Nordic Summer School of Cancer Epidemiology, phase III

Virrat Winter Symposium 2010

Virrat, Finland, 29-31 January 2010

Coordinated by Eero Pukkala
Finnish Cancer Registry & School of Public Health, University of Tampere

Program
+ abstracts
PROGRAM

FRIDAY, 29 January

16.00  Departure from Tampere railway station towards airport
(after arrival of the trains from Oulu and Helsinki at 15:56-15:57)

about 16.20  Departure from Tampere Airport for Virrat
(arrival of the last flight at 15.55)

at arrival to Virrat

Eero Pukkala: Opening of the Virrat Winter Symposium;
practical information (lecture hall)

Laufey Tryggvadóttir: Results of chairperson election; tasks of a chairman
of a scientific symposium (max 7 minute presentation)

Room occupation (wooden cottages at river-shore)
Poster hanging (coffee room next to the lecture hall)

19.0  Dinner (restaurant, other side of the road, walk 500 m)

SATURDAY, 30 January

8.00  Breakfast (restaurant)

8.30-9:45  SESSION I – Host factors and descriptive epidemiology

Chairperson: Díana Óskarsdóttir (co-chair: Laufey Tryggvadóttir)

Student presentations: 15 minutes plus 5 minutes discussion time

Johanna Sirkiä: Evaluation of 15 cancer candidate genes in familial
colorectal cancer predisposition

Eevi Kaasinen: Low-penetrance susceptibility variants underlying familial
colorectal cancer

Kim K. B. Clemmensen: Trends in incidence of malignant melanoma in
Denmark 1943-2007. A descriptive study
**Poster highlights**

(3 minute oral presentations of selected posters)

Juha Kivelä: Cause-specific mortality of oral cancer in northern Finland: patients diagnosed during 1984 - 2004


Riitta Niinimäki: High risk of osteonecrosis requiring total joint arthroplasty in young patients treated for myeloid leukaemias – a nationwide, register-based study

9:45 Break, poster viewing

10:15-11:35 **SESSION II – Life habits & cancer risk**

Chairperson: Camilla Böckelman (co-chair: Esa Läärä)

Aksel Jensen: Risk of skin melanoma following phototherapy for neonatal jaundice – a retrospective cohort study

Mohammad-Ali Haghsheno: The association of vitamin D, bone mineral density and skeleton fractures with prostate cancer

Elisabeth Möller: Adherence to the Nordic nutrition recommendations does not protect against prostate cancer

Angelica Siew: Exposure to ‘iron and welding fumes’, ‘wood dust and formaldehyde’ and the risk of respiratory cancers

12.00 Lunch (restaurant), poster viewing

13:00-13:30 Bendix Carstensen: R
13:40-15:00 SESSION III – Interventions, risk factor control, diagnostics
Chairperson: Nis Frederik Palm Suppli (co-chair: Inge Haunstrup Clemmensen)
Amy Levál: STI risk perception and condom use with temporary partners: a national population based study among young adults
Tina Bech Olesen: “LIVA” – a population-based study of sexual habits among more than 20,000 women in Denmark
Tuomas Kilpeläinen: Results of the three rounds of the Finnish Prostate Cancer Screening Trial
Díana Öskarsdóttir: Vertebral assessment of vertebral fractures with DXA: comparision of two different methods

15:00 Coffee break, poster viewing

15:20-16:40 SESSION IV – Effects of cancer to later life
Chairperson: Amy Levál (co-chair: Gerda Engholm)
Nis P. Suppli: Factors associated with the prescription of anti-depressive medication in breast cancer patients – a rehabilitation perspective
Marie Höyer: The complexity of assessing patient reported outcomes among women with breast cancer – a population-based cross-sectional study in central Sweden
Lars Henrik Damkjær: The association between cancer treatment, rehabilitation and permanent work market withdrawal in danish breast cancer survivors
Heidi Filppa: Relative survival of oral cancer patients at the Oulu University Hospital area in 1984-2004
Camilla Böckelman: CIP2A is a marker of reduced survival in serous ovarian cancer patients

16:50-17:10 Gerda Engholm: Cancer patient survival in the Nordic countries

17.30 Sport-like winter events
(outdoors, instructions in loud Finnish language)
18.45 Dinner, multicultural discussions on scientific and other mutually interesting topics  
(old country restaurant Mikonhovi)

ICEHOLE SESSION - (river shore sauna, fire place)  
Chairperson: Bendix Carstensen

21.30∞ Sauna, ice-hole swimming, sauna-disco  
Advanced jenkka dance lessons given by surrogates of Prof. Matti Hakama

SUNDAY, 31 January

9.00 Breakfast (restaurant)

9.50 SESSION VI – Closure  
Joint presentation by the tutors: How to submit a paper and what happens to it in the journal

10.20 Awards, certificates and closing remarks  
Packing, leaving the rooms

11:15 Bus leaves towards Tampere

13.00 arrival Tampere Airport (farewell to Icelanders, whose flight is at 14:00)

before 14.00 arrival to Tampere railway station  
Possibility to see around in Tampere  
Chairperson: Tuomas Kilpeläinen

before 19.00 arrival Tampere Airport (flight back to Western civilisation at 19:50)
ABSTRACTS

(in alphabetical order according to surname of the first presenting author)
CIP2A IS A MARKER OF REDUCED SURVIVAL IN SEROUS OVARIAN CANCER PATIENTS

Camilla Böckelmann1,2,3, Heini Lassus4, Annabrita Hemmes1,2, Arto Leminen4, Jukka Westermarck5,6, Caj Haglund3, Ralf Bützow2,4, Ari Ristimäki1,2,7

1Genome-Scale Biology Research Program, Biomedicum Helsinki, University of Helsinki, Helsinki, Finland. 2Department of Pathology, HUSLAB and Haartman Institute, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland. 3Department of Surgery, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland. 4Department of Obstetrics and Gynecology, Helsinki University Central Hospital and University of Helsinki, Helsinki, Finland. 5Centre for Biotechnology, University of Turku and Åbo Akademi University, Turku, Finland. 6Department of Pathology, University of Turku, Turku, Finland. 7Department of Pathology, Institute of Diagnostics, University of Oulu and Oulu University Hospital, Oulu, Finland.

Cancerous inhibitor of PP2A (CIP2A) is a recently identified oncoprotein, but its role in ovarian cancer is not known. We analyzed CIP2A protein expression in 562 consecutive serous ovarian cancer patients, of which 524 were scored successfully and analyzed for presence of CIP2A immunopositivity using tissue microarrays. The association of CIP2A expression with survival was evaluated according to the Kaplan-Meier method. We found strong CIP2A positive immunostaining in 212 (40.4%) specimens, 222 (42.4%) were weakly positive, while the rest (n = 90, 17.2%) were immunonegative for CIP2A protein. Our results demonstrate that CIP2A immunopositivity is a marker of reduced overall survival in ovarian cancer patients (P < 0.0001). In addition, positive CIP2A expression was significantly more frequent in specimens with high grade (P < 0.0001), advanced stage (P = 0.0005), aberrant p53 immunoreactivity (P < 0.0001), high proliferation index (P < 0.0001), and aneuploidy (P = 0.001). Interestingly, in subgroups of patients with favorable clinical factors (i.e. low stage and optimal debulking surgery) CIP2A expression was strongly associated with reduced survival (P < 0.0001 for both parameters). This shows that CIP2A could be used to predict biological behavior in the group of patients with otherwise favorable prognosis. In conclusion, our results show that CIP2A protein expression is a novel marker of reduced survival in patients with serous ovarian carcinoma. Furthermore, these results suggest that CIP2A characterizes the aggressive type of this disease even within subgroups with initially favorable prognosis.
Trends in incidence of malignant melanoma and non melanoma skin cancer in Denmark 1943-2007. A descriptive study

Astrid Knudsen* and Kim K. B. Clemmensen*

*The Danish Cancer Registry

**Background** In 2007 Danish Cancer Society launched an ongoing sun protection campaign. In connection with this campaign we plan to further investigate recreational UV-exposure. As an initial introduction to this subject, we here want to describe how the incidence of cancers related to UV-exposure (non melanoma skin cancer (NMSC) and malignant melanoma (MM)) has developed in Denmark since 1943. Multiple factors influence the incidence trends i.e. changes in intermittent UV-exposure patterns from vacations, sunbed use and intentional tanning.

**Material** The Danish Cancer Registry is a population-based registry containing data on the incidence of cancer throughout Denmark since 1943. Reporting of cancer was made mandatory by administrative order in 1987. Details of individual cases of cancer are available according to the 7th revision of the International Classification of Diseases (ICD) for all years, and according to the ICD-O since 1978. A core data set is kept on each individual which includes date of birth, sex, date of cancer diagnosis, method of verification, date of death and cause of death.

**Methods** Data from The Danish Cancer Registry 1943-2007. SAS-programmes: Niels Christensen, The Danish Cancer Society. The incidence rates were age-standardized to WSP (world). MM data: the ICD-10 codes C430-C439. NMSC data: the ICD-10 codes C440-C449, C60.

**Results**

**Time trends:** Overall the incidence of MM for both women and men in Denmark has increased steeply since 1943. NMSC incidence in Denmark has increased since 1960 and especially since 1975.

**Age incidence:** The incidence of MM increases with age, but the disease occurs among young individuals from 15 years of age. The NMSC incidence increases steadily with age, however the disease is rare before the age of 40 years.

**Conclusions** The incidence of both MM and SC has increased in Denmark. One factor which might contribute to the rise in incidence of these cancers is increased intermittent UV exposure during vacations. This we plan to address in further investigation of recreational UV-exposure looking at travelling patterns in the Danish population.
THE ASSOCIATION BETWEEN CANCER TREATMENT, REHABILITATION AND PERMANENT WORK MARKET WITHDRAWAL IN DANISH BREAST CANCER SURVIVORS.

Lars Henrik Damkjær

Institute for Cancer Epidemiology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen, Denmark

The purpose of this register-based study was to identify cancer-, treatment- and sociodemographic factors associated with taking Early Retirement Pension (ERP) in women treated for breast cancer and further to evaluate the risk of taking ERP in breast cancer survivors who attended a 6-day rehabilitation course compared to a matched control group of breast cancer survivors who did not attend the rehabilitation course, when adjusting for known risk factors. The study population consisted of 856 women who had attended the rehabilitation course and a comparison group of 1805 women registered by the Danish Breast cancer Coorperation Group (DBCG). We obtained information on receipt of unemployment benefits, sickness benefits and ERP for each of the years 1996 through 2007. The rate of ERP was higher among women suffering somatic comorbidity, prior depression or had received sickness benefits in the year prior to their breast cancer diagnosis. Living with a partner was associated with a reduced hazard ratio for taking ERP. The rate of ERP was higher among the women having attended the rehabilitation course in the year following the stay but it returned to unity in the course of three years. The knowledge gained from this study contributes to the identification of at-risk women and points to the need for tailored rehabilitation efforts in order to avoid unnecessary marginalisation of breast cancer survivors.
RELATIVE SURVIVAL OF ORAL CANCER PATIENTS AT THE OULU UNIVERSITY HOSPITAL AREA IN 1984-2004

Heidi Filppa¹
¹University of Oulu, Finland

The aim of the study is to determine if the survival of oral cancer patients at the Oulu university hospital area differs from the survival of the whole population of Finland between years 1984 and 2004.

The data includes all oral cancer patients diagnosed between 1984 and 2004 at the Oulu university hospital area, 384 patients total. Information from Finnish Cancer Registry has been used as well. Interesting variables are, for example, age, sex and stage of the cancer. Five years after the diagnosis 68.5% of 0-65-year-old oral cancer patients and 77.7% of over 65-year-old patients were alive. For males the same proportion was 71.5% and for females 66.7%. Analysis is still going on and the next step is to compare these proportions to national total mortality and draw survival functions.
We investigated the association between Vitamin D, bone mineral density (BMD) and skeleton fractures in men with prostate cancer enrolled in Mr Ös population study in Sweden.

In accordance with the results of previous studies we hypothesised that men with lower BMD and lower D-vitamin levels would have increased incidence of prostate cancer and that men with prostate cancer would have increased incidence of skeleton fractures.

Our cohort consisted of a total of 3011 men enrolled in Mr Ös community based population study from three centres in Sweden. The catchment areas were Gothenburg, Malmö and Uppsala, each of which having around 1000 men included in the study.

Baseline total body BMD, lumbar Spine BMD, total hip BMD, femoral neck BMD, trochanter standardized BMD, hip wards standardized BMD, and vitamin D levels were measured. Skeleton fractures were recorded before (by questionnaires and hospital records) and during the study. Follow up time was around nine years. Binary logistic regression model, Pearson’s, Cochran-Armitage- and Chi-Square analyses were conducted to assess the association between BMD, vitamin D levels, skeleton fractures and the prevalence and the incidence of prostate cancer in the cohort.

Our results showed no significant association between BMD, skeleton fractures and vitamin D levels and incidence of prostate cancer. We could however see a trend towards a decrease in prostate cancer incidence with increased BMD, but only in the prevalent cases of prostate cancer population cohort in Gothenburg. This population consisted of 88 men. We could also see a trend towards an increased incidence of prostate cancer with increased level of vitamin D in the Gothenburg cohort population consisting of 63 cases.

The failure to reach significance might mirror a relatively low number of cases. By expanding the follow up time more cases will be recruited to the study. In future studies we plan to subdivide men with prostate cancer according to their Gleason score and T-classification. Furthermore we plan to study the whole population regarding the association between vitamin D and prostate cancer.
The complexity of assessing patient reported outcomes among women with breast cancer – a population-based cross-sectional study in central Sweden

Author: Höyer M\textsuperscript{1,2}, representing the project group
\textsuperscript{1}Regional Oncologic Centre, Uppsala University Hospital, Uppsala, Sweden
\textsuperscript{2}Department of Public Health and Caring Sciences, Uppsala University, Uppsala, Sweden

Background: The increasing incidence of breast cancer demands a thorough knowledge about patient reported outcomes (PROs) subsequent to diagnosis and during treatment. The aim of the study was to describe health-related quality of life (HRQoL), anxiety, depression, and patient satisfaction among women with breast cancer early on in the course of the disease. Furthermore, the aim was to investigate the influence (association and contribution) of medical, demographic, socio-economic factors as well as psychosocial support on HRQoL, anxiety, depression, and patient satisfaction.

Material and methods: The study was conducted as a cross-sectional questionnaire study based on the Regional Breast Cancer Register of the Uppsala/Örebro Region in central Sweden. All women registered within a one-year period (2007-08) were included. Of 1574 eligible women diagnosed with breast cancer 1094 women accepted participation (70 %). Participants completed a questionnaire including instruments measuring HRQoL (EORTC QLQ-C30 + BR23), anxiety and depression (HADS), and patient satisfaction (PatSatBCQ50), as well as questions regarding demographic and socio-economic factors, psychosocial support, and comorbidity. The questionnaire data was supplemented with disease and treatment specific data from the Regional Breast Cancer Register. Descriptive statistics and sequential multiple linear regression models were used for data analysis.

Results: The breast cancer patients experienced problems with several dimensions of their HRQoL, as well as fatigue, sleep disturbances and systematic therapy side effects. Clinically significant anxiety and depression were found in 13.7 % and 5.6 % of the women, respectively. There was a high degree of patient satisfaction, especially in regards to emotional support. Certain medical factors and a younger age were related to a worse HRQoL, more anxiety and depression, and a lower degree of patient satisfaction (p<0.05). When other demographic factors, psychosocial support, and socio-economic factors were entered into the equation, all the models were significantly improved (p<0.05). Only a few associations with age remained significant (p<0.05). In all models sick leave/temporary disability pension and a worse financial situation were related to a worse HRQoL, more anxiety and depression, and a lower degree of patient satisfaction (p<0.05). Between 7 % and 47 % of the variance in the PROs were explained by the included factors.

Conclusion: The preliminary results have provided new knowledge about patient reported problems/symptoms and satisfaction with care among women undergoing modern breast cancer treatment in Sweden. The results have shown that PROs are complex phenomenons as they are only partly explained by established medical and individual factors. The present study has created new hypotheses as part of a longitudinal study aiming at improving the care of breast cancer patients.
Risk of skin cancer following phototherapy for neonatal jaundice – a retrospective cohort study

Authors: Aksel Jensen, Anne Mette Tranberg Kejs, Gerda Engholm

Affiliation: Danish Cancer Society, Department of Cancer Prevention & Documentation

Background: Neonatal jaundice is a very common state among newborn. In Denmark approximately 4000 newborn each year are therefore treated with phototherapy, lasting normally 24, 48, or 72 hours. This is suspected to be a potential risk factor for subsequent skin cancer (excluding basal cell carcinoma). The literature concerning this potential risk, though, has been very limited.

Material: Since 1977 all cases of Neonatal jaundice in Denmark have been registred in the nationwide hospital inpatient register (Landspatientregistret). These data are included in the cohort although part of the 1977-1993 data is incomplete. This is mainly due to inconsistencies in coding and registration in that period. Data is linked to known cases of cutaneous melanoma from the Danish Cancer Register since 1977. Finally data concerning death certificates, migration, etc regarding the Neonatal jaundice cohort are included.

Methods: Person years at risk are counted from the first diagnosis of neonatal jaundice to first observation of skin cancer, death, emigration, or end of study (2007). The expected number of cancers are calculated using skin cancer incidence rates for the population and compared to the observed numbers calculating SIR (standardised incidence ratio) and 95% confidence intervals. Poisson regression is applied for further analysis of SIR.

Results: Preliminary results suggest a 2 times increased risk of skin cancer, but these results are based on only 11 cases and must therefore be considered with great caution. The main problem is the lack of identified cases of neonatal jaundice from the period 1977-1993, since this part of the cohort span the ages where skin cancer mainly begin to emerge.

Conclusion: Main conclusions especially regarding uncertainty will be presented in Virrat.
Family history is a major risk factor for colorectal cancer (CRC), since individuals with an affected first-degree relative have more than twice as high risk of developing this malignancy than the general population. Based on twin studies, hereditary factors are estimated to underlie approximately ~35% of CRC. However, germline mutations in high-penetrance genes, including $MLH1$, $MSH2$, $APC$, and $MYH$ account for only ~5% of all CRC. Genome-wide association studies have recently identified ten independent chromosomal loci that predispose to CRC with allelic odds ratios of ~1.2. Although the individual effect of each variant is modest, the proportion of CRC attributed to the ten variants is large due to the high frequencies of risk alleles in the population. The aim of this study was to evaluate the combined contribution of the ten common low-penetrance loci on familial CRC and other clinical characteristics. The analyzed variants were rs6983267 at 8q24, rs4779584 at 15q13, rs4939827 at 18q21, rs16892766 at 8q23, rs10795668 at 10p14, rs3802842 at 11q23, rs4944235 at 14q22, rs9929218 at 16q22, rs10411210 at 19q13, and rs961253 at 20p12. Our population-based study cohort consisted of 826 CRC patients, of which normal tissue or blood samples were collected between 1994 and 1998 from nine central hospitals in south-eastern Finland. Genotypes in the ten loci and comprehensive clinical data, including family history of cancer verified from the Finnish Cancer Registry, were available for all the cases. There were 37 cases known to carry high-penetrance germline mutations, and these were excluded from the analysis. The remaining cases consisted of 97 patients with at least one affected first-degree relative and 691 with no affected first-degree relatives. The overall number of risk alleles (0-20) was counted for each individual, after which their association with familial CRC and other clinical characteristics was analyzed by logistic regression. Adjustment with age at diagnosis was included in the logistic regression analysis to improve the model fit. We observed a linear association between increasing numbers of risk alleles in the ten loci and odds of having familial CRC ($P=0.006$). With each one unit increase in the number of risk alleles, the odds of having an affected first-degree family member increased by a factor of 1.16 (95% confidence interval 1.04-1.30). Our results support the previous observation that a significant enrichment of risk alleles in the ten low-penetrance variants is observed in familial CRC. Characterization of the molecular basis of familial CRC patients is important in order to stratify individuals according to their inherited predisposition and provide high-risk patients preventive interventions in the future.
RESULTS OF THE THREE ROUNDS OF THE FINNISH PROSTATE CANCER SCREENING TRIAL

Kilpeläinen Tuomas P (1,2), Auvinen Anssi (2), Määttänen Liisa (3), Kujala Paula (4), Ruutu Mirja (5), Stenman Ulf-Håkan (6), Tammela Teuvo LJ (1)

(1) Department of Urology, Tampere University Hospital, Tampere, Finland
(2) Tampere School of Public Health, University of Tampere, Tampere, Finland
(3) Finnish Cancer Registry, Pieni Roobertinkatu 9, Helsinki, Finland
(4) Department of Pathology, Tampere University Hospital, Tampere, Finland
(5) Department of Urology, Helsinki University Hospital, Helsinki, Finland
(6) Department of Clinical Chemistry, Helsinki University Hospital, Helsinki, Finland

Screening for prostate cancer (PC) remains a controversial issue despite some new evidence on the mortality benefits of PC screening. We conducted a prospective, randomized screening trial in Finland to investigate whether screening decreases PC incidence. Here we report the incidence results from three screening rounds during a 12-year period. Of the 80,379 men enrolled, 30,195 men were randomized to the screening arm (SA) and invited for screening with prostate-specific antigen test (cut-off 4.0 ng/ml) every 4 years, while the remaining men formed the control arm (CA) that received no interventions. The mean follow-up time for PC incidence in both arms was over nine years.

The incidence rate of PC (including screen-detected and interval cancers as well as cases among non-participants) was 9.1 per 1,000 person-years in the SA and 6.2 in the CA, yielding an incidence rate ratio (IRR) 1.5 (95% confidence interval 1.4-1.6). The incidence of advanced PC was 1.1 in the SA and 1.5 in the CA, IRR = 0.7 (0.6-0.8) and the difference emerges after 5-6 years of follow-up. The incidence of localized PC was 7.9 in the SA and 4.6 in the CA, IRR = 1.7 (1.6-1.8).

The results from our large population-based trial indicate that screening for PC decreases the incidence of advanced PC. As compared to the CA, the PC detected in the SA there were substantially more often localized, low-grade PCs due to overdiagnosis.
CAUSE-SPECIFIC MORTALITY OF ORAL CANCER IN NORTHERN FINLAND:
PATIENTS DIAGNOSED DURING 1984 - 2004

Juha Kivelä
University of Oulu, Finland.

The aim of the study is to estimate the cumulative mortality from oral cancer since the
diagnosis among patients contracting this diseases. I am also trying to find out how some
prognostic factors affect the mortality.

The data was gathered by the Institute of Dentistry at the University of Oulu on all 339
patients who were treated at the Oulu University Hospital between 1984 and 2004. The
catchment population covers the provinces of Oulu and Lapland in Northern Finland.

The data were analysed using non-parametric statistical methods such as the Kaplan-
Meier method modified to handle competing risks. As most patients were on average older
than 50 years at diagnosis, many of them died from other causes than from the cancer itself.
Death from other causes is hence treated as a competing event.

The cumulative mortality from oral cancer in these patients was 31% at 5 years since
diagnosis and 36% at 10 years. The cumulative mortalities from other causes were 16% and
27% respectively. Between genders there doesn’t seem to be any significant difference on
mortality from oral cancer: the cumulative mortality due to oral cancer at 10 years was 35% in
females and 36% in males. The stage of cancer highly affects on the cause-specific mortality
of the patients.
Title: STI RISK PERCEPTION AND CONDOM USE WITH TEMPORARY PARTNERS: A NATIONAL POPULATION BASED STUDY AMONG YOUNG ADULTS

Authors: Amy Levål₁, Karin Sundström₁, Alexander Ploner₁, Carol Tishelman₂, Lisen Arnheim Dahlström₁, Catarina Widmark₂, Pär Sparén₁

₁ Dept. of Medical Epidemiology and Biostatistics, Karolinska Institute, Stockholm Sweden
₂ Dept. of Learning, Informatics, Management and Ethics, Karolinska Institute, Stockholm, Sweden

Background: The role of sexually transmitted infections (STIs) in causing cancer has received increased attention. This due to the introduction of vaccinations against certain human papilloma virus (HPV) types associated with cervical cancer and condyloma. In light of these developments, STI risk perception becomes more relevant in terms of cancer risk and condom use becomes a primary cancer prevention strategy. The association between condom use and STI risk perception in the age of new vaccines is therefore investigated here.

Methods: A national population-based HPV awareness survey of 20,000 young adults aged 18-30 residing in Sweden in 2007, linked with socio-demographic databases. Descriptive and stratified logistic and multinomial regression analyses were performed to measure STI risk perception and condom use with temporary partners.

Results: Correlates to STI risk perception differ drastically between sexes. Men’s STI risk perception is not associated with condom use. Women younger than 15 at sexual debut had two-fold odds of reporting non-condom use with temporary partners compared to women with later sexual debuts (OR 1.95 CI:1.46-2.60). Women with immigrant mothers were 50% less likely to report seldom/never use of condoms with temporary partners compared to women with Swedish-born mothers (OR 0.53 CI: 0.37-0.77).

Conclusions: Being of young age at sexual debut is a well-known risk factor for developing cervical cancer. This due to exposing the cervical transformation zone to HPV infection for a longer time-period and/or an average increased number of lifetime sexual partners. When considering these factors with our results of young sexual debut age related to an increased risk taking later in life in terms of non-condom use with temporary partners, an interaction effect could be indicated. Factors influencing and confounding the effect of age at first intercourse on cervical cancer development warrant further investigation. STI risk perception is low and correlates differ between sexes. Men report condom use with temporary partners more than women but do not associate use with STI risk. There is a need for more finely tuned gender-specific messages in order to reduce the spread of STIs. Also, maternal and cultural influences on STI prevention behavior could be further emphasized in light of our findings.
THE ESTIMATION OF ABSOLUTE RISK FOR COLON AND RECTAL CANCER IN FINLAND 2003 – 2007
Marko Merikukka¹, Esa Läära¹
¹Department of Mathematical Sciences, University of Oulu, Finland

Background: The absolute risk is defined as the probability that a disease-free individual will develop a given disease over a specified time interval given current age and presence of competing risks. Competing risks can prevent a disease in interest. In this study the interest disease is colon and rectal cancer and the competing risk is death. Aim of the study is to calculate the absolute risk for colon and rectal cancer.

Material: Data are collected from website of Finnish Cancer Registry (cancerregistry.fi) and Statistics Finland (stat.fi). Data including the number of first colon and rectal cancer incident cases, colon and rectal cancer deaths, other deaths occurring at 5-year interval during the calendar time 2003 – 2007 separately for men and women. Data are also including the midyear populations. The last interval 85+ includes the 85 years old and the older.

Methods: We use cross-sectional cancer rates and death rates to estimate absolute risk in a hypothetical cohort.

Results: To estimate absolute risk we need rates per person-years alive and disease free. However, many disease registries provide rates per person-years alive only. Fay, Pfeiffer, Cronin, Le and Feuer (Statist. Med. 2003; 22:1837 - 1848) showed how to write the age-conditional probability of developing cancer as a function of the available rates, under a simple, standard assumption. They assumed that the rate of non-cancer deaths is the same for all people regardless of whether or not they have had a cancer. Next step will be to compute the estimate of absolute risk for colon and rectal cancer using our data under this assumption.

Conclusions: The absolute risk is more realistic than other risks, because it takes account of competing risks.
Title: ADHERENCE TO THE NORDIC NUTRITION RECOMMENDATIONS DOES NOT PROTECT AGAINST PROSTATE CANCER

Authors: Elisabeth Möller¹, Carlotta Galeone², Rino Bellocco¹,³, Henrik Grönberg¹, Hans-Olov Adami¹,⁴, Katarina Bälter¹

Affiliations:
¹ Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
² Department of Epidemiology, Istituto di Ricerche Farmacologiche “Mario Negri”, Milan, Italy
³ Department of Statistics, University of Milan-Bicocca, Milan, Italy
⁴ Department of Epidemiology, Harvard School of Public Health, Boston, USA

Background: The etiology behind prostate cancer is poorly understood, but there is increasing evidence that lifestyle factors such as diet and physical activity play important roles. The Nordic Nutrition Recommendations (NNR) are guidelines for nutrient intakes and physical activity based on scientific data and aiming at preventing major chronic diseases in the Nordic population. We have investigated the hypothesis that good adherence to the NNR reduces the risk of prostate cancer in Swedish men.

Material and methods: In a Swedish population-based case-control study, questionnaire-data on diet and physical activity were available for 1,499 incident prostate cancer cases and 1,118 population controls. Categorization of adherence to the NNR was done by evaluating nine variables: intake of fat, carbohydrates, protein, fiber, vitamins, minerals, sodium, and alcohol, and level of physical activity. Each variable was graded, giving 1 point for poor adherence, 2 points for moderate adherence and 3 points for good adherence, and then summarized into a total score for each person. The relative risk of prostate cancer for good versus poor adherence to the NNR was estimated by unconditional logistic regression to generate multivariate odds ratios (ORs) and 95% confidence intervals (CIs). Analyses were performed for all cases and for advanced and localized prostate cancer cases separately.

Results: We found a slightly increased risk of prostate cancer for men with moderate and good adherence to the NNR. The OR comparing the moderate vs. the poor adherence group was 1.22 (95% CI: 0.99-1.51) and the OR for good vs. poor adherence was 1.27 (95% CI: 1.01-1.59). For advanced cases there was a non-significant association between adherence to the NNR and prostate cancer risk, whereas for localized cases there was a marginally significant positive association, with an OR of 1.29 (95% CI: 1.00-1.67) for moderate vs. poor adherence and an OR of 1.35 (95% CI: 1.03-1.78) for good vs. poor adherence. Our next step is to explore whether these associations are modified by genetic factors known to be related to prostate cancer.

Conclusions: Our results do not support the hypothesis that men who follow the NNR have a reduced risk of prostate cancer. However, since the observed positive association was weak and only marginally significant we cannot conclude that there is an increased risk of prostate cancer for men who adhere to the NNR.
HIGH RISK OF OSTEONECROSIS REQUIRING TOTAL JOINT ARTHROPLASTY IN YOUNG PATIENTS TREATED FOR MYELOID LEUKAEMIAS – A NATIONWIDE, REGISTER-BASED STUDY

Niinimäki, Riitta¹; Niinimäki, Tuukka²; Sankila, Risto³; Harila-Saari, Arja¹
¹ Department of Paediatrics, University of Oulu, Finland
² Department of Surgery, Oulu University Hospital, Finland
³ Finnish Cancer Registry, Helsinki, Finland

Objectives: The risk of osteonecrosis (ON) requiring total joint arthroplasty (TJA) in patients treated for cancer in childhood or early adulthood was studied in a nationwide, population-based study.

Methods: All Finnish patients diagnosed with cancer at age 0-30 years in 1975-2000 and who survived at least two years after diagnosis were identified from the Finnish Cancer Registry (FCR). Non-melanoma skin cancers were excluded. The patients were linked to the databases on orthopaedic diagnoses and procedures in the National Hospital Discharge Register and the Finnish Arthroplasty Register for years 1980-2005.

Results: Of the 9903 patients, 25 had undergone TJA because of ON. The median time from diagnosis to TJA was 5 years (range 1-10 years). The proportion of ON requiring TJA was highest among patients treated for chronic myeloid leukaemia (6.25 %, 6 out of 96) and for acute myeloid leukaemia (3.5 %, 6 out of 172). TJA was required for a small proportion of patients with acute lymphoblastic leukaemia (ALL) (0.4 %, 4 out of 990), Hodgkin lymphoma (HL) (0.4 %, 4 out of 996) or non-Hodgkin lymphoma (NHL) (0.5 %, 3 out of 570). Only two patients with any other cancer (1 colon carcinoma and 1 testicular cancer) had undergone TJA because of ON. Hip was the involved joint in 24 patients and knee in one patient.

Conclusions: Osteonecrosis requiring total hip arthroplasty is an important cancer-related complication in children and in young adults treated for myeloid leukemias. Also patients with ALL, HL or NHL have a risk of ON requiring TJA. The risk was very low in patients diagnosed with other cancers than leukemias and lymphomas.
Title
“LIVA” – A POPULATION-BASED STUDY OF SEXUAL HABITS AMONG MORE THAN 20,000 WOMEN IN DENMARK

Authors
Tina Bech Olesen¹, Kirsten Egebjerg Jensen¹, Christian Munk¹, Janne Schurmann Tolstrup², Susanne Krüger Kjær¹,³

Affiliation
¹ Department of Virus, Hormones and Cancer, Institute of Cancer Epidemiology, Danish Cancer Society
² National Institute of Public Health, University of Southern Denmark
³ Juliane Marie Centre, Gynecologic Clinic, Rigshospitalet, University of Copenhagen

Introduction
Sexual and contraceptive habits, in particular early age at first intercourse, multiple sexual partners and non-use of condoms, are well-established risk factors for sexually transmitted infections and unwanted pregnancy. The aim of this study was to examine if and how educational level and degree of urbanization are related to age at first intercourse, lifetime number of sexual partners and condom use.

Material and methods
We used data from a large population-based questionnaire survey conducted 2004-2005 including a random sample of 20,478 women (18-45 years) (participation rate: 81.4%). We used multiple logistic regression analysis to estimate odds ratios (OR) of early sexual debut (≤15 years old), having had >5 lifetime number of sexual partners and never-use of condoms associated with educational level and degree of urbanization.

Results
OR of having had early sexual debut was almost twofold higher among women with lower educational level (9th grade) (OR=1.93; 95% CI: 1.73-2.15) compared to women with higher educational level (gymnasium) and the OR of having had >5 lifetime sexual partners was highest among women in the capital area (OR=2.36; 95% CI: 2.16-2.57) compared to women in the large provincial town areas. Furthermore, OR of never-use of condoms was 2.53 (95% CI: 2.15-2.97) for women with lower educational level compared to those with higher educational level (mutually adjusted for age, degree of urbanization and educational level).

Conclusion
Low educational level is associated with young age at first sexual intercourse and never-use of condoms, and living in an area of high urbanization is associated with a higher lifetime number of sexual partners. This information may be of importance for prevention in relation to women’s reproductive health.
Background. Vertebral fractures are common osteoporotic problems among women older than 65 years, but the prevalence and incidence are not known. Diagnosing vertebral fractures is important, as they increase the probability of further fractures. The goal was to assess the ability of two different diagnostic methods to detect vertebral fractures with dual energy X-ray assessment (DXA).

Material and methods. Two methods: ABQ, a visual method which requires the depression of the vertebral endplate and McCloskey a quantitative method based on direct height measurements of vertebrae were compared to the golden standard, e.e radiographic examinations evaluated with the Genant method (a semiquantitative method). The prevalence and incidence of vertebral fractures among Icelandic women aged 75–80 were assessed at the same time as well as the fraction of women not aware of the fractures. The subjects were 166 women, born in 1927 and resident in Reykjavik. The came twice for bone density measurement, first in 2003 and again, in 2007. At each visit a DXA spine was acquired, and in addition 108 women had an x-ray of the spine in 2007.

Results. The research did not show a statistically significant difference between the ABQ and McCloskey methods considering diagnoses of the frequency of vertebral fractures in the years 2003 and 2007. At the age of 75 the frequency was 31.3% (ABQ) and 24.1% (McCloskey) and at the age of 80 36.7% (ABQ) and 38.0% (McCloskey). Statistically significantly more fractures were diagnosed with McCloskey at the subsequent measurement. The positive predictive value of fracture was 82% for both ABQ and McCloskey. Around 70% of the women were unaware of their vertebral fractures.

Conclusion. An organized search for vertebral fractures at the same time as DXA-bone measurement among older women in Iceland is likely to be beneficial. Vertebral fractures in older women are common and are usually ensued by an impaired quality of life. It is therefore important to diagnose them early in order to proceed with the appropriate treatment and preventive measures.
EXPOSURE TO ‘IRON AND WELDING FUMES’, ‘WOOD DUST AND FORMALDEHYDE’ AND THE RISK OF RESPIRATORY CANCERS

Sie Sie Siew1(Angelica Siew), Timo Kauppinen, Pentti Kyyrönen, Pirjo Heikkilä, Eero Pukkala2,3

1 Finnish Institute of Occupational Health, Helsinki, Finland.
2 Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland.
3 School of Public Health, University of Tampere, Tampere, Finland.

Background Exposure to iron, welding fumes, wood dust and formaldehyde is widespread and may increase the risk of respiratory cancers. The aim of the first study was to identify associations between exposure to iron and/or welding fumes and the incidence of lung cancer among Finnish men. In the second study, we identified the associations between exposure to wood dust and/or formaldehyde and risk of nasal cancer, nasopharyngeal cancer and lung cancer among the same cohort.

Material and Methods The cohort of all economically active Finnish men, born in 1906–1945, who participated in the national census in 1970 was followed through the Finnish Cancer Registry for lung cancer cases (N=30 137) during 1971–1995. Their census occupations in 1970 were converted to estimates of cumulative exposure to iron and welding fumes with the Finnish job-exposure matrix on the basis of likelihood, average level, and estimated duration of exposure. Relative risk estimates for categorized cumulative exposure were defined by a Poisson regression, adjusted for smoking, socioeconomic status, and exposure to asbestos and silica dust.

Results The relative risks for lung cancer increased as the cumulative exposure to iron and welding fumes increased. The relative risks in the highest exposure category was 1.35 [95% confidence interval (95% CI) 1.05–1.73] for iron and 1.15 (95% CI 0.90–1.46) for welding fumes. The respective relative risks estimated for squamous-cell carcinoma of the lungs were 1.94 (95% CI 1.35–2.78) and 1.55 (95% CI 1.08–2.24). There was no excess risk of small-cell carcinoma in any exposure category. Men exposed to wood dust had a significant excess of nasal cancer overall (RR 1.59, 95% CI 1.06-2.38) and specifically in nasal squamous cell carcinoma (1.98, 1.19-3.31). Workers with lower exposure (0.1-0.9 ppm-years) to formaldehyde had a RR of 1.22 (1.16-1.29) for lung cancer while there was no excess attributable to higher CE. There was no indication that CE to wood dust or formaldehyde would increase the risk of the nasopharyngeal cancer.

Conclusions Occupational exposure to iron and welding fumes was associated with an increase in lung cancer risk, mainly that of squamous-cell carcinoma. The simultaneous exposure to both of these agents and other potential work-related carcinogens complicates the interpretation of the independent roles of the risk factors. Occupational exposure to wood dust in Finland appeared to increase the risk of nasal cancer but not that of nasopharyngeal cancer or lung cancer. Formaldehyde appeared to have no risk increasing effect whatsoever.
EVALUATION OF 15 CANCER CANDIDATE GENES IN FAMILIAL COLORECTAL CANCER PREDISPOSITION

Alexandra Gylfe, Johanna Sirkiä, Auli Karhu, Lauri Aaltonen
University of Helsinki, Finland

Background
Colorectal cancer (CRC) is the third most common cancer in Western countries. It is a disease of the genome and thus genetic alterations play a key role in its predisposition. In a recent systematic sequencing study, 13,000 protein coding genes in 11 colorectal cancers were analyzed. By a statistical method that took into account variations in mutation frequency, affected nucleotide type and context, a set of candidate cancer genes (CAN genes) was identified. A follow-up study included the analysis of 18,191 genes and produced a set of 140 colorectal CAN genes. It is estimated that 10% of cancer predisposing genes are involved in both somatic and hereditary cancer forms. The somatically mutated CAN genes thus serve as a distinct set of candidates for hereditary susceptibility. The aim of this cross-sectional study is to examine the possible role of somatically mutated colorectal CAN genes in familial colorectal cancer. The mutational profile of the 15 top-ranked CAN genes was analyzed for somatic and germline variations in a series of familial CRC patients.

Material
The CRC samples and corresponding normal tissues were selected from a population-based set of 1042 samples. These were prospectively collected at nine Finnish central hospitals between years 1994 and 1998. After extensive analyses, 113 of these samples have remained mutation negative familial cases where there are one or more diagnosed CRC cases in first-degree relatives. From these, 45 samples previously evaluated by a pathologist were selected. Blood DNA samples from population-matched healthy individuals from the Finnish Red Cross Blood Transfusion Service were used as controls.

Methods
Of the 140 colon cancer CAN genes identified in a previous sequencing study, previously known CRC predisposing genes such as APC, KRAS, TP53, SMAD4 and PTEN were excluded. From those remaining, the top 15 were selected and analyzed for mutation profile. In mutation analysis, all coding exons and adjacent splice sites were covered in reference to the transcript with the longest coding region.

Preliminary Results
A total of 6 non-synonymous germline variants were identified in five CAN genes. These novel variants were not reported in SNP databases and were not present in around 450 cancer-free controls. In addition, 14 somatic mutations in four CAN genes were identified. Further studies are needed to unravel the potential role of these CAN genes in CRC predisposition.

1 Sjöblom et al. 2006, Science 5797: 268-274
2 Wood et al. 2007, Science 5853: 1108-1113
Factors associated with the prescription of anti-depressive medication in breast cancer patients – a rehabilitation perspective

Nis P. Suppli
Institute of Cancer Epidemiology, Danish Cancer Society, Copenhagen, Denmark
Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark

Purpose This study evaluated factors associated with use of antidepressant medication (AD) subsequent to a diagnosis of breast cancer (BC). Further, we evaluated the effect of participation in a cancer rehabilitation program on use of AD.

Material and methods A register-based cohort study included 1247 women diagnosed with BC from 1998 until 2006 and who attended a week-long rehabilitation program as well as a matched comparison group of 2903 women who did not attend the program. The associations between BC-related, treatment related and socio-demographic factors with use of AD were evaluated in multivariate Cox proportional hazard models separated on use of AD prior to diagnosis of BC.

Results In women who were not users of AD prior to BC, a relapse increased the hazard ratio (HR) of first use of AD to 2.53 (95% CI, 1.16-2.09) whereas a diagnosis of a new primary cancer increased the HR to 3.36 (95% CI 1.48 to 7.65). Further, number of tumour-positive axillary lymph nodes and unemployment was associated with significantly increased HRs for use of AD, whereas having children living at home, education and income was borderline associated with AD use. No effect of the rehabilitation program was observed on first use of AD after BC.

Conclusion Socio-demographic rather than disease- and treatment characteristics at time of diagnosis were associated with first time use of AD following a breast cancer diagnosis. However, a subsequent recurrence or the diagnosis of a new cancer considerably increased the rate of AD use.