Nordic Summer School of Cancer Epidemiology, phase III

Virrat Winter Symposium 2012

Virrat, Finland, 3-5 February 2012

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

Program + abstracts
## Participants

### Students

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<td>Vesal Khalid</td>
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<td>Christiane Bay</td>
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### Faculty

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<td>Prof. Laufey Tryggvadóttir</td>
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Nordic Summer School of Cancer Epidemiology
Phase III: Virrat Winter Symposium 2012
Virrat, Finland, 3-5 February 2012

PROGRAM

FRIDAY, 3 February

12:00  Departure from Tampere railway station towards airport
       (after arrival of the trains from Helsinki at 11:52
       and from Oulu at 11:56)

about 12:30  Departure from Tampere Airport for Virrat (arrival of the flight at 11:55)

at arrival  Room occupation
           (wooden cottages at river-shore)

15:00  Welcome snack (main restaurant)

16:00  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)
       Hans Storm: Future of cancer epidemiology (max 7 minute presentation)

16:20  Break / Poster hanging (coffee room next to the lecture hall)

16:30-18:00  SESSION I – Host factors and descriptive epidemiology
              Chairperson: Sunniva Todnem Sakkestad (co-chair: Hans Storm)

16:30-16:50  Gerda Engholm: NORDCAN – goldmine of cancer facts
              Student presentations: 15 minutes plus 5 minutes discussion time

17:00-17:20  Siv Mjøs: Gene mutations and amplifications in endometrial cancer

17:20-17:40  Vesal Khalid: Uterine carcinosarcomas – a retrospective pilot study of the clinical features and outcomes

17:40-18:00  Jens Anibal Juul: Non melanoma and non basal cell carcinoma skin cancer mortality in Denmark, 1995-1999

19:00  Dinner, multicultural discussions on scientific and other mutually interesting topics (old country restaurant Mikonhovi, other side of the road, walk 500 m)
SATURDAY, 4 February

8.00 Breakfast (restaurant)

9:00-11:35 SESSION II – Life habits & diseases
Chairperson: Hrafnkell Stefánsson (co-chair: Esa Lääärä)

9:00-9:20 Louise Nørreslet Gimsing: The risk for dementia, Alzheimer’s disease, Parkinson’s disease and epilepsy among members of Seventh Day Adventists and Baptists in Denmark, 1977-2009

9:20-9:40 Helka Sahi: Incidence of Merkel cell carcinoma is increased significantly among younger statin users in Finland

9:40-10:00 Bendix Carstensen: Cancer in diabetes patients – basing a wrong conclusion on a wrong or on a correct analyses

(Break)

10:10-10:30 Erika Ax: Dietary patterns and prostate cancer risk: a prospective cohort study in elderly Swedish men

10:30-10:50 Toni Similä: Estimation of absolute risk from nested case-control design – risk of hepatocellular carcinoma associated with hepatitis viruses

11:00-11:30 SESSION III – Poster highlights
Guided walk and interesting discussions in the poster room
Chairperson: Vesal Khalid (co-chair: Laufey Tryggvadóttir)

Christiane Bay: Trends in malignant melanoma of the skin in Denmark – an epidemic of superficial spreading melanoma? A descriptive register study

Ulla Holten Nielsen: Characterization of deaths without a cause in the Danish Register of Causes of Death

Faisal Shahzad: Subsite specific incidence of colorectal cancer, a comparison of incidence rates in Norway and Denmark
11:45 Lunch *(main restaurant)*

12:40-15:00 **SESSION IV – Interventions, risk factor control, diagnostics**
Chairperson: Rebecka Godtman (co-chair: Nea Malila)

12:40-13:00 **Terese Matthesen**: Risk of cervical dysplasia and cancer in users of copper intrauterine device – An epidemiological historically controlled cohort study

13:00-13:30 **Laura Järvelä & Marjukka Viita-aho**: Rubber workers and cancer

13:30-13:50 **Ville Karhunen**: Incidence of cancer of the oral cavity by occupational category in Finland 1971-2005

Break

14:00-14:20 **Hrafnkell Stefánsson**: Trends in Breslow’s tumour thickness of cutaneous melanoma in Iceland 1980-2009

14:20-14:40 **Nannan Yang**: Tumor characteristics in prevalent versus subsequent screened women in the Norwegian Breast Cancer Screening Program

14:40-15:00 **Annika Helin**: Colorectal cancer screening – is there seasonal variation in the test performance?

15:00-15:15 **Nea Malila**: Stories on fecal test and other screening issues – an appetizer

15:30 Coffee & energy input *(main restaurant)*

16:00 Practical SURVIVAL exercise:
*going in the forest, trying to find out of the forest, competing causes, effects of open fire food*

**ICEHOLE SESSION** - *(river shore sauna, fire place)*

Chairperson: Bendix Carstensen

21.00++ Sauna, ice-hole swimming, sauna disco, fire place sausages

*Advanced senior jenkka dance lessons given by Prof. Matti Hakama*
SUNDAY, 5 February

8.40 Breakfast (restaurant)

9:40-11:00 SESSION V – Effects of cancer to later life
Chairperson: Marjukka Viita-aho (co-chair: Gerda Engholm)

9:40-10:00 Anna Odgaard: Danish childhood cancer patients with congenital heart defects: a nationwide mortality study

10:00-10:20 Thorgerdur Gudmundsdottir: Cardiovascular complications in adult life after childhood cancer in Scandinavia

10:20-10:40 Rebecka Godtman: Surveillance for men with screen-detected prostate cancer, results from the Gothenburg randomised population-based prostate-cancer screening trial

10:40-11:00 Sunniva Todnem Sakkestad: The impact of pre-operative chemoradiotherapy on local recurrence and survival in rectal cancer – retrospective cohort study

11.10-12:00 SESSION VI – Closure

Joint presentation by the tutors: How to submit a paper and what happens to it in the journal

Awards, certificates and closing remarks

12:00 Packing, leaving the rooms

13:00 Farewell lunch

14:00 Bus leaves towards Tampere

before 16.00 arrival to Tampere railway station
(before departure of the trains to Oulu at 16:00 and to Helsinki at 16:07)

before 17.00 arrival Tampere Airport
(flight back to Western civilisation at 18:00 and to Sweden at 18:40)
ABSTRACTS

(in alphabetical order according to surname of the first presenting author)
Dietary Patterns and prostate cancer risk: a prospective cohort study in elderly Swedish men

Erika Ax¹, Tommy Cederholm¹, Björn Zethelius¹,⁵, Birgitta Grundmark²,⁴,⁵, Anna Bill-Axelson², Wulf Becker¹,³, Hans Garmo⁴,⁶, Lars Holmberg⁴,⁶, Anna Bill-Axelson², Wulf Becker¹,³, Hans Garmo⁴,⁶, Lars Holmberg⁴,⁶, Per Sjögren¹

¹Dept. of Public Health and Caring Sciences and ²Dept. of Surgical Sciences, Uppsala University, ³National Food Administration, ⁴Regional Oncologic Center, University Hospital, Uppsala, ⁵Medical Products Agency, ⁶the Division of Cancer Studies, School of Medicine, King’s College, London, UK

Background: There is a growing body of evidence linking nutrition to prostate cancer (PCa), but the results regarding the impact of single food components are conflicting and studies of dietary patterns and PCa are rare. Objective: To assess the relationship between adherence to a Mediterranean-like and a low carbohydrate-high protein dietary pattern and PCa incidence in elderly Swedish men. Design: We used data from the Uppsala Longitudinal Study of Adult Men, a Swedish population-based cohort of 1138 men (mean age 71±1). Seven-day food records determined dietary habits, and nonadequate reporters of energy intake were excluded. After additional exclusions, 566 individuals remained for analysis. Adherence to a modified Mediterranean Diet Score (mMDS) and a low carbohydrate-high protein score (LCHP-score) were assessed, and individuals were grouped as low, medium, or high adherent to each diet. PCa cases were identified in the Swedish Cancer Register. Risk of PCa was analyzed with Cox proportional hazard regression. Exploratory analyses of selected nutrients were conducted and competing risk of death was taken under consideration. Results: During median follow-up of 13.3 years 72 cases of PCa were identified. The mMDS was not associated with PCa. Adherence to the LCHP-score was inversely related to PCa, with adjusted hazard ratios (HR) of 0.55 (0.32-0.96) for medium-, and 0.47 (0.21-1.04) for high-, compared with low adherent individuals. Stratified analyses implied a selenium dependent effect of the LCHP-score. Risk relations could not be explained by competing risk of death. Conclusions: In this study, a dietary pattern with lower carbohydrate and higher protein intake was associated with lower PCa incidence. A higher intake of selenium associated with the LCHP-score might have contributed to observed relations.
Title: TRENDS IN MALIGNANT MELANOMA OF THE SKIN IN DENMARK - AN EPIDEMIC OF SUPERFICIAL SPREADING MELANOMA? A DESCRIPTIVE REGISTER STUDY

Authors: Christiane Bay, Anne Mette Tranberg Kejs, Ida Marie Castberg, Hans Storm, Gerda Engholm

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

Background: Denmark has experienced a striking increase in malignant melanoma since 2004 and Danish women aged 15-39 years were in GLOBOCAN 2008 estimated to have the highest risk of malignant melanoma in the world. The increased risk may be associated with increased UV exposure in the population, but also changes in reporting and classification of early and slow/non-progressing or borderline melanomas may have caused diagnostic drift. Further, coding was changed in 2004 to ICDO-3, and the Cancer Registry modernized data capture as of 2004 to electronic notification through the Danish National Patient Register (NPR) supplemented with information on histology from the Danish Pathology Register.

Objective: To evaluate possible causes of the extensive increase in incidence of malignant melanoma in Denmark in the recent years.

Material: Anonymized, individual-level data was extracted from the Danish Cancer Register of all patients with malignant melanoma of the skin (ICD-10=C43) in the period 1990–2009. Morphology (M) was categorized in 5 subgroups: superficial spreading melanoma (SSM) (M-8743), nodular melanoma (NM) (M-8721), lentigo maligna melanoma (M-8742), melanoma not otherwise specified (NOS) (M-8720) and the remaining cutaneous melanomas. Equivalent data for Norway were drawn from the NORDCAN.

Methods: Incidence rates were calculated and standardized to the age distribution of the Danish population in 2000. Homogeneity of morphology distribution over time was evaluated with chi square tests. We also evaluated the trend in 3-year relative survival by morphology.

Results: 22,099 cases of melanomas were diagnosed in 1990-2009. An increase was seen from 1128 cases in 2004 to 1813 cases in 2009 compared to 829 cases in 1990. In 2004-2009 the proportion of SSM incidence increased from 55% to 65% corresponding to an absolute increase of 92% (n=1180 in 2009), and the incidence of NM increased 61% (n=190 in 2009), whereas melanoma NOS decreased 31% (n=368 in 2009) from 2003. The 3-year relative survival (%) (95% CI) in 1995-2009 for NM and melanoma NOS decreased from 81 (78-85) to 77 (74-79) for males and 89 (87-92) to 87 (85-89) for females, whereas it for SSM increased from 94 (91-98) to 95 (94-97) for males and 96 (93-99) to 98 (96-99) for females. In Norway the age adjusted rate of SSM increased from 26 to 28 pr. 100,000 persons from 2000 to 2009 compared to an increase from 17 to 40 pr. 100,000 persons in Denmark.

Conclusions: There has been a superficial spreading melanoma epidemic in Denmark, accounting for the increase seen in the overall incidence from 2004-2009. It was mainly seen among women. A similar pattern was not seen in Norway. The relative survival for SSM was stable, while the survival in the NOS group decreased over time. The possible occurrence of a diagnostic drift could not be rejected, but at any case it didn't influence the overall relative survival rates. The decrease in melanoma NOS incidence from 2004 was likely due to capture of high quality data by the linkage between the Cancer Registry and Danish Pathology Register as previously reported melanomas NOS were now notified as SSM. It is possible that the melanoma epidemic is a consequence of sun campaigns launched by The Danish Cancer Society in the recent years, because these have raised public awareness with increased skin self-examination and physician consultations. Since SSM is not life threatening as long as an early diagnosis is obtained followed by prompt treatment the sun campaigns may prevent future increases in melanoma mortality rates, though it might also result in removal of larger numbers of benign or non-progressing melanomas.
The risk for Dementia, Alzheimer's disease, Parkinson's disease and epilepsy among members of Seventh Day Adventists and Baptists in Denmark, 1977-2009.

Louise Nørreslet Gimsing, Lau Caspar, Christoffer Johansen.

Institute for Cancer Epidemiology. Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen.
The National Institute of Public Health, Øster Farimagsgade 5A, 2nd floor, 1353, Copenhagen K.

Background Some religious groups anticipate that their belief-system influences the risk and prognosis of several chronic diseases.
Most studies published so far point to the healthy lifestyle among members of religious societies as the causal explanation for reduced risk for (among others) cancer, diabetes and severe psychiatric illness.
The aim of this study is to investigate the risk for four frequent chronic diseases of the central nervous system (CNS) among members of two Danish religious cohorts.
The study is a part of The Danish Religious Societies Health Study (2003). A protective effect of membership in the same two cohorts was shown on survival and incidence of cancer.

Material We obtained information on all members of the society of Seventh Day Adventists and the Baptists Societies in Denmark: name and date of birth as well as date of membership and a date if leaving the society.

Methods We identified 4882 (62.9% women) Seventh Day Adventists and 3514 (58.3% women) Baptists. Via the Danish Civil Registration System their personal identification number (PIN) and vital status was obtained. They were followed up from 1977 until 2009 by using the PIN as key variable in the linkage procedures. We linked the cohorts to the Danish Hospital Discharge Register which since 1977 has kept information on all hospital discharges. The exposure is defined as membership of one of the two religious societies. The outcome is defined as first hospital discharge with a diagnosis of Dementia, Alzheimer's disease, Parkinson's disease and epilepsy, classified by ICD8 (1977-1993) and ICD10 (1994-2009). We compare the observed number of cases in the cohort with the general Danish population by standardised incidence ratios (SIRs) including 95 % confidence interval. Statistic Denmark provided the yearly demography of the Danish population.

Results and conclusion During the study period a total number of 243 cases of Dementia and Alzheimer's disease, 118 cases of Parkinson's disease and 206 cases of epilepsy were observed in the cohorts. The preliminary results cannot document a protective effect of membership of the Danish Seventh Day Adventists or Baptists on the risk for the neurological diseases under study. The strength of the study is the long follow up time and the high quality and completeness of the population based registers. The study shows the potentials of the Danish registers in the field of Religion and Health. We suggest a future Danish cohort study combining more detailed definitions of exposure.
Surveillance for Men with Screen-detected Prostate Cancer, Results from the Gothenburg Randomised Population-based Prostate-cancer Screening trial

R. Godtman 1, J. Stranne 1, J. Hugosson 1 (1) Institute of Clinical Sciences, Sahlgrenska Academy At Göteborg University, Dept. of Urology, Göteborg, Sweden

Introduction: Overdiagnosis, diagnosis of clinically insignificant cancer, and overtreatment are major potential drawbacks of screening for prostate cancer (PC) with prostate-specific antigen (PSA). Surveillance has emerged as a treatment alternative in order to reduce overtreatment. The aim of surveillance is to avoid or postpone active treatment in men with low risk PC without missing the opportunity for cure if there are signs of disease progression. The present study investigates surveillance as a strategy for men with screen-detected PC in the Gothenburg randomised population-based prostate-cancer screening trial

Material and methods: The 10 000 men randomized to screening in the Gothenburg trial have, since 1995, been invited every second year for a PSA test until the upper age limit of 67-71 (median 69) years. Men with a PSA above threshold, ≥2.5 ng/mL, were offered further urological investigation including a prostate biopsy. These men form the basis of the present study. Up to Dec 31, 2010, 968 men had been diagnosed with screen-detected PC and 439 of those were primarily managed with surveillance and included in this study. They have been followed at a 3-12 months interval and in case of a progression in PSA, stage or grade been recommended a switch to active treatment (radical prostatectomy, radiation therapy or hormonal treatment). Tumours were divided in to risk groups to investigate if risk group and/or age at diagnosis were associated with failure after surveillance (death from PC, diagnosis of PC metastases, initiation of hormonal treatment or PSA relapse after radical prostatectomy or radiation therapy). The risk groups were; lowlow (T1c, Gleason score ≤6, < 3 cores with cancer and ≤50% cancer in any core), low (T1, Gleason score ≤6 and PSA <10 ng/mL and not fulfilling lowlow criteria), intermediate (T1-2, Gleason score ≤7 and/or PSA <20 ng/mL and not fulfilling lowlow or low criteria) and high (T1-4, Gleason score ≥8 and/or PSA <100 ng/mL and not fulfilling other risk group criteria). Kaplan Meier analyses and Cox proportional hazard models were used.

Results: Median age at diagnosis was 65.4 years and median follow up (FU) was 6.0 years. During FU, 162 men switched from surveillance to active treatment resulting in a 10-year treatment-free survival of 45.4%. The reason for terminating surveillance was an increase in cancer involvement, Gleason grade or PSA in 80%; only 4 men (2.5%) terminated surveillance due to anxiety. Sixty men died during FU, 59 men due to non-PC causes and one man due to PC, resulting in a 10-year overall survival of 81.1%. Forty-two men had a failure after surveillance and the 10-year failure-free survival was 85.0%. Compared with men in the lowlow risk group, men with low and intermediate/high risk PC had a hazard ratio of failure or 2.0 (p=0.08) and 3.6 (p<0.001) respectively.

Conclusion: A large proportion of men with screen-detected PC can be suitable for surveillance, potentially reducing overtreatment. Surveillance appears as a safe strategy for men with low risk PC and maybe also for selected men with intermediate risk PC, however, longer follow up is needed.
CARDIOVASCULAR COMPLICATIONS IN ADULT LIFE AFTER CHILDHOOD CANCER IN SCANDINAVIA (ALiCCS) - A large population-based patient cohort

Thorgerdur Gudmundsdottir, MD1, Jeanette Falck Winther, MD1, Klaus Kaae Andersen, MSc, PhD1, Henrik Hasle, Professor, MD, PhD2, Jørgen H Olsen, MD, DMSc1.

1 Danish Cancer Society Research Center, Survivorship Unit, Copenhagen, Denmark
2 Aarhus University Hospital Skejby, Department of Paediatrics, Aarhus, Denmark

Purpose
Survival has improved remarkably after introduction of aggressive multimodal chemotherapy for childhood cancer. However, morbidities now become more apparent. Findings of previous studies indicate an increased risk for cardiovascular disease. Yet, the life-long risk of late complications remains to be fully explored.

Patients and methods
A complete population-based series of 19 887 childhood cancer survivors and 126 061 population comparison cohort members (randomly selected and matched by country, gender and age) have been established from Denmark, Iceland and Sweden in a retrospective cohort study. Survivors were diagnosed with cancer before age 20 and recruited from beginning of cancer registration in the 1940s through 2010. Cohort members were followed-up individually for cardiovascular diseases through register linkages.

In a multivariate analysis the Cox proportional hazard model was used to estimate the relative risk of cardiovascular disease in survivors of childhood cancer in comparison to population comparisons.

Results
Preliminary results show a total of 308 ischemic heart disease (IHD) discharge diagnoses, 596 heart failure (HF), 190 valvular abnormality, 240 cerebrovascular incident and 389 cardiomyopathy diagnoses observed in the survivor cohort. Survivors were significantly more likely to be diagnosed with IHD (hazard ratio, HR 1.63, 95% CI 1.44 to 1.84), HF (HR 3.71, 95% CI 3.36 to 4.09), valvular abnormality (HR 4.25, 95% CI 3.56 to 5.08), cerebrovascular incidents (HR 2.36, 95% CI 2.04 to 2.73) and cardiomyopathy (HR 1.67, 95% CI 1.50 to 1.87) than comparisons. The highest risk for IHD, HF and cardiomyopathy was observed among survivors of haematologic cancers. The probability of being hospitalized for cardiovascular diseases was higher among survivors than comparisons in the total follow-up period.

Conclusions
Survivors of childhood cancer are at increased risk for cardiovascular disease compared to the general population. Awareness of this excess risk is important for this growing population of cancer survivors. More final results will be presented at the Nordic Summer School meeting. Next step will be to interpret the epidemiologic results for selected cardiac outcomes in light of dose-response evaluations based on computation of individual radiation doses to the heart estimated at MD Anderson Cancer Center in Houston, TX.
COLORECTAL CANCER SCREENING – IS THERE SEASONAL VARIATION IN THE TEST PERFORMANCE?

Annika Helin1, Nea Malila2
1Tampere School of Public Health, Tampere, Finland
2Finnish Cancer Registry, Helsinki, Finland

Background: Colorectal cancer is the third most common cancer in Finland. Screening with faecal occult blood (FOB) testing has been proven to be effective in reducing colorectal cancer mortality. Colorectal cancer screening has been launched in Finland in 2004 with a gradually expanding programme. The screening consists of biannual guaiac-based FOB testing (Hemoccult) for men and women aged 60-69 and those with positive test results are referred to colonoscopy. The screening tests are sent by mail to the target population and back for analysis and are therefore exposed to environmental conditions such as temperature and humidity. There have been some reports on seasonal variation in FOB test performance. The purpose of this study is to examine if there is any seasonal variation in the FOB test performance measured by proportion of test positives in Finland.

Material: Individual data from the screening programme from 61026 men and 62123 women covering the years 2004 to 2009. The data includes information of the test date, test result (negative, positive), sex, age and residential district. Seasons have been defined by the average monthly temperatures. Also data of all colorectal cancer cases among the cohort has been obtained by linkage with the Finnish Cancer Registry.

Methods: Logistic regression was used to examine if there is seasonal variation in the proportion of test positives.

Results: The proportion of test positives was 3,9% for men and 2,1% for women. The logistic regression showed statistically significant differences between age groups and test years. By age group the positivity rates were 2,9% for ages 60-61, 2,6% for ages 62-63 and 3,1% for ages 64-68. We found no statistically significant differences in the test positivity rates between seasons. Also no regional differences were observed.

Conclusions: The guaiac-based FOB test performs well in the Finnish environmental conditions. The test is considered quite stable. The immunochemical tests have proven to be more sensitive to changes in temperature and moisture content of the air than the guaiac test. With big temperature variations between seasons in Finland changing to another test should be carefully planned and tested before decision making.
Rubber workers and cancer

Laura Järvelä¹, Iiro Kilpikari, Eero Pukkala, Marjukka Viita-aho¹
¹Tampere School of Public Health, Finland

Background:
The rubber workers are exposed to several chemicals in their work environment and the exposure happens mostly through respiratory track and skin contact. Thus, it is hard to determine the overall exposure. The cancer incidence of rubber workers has been known to be higher than the average population. The research done in the last decades shows at least a moderate increase in the cancer risk among rubber workers. In bladder, laryngeal, lung cancer and leukemia risks the results were most consistent. The recent studies do not provide information on the association of specific exposures with cancer risk or how the improved conditions at the factories have decreased the risk. The aim of this study was to assess the excess of cancer incidence and mortality among the rubber workers of the rubber plant workers of Oy Nokia ab.

Material and methods:
The original data was collected by I. Kilpikari in a study “Estimation of exposure, incidence of cancer, and mortality in the rubber industry”. The study was done as a nested case-control study and the data was taken from an earlier cohort study which included 1318 workers. There were 78 cases and each of them had five controls. The controls were matched by sex and age (+/-1 year). The exposure in this study was evaluated by work code, duration of the exposure and thioether levels of the urine. 43 of the workers had given the urine sample and information about their smoking, drinking and use of medicine.

The analysis was done using SPSS and R statistical programs. In statistical analysis the risk of cancer between cases and controls were estimated by using odds ratios. The odds ratios were compared to the SIRs of the original cohort.

Results:
The mean worktime was 4.4 years. 52 of the workers had died during the follow up. There were 78 cancer cases of which 22 breast cancers, 13 cancers of the skin, 11 prostate cancers, 11 cancers of the gastroenteral track, 8 gynecological cancers, 6 cancers of the respiratory track and 7 other cancers. Thus there were 78 observed cancers in the cohort of 398. Most of the workers were exposed by the respiratory track (92.2%) and the rest by skin contact.

Conclusions:
Non melanoma & non basal cell carcinoma skin cancer mortality in Denmark between 1995-1999

Jens Anibal Juul, Niels Christensen, Gerda Engholm
Department of Cancer Prevention and Documentation, Danish Cancer Society, Strandboulevarden 49, Copenhagen, Denmark

Abstract
Given the generally accepted assumption that non melanoma and non basal cell carcinoma skin cancer (NMNB) are rarely fatal, statistics from NORDCAN (Association of the Nordic Cancer Registries) show a surprisingly high mortality among patients with an average of more than 50 annually deaths with NMNB as primary death cause in Denmark. The goal of this project is to elucidate what contributes to these deaths. Can death among rarer skin cancers and among skin cancer patients with previous organ transplant account for most NMNB deaths? -The generated knowledge may in turn contribute to the generation of new hypothesis as starting ground for further investigation and the development of prognostic factors with clinical value for when giving skin cancer patients medical advice and treatment.

Material and Method:
The project has yet to be completed. The material consists of data from the Danish registries; Cancer Registry, Cause of Death Registry and the National Patient Registry (Years). We have investigated predefined hypotheses; difference in mortality of NMNB skin cancer as the primary cause of death between age, gender, geography and morphology. We further plan to examine the data with NMNB skin cancers excluded rarer skin cancers (Mainly neuroendocrine skin cancers) and patients under immunosuppressive treatment. We will analyze incidence, mortality and relative survival.

Results:
So far, results of the project has rejected the hypothesis of significant differences in distribution of NMNB skin cancer mortality and geography, age, morphology and sex in Denmark.

Conclusion:
Further results will be shown at the presentation.
Incidence of cancer of the oral cavity by occupational category in Finland 1971-2005
Ville Karhunen
University of Oulu, Finland

In this study the incidence of cancer of the oral cavity in different occupational categories in Finland 1971-2005 was analyzed by two different models. In the first model standardized incidence ratios (SIRs) were calculated for men and women in each occupational category adjusted for age and calendar period.

Smoking and alcohol consumption are known to be major risk factors for cancers of the oral cavity. Thus, in the second model, lung cancer incidence, liver cirrhosis mortality and liver cancer incidence in occupational groups are taken into account as surrogate variables in an attempt to adjust for the confounding effects of these risk factors. SIRs are calculated for men and women in each occupational category adjusted for age, calendar period and the surrogate variables.
UTERINE CARCINOSARCOMAS - A RETROSPECTIVE PILOT STUDY OF THE CLINICAL FEATURES AND OUTCOMES.

Vesal Khalid MS¹, Lone Kjeld Pedersen D.M.Sc.²
¹University of Aarhus, Aarhus, Denmark, ²Department of Gynecology and Obstetrics, Aarhus University Hospital, Aarhus, Denmark.

Background:
Uterine carcinosarcoma (CS) is a rare and highly aggressive neoplasm. It represents both malignant epithelial and malignant sarcomatous components. The clinical course is associated with poor outcome. The diagnosis of CS is histological and mostly made after surgical treatment. Diagnostic and treatment evaluation is seldom described in literature. The objective of this pilot study was to describe the clinical presentation and outcomes of CS. Furthermore the demographics were evaluated.

Material:
A retrospective review was performed for patients treated at the University Hospital of Aarhus, Denmark between 1995 and 2010. All patients with histologically confirmed CS within the period were included in this study.

Methods:
Patients were identified from the Danish Pathology Databank. Medical records were retrieved and assessed. Information regarding demographics, clinical presentation, treatment and outcome were collected in a database.

Results:
38 patients were identified. Mean age 69.4 (±10.5), mean BMI 28.2 (± 7.4). The majority of patients (74%) presented with postmenopausal bleeding. The mean observation period was 12.8 months (±8.8). Overall, 55% of the women were dead, 43% after recurrence. Advanced stage of disease at the time of diagnosis was found in 38.9% of the dead. Grade III tumours were more frequent among women who died from disease compared to those without recurrence (62% versus 18%).

CS as a preoperative diagnosis was known in 21%. The diagnosis was obtained by cytology in 12.5% and by hysteroscopy directed biopsies in 87.5%.

Local recurrence at the vaginal vault was most frequent (60% of recurrent disease). 5 patients only contributed with data regarding histology and living status.

Conclusions:
In the present study we found that CS is a highly aggressive neoplasm with a rapid course. Tumor stage and grade were found to be a key factor for survival. This study indicates a possible advantage of preoperative staging as preoperative diagnosis of CS given by Hysteroscopy directed biopsies enables the surgeon to select more extensive surgery in an effort to improve survival. This pilot study reinforces the need for a larger national study.
Risk of cervical dysplasia and cancer in users of copper intrauterine device

An epidemiological historically controlled cohort study
Terese Matthesen Student, Øjvind Lidegaard Professor RH, Charlotte Wessel Skougaard

In 2008, 397 Danish women were diagnosed with cervical cancer and 128 died of the disease. Of prophylactic measures, Denmark has introduced a national screening program that aims to detect early stages of cervical cancer. Danish women between 12 and 26 years are also offered free vaccination against human papilloma virus.

Intrauterine copper IUD has been shown to protect against endometrial cancer and it is suggested that it also protects against cervical cancer. If this hypothesis can be confirmed, incidence and mortality of cervical cancer could be reduced further. However, there has not been conducted long term follow-up register-based epidemiological studies that examine this hypothesis.

The purpose of this study is to examining the incidence of cervical dysplasia and cancer for users or former users of copper IUD and comparing this with a control group who never have been registered with a copper IUD.

The method is to first map the 15-49 year old Danish women using copper IUD over time in the period 1994-2010. Data is extracted from the Danish National Patient Register and The National Health Insurance Service Registry, which makes it possible to trace every single woman in regard to decommissioning and removal of the IUD. These women are investigated whether they are registered with dysplasia and or cancer. Outcome compares with the occurrence of cervical dysplasia and cancer in a control group of women with matching age to the group of exposed women. We adjust for relevant covariates such as hpv-vaccination, use of contraceptive pills, hysterectomy and previous dysplasia or cancer. We calculate rateratio and 95% CI.

The results of the study is not yet clear, since the permissions from the authorities involved have not yet been approved.
GENE MUTATIONS AND AMPLIFICATIONS IN ENDOMETRIAL CANCER

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Aim and background:
Endometrial cancer is among the most common gynecological malignancies in industrialized countries. Although 75% of cancers are treated at an early stage, 15% to 20% recur. Due to these recurrences the demand for systemic therapies and better prognostic markers are vital. The aim of this study was to validate the phenotype related to gene amplification and mutations in PIK3CA.

Materials and methods:
We used a population based prospectively collected sample series from primary tumors and corresponding metastatic lesions from patients with endometrial cancer. Primary tumors from 375 patients and 50 with one or more corresponding metastatic lesions were analysed for amplification of the PIK3CA gene using fluorescence in situ hybridization (FISH). We wanted to analyze point mutations in exons 9 and 20 of the PIK3CA gene. For this we used polymerase chain reaction (PCR).

Results:
We find that 5% of patient samples harbor PIK3CA gene amplifications or gain. These gene copy number changes are associated with poor survival, high FIGO-stage, and non-endometroid tumors. Mutational status data are yet to be analyzed.

Conclusion:
We conclude that the PIK3CA signalling pathway is affected in endometrial cancer. Changes such as PIK3CA gene amplification leads to poor prognosis and survival, however further research is needed.
Characterization of deaths without a cause in the Danish Register of Causes of Death.

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Background
In 2007 the Danish Registry of Causes of Death changed registration from paper forms to be electronically based. Following that, some deaths did not get at cause of death attached - the Danish Register of Causes of Death was no longer complete. This induces an underreporting of cancer deaths in for instance in NORDCAN. In 2007 3.5% of the deaths missed the information and in 2008 and 2009 percentages missing were 4.0 and 5.3%. We will characterize the demographic pattern and search for probable causes of death among cancer registrations and - if the time permits – other diseases in hospital information the preceding three years.

Material
Around 6000 persons with unknown cause of death 2007-2009 are identified in the Danish Register of Causes of Deaths. The register is population-based and contains data on all deaths in among Danish residents dying in Denmark, including information on date of birth, sex, date of death and home municipality at death for all deaths.

Methods
Using the personal identification number for persons without a cause of death we search for registrations of cancer and - if time permits – other diseases in the three years preceding death by linkage to the Cancer Register and the Hospital Inpatient Register.
It will be evaluated whether the persons without a cause of death are missing completely at random and after estimating 1 and 5 years survival probability we will compare with the national based survival probabilities and see if the cancer diagnoses seem a reliable cause of death.

Results
Among the deaths without a cause of death 47.3 percent had a cancer diagnosis in the year prior to death. Among those were 91 percent a malign tumor. The three main malign cancers of which most persons die within a year after diagnosis are lung cancer (20.7 percent), colon cancer (9.9 percent) and pancreatic cancer (7.7 percent) out of all the diagnosed the year prior to death.

Conclusions
Further results from the characterizations of the deaths without a cause of death and results from the linkages will be shown at the meeting.
DANISH CHILDHOOD CANCER PATIENTS WITH CONGENITAL HEART DEFECTS: A NATIONWIDE MORTALITY STUDY.

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**Background:** Comorbidity is known to affect mortality of cancer patients. Congenital heart defects (CHD) are the most common congenital defects, and mortality of CHD patients with childhood cancer is unknown. We aimed to examine whether there is an increased mortality among paediatric cancer patients who are born with a CHD compared with childhood cancer patients without CHD.

**Material and methods:** The study was carried out as a cohort study based on the Danish Cancer Registry and the Danish National Registry of Patients. We identified an exposed cohort including children born 1977-2008 with cancer and CHD and a comparison-cohort of children with cancer born without a CHD. The comparison-cohort was matched with the exposed cohort on sex, year of birth, age at diagnosis of cancer, and cancer type. Information on the included patients' vital status was obtained from the Danish Civil Registration System. We computed cumulative mortality of the exposed and comparison cohorts based on the Kaplan-Meier estimator.

**Preliminary results:** We identified 36 patients born with CHD and diagnosed with a paediatric cancer. We did not identify comparison cohort members fulfilling all matching criteria for all CHD patients. The Kaplan-Meier curves for the cumulative 5-year mortality show a higher mortality of the exposed cohort compared with the comparison-cohort when only matching on sex, year of birth, and age at cancer diagnosis.

**Conclusion:** The childhood cancer patients with CHD had a higher mortality compared with childhood cancer patients without CHD. Potential explanations will be discussed.
INCIDENCE OF MERKEL CELL CARCINOMA IS INCREASED SIGNIFICANTLY AMONG YOUNGER STATIN USERS IN FINLAND

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Background: Statins (HMG-CoA-reductase inhibitors) are suggested to act as a predisposing factor for autoimmune diseases, have immunomodulatory effects, and possibly prevent some cancer types – the sum of these effects is unknown in cancers of viral aetiology, such as Merkel cell carcinoma (MCC). Aim of our study was to find out whether statin users in Finland have an increased incidence of MCC.

Materials and Methods: A cohort of 224,715 male and 230,220 female statin users during 1994-2009 was identified from the Prescription Register of the National Social Insurance Institution. This cohort was followed up through the Finnish Cancer Registry for MCC up to 2009.

Results: There were 50 cases of MCC, while the expected number of cases, based on the MCC incidence in comparable Finnish population, was 39.9. The standardized incidence ratio (SIR) for MCC in ages <60 years was 3.16 (95% CI 0.65-9.23), in ages 60-74 years 1.94 (95% CI 1.23-2.90) and in ages ≥75 years 0.89 (95% CI 0.57-1.31). The relative risk of MCC decreased significantly, 0.79 fold (95% CI 0.67-0.92), at each 5 year step when moving towards older age groups. There was no significant variation in SIR related to length of follow-up or between the genders.

Conclusions: MCC is the first neuroendocrine cancer linked to statin use. The association is statistically significant and biologically plausible through immunomodulatory effects of statins. The excess of MCCs was observed in atypically young patients, a similar phenomenon as noted earlier in patients with immunocompromising states.
THE IMPACT OF PRE-OPERATIVE CHEMORADIOThERAPY ON LOCAL RECURRENCE AND SURVIVAL IN RECTAL CANCER – RETROSPECTIVE COHORT STUDY

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Background The treatment of rectal cancer in Norway has been through some major changes in the last 20 years. Large focus has been aimed at the frequent problem of locally recurrent cancer, a feared post-operative event that is predictive of higher morbidity and mortality. The national implementation of total mesorectal excision in 1993 has yielded a significant reduction in local recurrence-rate, and this surgical technique is now the gold standard at all hospitals treating rectal cancer in Norway. The more recent introduction of pre-operative chemoradiotherapy for advanced rectal cancer has also been an important improvement in the treatment. As opposed to most other countries, these two treatment measures were not implemented simultaneously in Norway. The aim of the present project is to investigate the separate effect of pre-operative chemoradiotherapy on local recurrence and survival in rectal cancer at a major Norwegian hospital.

Material and methods All 588 patients treated surgically for rectal cancer at the Haukeland University Hospital between 1994 and 2006 were identified from the Norwegian Rectal Cancer Registry. The 5-year relative survival will be used to compare the outcomes of the patients treated in the time interval of 1997-2000 with surgery alone, and patients treated in the time interval of 2002-2005 who received chemoradiotherapy before surgery. The 5-year local recurrence rate will also be calculated for each time interval.

Results The project is currently collecting and controlling data, and results are thus not yet available. It is, however, possible to outline some future challenges when analysing and interpreting the results. As the two patient groups are treated in different time-intervals (1997-2000 vs 2002-2005) one would expect a natural improvement in survival from the earlier period to the later regardless of treatment method. Data from the Cancer Registry of Norway shows that there has been an overall increase in the relative survival for rectal cancer from 55 % (men) and 58 % (women) in 1995-1997, to 63 % (men) 66 % (women) in 2000-2004. These figures are for all stages combined, but the increase is even more pronounced for localized and regional stages. Caution is therefore required when comparing the patient groups and interpreting the results. Also, obtaining an adequate sample size can prove to be difficult.

Conclusion It is not yet possible to draw any conclusions in the project, but the database will hopefully be completed by the end of February after which the statistical analysis can begin.
Title: Subsite specific incidence of colorectal cancer, A comparison of incidence rates in Norway and Denmark.

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Text: There have been a rapid increase in the colorectal cancer in Norway and Denmark since 1960’s and several studies have reported a rising proportion of right-sided colon tumors. Referred to as a left to right shift of colon cancer. The prospect of this study have pointed to some risk factors being stronger associated to one one subsite than another. The comparison of subsite-specific incidence trends in Norway and Denmark is interesting as these countries have about the same incidence today, but have had different incidence trends during the last decades. So, the aim of this study is to compare incidence rates of left and right sided colon, and rectal cancer in Norway and Denmark.

An aggregated data set has been made by dividing the data in age-groups and five years period for the different subsites, for men and women separately. Then applied the techniques of survival analysis to see the incidence of colorectal cancer in Norway and Denmark and the results shows that overall Norway and Denmark both have really high incidence of this disease and the colon cancer in males and females in all ages have increasing trend while the proximal cancer in females is found to be bit higher than the males. At the same time, rectal cancer in the middle/young age group people is found to be higher in men than the women. Denmark is found to be higher incidence rates than Norway and also having more deaths by this type of cancer. Similarly, colon cancer in Norway has smaller amount of new cases than Danmark.
ESTIMATION OF ABSOLUTE RISK FROM NESTED CASE-CONTROL DESIGN: RISK OF HEPATOCELULAR CARCINOMA ASSOCIATED WITH HEPATITIS VIRUSES

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Langholz and Borgan (1997, Biometrics 53, 767-774) have described methods for estimating absolute risk of getting an interesting disease from nested case-control data. These methods are relatively little used, though such estimates would often be highly relevant in epidemiological contexts. These principles are introduced in this ongoing study and are used to estimate the absolute risk of hepatocellular carcinoma (HCC, the most common type of liver cancer) associated with exposure to different hepatitis viruses.

Analyses are based on data derived from Nordic biobanks and national cancer registries. Actually, a Nordic biobank network NBSBCCC (Nordic Biological Specimen Banks working group on Cancer Causes & Control) maintains these data sources for epidemiological studies. This network covers 17 independent biobank cohorts in total and some of these have been created for specific epidemiological studies. Therefore, these cohorts are typically not representative of the respective national or “general” populations, and they are not comparable with each other either. Three of these cohorts are used in this study, one from each country (Norway, Sweden and Finland). For each cohort, separate data frames exist for cohort and nested case-control data. Remes (2010) has already done analysis based on nested case-control data from these (and few other) cohorts. One major conclusion is that hepatitis C in particular seems to be strongly associated with HCC.

Data on actual hepatitis virus infections are obtained by laboratory analyses from stored blood serum samples. Many possible sources of error are involved in these samples that may ultimately result to biased estimates of effect. Because of this, the effects of analytic batch, storage time and freeze-thaw cycles in biological samples are also discussed in this study.

Key words
Absolute risk, Nested case-control, Hepatocellular carcinoma, Hepatitis, Biobank, Biological sample

References

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¹ In English: Hepatitis virus infection and liver cancer - matched case-control study.
TRENDS IN BRESLOW’S TUMOUR THICKNESS OF CUTANEOUS MELANOMA IN ICELAND 1980-2009

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Background: Cutaneous melanoma incidence has increased dramatically in Iceland in spite of its northern hemispheric location. A reason for this might include more frequent travel abroad and increasing prevalence of sunbed use. The aim of this study was to evaluate the trend in Breslow’s tumour thickness in the years 1980-2009.

Materials & Methods: The population based Icelandic Cancer Registry provided information on 854 cases of melanoma between January 1980 through December 2009. Incidence rates were calculated per 100.000 and the lesions were stratified according to gender, age at diagnosis (<50, ≥50), year of diagnosis (1980-1989, 1990-1999 and 2000-2009), Breslow tumor thickness (≤1.0, 1.01-2.0, 2.01-4.0 and >4.0 mm).

Results: The median Breslow’s thickness in 10 year time periods declined from 2.15 and 1.0 in 1980-1989 to 0.9 and 0.6 in 2000-2009 for males and females, respectively. When stratified by gender and age, the incidence of thin (≤1.0 mm) melanomas increased dramatically in all subgroups, while intermediate (1.01-2.0 and 2.01-4) tumours increased in older (≥50) men only. The proportion of thin melanomas (≤1.0 mm) increased from 42% in 1980-1989 to 69% in 2000-2009. The proportion of thin melanomas in 2000-2009 was higher among females (78%) than males (56%), and especially high among young (<50) females (85%).

Conclusion: Breslow’s tumour thickness has declined markedly and the increasing melanoma incidence is mainly among thinner tumours. Females have higher proportion of thinner tumours than males and there is an increase in intermediate tumours in older men. This might indicate that women are more alert of new or irregular nevi’s than men. The authors conclude that future melanoma educational campaigns in Iceland should be more focused on men, and in particular, older men.
Background: Norwegian women aged 50-69 years are invited to the Norwegian Breast Cancer Screening Program (NBCSP) every second year from 1996. Until 2009, some women attended the screening seven times. The aim NBCSP is to reduce the mortality from the disease by detecting the cancers in an early stage. Several studies have shown that screen-detected cancers have prognostic favorable tumor characteristics compared with clinical detected cancers. In addition, women who attend regularly have prognostic favorable tumor characteristics compared with irregular participants. However, the tumor characteristics in women who attend regularly is less known. In order to investigate the possible benefit of regular participation in the NBCSP, prognostic tumor characteristics will be identified in cancers detected in women after one, two, three, four, five, six and seven screening tests. The following hypothesis will be tested:

1. Tumor characteristics do not differ in women who have their first, second, third, fourth, fifth, sixth or seventh screening test.
2. Tumor characteristics in women defined in Pt#1 do not differ from age and calendar year matched controls with cancer diagnosed outside the screening program.

Material: Women diagnosed with screen-detected or interval cancer will be included in the analyses. All groups will be divided into NBCSP-cancers (screen-detected and interval cancer) and those detected among women outside the screening program. We assume about 800 breast cancer cases among the women aged 50-69 years old, decreasing with 80-100 every second year, giving about 200 breast cancer cases detected among women screened seven times.

Methods: Chi square test will be used to compare the tumor characteristics, both between the age groups of NBCSP-cancers and between NBCSP-cancers and cancers detected outside the screening program. Two-sided chi-square tests will be used to determine statistical significance between groups. Statistical power is not calculated for the study since it is considered a part of the quality control of the Norwegian Breast Cancer Screening Program.

Data is not received yet, thus no results can be presented here. Hopefully I can get data and find some results before I travel to Tampere.