4.4 PHARMACOEPIDEMIOLOGY

Chair: Dr. John Frank, Canada

04-4.1 NON-STEROIDAL ANTI-INFLAMMATORY DRUG AND ASPIRIN USE AND THE RISK OF HEAD AND NECK CANCER

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Introduction The use of non-steroidal anti-inflammatory drugs (NSAIDs) has been associated with a reduced risk of several cancers. Evidence for NSAIDs preventing head and neck cancer (HNC) is inconclusive. We conducted a prospective cohort study to examine the association between NSAID use and HNC risk.
Methods Using data from the National Cancer Institute (NCI) Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, we examined the association between aspirin / NSAID use and HNC incidence among 142 034 men and women aged 55–74 years. Information regarding regular use and frequency of use of aspirin and NSAIDs over the last 12 months was reported at enrolment. (1993–2001). Individuals were followed-up until 2006. HRs and 95% CIs were calculated using multivariable cox proportional hazards regression with adjustment for potential confounders including tobacco use, gender, body mass index and age.
Results Over the follow-up period 316 individuals were diagnosed with HNC. Regular aspirin use, compared to non-use, was associated with a significantly reduced incidence of HNC (Adjusted HR 0.78; 95% CI 0.62 to 0.98). No association was observed with regular NSAID use, compared to non-use, and HNC incidence (adjusted HR 0.99, 95% CI 0.76 to 1.28).
Conclusions Our study suggests that aspirin may have potential as a chemopreventative agent for HNC however further investigation is warranted.

04-4.2 CHOLESTEROL-LOWERING DRUGS AND INCIDENT OPEN-ANGLE GLAUCOMA

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Purpose To determine the association between the use of statins and non-statin cholesterol-lowering drugs and incident open-angle glaucoma.
Methods In a prospective population-based cohort study among 3939 participants aged 55 years and above, ophthalmic examinations including measurement of the intraocular pressure, assessment of the optic nerve head and perimetry were performed at baseline and after an average follow-up duration of 9.8 years. The use of statins and non-statin cholesterol-lowering drugs was monitored continuously during follow-up. Associations between incident glaucomatous visual field loss and the use of statins and non-statin cholesterol-lowering drugs were assessed using cox-regression models adjusted for age, gender, intraocular pressure lowering treatment and potential (mainly cardiovascular) confounders.
Results During follow-up, 108 participants (2.7%) developed glaucomatous visual field loss. The HR for statin use was 0.56 (95% CI 0.32 to 0.99; p=0.045) and for non-statin cholesterol lowering drugs 1.82 (0.71 to 4.66; p=0.21). There was a significant trend towards a reduced risk of developing OAG with prolonged statin use (HR 0.89, 95% CI 0.41 to 1.93 for use during 2 years or less; HR 0.44, 95% CI 0.22 to 0.89 for use during more than 2 years).
Conclusions Long-term use of statins seems to be associated with a reduced risk of open-angle glaucoma. This result is consistent with an earlier study and suggests that statins should be further explored as a new class of medications for the treatment of glaucoma, especially for those patients in whom disease progression continues despite an apparently sufficient intraocular pressure reduction.

04-4.3 CANCER INCIDENCE AND INSULIN THERAPY IN A COHORT OF DIABETIC PATIENTS

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The risk of incident cancer seems increased in patients with type 2 diabetes (T2D) and therapeutic regimens (metformin; insulin, analogues) may be involved. We investigated in a cohort of 26 742 T2D patients from a statewide disease management program the risk of incident cancer over a median follow-up time of 3.5 years. Data from all T2D patients in the age 40–79 years residing in the Muenster District were linked to cancer cases in the population-based regional cancer registry. Invasive cancer cases were identified using probabilistic record linkage procedures and pseudonymised personal identifiers, including only first cancers but no DCO cases. Censuring date was 31 December 2008. We computed standardised incidence ratios (SIR) and employed Cox regression models. We identified 759 first cancers among male T2D patients (18.7 per 1000 py) and 605 among females (12.7 per 1000 py). Relative to the general population, the risk of any incident cancer was raised (SIR 1.14; 95% CI [1.10 to 1.21]), it was particularly high for cancer of the liver (SIR 1.95 [1.18 to −2.99]) and pancreas (SIR 1.45 [1.07 to 1.92]). In Cox models, adjusting for diabetes duration, body mass index and sex, insulin therapy was related to higher cancer risk (HR 1.69 [1.55 to 1.84]). No effect was seen for metformin. Limitations relate to lack of numbers for analysing specific cancer types and lack of detail on medication type, duration and dosage. Our results seem to confirm previous reports of increased cancer risk with insulin therapy.

04-4.4 EXPOSURE TO CYCLO-OXYGENASE-2 INHIBITORS AND RISK OF CANCER: NESTED CASE-CONTROL STUDIES

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Introduction Selective cyclo-oxygenase-2 (COX2) inhibitors are a widely used analgesic for patients with intolerance to traditional non-steroidal anti-inflammatory drugs and it is unclear how long-term use affects cancer risk.
Methods A series of nested case-control studies were conducted using data from 574 UK general practices in the QResearch primary care database. All patients diagnosed with cancer between 1998 and 2008 were matched with up to 5 controls. Associations of COX2 inhibitors with risk of all cancers and 10 site-specific cancers (breast, prostate, lung, colorectal, haematological, bladder, melanoma, gastric, pancreatic and oesophageal) were estimated using conditional logistic regression adjusted for co-morbidities, smoking status, socio-economic status and use of non-steroidal anti-inflammatory drugs, aspirin and statins.
Results 88 125 cases with cancer and 362 254 matched controls with at least 6 years of records were analysed. Use of COX2 inhibitors for more than a year was associated with significantly increased overall risk of cancer (OR 1.06, 95% CI 1.03 to 1.09), particularly breast cancer (OR 1.24, 95% CI 1.08 to 1.42) and haematological

malignancies (OR 1.38, 95% CI 1.12 to 1.69). Risk of colorectal cancer was significantly decreased (OR 0.76, 95% CI 0.63 to 0.92) for COX2 inhibitor usage of more than a year. There were no other significant associations.

Conclusion In this large population-based case-control study, prolonged use of COX2 inhibitors was associated with increased risk of breast and haematological cancers and decreased risk of colorectal cancer. These findings need to be confirmed using other data sources.

04-4.5 ASSOCIATIONS OF ANGIOTENSIN-II RECEPTOR BLOCKERS AND ACE INHIBITORS WITH ALZHEIMER'S DISEASE: A NESTED CASE-CONTROL STUDY WITHIN THE UK GENERAL PRACTICE RESEARCH DATABASE

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Objectives To investigate whether angiotensin II receptor blockers (ARBs) and ACE inhibitors (ACE-Is) are more strongly associated with Alzheimer's disease (AD) than other anti-hypertensive drugs.

Methods Nested case-control analysis within the UK general practice research database (n≈10 million), with prospectively recorded anti-hypertensive prescribing data. Cases aged ≥60 years and diagnosed between 1997 and 2008 (5797 with AD, 2186 with vascular dementia, 1214 with unspecified / other dementia) were matched to up to four controls by age, general practice and gender. We computed ORs and dose response effects for AD, vascular and unspecified / other dementia, comparing those prescribed ARBs or ACE-Is for at least 6 months with patients prescribed other anti-hypertensives. We controlled for matching factors, co-morbidities, smoking status, an area measure of socio-economic status, consultation rate and blood pressure and accounted for reverse causality by introducing time-lags of up to 8 years prior to diagnosis / index date.

Results Patients diagnosed with AD, vascular and unspecified / other dementia had fewer prescriptions for ARBs and ACE-Is. Inverse associations with AD were strongest for ARBs (OR 0.47, 95% CI 0.37 to 0.58) compared with ACE-Is (OR 0.76, 95% CI 0.69 to 0.84) (p difference <0.001). Associations of ARBs with AD were stronger than for vascular dementia (p difference=0.01) and unspecified / other dementia (p difference=0.23). There were inverse dose-response relationships between ARBs and ACE-Is with AD (both p trend <0.01). The inverse association of ACE-Is with AD diminished when using longer time lags but the ARB-AD association persisted.

Conclusions Patients with AD were around half as likely to be prescribed ARBs. Further randomised controlled trial evidence is required to rigorously test these findings.

04-4.6 ROLE OF MEDICAL FACTORS IN THE AETIOLOGY OF UPPER AERODIGESTIVE TRACT CANCERS IN EUROPE: THE ARCAGE STUDY

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Background Cancer of the upper aerodigestive tract (UADT) (oral cavity, pharynx, larynx and oesophagus) is, globally, the fourth most common cancer and cause of cancer mortality. In addition to established risk factors such as tobacco and alcohol consumption, other risk factors were suggested, including human papillomavirus infection.

Objective To investigate the role of medical history (skin warts / verrucae; *Candida albicans* / thrush; herpetic lesions / cold sores; heartburn; regurgitation) and medication (for heartburn; for regurgitation; aspirin) use in UADT cancer risk.

Methods A case-control study conducted in 10 European countries.

Results There were 1779 cases of UADT cancer (all SCC) and 1993 controls. Having had warts / verrucae and history of Candida / thrush infection protective for UADT cancers (OR 0.80, 95% CI (0.68 to 0.94) and 0.73 (0.60 to 0.89), respectively) but there was no association with herpetic lesions.

Neither symptoms of gastro-oesophageal reflux (heartburn or regurgitation) nor medication for associated symptoms were associated with risk of UADT cancer. When considered by sub-site, regurgitation was associated with a non-significant increased risk for cancer of the oesophagus (1.47; 0.98 to 2.21).

Regular aspirin use (at least once a week for a year) was not associated with risk of UADT cancer. When considered by sub-site, it had protective effect for cancer of oesophagus (0.51; 0.28 to 0.96) and non-significant protective effect for cancers of hypopharynx (0.53; 0.28 to 1.02) and larynx (0.74; 0.54 to 1.01).

Conclusion There is conflicting evidence regarding association between medical history and medication use and UADT cancer risk.

4.5 PREVENTING CHRONIC DISEASE LOCALLY AND GLOBALLY: DELIVERY OF PREVENTION INTERVENTION VIA THE SUPERCOURSE

Chair: Prof. Ronald LaPorte, USA

04-5.1 TELEPREVENTIVE MEDICINE AS THE FUTURE OF EPIDEMIOLOGY AND DISEASE PREVENTION

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The problem of chronic disease around the world can be improved only through the means of prevention. Effective prevention of chronic disease cannot be achieved without what we call "Telepreventive Medicine." The fundamental underlying concept is that information about disease prevention should be distributed using inexpensive Internet pathways. The birth of the discipline started a few years ago and has been recognised in the *The British Medical Journal* article. In the global public health arena, the concept of telepreventive medicine is an integral part of the Global Health Network Supercourse project, a global online library of nearly 5000 lectures and a network of 48 000 individuals in 174 countries. Telepreventive medicine has a great potential to improve global health, in both communicable and non-communicable diseases. For example, utilising the power of the Supercourse network and telepreventive medicine, Supercourse team was able to distribute information about H1N1 infection even before it made it to news media. We must differentiate telepreventive medicine from telemedicine. Telemedicine is designed to "cure" and it is expensive (like "telesurgery", it is unlikely that telemedicine can have any effect on global health as it does not reach too many people. In contrast with telepreventive medicine we can reach millions with the prevention message. Through the Supercourse, telepreventive medicine epidemiology and new mobile global health approaches, information can be shared more rapidly with all students through their instructors.

Visit the Telepreventive Medicine Supercourse lecture at http://www.pitt.edu/~super1/lecture/lec10431/index.htm.