly to the hazard and risk identification and to the development of cost effective abatement strategies.

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Cancer risk in Norwegian elite athletes performing in the period 1936-2006

Trude Eid Robsahm

The Cancer Registry of Norway

Correspondence: Trude Eid Robsahm, e-mail: trude.eid.robsahm@kreftregisteret.no, telephone: +47 23333932

Background: Physical activity is suggested to inhibit cancer processes and thus, reduce the risk of cancer diseases. However, results from association studies are mainly weak.

Aim: The study aims to investigate whether the level of physical activity influence cancer development, using a study population of Norwegian world class elite athletes, who performed a sport career within the 70-year period 1936-2006.

Material and methods: Altogether, 3 427 athletes are included in the study population. They have completed a questionnaire which gave information about physical activity throughout life, health, alcohol habits, tobacco use, educational level, anthropometry (during life), puberty, hormones, parity and some health problems of current interest. Athlete groups were established based on discipline, lifetime activity level and period of sport career. To elucidate variations in cancer risk, groups of athletes were compared to the general Norwegian population (SIR, STATA), and to each other (Poisson regression, STATA).

Results: A significant reduced risk of total cancer, lung cancer and leukemia/lymphoma was observed in the athlete cohort. In females, a 3-fold risk of thyroid cancer was observed and males tend to have an elevated risk of testicular- and pancreas cancer. The most significant risk reduction was seen in athletes who mainly perform a high frequency of moderate intensive activity (ball sport; moderate level of lifetime activity). Prolonged strenuous training may increase the risk of selected cancer forms.

Conclusion: The observed results indicate a threshold limit for effect rather than a dose response relationship, between physical activity and cancer risk. Lifetime activity with moderate intensity seems to reduce the risk of cancer.

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Assessing interactions between established susceptibility polymorphisms and putative environmental factors in type 1 diabetesLars C. Stene¹, Dag E. Undlien², Kjersti S. Rønningen¹ and Geir Joner³

1) Division of Epidemiology, Norwegian Institute of Public Health, NO-0403 Oslo, Norway

2) Department of Medical Genetics, Oslo University Hospital Ullevål, NO-0407 Oslo, Norway

3) Department of Paediatrics, Oslo University Hospital Ullevål, NO-0407 Oslo, Norway

Correspondence: Lars Christian Stene, e-mail: Lars.Christian.Stene@fhi.no, telephone: +47 2107 8176

Objective: HLA-DQ and PTPN22 are well established susceptibility loci for type 1 diabetes (T1D). Long duration of breastfeeding and use of cod liver oil in the first year of life have been associated with lower risk of T1D in epidemiological studies. We aimed to assess whether the joint effects of pairs of these genetic and non-genetic factors indicated multiplicative effects or stronger “synergistic” effects.

Material and methods: We designed a case-control study with 470 cases of type 1 diabetes diagnosed before 15 years of age in Norway, and 1400 population-based control children. Data on use of cod liver oil and duration of exclusive breastfeeding were obtained from a structured questionnaire administered to the parents of the participating children. HLA genotypes (high- to moderate risk: DQ8/DQ2, DQ8/DQ8, DQ8/X, DQ2/DQ2, vs. all other genotypes) and PTPN22 (TT and CT vs. CC) were divided in two categories.

Results: Non-use of cod liver oil in the first year of life alone was associated with significantly increased risk compared to use of cod liver oil. The two-way joint effect of cod-liver oil with both HLA and PTPN22 was near multiplicative (no evidence for deviation from a multiplicative model, $P=0.86$ and $P=0.87$, respectively, in case-only analysis). Exclusive breast-feeding ≤ 3 months alone were non-significantly associated with higher risk. There was no evidence for a deviation from a multiplicative model for the joint effect of short breastfeeding and HLA ($P=0.48$). There was also no evidence for a deviation from a multiplicative model for the joint effects of short breast-feeding and PTPN22 ($P=0.87$).

Conclusion: The relative risks estimated for the established susceptibility polymorphisms and the non-genetic factors seem to be independent of each other. However, we cannot exclude a role of non-measured confounding factors or some sort of bias explaining the putative association between the non-genetic factors and T1D in this study.

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Cod liver oil, other dietary supplements and survival among cancer patients with solid tumours

Guri Skeie¹, Tonje Braaten¹, Anette Hjartåker², Magritt Brustad¹ and Eiliv Lund¹

1) Institute of community medicine, University of Tromsø, Tromsø, Norway

2) Cancer Registry of Norway, Oslo, Norway

Correspondence: Guri Skeie, e-mail: guri.skeie@uit.no, telephone: 0047 77646594

Background: The effect of various dietary supplements on chronic diseases and mortality has been widely studied, but few convincing results have emerged from studies in well-nourished populations. In Norway, both cod liver oil and other dietary supplements are frequently used. In the Norwegian Women and Cancer cohort study we explored if supplement use before diagnosis affected survival of cancer patients with solid tumours.

Methods: We performed Cox proportional hazards analyses, adjusting for age at diagnosis, smoking and stage.

Results: Cod liver oil was the most frequently used dietary supplement, followed by multivitamins and -minerals. Whole year daily use of cod-liver oil was associated with lower risk of death in patients with solid tumours (RR=0.77 [95% CI 0.61-0.97]) and in lung cancer patients (RR=0.56 [95% CI 0.34-0.92]). Also daily and occasional use of other dietary supplements decreased the risk of death among lung cancer patients (RR=0.70 [95% CI 0.49-0.99] and 0.55 [95% CI 0.31-0.97]). Combined use of cod liver oil and other dietary supplements was associated with reduced risk of dying in lung cancer patients (RR=0.57 [95% CI 0.35-0.94]).

Conclusion: More research is needed in order to clarify the association; meanwhile adjustment for dietary supplement use should be performed in survival analyses of lung cancer patients.

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Incidence of type 2 diabetes in groups stratified according to criteria of metabolic syndrome. The Tromsø StudyJosepha Joseph¹, Johan Svartberg^{2,3}, Inger Njølstad¹ and Henrik Schirmer^{1,4}

1) Department of Community Medicine, University of Tromsø, Tromsø, Norway

2) Department of Medicine, University Hospital of North Norway, Tromsø, Norway

3) Institute of Clinical Medicine, University of Tromsø, Tromsø, Norway

4) Department of Cardiology, University Hospital of North Norway, Tromsø, Norway

Correspondence: Josepha Joseph, e-mail: josepha.joseph@uit.no, telephone: +4777620719

Objective: Metabolic syndrome is known as a precursor of type 2 diabetes. Less is known about the subjects who develop type 2 diabetes without fulfilling the metabolic syndrome criteria. The aim of this study is to evaluate the incidence of type 2 diabetes in groups stratified according to criteria of metabolic syndrome and to describe the subgroup which develops diabetes without metabolic syndrome at baseline.

Material and methods: This is a population based 11 years follow up of 26,957 subjects from municipality of Tromsø followed from 1994 to 2005, age range was 25-98 years. 7191 of these subjects were rescreened in 2001. Non fasting serum level of high density lipoprotein (HDL), triglycerides and glucose, blood pressure (BP), weight and height were measured at baseline. A total of 522 new cases of type 2 diabetes were registered, 308 among men and 214 among women. Of these 198 developed diabetes after 2001. The metabolic syndrome defined by the NCEP was applied to examine the risk of developing diabetes. (Body mass index) BMI was used instead of waist circumferences (>28,3 kg/m² for men and 27,0 kg/m² for women). Triglycerides > 1,695 mmol/L, Blood pressure > 135/85, HDL < 1,036 mmol/L for men and < 1,295 mmol/L for women. The sums of these criteria were calculated with 3 or more as metabolic syndrome. The hazard ratio (HR) of type 2 diabetes was calculated using Cox proportional hazard model adjusting for age. All analysis was performed stratified by gender.

Results: The absolute risk of developing type 2 diabetes over 11 years increased from 0,5% in men and 0,1% in women for those without any metabolic risk factors to 10 and 11% for those men and women fulfilling 4 of the metabolic score criteria. The age adjusted HR for highest metabolic score compared to lowest were 50 (CI95% 22-114) for women and 16 (CI95% 8.6-30) for men. There was a significant risk already from a score of 1 in each gender. Of new cases of type 2 diabetes, 53% of the men and 40% of the women did not fulfil the metabolic criteria at baseline by scoring 2 or less. In the 7191 with screening data in 2001, of those who developed type 2 diabetes after 2001 with low metabolic score in 1994; 44% had changed to high metabolic score before being diagnosed with diabetes. In total, 52% and 88% had an unfavourable change in triglycerides, 60.9% and 77.8% in BMI, 69.6% and 77.8% in HDL and 14.5% and 14.6% became hypertensive in men and women respectively. Those who developed diabetes despite a low score at baseline were most likely hypertensive at baseline (84.6% of the men and 85.2% of the women).

Conclusion: As expected the metabolic syndrome predicts diabetes type 2. Of new cases of type 2 diabetes only 53% fulfilled 3 or more metabolic syndrome criteria at baseline, but in the subjects with a low metabolic score at baseline, unfavourable change in these factors left only 38% of these subjects with a low metabolic score before development of diabetes. A majority of these had hypertension at baseline and more than 95% had unfavourable change in one or more of the metabolic risk factors before diagnosis.

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Ultraviolet exposure in five life decades and risk of cutaneous malignant melanoma

Marit B. Veierød¹, Hans-Olov Adami^{2,3}, Eiliv Lund⁴, Bruce Armstrong⁵ and Elisabete Weiderpass^{2,4,6,7}

1) Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

2) Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

3) Department of Epidemiology, Harvard School of Public Health and Dana Farber Harvard Cancer Center, Boston, MA

4) Institute of Community Medicine, University of Tromsø, Tromsø, Norway

5) School of Public Health, University of Sydney, Sydney, Australia

6) Department of Etiological Research, Cancer Registry of Norway, Oslo, Norway

7) Department of Genetic Epidemiology, Folkhälsan Research Center, Helsinki, Finland

Correspondence: Marit B. Veierød, e-mail: m.b.veierod@medisin.uio.no, telephone: +47 22 85 14 32

Objective: The major established and modifiable risk factor for cutaneous malignant melanoma is sun exposure. Use of indoor tanning devices (solariums) has also been associated with increased risk, but the evidence is less consistent. Previous results derive mainly from case-control and nested case-control studies. The current aim is to study the importance of exposure to sun and solariums in different periods of life and possible effect modification by host factors in a cohort.

Material and methods: The Norwegian-Swedish Women's Lifestyle and Health Cohort Study included more than 100 000 women aged 30-50 years in 1991/92. Ultraviolet (UV) exposure and host factors were collected at inclusion through a self-administered questionnaire. The women were asked about their histories of sunburn, sunbathing vacations and use of a solarium when they were aged 0-9, 10-19, 20-29, 30-39 or 40-49 years. Follow-up was achieved by linkages to national registries in Norway and Sweden through 2005. Relative risks are estimated by Poisson regression.

Results: A total of 412 cases of melanoma were diagnosed during an average follow-up of 14 years. The mean age at diagnosis was 49 years. Increased risks of melanoma were found following sunburns and bathing vacations in the first three decades of life. Solarium use in childhood and teenage years was rare in this cohort. Solarium use in early adulthood and midlife increased the risk of melanoma. Interactions between UV exposure and host factors will be discussed. Both UVA and UVB may play a role for melanoma, and we will also discuss the potential impact of national regulations on indoor tanning devices implemented in 1982/83 resulting in changes in the UVB to UVA ratio.

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Seasonal variation in incidence of acute myocardial infarction and all-cause mortality in a subarctic population. The Tromsø Study 1974-2004.

Laila Arnesdatter Hopstock¹, Tom Wilsgaard¹, Inger Njølstad¹, Jan Mannsverk², Ellisiv B. Mathiesen^{3,4}, Maja-Lisa Løchen^{1,2} and Kaare Harald Børnaa^{1,2}

1) Institute of Community Medicine, University of Tromsø, Norway

2) Department of Cardiology, University Hospital of Northern Norway, Tromsø, Norway

3) Department of Neurology, University Hospital of Northern Norway, Tromsø, Norway

4) Institute of Clinical Medicine, University of Tromsø, Norway

Correspondence: Laila A. Hopstock, e-mail: laila.hopstock@uit.no, telephone +47 90 01 08 11

Background: A seasonal pattern with higher morbidity and mortality in winter has been reported for both acute myocardial infarction (MI), cardiovascular diseases and total mortality. The quantity of difference between peak and nadir season has been associated with latitude, but the results are inconsistent. Studies of monthly variation of MI in population-based cohorts, based on adjudicated MI cases, are few. We investigated the monthly variation in incident non-fatal and fatal MI and total mortality in the population of Tromsø in Northern Norway, a region with a harsh climate and extreme seasonal variation in daylight exposure.

Materials and methods: A total of 37,392 participants from the population-based Tromsø Study enrolled between 1974 and 2001 were followed from date of study entry throughout 2004. Each incident case of MI was validated via review of full medical records and death certificates. Event ascertainment followed a detailed protocol.

Results: A total of 1,893 first-ever MI were registered, of which 592 were fatal. A total of 3,067 deaths from any cause occurred in the period. No evident seasonal variation in non-fatal or fatal MI incidence or case-fatality was found. All-cause mortality had a significant seasonal pattern with lower mortality in April, May and June ($p=0.0057$).

Conclusion: We found no evident seasonal pattern in incident fatal and non-fatal MI. In contrast, all-cause mortality had a significant seasonal pattern. A non-uniform definition of outcome and season may explain some of the inconsistency in results from previous studies. The populations living in the subarctic areas may be more adapted to face winter month exposures through behavioural protection.

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Menopausal hormone therapy and breast cancer risk – impact of different treatments (The EPIC-study)

Kjersti Bakken¹, Agnès Fournier², Eiliv Lund¹, Françoise Clavel-Chapelon², Bertrand Hémon³ and Franco Berrino⁴

1) Department of Community Medicine, University of Tromsø, Tromsø, Norway

2) Inserm, (Institut National de la Santé et de la Recherche Médicale), ERI 20 / Institut Gustave-Roussy / University Paris-South 11, EA 4045, IFR69, Villejuif, France

3) International Agency for Research on Cancer, Lyon, France

4) Epidemiology Unit, National Cancer Institute, Milan, Italy

Correspondence: Kjersti Bakken, e-mail:kjersti.bakken@uit.no, telephone: 77646434

Background: There is considerable epidemiological evidence that menopausal exposure to exogenous sex steroid hormones plays an important role in the development of breast cancer in women. Menopausal hormone therapy (MHT) is characterized by the use of different constituents, regimens and routes of administration. We therefore conducted an analysis of the relation between use of MHT and the risk of breast cancer according to different hormones, regimens and administration routes using data from the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. The ultimate aim of the study was to identify the safest modalities of MHT use.

Methods: The EPIC-cohort is a multi-centre prospective cohort with 23 contributing centres in ten European countries. Altogether 133 744 postmenopausal women were followed in eight of the ten countries. Information on MHT use was derived from country-specific self-administered questionnaires with a single baseline assessment. Incident breast cancers were identified through population cancer registries or by active follow-up. Overall relative risks (RR) and their 95% confidence interval (CI) were derived from country-specific Cox proportional hazard models estimates, combined based on random effects model.

Results: A total of 4,312 primary breast cancers were diagnosed during 1,153,747 person-years of follow-up. Overall, MHT ever use was reported by 46.0% of postmenopausal women in the cohort, 67.1% of these being current users. Among current users, combinations of estrogens and progestin were predominant (65.0%) over estrogen-only (21.7%). The most frequently used progestin in combined MHT was norethisterone acetate (NETA), followed by progesterone and norgestrel. Compared to MHT never-users, we found increased breast cancer risks in current users of estrogen-only (RR 1.42, 95% CI 1.23-1.64) and of combined MHT (RR 1.77, 95% CI 1.40-2.24). Compared to estrogen-only, use of combined MHT was associated with a significant increase in risk ($p=0.02$). Continuous combined regimens conferred a 43% (95% CI 19%-72%) greater risk compared to sequential regimens. There was no significant difference between progesterone- and testosterone-derivatives in sequential regimens (RR 1.09, 95% CI 0.81-1.48 for testosterone- compared with progesterone-derivatives). We found no significant variation in risk linked to the estrogenic component of MHT, neither for oral vs. cutaneous administration, nor for estradiol compounds vs. conjugated equine estrogens.

Conclusions: Use of MHT was associated with a significant increase in risk of breast cancer in women, and the highest estimates were found in current users of combined MHT. Relative to sequential regimens, continuous regimens were associated with a 43% greater risk of breast cancer. A comparison of risk of breast cancer between testosterone- and progesterone-like progestins was only possible for sequential regimens and yielded no significant difference. This study adds to the increasing evidence that breast cancer risk may vary according to the characteristics of the progestin component of combined MHT, especially the number of days it is administered each month. Further studies are needed to disentangle the effects of these parameters and of the monthly progestin dose.

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Combined results and long-term follow-up in NORVIT and WENBIT of 6837 coronary artery disease patients: Homocysteine-lowering B-vitamin treatment does not prevent major cardiovascular events

Ottar Nygård^{1,4}, Marta Ebbing¹, Kaare Harald Bønaa^{2,3}, Per Magne Ueland⁴, Jan Erik Nordrehaug^{1,4}, Knut Rasmussen^{2,5}, Inger Njølstad³, Dennis W. Nilsen^{6,4}, Øyvind Bleie¹, Helga Refsum⁷, Aage Tverdal⁸, Stein Emil Vollset^{8,9} and Egil Arnesen³

1) Department of Heart Disease, Haukeland University Hospital, Bergen, Norway

2) Department of Heart Disease, University Hospital of North Norway, Tromsø, Norway

3) Institute of Community Medicine, University of Tromsø, Norway

4) Institute of Medicine, University of Bergen, Norway

5) Institute of Medicine, University of Tromsø, Norway

6) Department of Cardiology, Stavanger University Hospital, Stavanger, Norway

7) Institute of Basic Medical Sciences, University of Oslo, Norway

8) Department of Epidemiology, the Norwegian Institute of Public Health, Oslo, Norway

9) Department of Public Health and Primary Health Care, University of Bergen, Norway

Correspondence: Marta Ebbing, e-mail: marta.ebbing@helse-bergen.no, telephone: +4755972196

Objectives: Observational studies have reported associations between circulating total homocysteine concentration and risk of cardiovascular disease. Our purpose was to assess the effects of homocysteine-lowering treatment in the Norwegian Vitamin Trial (NORVIT) and the Western Norway B-vitamin Intervention Trial (WENBIT) by combined analyses of trial results and long-time follow-up of the two study populations.

Methods: A total of 6837 patients, 76.5% male, mean (SD) age 62.3 (11.0) years, with acute myocardial infarction or angiographically verified coronary artery disease, were included during the period from December, 1998 to April, 2004. They were randomly assigned to four groups receiving daily oral treatment with 1) folic acid (0.8 mg)/vitamin B₁₂ (0.4 mg)/vitamin B₆ (40 mg), 2) folic acid/vitamin B₁₂, 3) vitamin B₆ alone or 4) placebo. The primary end point during the intervention was a composite of non-fatal acute myocardial infarction, non-fatal thromboembolic stroke or cardiovascular death. The end point during long-time follow-up was cardiovascular death. Estimates of the hazard ratios (HR) and 95% confidence intervals (CI) were obtained using Cox proportional hazard regression with adjustment for trial.

Results: By 1-2 months after randomization, plasma total homocysteine concentration was lowered by median 25% in the groups receiving folic acid and vitamin B₁₂. During median in-trial follow-up of 39 months, 531 (15.6%) of participants receiving folic acid plus vitamin B₁₂ vs 503 (14.7%) of those not receiving such treatment experienced the primary end point (HR, 1.07; 95% CI, 0.95–1.21; P=.28). In the vitamin B₆ groups, a total of 524 (15.4%) of participants experienced the primary end point vs 510 (14.9%) of participants in the non-vitamin B₆ groups (HR, 1.04; 95% CI, 0.92–1.18; P=.53). Long-term cardiovascular mortality during median 78 months of extended follow-up was also similar according to treatment with folic acid plus vitamin B₁₂ or not (HR, 1.12; 95% CI 0.95–1.31; P=.18) and vitamin B₆ or not (HR, 1.06; 95% CI, 0.90–1.24; P=.51). After adjustment for study treatment, age, gender, smoking status and serum creatinine concentration, every 5- μ mol/L increment in baseline plasma total homocysteine was associated with a 7% increased risk for the primary end point during trials (HR, 1.07; 95% CI, 1.01–1.13, P=.02) and a 12% increased risk for long-term cardiovascular death (HR, 1.12; 95% CI, 1.05–1.19; P<.001).

Conclusions: The combined results and long-time follow-up of these two large randomized clinical trials in Norway do not justify the use of homocysteine-lowering B vitamin supplements as secondary prevention in patients with ischemic heart disease.

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Smoking and risk of ovarian cancer; results from the EPIC study

Inger T. Gram^{1,2}, Tonje Braaten¹, Ilene Brill³, Eiliv Lund¹, Laure Dossius⁴, Annie Lukanova⁴ and Rudolf Kaaks⁴

1) Institute of Community Medicine, University of Tromsø, Norway

2) Norwegian Centre for Telemedicine, University Hospital of North Norway, Tromsø

3) School of Public Health, University of Alabama at Birmingham, Alabama, USA

4) Division of Cancer Epidemiology, German Cancer Research Centre, Heidelberg, Germany

Correspondence: Inger Torhild Gram, e-mail: inger.gram@uit.no, telephone: +47 77 64 48 16

Objective: As of today we do not know if ovarian cancer is a smoking related disease. Studies regarding the association between smoking and risk of epithelial ovarian cancer (EOC) are few and inconsistent. The purpose of this study was to examine the association between smoking and EOC in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort.

Material and methods: The EPIC cohort is a large, multi-centre prospective study to investigate the relations of nutritional, lifestyle, metabolic and genetic risk factors and cancer incidence. It was initiated in 1992 in ten European countries (Sweden, Denmark, Norway, the Netherlands, United Kingdom, France, Germany, Spain, Italy and Greece). The questionnaires included data about dietary, lifestyle and health factors. Information about tobacco smoking was collected from individuals in all participating countries. Subjects were asked if they smoked cigarettes currently and whether they had smoked in the past. Information was available on number of cigarettes per day, duration of smoking, age started smoking and age of smoking cessation (for former smokers). Incident cancer cases were identified through several methods, including record linkage with regional cancer registries (Denmark, Sweden, Norway, Italy, the Netherlands, Spain and the United Kingdom), health insurance records, cancer and pathology registries and active follow-up of study subjects (France, Germany, and Greece). We used Cox proportional hazard regression models to estimate hazard ratio (RR) of EOC with 95% confidence intervals (CIs) associated with different measures of smoking exposures adjusting for confounding variables.

Results: Altogether 836 [731 (87%) invasive, 67(8%) borderline and 38(5%) unclassified] incident EOC cases were identified among the 326,831 women during an average of 6 years of follow-up. The tumours were classified as 400 serous, 83 mucinous and 353 endometrioid /clear cell/unspecified. Forty-three percent of the women reported to be ever smokers, 23% former and 20% current smokers. Current smokers had a 20% increased risk for EOC overall [RR=1.2 (95% CI 1.0–1.4)] and an 80% increased risk of borderline tumors [RR=1.8 (95% CI 1.0–3.1)] compared with the reference group of never smokers. Ever smokers who started to smoke before the age of 16 years had a 50% increased risk for invasive EOC [RR=1.5 (95% CI 1.1–2.0)] compared with the reference group. Furthermore, ever smokers who had smoked for 30 years or more had a 30% increased risk for EOC overall [RR=1.3 (95% CI 1.1–1.6)], a 30% increased risk for invasive EOC [RR=1.3 (95% CI 1.0–1.5)] and a 90% increased risk of borderline tumors [RR=1.9 (95% CI 0.9–3.9)] compared with the reference group.

Conclusion: In conclusion, smoking of long duration may increase the risk of both invasive and borderline EOC.

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Cholesteryl ester transfer protein (CETP) TaqIB polymorphism, HDL-cholesterol, alcohol consumption and the risk of coronary heart disease; a case-cohort study (INTERGENE)

E. Strandhagen¹, K. Mehlig¹, L. Nunez¹, P.A. Svensson², A. Rosengren³, K. Toren¹, L. Lissner¹ and D.S. Thelle^{1,4}

1) Sahlgrenska School of Public Health and Community Medicine, Institute of Medicine, University of Gothenburg, Sweden

2) Department of Molecular and Clinical Medicine, Institute of Medicine, University of Gothenburg, Sweden

3) Department of Emergency and Cardiovascular Medicine, Institute of Medicine, University of Gothenburg, Sweden

4) Department of Biostatistics, Institute of Basic Medical Sciences, Faculty of Medicine, University of Oslo, Norway

Correspondence: Elisabeth Strandhagen, e-mail: elisabeth.strandhagen@gu.se

Objective: To investigate whether CETP TaqIB (G+279A/In1- rs708272) polymorphism, alcohol consumption and high density lipoprotein cholesterol (HDL-C) and their co-variation is modifying the risk of coronary heart disease (CHD) in a case-cohort study.

Methods and results: 618 cases of CHD (165 female) were analyzed in relation to 1908 women and 1702 men from the INTERGENE cohort using unconditional logistic regression. The alcohol consumption was categorized as tertiles of ethanol intake (g/day), with non-drinkers constituting a fourth category. CETP TaqIB genotypes and blood lipid levels were determined. The CETP TaqIB T homozygotes had significantly lower risk of CHD (OR 0.72, 95% CI 0.55–0.96, adjusted for age and sex), than C homozygotes. The protective effect of being in the 2 highest quartiles of HDL-C was stronger in the TT group (4th vs. 1st quartile OR 0.12, 95% CI (0.06–0.25 and 3rd vs. 1st quartile OR 0.18, 95% CI (0.09–0.36)) than in the (CT+CC) group, p-value for interaction between HDL-C and genotype 0.05 and 0.03, respectively (results adjusted for age, sex, BMI, ever smoking and ethanol).

Intermediate ethanol intake is associated with a reduced risk for CHD in T homozygotes, 2nd tertile vs. zero consumption OR 0.26, 95% CI 0.11–0.64 (adjusted for age, sex, BMI, ever smoking and quartiles of HDL-C, p-value for interaction between ethanol and genotype 0.05).

Conclusions: The CETP TaqIB polymorphism may affect the risk of CHD depending on HDL-C levels and alcohol intake. CETP TaqIB TT homozygotes have lower risk for CHD, a risk which decreases further with high values of HDL-C and consumption of moderate amounts of alcohol.

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Breast cancer mortality in Norway after the introduction of mammography screening

Anne Helene Olsen and Eiliv Lund

Department of Epidemiology and Medical Statistics, Institute of Community Medicine, Faculty of Medicine, University of Tromsø

Correspondence: Anne Helene Olsen, e-mail: anne.h.olsen@uit.no, telephone: +45 26 25 81 06

Objective: Organised mammography screening for women aged 50 to 69 started in Rogaland, Oslo, Hordaland and Akershus in 1996 (the early starting counties). The programme was gradually expanded across Norway. The last counties to be included were Oppland, Møre & Romsdal in 2002, Sogn & Fjordane and Hedmark in 2003, and Vestfold in 2004 (the late starting counties). We will study the change in breast cancer mortality from the period before screening to the period during screening in the early starting countries, controlling for the change in breast cancer mortality between the same periods in the late starting counties. The purpose of this presentation is to explain the methods developed for this study.

Material and methods: The study group consists of women aged 50-69 living in the early starting counties during the screening period. These women will be compared with women in the same age group living in the early starting counties during the period before screening started (historical control group), and with women aged 50-69 living in the late starting counties during the same two periods (regional and historical regional control groups). The women will be followed up until death, emigration or end of follow-up, whichever comes first. End of follow-up is before start of screening in the late starting counties for the study group and the regional control group, and a similar follow-up system will be constructed for the historical and the historical regional control group. Person time will be calculated individually for each woman. The end point studied is death from breast cancer. After a preliminary analysis of breast cancer mortality we will use data from the Norwegian Women and Cancer study (NOWAC) to adjust the results for opportunistic screening and life style factors affecting breast cancer incidence and mortality. Poisson regression is used for the analyses, controlling for region (early and late starting counties), period (before and during screening in early starting counties), and age (50-54, 55-59, 60-64, 65-69, 70-74, 75-79, and 80-84 years).

Results: Results are not yet available and will therefore not be presented. A study of the Copenhagen mammography screening programme in Denmark showed a 25% reduction in breast cancer mortality for women invited to the programme using a similar study design.

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Explaining the massive declines in coronary heart disease mortality rates in Iceland, 1981-2006

Thor Aspelund^{1,2}, Vilmundur Gudnason^{1,2}, Bergrun T. Magnusdottir¹, Karl Andersen^{1,2}, Bolli Thorsson¹, Gunnar Sigurdsson^{1,2}, Julia Critchley³, Martin O'Flaherty⁴ and Simon Capewell⁴

1) Icelandic Heart Association, Heart Preventive Clinic and Research Institute

2) University of Iceland

3) Institute of Health and Society, University of Newcastle, UK

4) Department of Public Health, University of Liverpool, England

Background: Coronary heart disease mortality rates have been decreasing in Iceland since the 1980s. We used the IMPACT model to examine how much of the decrease in Iceland between 1981 and 2006 could be attributed to medical and surgical treatments and changes in risk factors.

Methods: The previously validated IMPACT model was used to combine and analyse data on uptake and effectiveness of cardiological treatments and risk factor trends in the Icelandic population. The main data sources were official statistics, national registers, published trials and meta-analyses, clinical audits and national population surveys.

Results: Between 1981 and 2006, coronary heart disease mortality rates in Iceland decreased by 80% in men and women aged 25 to 74 years. This fall resulted in 295 fewer deaths in 2006. One quarter of this decrease was attributable to treatments in individuals. Three quarters of the decrease was attributable to population risk factor reductions (principally cholesterol 36%; smoking 20%; systolic blood pressure 26% and physical activity 5%). Adverse trends were seen for diabetes (-5%), and obesity (-4%).

Conclusions: Three quarters of the coronary heart disease mortality decrease in Iceland between 1981 and 2006 was attributable to reductions in major cardiovascular risk factors in population, (mainly decreases in total serum cholesterol, smoking and blood pressure levels). These findings emphasize the value of a comprehensive strategy that promotes tobacco control and a healthier diet. It also highlights the potential importance of effective, evidence based medical treatments.

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Swedish mammography screening trials revisited

Per-Henrik Zahl

Norwegian Institute of Public Health, Oslo

Correspondence: Per-Henrik Zahl, e-mail: Per-Henrik.Zahl@fhi.no, telephone: +47 21078150

Objective: In Norway and Sweden mammography screening was associated with a 50% increase in breast cancer incidence rates. In Norway we have previously compared two matched cohorts of 109,784 (control) and 119,472 (study) women who were followed in 6 years. The study cohort was screened biennial in the first 4 years but not the controls. After 4 years the difference in the cumulative rates was 458 per 100,000 women. In years 5-6 both cohorts were screened simultaneously. After 6 years there were 345 more breast cancers per 100,000 in the triple screened group. This corresponds to that $(345 \text{ of } 458) = 75\%$ of all extra breast cancers detected in the first two screening rounds have disappeared before screening in year 5-6. We suggested that overdiagnosis to a large extent is explained by the detection of tumors that otherwise would spontaneously regress.

Methods: In Sweden screening started ten years earlier than in Norway. We have constructed two cohorts of 317,404 (control) and 328,927 (study) women, respectively, and followed the age groups 40-4, 45-9, 50-4, 55-9, 60-64 and 65-9 in six years as previously done in Norway. We have also calculated the differences in the breast cancer mortality rates. This study design is also mimicking the Swedish randomized screening trials.

Results: There were significantly ($P < 0.001$) more breast cancers in the triple screened cohorts for all 5-year age groups and the differences were similar to those observed in Norway. The difference was biggest for the age groups 40-54.

Conclusions: We have shown that the screening related incidence increase in the first 4 years of the 6-year observation period in the study cohort was not compensated for by a corresponding incidence increase when the previously un-screened women in the control cohort were invited in year 5-6. In this study hormone therapy do not confound the analyses because most women did not use these drugs.

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Low serum 25-hydroxyvitamin D levels are associated with increased all-cause and cardiovascular disease mortality risk in a general population. The Tromsø study.

M.S. Hutchinson, G. Grimnes, R. Joakimsen, Y. Figenschau and R. Jorde

Correspondence: Moira Strand Hutchinson, e-mail: moira-ylva.hutchinson@uit.no

Objectives: Ecologic and observational studies have suggested an association between serum 25-hydroxyvitamin D (25(OH)D) levels and cardiovascular disease (CVD) risk factors, CVD mortality, and cancer mortality. Based on this, low serum 25(OH)D levels should be associated with higher all-cause mortality in a general population. This hypothesis was tested in the present study.

Design: The Tromsø study is a longitudinal population based multipurpose study initiated in 1974 with focus on lifestyle-related diseases. In the fourth Tromsø study the attendance rate was 77%, resulting in 27 159 participants \geq 25 years of age. Serum 25(OH)D was measured in 7161 participants. Current smokers were excluded from the analyses, leaving 4751 subjects for the present analysis.

Results: During a mean 11.8 years of follow up 798 (16.8%) participants died. In multivariate regression models there was a significantly increased risk of all-cause (hazard ratio (HR) 1.24 confidence interval (CI) 1.06-1.45) and CVD mortality (HR 1.29 CI 1.01-1.65) among participants in the lowest serum 25(OH)D quartile when compared to participants in the upper three quartiles.

Conclusions: Low serum 25(OH)D levels are associated with increased all-cause and CVD mortality risk. However, low serum 25(OH)D levels are associated with impaired general health and we can not draw conclusions about causality. Randomized controlled studies are needed to address this question.

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Histological type and grade of breast cancer tumors by time since a childbirth

Grethe Albrektsen¹, Ivar Heuch² and Steinar Østerbø Thoresen³

1) Department of Public Health and Primary Health Care, University of Bergen, Norway

2) Department of Mathematics, University of Bergen, Norway

3) The Gade institute, University of Bergen, Norway

Correspondence: Grethe Albrektsen, e-mail: msega@uib.no, telephone: +47 55 58 61 54

Objective: The long-term protective effect of a pregnancy in relation to breast cancer risk is preceded by a short-term adverse effect. A main aim of the present study was to examine whether pregnancy-related breast cancer tumors, and tumors diagnosed during the high-risk period after birth, tended to be of a particular histological type or grade.

Material and methods: Results are based on information for 9709 parous women diagnosed with breast cancer before age 50 years in Norway during the period 1955-1999. Information on reproductive history and cancer diagnoses was obtained from the national population- and cancer registers, respectively. Chi-square tests were applied for comparing proportions, whereas odds ratios (each histological type vs. ductal, or grade 3-4 vs. grade 1-2) were estimated in polytomous and binary logistic regression analyses.

Results: Ductal tumors, and malignant sarcomas, mainly phyllodes tumors, seemed to occur at higher frequency in women diagnosed <2 years after a childbirth compared to women with a longer time interval since delivery at date of diagnosis. The proportions of medullary tumors and Paget disease were particularly high among women diagnosed 2-5 years after birth, but the absolute numbers were rather low. In age-adjusted analyses, only unspecified carcinomas and lobular tumors showed a significant inverse linear relationship with increasing time since first and last birth. The observed high proportion of poorly differentiated tumors in women with a recent childbirth was partly explained by young age.

Conclusion: The present results indicate that a pregnancy may affect histological types of breast cancer tumors differently.

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Parental-offspring associations in body mass index in the Norwegian Mother and Child Cohort Study

Caroline Fleten¹, Wenche Nystad¹, Hein Stigum¹, Debbie Lawlor², George Davey Smith², Rolv Skjærven³ and Øyvind Næss¹

1) Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

2) Division of Epidemiology, University of Bristol, England

3) Medical Birth Registry of Norway, Norwegian Institute of Public Health, Bergen, Norway

Correspondence: Caroline Fleten, e-mail: anne.caroline.fleten@fhi.no, telephone: +47 21 07 82 62

Objective: The aim of this study is to compare the association between maternal pre-pregnancy body mass index (BMI) and offspring BMI at three years of age with the paternal-offspring association in BMI. Furthermore, the study explores the role of other pre-, peri- and postnatal determinants of offspring BMI on the maternal-offspring association in BMI.

Material and methods: This study included pregnant women and their offspring recruited from 1999-2008 in the Norwegian Mother and Child Cohort Study conducted by The Norwegian Institute of Public Health. Linear regression analyses were based on data from self-administered questionnaires during and after pregnancy.

Preliminary results: 26,826 offspring-parents trios were included. The mean BMI at three years of age was 16.1 kg/m², mean maternal BMI was 24.1 kg/m² and paternal BMI was 25.8 kg/m². The crude association between maternal and offspring BMI showed an increase in offspring BMI of 0.033 kg/m² ($P < 0.001$; confidence interval (CI) 0.028 to 0.038) per unit increase in maternal BMI (1 kg/m²). The association between paternal and offspring BMI showed an increase in offspring BMI of 0.043 kg/m² ($P < 0.001$; CI 0.036 to 0.049). When adjusting the maternal-offspring association in BMI for paternal BMI, both associations appeared approximately the same with increases of 0.027 kg/m² and 0.035 kg/m² in offspring BMI, respectively, for mother's and father's increase in BMI by one unit. All regression models adjusted for pre-, peri- or postnatal factors showed similar results, including parental height, age and education, maternal smoking during pregnancy, breast-feeding, parents living together or not, institution of daycare, mother in work, offspring time in front of television/video, and offspring time spent outdoor at the age of three.

Conclusion: The results show similar associations between maternal-offspring and paternal-offspring BMI. None of the included pre-, peri- or postnatal determinants of offspring BMI changed the maternal-offspring association in BMI.

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**Trends in colorectal cancer incidence in Norway 1962-2006:
an interpretation of the temporal patterns by anatomic subsite**Inger Kristin Larsen¹ and Freddie Bray^{1,2}

1) Department of Clinical and Registry-based Research, Cancer Registry of Norway, Institute of Population-based Cancer Research, Oslo, Norway

2) Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Norway

Correspondence: Inger Kristin Larsen, e-mail: Inger.Kristin.Larsen@kreftregisteret.no, telephone: +47 23 33 39 18

Objective: There have been rapid increases in the incidence of colorectal cancer in Norway since the 1960s, and rates rank among the highest worldwide. The primary objectives of this study has been to describe the Norwegian trends in subsite-specific colorectal cancer incidence, and to summarize the available evidence from prospective studies on the associations between established risk factors and cancer of the colorectal subsites.

Material and methods: Diagnoses of colorectal cancer were extracted from the Cancer Registry of Norway for 1962-2006 by year of diagnosis, sex, and age and (ICD-7 4-digit) topography codes, yielding material on 101 034 persons and 102 882 primary colorectal cancer tumours. Aggregated age-specific and age-standardised (world58) incidence rates per 100,000 were computed by anatomic subsite in five-year periods (1962-6, 1967-71, ..., 2002-6) by sex.

Results: While the age-adjusted incidence rates of CRC increased in Norway in both sexes up to the 1980s, subsite- and age-specific analyses reveal a deceleration in the rate of increase thereafter, an observation apparent in the rates of both left-sided colon and rectal cancer. Overall trends in incidence of right-sided colon cancer continue to increase in both sexes. The all-ages rates are thus in keeping with the commonly-reported "left to right shift" of colon cancer. The cohort patterns provide further evidence that factors earlier in life are important, and while the complex aetiology makes interpretation difficult, modifications in diet, obesity and physical activity in Norway are likely among the drivers of the trends, although the associations differs across the colorectal subsites.

Conclusion: The recent downturn in the disease at younger ages provides some reason for optimism, although possible increases in rectal cancer among recent birth cohorts are of concern.

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Trends in incidence and mortality for triplets in Norway 1967-2006. The influence of assisted reproductive technologies.

Anne Tandberg^{1,2}, Tone Bjørge^{2,3}, Ottar Nygård⁴, Per E. Børdahl^{1,5} and Rolv Skjærven^{2,3}

1) Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen

2) Department of Public Health and Primary Health Care, University of Bergen

3) Medical Birth Registry of Norway, Norwegian Institute of Public Health, Bergen

4) Institute of Medicine, University of Bergen

5) Institute of Clinical medicine, Section for Gynaecology and Obstetrics, University of Bergen

Correspondence: Anne Tandberg, e-mail: anne.tandberg@isf.uib.no, telephone: +4755588514

Objective: To assess changes in incidence rates and outcomes of triplets during forty years with a particular focus on the influence of assisted reproductive technology (ART).

Design: Population-based cohort study from the Medical Birth Registry of Norway.

Material and methods: 2.18 million pregnancies, inclusive 448 sets of triplets and 27,575 twin pairs covering the years 1967-2006. Since 1988, pregnancies from ART were available through a separate registry and linked with the birth record. Incidence rates and outcomes for triplets were analyzed and compared with singletons and twins. Relative risks (RR) were estimated between time periods, and between ART and non-ART pregnancies, respectively.

Results: The total triplet rate per 10,000 pregnancies increased from 1.0 in 1967-71 to 3.5 in 1987-92, followed by a decline to 2.7 in 2002-06. After excluding ART-pregnancies, the incidence was more than doubled at the end of the study period. The mean gestational age and the birth weight of triplets were significantly lower in 1988-2006 compared to 1967-1987, similar for ART- and non-ART triplets in the last period. The cesarean rate in triplets increased from 47% to 92%. The RR of perinatal death in triplets compared to singletons did not change after the introduction of ART, RR 8.9 (95% CI 6.8-11.7) and 10.4 (95% CI 8.3-13.0), comparing the two periods.

Conclusions: The triplet incidence rate in Norway has more than doubled during the last forty years, even after excluding ART pregnancies. The risk of perinatal death in triplets was ten times higher compared to singletons and has not changed during this forty years period, independent of introduction of ART.

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Use of drugs with an abuse potential among disability pensioners in NorwayIngeborg Hartz^{1,2,3}, Aage Tverdal³ and Svetlana Skurtveit^{3,4}

1) Department of Health and Sports, Hedmark University College, Elverum, Norway

2) Institute of Pharmacy, University of Tromsø, Norway

3) Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

4) Norwegian Centre for Addiction Research, University of Oslo, Norway

Correspondence: Ingeborg Hartz, e-mail: ingeborg.hartz@hihm.no, telephone: +4797703853

Objective: The Norwegian Government urges that actions are needed to stimulate the working capacity in disability pensioners with such a potential. Information on factors that may impair rehabilitation efforts, including unfavourable use of drugs with an abuse potential, may be useful in this context. Thus, the aim of the study was to describe the association between receipt of disability pension (DP) and later prescriptions of benzodiazepines (BZDs), and other potentially abusive drugs, among non-users of BZDs at baseline.

Material and Methods: We followed a cohort 9409 men and 11236 women aged 40, 45, 60 years who underwent health surveys in 2000-01 in three Norwegian counties (Hedmark, Oppland and Oslo), with respect to incident use of BZDs, and other potentially abusive drugs, by linkage to the Norwegian Prescription Database for 2004-2007. Information on disability pension status was retrieved from Statistics Norway. Predictors of incident BZD use in 2004 were analysed, as well as patterns of continued BZD use throughout the period 2004-2007.

Results: Incident BZD use 3-4 years later were significantly higher among disability pensioners, Highest initiation rates were observed among female disability pensioners, of whom 18-20% had started BZDs, as compared to 5-8% of the non-receivers of a disability pension at baseline. Multivariable analyses revealed an independent effect of disability pension on initiation of BZDs 3-4 years later (OR 1.6 (95% CI 1.4-2.0)). Among users in 2004, 51% of the youngest (40+45 years at baseline) and 60% of the oldest (60 years at baseline) disability pensioners continued to retrieve BZDs throughout the period 2004-07, as compared to 32-33% of the non-receivers of a disability pension. The annual median defined daily doses (DDD) of BZDs among continued users increased steadily throughout the period, most pronounced in the youngest disability pensioners (50 (IQR 14,140) DDD in 2004 to 205 (25,352) DDD in 2007).

Conclusions: The chance of being prescribed benzodiazepines was higher among those reporting to be DP recipients 3-4 years in the past. High continuation rates, with a steadily increasing annual amount of use among the continued users may reflect an unfavourable use pattern of potentially abusive drugs among disability pensioners, most worrisome among the youngest.

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Noise-annoyance from traffic and plasma cortisol in a population based study

Ruhina Tasmin Biswas¹, Bente Oftedal¹, Gunn Marit Aasvang¹, Per Schwarze¹, Per Nafstad^{2,3}, Wenche Nystad² and Stein Knardahl⁴

1) Norwegian Institute of Public Health, Division of Environmental Medicine, Oslo

2) Norwegian Institute of Public Health, Division of Epidemiology, Oslo

3) Institute of General Practice and Community Medicine, University of Oslo

4) The National Institute of Occupational Health

Correspondence: Ruhina T. Biswas, e-mail: RuhinaTasmin.Biswas@fhi.no, telephone: +4721076608

Background: Experimental studies have shown that noise can affect cortisol levels acutely as well as chronically. Cortisol influences both metabolic factors and the immune system. At moderate to high levels, transportation noise is considered as an environmental stressor by influencing behavioural, psychological and physiological processes. Several studies have suggested that long term exposure to transportation noise may increase the risk of ischemic heart disease and hypertension. One of the possible mechanisms that are proposed to link elevated noise levels to the development of these diseases includes the increase in hormone levels such as cortisol. An important indicator of the noise-cortisol relationship could be annoyance from traffic noise, as perception of as well as coping with noise differs in people. So far this potential relationship has not been studied in large epidemiological studies.

Objective: The aim of the study is to examine the relationship between noise-induced annoyance and plasma cortisol levels.

Method: Blood samples of 1470 subjects aged 30 and 45 year were taken at afternoon (11 a.m to 1 p.m.) in the Oslo Health Study (HUBRO) and were later analysed for cortisol levels. Time of last meal was also noted. Hopkins Symptoms Checklist- a ten questions based check list (HSC-10) was used to assess psychological distress. A general linear model was used to investigate the association between noise annoyance and plasma cortisol levels adjusting for relevant confounders including HSC-10, use of sedatives in the last month and time of last meal.

Result: 19% of the subjects were moderately and 2.6% were very annoyed by traffic noise. 9.1% of the moderately annoyed and 21.4% of the very annoyed persons reported sleep disturbance in the last week according to HSC-10. The mean cortisol level was 442 nmol/L (95%CI, 430-455) in men and 426 nmol/L (95% CI, 409-443) in women. Preliminary results did not reveal an association between noise annoyance and plasma cortisol levels. The association between noise annoyance and plasma cortisol remained insignificant after adjusting for age, sex, BMI, HSC-10, use of sedatives and time of last meal.

Conclusion: We found no simple association between noise annoyance and plasma levels of cortisol.

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**Nicotine dependence predicts problematic use of prescribed opioids.
Prospective population-based cohort study.**Svetlana Skurtveit^{1,2}, Kari Furu¹, Randi Selmer¹, Marte Handal¹ and Aage Tverdal¹

1) Department of Pharmacoepidemiology, Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, 0403 Oslo, Norway

2) Norwegian Centre for Addiction Research, University of Oslo, Norway

Correspondence: Svetlana Skurtveit, e-mail: svetlana.skurtveit@fhi.no, telephone: +47 21078172

Objectives: Use of repeated opioid therapy for chronic non-cancer pain has increased substantially. Optimal use of opioids should balance the benefits with the potential abuse of opioids medication. Nicotine and opioids have been shown to interact in various experimental settings of drug addiction, and chronic nicotine treatment has been shown to sensitize the dopaminergic reward system to morphine. An association between smoking and the use of prescribed opioids has been suggested in cross-sectional population-based studies. More data on opioid use in the general population is required to determine the factors that may increase unfavourable use in patients with chronic, non-malignant pain. The aim of our study was to evaluate prospectively smoking dependence as predictor of moderate-high use of prescribed opioids in non-cancer patients.

Design: Prospective population-based study cohort.

Setting: Five counties in Norway.

Participants: 12848 men and 15894 women, aged 30-75 years, participated in health surveys in Norway 2000-2002 and followed throughout 2007.

Measurements: Moderate-high opioid prescriptions (12+ times during 2004-2007) recorded in the Norwegian Prescription Database. Information on history of smoking and potential confounders were obtained at baseline by self-administered questionnaires. For smoking, participants were divided into four categories: never; previously heavy (stopped max. 5 year ago; 10+ cigarettes daily); daily not heavy (1-9); dependent daily smokers (10+) and category others (previously and/or not daily). Odds ratios (OR) with 95% confidence intervals (CI) were estimated by logistic regression.

Findings: During follow-up, 335 (1.5%) of survey participants were registered with 12+ prescriptions of opioids during 2004-2007. The prevalence of moderate to high prescription frequency of opioids was higher for men and women with a history of smoking. The adjusted OR for prescribed opioids for dependent daily smokers was 3.1 (95% CI: 2.3-4.1), for daily non heavy smokers 1.8 (1.2-2.7), for previous heavy smokers 1.8 (1.1-3.0), compared with never smokers as reference.

Conclusions: We found a dose-response relationship between cigarette consumption and subsequent use of opioids. When prescribing opioids for chronic non-cancer pain, clinicians need to balance the risks of prescription drug abuse and dependence with the benefits of pain relief. Our study suggests that smoking dependence may predict more frequent use of opioids.

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Exposure to long-term traffic noise, noise annoyance and blood pressure

Bente Oftedal¹, Gunn Marit Aasvang¹, Ruhina Tasmin Biswas¹, Per Nafstad^{2,3}, Wenche Nystad² and Per Schwarze¹

1) Norwegian Institute of Public Health, Division of Environmental Medicine, Oslo

2) Norwegian Institute of Public Health, Division of Epidemiology, Oslo

3) Institute of General Practice and Community Medicine, University of Oslo

Correspondence: Bente Oftedal, e-mail: bente.oftedal@fhi.no, telephone: +47 21 07 65 92

Background: Based on a general stress model, it is hypothesized that long-term exposure to noise may have adverse effects on health, including cardiovascular outcomes. Several epidemiological studies have reported higher risk of hypertension in areas with high exposure to aircraft noise, whereas the relationship with exposure to road traffic noise is more unclear. In Norway about 1.7 million people are exposed to environmental noise above recommended level at their home address of whom more than 10% have reported being highly annoyed by noise. Noise annoyance depends on individual perception, and may be able to mediate associations between noise levels and health outcomes. Road traffic is the main source of both noise and air pollution in Norway, and air pollution has also been linked to cardiovascular outcomes. So far, the relative importance of noise and air pollution for developing cardiovascular diseases is limited, and more studies are needed.

Objective: The aim is to gain more knowledge on the relationships between residential traffic noise, noise annoyance and blood pressure by simultaneously controlling for residential traffic-related air pollution.

Material and methods: The study population consisted of the participants from The Oslo Health Study (HUBRO) and from the additional cohorts (N=21,363 in total). The participants were from 30 to 76 years of age. Systolic and diastolic blood pressures were measured by an automatic device on the right arm in sitting position, with three recordings at one-minute intervals. The mean value of the second and third measurement was used as outcome. Annoyance from traffic noise was obtained from the questionnaire. The assessment of environmental noise in Oslo for 2006 was conducted by the Municipality of Oslo in compliance with the EU Directive on Environmental Noise. The outdoor noise levels were calculated separately for road traffic and rail traffic (tram, subway and railway) according to the Nordic Prediction Method. By including rail traffic data and road traffic data together with digitalised terrain data, buildings and noise screens in 3 dimensions, the software program CadnaA calculated the noise levels in 5 x 5 m² grids. The noise indicators L_{den} (day-evening-night) and L_{night} were calculated outside the most exposed façade and outside the bedroom façade, respectively. Using the geographical coordinates for each participant's home addresses during 1992-2006, long-term residential traffic noise exposure will be assigned. The Norwegian Institute of Air Research will provide residential traffic-related air pollution levels from the same period. A general linear model will be used to analyse the relationships between traffic noise, noise annoyance and blood pressure, adjusting for relevant potential confounders including air pollution.

Results: 2.5% reported being very annoyed and 17.3% reported being moderately annoyed by traffic noise. Systolic blood pressure was 2.5 mmHg (95% CI: 0.7, 4.3) lower in those reporting being very annoyed and 0.9 mmHg (0.2, 1.7) lower in those reporting being moderately annoyed by traffic noise, compared to those not being annoyed. Further results including residential traffic noise exposure, will be presented at the conference.

Conclusion: As residential traffic noise levels are not yet available, it is not possible to draw any conclusions on the relationships between traffic noise, noise annoyance and blood pressure.

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Congenital anomalies in newborns of women with type 1 diabetes: Nation-wide population based study in Norway 1999-2004

Ingvild Eidem^{1,2}, Lars C. Stene², Tore Henriksen^{3,4}, Kristian F. Hanssen⁵, Siri Vangen^{2,6}, Stein E. Vollset^{7,8} and Geir Joner^{1,9}

1) Department of Paediatrics, Oslo University Hospital Ullevål, Oslo, Norway

2) Division of Epidemiology, Norwegian Institute of Public Health, Oslo

3) Department of Gynecology and Obstetrics, Oslo University Hospital Rikshospitalet, Oslo

4) Faculty Division Rikshospitalet, University of Oslo

5) Department of Endocrinology, Oslo University Hospital Aker, Oslo

6) National Centre of Women's Health, Department of Gynecology and Obstetrics, Oslo University Hospital Rikshospitalet, Oslo

7) Medical Birth Registry, Norwegian Institute of Public Health, Bergen, Norway

8) Department of Public Health and Primary Health Care, University of Bergen

9) Institute of Health Management and Health Economics, University of Oslo

Correspondence: Ingvild Eidem, e-mail: Ingvild.eidem@fhi.no, telephone: +4721078181

Objective: To estimate the risk of congenital anomalies in offspring of birth giving women with type 1 diabetes in Norway during recent years.

Design: Nation-wide population based study using the Medical Birth Registry of Norway and the Norwegian type 1 Diabetes Registry.

Participants: All births in Norway 1999-2004 (n=350 961). 1583 were births by a mother registered with pregestational type 1 diabetes.

Main outcome measure: Congenital anomalies, excluding minor anomalies according to the EUROCAT system.

Results: Anomalies were registered in 5.7% of offspring of women with type 1 diabetes, and in 2.9% among the background population (odds ratio 2.1, 95% confidence interval: 1.7-2.6). Cardiovascular anomalies were registered in 3.2% in the diabetes group and 0.94% in the background population (odds ratio 3.5, 95% confidence interval: 2.7-4.7). Results were similar when restricted to women identified with type 1 diabetes through the diabetes registry.

Conclusion: Women with type 1 diabetes experience a significantly higher risk of congenital anomalies in their babies, also during recent years in Norway.

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Smokers have an increased risk of developing genital warts

Bo Terning Hansen¹, Maria Hagerup-Jenssen¹, Susanne Krüger Kjær^{2,3}, Christian Munk², Laufey Tryggvadottir⁴, Pär Sparén⁵, Kai-Li Liaw⁶ and Mari Nygård¹

1) Department of Screening-based Research, Cancer Registry of Norway, Oslo, Norway

2) Institute of Cancer Epidemiology, Danish Cancer Society

3) Department of Obstetrics and Gynecology, Rigshospitalet, University of Copenhagen, Denmark

4) Icelandic Cancer Society, Reykjavik, Iceland

5) Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm, Sweden

6) Merck Research Laboratories, Merck & Co., Inc., Upper Gwynedd, Pennsylvania, USA

Correspondence: Bo Terning Hansen, e-mail: bo.terning.hansen@kreftregisteret.no, telephone: +4723333959

Objective: To assess the association between smoking and the occurrence of genital warts.

Methods: A sample of 59489 women (aged 18-45) from the general female population of Denmark, Iceland, Norway and Sweden answered a questionnaire on lifestyle and health. We reconstructed longitudinal data based on self report of age at first clinical diagnosis of genital warts, as well as age-specific smoking doses and ages at onset of smoking, sexual intercourse, condom use, hormonal contraceptive use, first pregnancy and alcohol drinking.

Results: In an adjusted time-dependent Cox regression model, smokers had an elevated risk of developing genital warts compared to nonsmokers (hazard ratio 1.31, 95% CI 1.21 to 1.41). There was an additional dose-response effect of smoking, with smokers experiencing a 1.1% increased risk of developing genital warts per additional cigarette smoked daily (hazard ratio 1.011, 95% CI 1.005 to 1.016).

Conclusion: Smokers had a moderately increased risk of developing genital warts.

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Calculation of volume of health services that are registered in the Norwegian Patient Registry

Lise Lund Håheim^{1,2}, Katrine Damgaard¹ and Doris Tove Kristoffersen¹

1) Norwegian Knowledge Centre for the Health Service, Oslo

2) Institute of Basal Medicine, Medical Faculty; Institute of Oral Biology, Dental Faculty: University of Oslo

Correspondence: Lise Lund Håheim, e-mail: llh@nokc.no, telephone: +47 90113398

Objective: The volume of treatment procedures is one way of illustrating the hospital activity. The Norwegian Directorate for Health requested the Norwegian Knowledge Centre for Health Services (NOKC) to identify the codes necessary to identify certain treatment procedures. The volumes to be calculated were those for which there is published waiting time for consultation and treatment on the web-site for Free Hospital Choice Norway (Fritt sykehusvalg Norge): <http://www.frittsykehusvalg.no/start/>

Material and method: The databases of the Norwegian Patient Registry (Norsk pasientregister (NPR)) for out-patients, day treatment and in-patients were used. NOKC, Section for Quality Measurements, carried out an assessment of the databases, and identified the codes for 58 surgical procedures in the first phase of the project. The second phase is in progress for coding the remaining examinations and different conditions.

Results: The work followed a process to quality assure the codes and calculations: a) NOKC made suggestions to codes for the surgical procedures. These were assessed by clinicians for codes and content. The alternative codes were ICD-10, DRG, The NOMESCO Classification of Surgical Procedures (NCSP), and consultation fees. b) The revised codes were used for calculations per hospital and per procedure using data from 2006. These calculations were sent to Free Hospital Choice Norway in Norway who administered the quality control with each hospital. Differences were observed between data from the hospitals and NPR. Most differences were due to the quality assurance process that NPR carries out on data from the hospitals. Some differences may be explained by differences in coding practice.

Conclusion: This project show that the NPR databases can be used for other purposes than it was first designed to cater for the financing of the hospital services. These volume data gives insight into the activities of the hospitals, but they are not linked to any specific quality outcomes.

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Participants

Adele Stornes	Kreftregisteret, Oslo	adele.stornes@kreftregisteret.no
Alena Bartonova	NILU, Kjeller	alena.bartonova@nilu.no
Andrew Gilman	Canada	andygilman@shaw.ca
Anna Sofia Veyhe	UiT, Tromsø	anna.sofia.veyhe@uit.no
Anne Caroline Fleten	Folkehelseinstituttet, Oslo	anne.caroline.fleten@fhi.no
Anne Helene Olsen	UiT, Tromsø	anne.h.olsen@uit.no
Anne Tandberg	UiB, Bergen	anne.tandberg@isf.uib.no
Annett Arntzen	Høgskolen i Vestfold	AA@hive.no
Bente Oftedal	Folkehelseinstituttet, Oslo	bente.oftedal@fhi.no
Bjørn Straume	UiT, Tromsø	bjorn.straume@uit.no
Bo Terning Hansen	Kreftregisteret, Oslo	bo.terning.hansen@kreftregisteret.no
Cecilie Kyrø	Fredriksberg, Danmark	cecilie@cancer.dk
Charlotta Rylander	UiT, Tromsø	charlotta.rylander@uit.no
Christine L. Parr	UiO, Oslo	c.l.parr@medisin.uio.no
Eiliv Lund	UiT, Tromsø	eiliv.lund@uit.no
Elisabeth Strandhagen	Göteborgs universitet	elisabeth.strandhagen@gu.se
Elja Arjas	Universitetet i Helsinki	elja.arjas@helsinki.fi
Erik Eik Anda	UiT, Tromsø	erik.anda@uit.no
Ernst I.S. Thomassen	UiT, Tromsø	eivsit@gmail.com
Grethe Albrektsen	UiB, Bergen	msega@uib.no
Gudrun Maria Waaler	Folkehelseinstituttet, Oslo	gudrun.maria.waaler@fhi.no
Guri Skeie	UiT, Tromsø	guri.skeie@uit.no
Hege M. Bøvelstad	UiO, Oslo	hegembo@math.uio.no
Helene M. Tvinnereim	UiB, Bergen	helene.tvinnereim@iko.uib.no
Hilde Langseth	Kreftregisteret, Oslo	hilde.langseth@kreftregisteret.no
Ingeborg Hartz	Høgskolen i Hedmark	ingeborg.hartz@hihm.no
Inger Cappelen	Folkehelseinstituttet, Oslo	inger.cappelen@fhi.no
Inger Kristin Larsen	Kreftregisteret, Oslo	inger.kristin.larsen@kreftregisteret.no
Inger Njølstad	UiT, Tromsø	inger.njolstad@uit.no
Inger Torhild Gram	UiT, Tromsø	inger.gram@uit.no
Ingvild Eidem	Folkehelseinstituttet, Oslo	ingvild.eidem@fhi.no
John-Arne Skolbekken	NTNU, Trondheim	johnas@svt.ntnu.no
Jon Michael Gran	UiO, Oslo	j.m.gran@medisin.uio.no
Josepha Joseph	UiT, Tromsø	josepha.joseph@uit.no
Kari Furu	Folkehelseinstituttet, Oslo	kari.furu@fhi.no
Karina Standahl Olsen	UiT, Tromsø	karina.s.olsen@uit.no
Kirsten Mehlig	Göteborgs universitet	kirsten.mehlig@gu.se
Kjersti Andersen Nerhus	Folkehelseinstituttet, Oslo	kjne@fhi.no
Kjersti Bakken	UiT, Tromsø	kjersti.bakken@uit.no
Knut Fylkesnes	UiB, Bergen	knut.fylkesnes@cih.uib.no
Koenraad Cuypers	HUNT, Verdal	kjcuype@online.no
Kristian Hveem	NTNU, Trondheim	kristian.hveem@ntnu.no

Kristin B. Borch	UiT, Tromsø	kristin.benjaminsen.borch@uit.no
Kristin Holvik	UiO, Oslo	kristin.holvik@medisin.uio.no
Kristin Steinsbekk	NTNU, Trondheim	kristin.steinsbekk@samfunn.ntnu.no
Kristin Sørensen	UiT, Tromsø	kristin.sorensen@uit.no
Laila Hopstock	UiT, Tromsø	laila.hopstock@uit.no
Lars Christian Stene	Folkehelseinstituttet, Oslo	lars.christian.stene@fhi.no
Leiv Bakketeig	Folkehelseinstituttet, Oslo	leiv.bakketeig@fhi.no
Lisa Forsén	Folkehelseinstituttet, Oslo	lisa.forsen@fhi.no
Lise Lund Håheim	Kunnskapssenteret, Oslo	llh@nokc.no
Lise Marie Fjellsbø	NILU, Kjeller	lbf@nilu.no
Magritt Brustad	UiT, Tromsø	magritt.brustad@uit.no
Mari Nygård	Kreftregisteret, Oslo	mari.nygard@kreftregisteret.no
Marianne Lauritzen	Kreftregisteret, Oslo	marianne.lauritzen@kreftregisteret.no
Marianne Riksheim	UiO, Oslo	marianneriksheim@gmail.com
Marit B. Veierød	UiO, Oslo	m.b.veierod@medisin.uio.no
Marit Waaseth	UiT, Tromsø	marit.waaseth@uit.no
Marte Handal	Folkehelseinstituttet, Oslo	marte.handal@fhi.no
Merethe Kumle	UNN, Tromsø	merethe.kumle@unn.no
Moira Yla Strand	UiT, Tromsø	moira-ylva.hutchinson@uit.no
Nanna Kurtze	SINTEF, Oslo	nanna.kurtze@sintef.no
Nannan Yang	UiT, Tromsø	nannan.yang@uit.no
Odd O. Aalen	UiO, Oslo	o.o.aalen@medisin.uio.no
Ottar Nygård	Helse Bergen	ottar.nygard@helse-bergen.no
Per Magnus	Folkehelseinstituttet, Oslo	per.magnus@fhi.no
Per-Henrik Zahl	Folkehelseinstituttet, Oslo	per-henrik.zahl@fhi.no
Petter Kristensen	Statens Arbeidsmiljøinstitutt	petter.kristensen@stami.no
Randi Gislefoss	Kreftregisteret, Oslo	randi.gislefoss@kreftregisteret.no
Randi Selmer	Folkehelseinstituttet, Oslo	rands@fhi.no
Ruhina Tasmin Biswa	Folkehelseinstituttet, Oslo	rubi@fhi.no
Saminda Pathmasiri	Canada	spathmasiri@3g.org
Sarah Sæther	UiT, Tromsø	fra-saet@hotmail.com
Sissel Andersen	UiT, Tromsø	sissel.andersen@uit.no
Solrunn Hansen	UiT, Tromsø	solrunn.hansen@uit.no
Stein Atle Lie	UiB, Bergen	stein.lie@unifob.uib.no
Svetlana Skurtveit	Folkehelseinstituttet, Oslo	svetlana.skurtveit@fhi.no
Thor Aspelund	Hjartavernd, Island	aspelund@hjarta.is
Tom Ivar Lund Nilsen	NTNU, Trondheim	tom.nilsen@svt.ntnu.no
Tom Wilsgaard	UiT, Tromsø	tom.wilsgaard@uit.no
Tormod Brenn	UiT, Tromsø	tormod.brenn@uit.no
Tron Anders Moger	UiO, Oslo	tronmo@medisin.uio.no
Trond Peder Flaten	NTNU, Trondheim	trond.flaten@chem.ntnu.no
Trude Eid Robsahm	Kreftregisteret, Oslo	trude.eid.robsahm@kreftregisteret.no
Vanessa Dumeaux	UiT, Tromsø	vanessa.dumeaux@uit.no
Vilmundur Gudnason	Hjartavernd, Island	v.gudnason@hjarta.is
Yiting Xue	UiO, Oslo	yiting.xue@medisin.uio.no
Øystein Karlstad	Folkehelseinstituttet, Oslo	oeka@fhi.no
Aage Tverdal	Folkehelseinstituttet, Oslo	aage.tverdal@fhi.no