ABSTRACT FROM CURRENT LITERATURE

Association of adherence to lifestyle recommendations and risk of colorectal cancer : a prospective Danish cohort study

H Kirkegaard, NF Johnsen, J Christensen et al.
BMJ 2010; 341 : 5504

Objectives: To evaluate the association between a simple lifestyle index based on the recommendations for five lifestyle factors and the incidence of colorectal cancer, and to estimate the proportion of colorectal cancer cases attributable to lack of adherence to the recommendations.

Design: Prospective cohort study.

Setting: General population of Copenhagen and Aarhus, Denmark.

Participants: 55487 men and women aged 50-64 years at baseline (1993-7), not previously diagnosed with cancer. Main outcome measure Risk of colorectal cancer in relation to points achieved in the lifestyle index (based on physical activity, waist circumference, smoking, alcohol intake, and diet (dietary fibre, energy percentage from fat, red and processed meat and fruits and vegetables)' modelled through Cox regression.

Results: During a median fellow-up of 9.9 years, 678 men and women had colorectal cancer diagnosed. After adjustment for potential confounders, each additional point achieved on the lifestyle index. corresponding to one additional recommendation that was met was associated with a lower risk of colorectal cancer (incidence rate ratio 0.89 (95% confidence interval 0.82 to 0.96), In this population an estimated total of 13% (9.5% Cl 4% to 22%) of the colorectal cancer cases were attributable to lack of adherence to merely one additional recommendation among all participants except the healthiest. If all participants had followed the five recommendations 23% (9% to 37%) of the colorectal cancer cases might have been prevented. Results were similar for colon and rectal cancer, but only statistically significant for colon cancer.

Conclusions: Adherence to the recommendations for physical activity, waist circumference, smoking, alcohol intake and diet may reduce colorectal cancer risk considerably, and in this population 23% of the cases might be attributable to lack of adherence to the five lifestyle recommendations. The simple structure of the lifestyle index facilitates its use in public health practice.

Paracetamol use in early life and asthma: prospective bir cohort study

AJ Loe, JB Carlin, CM Bennett et al.
BMJ 2010; 341 : 4616

Objective: To determine if use of paracetamol in early life is an independent risk factor for childhood asthma.

Design: Prospective birth cohort study.

Setting: Melboune Atopy Cohort Study.

Participants: 620 children with a family history of allergic disease, with paracetamol use pro spectively documented on 18 occasions from birth to 2 years of age, followed until age 7 years.

Main outcome measures: The primary outcome was childhood asthma, ascertained by questionnaire at 6 and 7 years. Secondary outcomes were infantile wheeze. allergic rhinitis, eczema, and skin prick test positivity.

Results: Paracetamol had been used in 51% (295/575) of children by 12 weeks of age and in 97%, (556/575) by 2 years. Between 6 and 7 years, 80% (495/620) were followed up 30% (148), had current asthma. Increasing frequency of paracetamol use was weakly associated with increase risk of childhood asthma (crude odds ratio 1,18.95% confidence interval 1.00 to 1.39, per doubling of days of use). However, after adjustment for frequency of respiratory infections, this association essentially disappeared (odds ratio 1.08. 0.91 to 1.29), Paracetamol use for non-respiratory causes was not associated with asthma (crude odds ratio 0.95, 0.81 to 1.12).

Conclusions: In children with a family history of allergic diseases, no association was found between early paracetamol use and risk of subsequent allergic disease after adjustment for respiratory infections or when paracetamal use was restricted to non-respiratory tract infections, These findings suggest that early paracetamol use does not increase the risk of asthma.

Oral Rivaroxaban for Symptomatic Venous Thromboembolism

The EINSTEIN Investigators
N Engl J Med 2010; 363: 2499-2510

Background: Rivaroxaban, an oral factor Xa inhibitor, may provide a simple, fixed-dose regimen for treating acute deep-vein thrombosis (DVT) and for continued treatment, without the need for laboratory monitoring.

Methods: We conducted an open-label, randomized, event-driven, noninferiority study that compared oral rivaroxaban alone (15 mg twice daily for 3 weeks,

followed by 20, mg once daily) with subcutaneous enoxaparin followed by a vitamin K antagonist (either warfarin or acenocoumarol) for 3, 6, or 12 months in patients with acute, symptomatic DVT. In parallel, we carried out a double-blind, randomized, event-driven superiority study that compared rivaroxaban alone (20 mg once daily) with placebo for an additional 6 or 12 months in patients who had completed 6 to 12 months of treatment for venous thromboembolism. The primary efficacy outcome for both studies was recurrent venous thromboembolism. The principal safety outcome was major bleeding or clinically relevant nonmajor bleeding in the initial-treatment study and major bleeding in the continued-treatment study.

Results: The study of rivaroxaban for acute DVT included 3449 patients: 1731 given rivaroxaban and 1718 given enoxaparin plus a vitamin K antagonist. Rivaroxaban had noninferior efficacy with respect to the primary outcome (36 events [2.1 %], vs. 51 events with enoxaparin-vitamin K antagonist [3.0%]; hazard ratio, 0.68; 95% confidence interval [CI], 0.44 to 1.04; P<0.001). The principal safety outcome occurred in 8.1 % of the patients in each group. In the continued-treatment study, which included 602 patients in the rivaroxaban group and 594 in the placebo group, rivaroxaban had superior efficacy (8 events (1.3%], vs. 42 with placebo [7.1%]; hazard ratio, 0.18; 95% CI, 0.09 to 0.39; P<0.001). Four patients in the rivaroxaban group had nonfatal major bleeding (0.7%), versus none in the placebo group (P=0.11).

Conclusions: Rivaroxaban offers a simple, single-drug approach to the short-term and continued treatment of venous thrombosis that may improve the benefit-to-risk profile of anticoagulation.

Cardiac-resynchronization therapy for mild-to-moderate heart failure

ASL Tang, GA Wells, M Talajic et al.
N Engl. J Med 2010: 363; 2385-95

Background: Cardiac-resynchronization therapy (CRT) benefits patients with left ventricular systolic dysfunction and a wide QRS complex, Most of these patients are candidates for an implantable cardioverter-defibrillator (ICD). We evaluated whether adding CRT to an ICD and optimal medical therapy might reduce mortality and morbidity among such patients

Methods: We randomly assigned patients with New York Heart Association (NYHA) class II or III heart failure, a left ventricular ejection fraction of 3% or less, and an intrinsic QRS duration of 120 msec or more or a paced QRS duration of 200 msec or more to receive either an ICD alone or an ICU plus CU The primary outcome was death from any cause or hospitalization for heart failure.

Results: We followed 1798 patients for a mean of 40 months. The primary outcome occurred in 297 of 894 patients (33.2%) in the ICD--CRT group and 364 of 904 patients (40.3%) in 6 c ICD group (hazared ratio in the ICL-CRT group, 0.75; 95%, confidence interval [CI], 0,64 to 0.87, P<0.001), In the ICD –CRT group, 186 patients died, as compared with 236 in the ICD group (hazard ratio, 0.75; 95% CI 0.62 to 0.91, P=O.O03), and 174 patients were hospitalized for heart fai1ure, as compared with 06 in the ICD group (hazard ratio, 0.68, 95% C1, 0.56 to 0.83; P<0.001). However, at 30 days after device implantation, adverse events had occurred in, 124 patients in the ICD-CRT group, as compared with 58 in the JCD group (P<0.001)

Conclusions: Among patients with NYHA class II or III heart failure, a wide QRS complex, and left ventricular systolic dysfunction, the addition of CPT to an ICU reduced rates of death and hospitalization for heart failure. This improvement was accompanied by more adverse events. (Funded by the Canadian Institutes of Health Research and Medtronic of Canada; Clinical Trials gov number, NCT00251251)

Pentavalent rotavirus vaccine in developing countries: safety and health care resource utilization

CDC Christie, ND Duncan, KA Thame et al.
Pediatrics 2010; 126: 1499-1506

Objective: In the international, placebo-controlled. Rotavirus Efficiacy and Safety Trial, the pentavalent rotavirus vaccine reduced the rate of rotavirus attributable hospitalizations and emergency department visits by 95%. This study investigated the effect in Jamaica.

Methods: The vaccine effect an rates of hospitalization and emergency department visits in Jamaica was evaluated in both modified intention to treat and per-protocol analyses. Rates or serious adverse events, including intussception, also were compared between groups.

Results: A total of 1804 Jamaican infants, 6 to 12 weeks of age at entry and primarily from low middle-income families of African heritage, received >1 doze. During the first year after dose 1, there were 2 and 11 hospitalization or emergency department visits attributable to rotavirus gastroentertis involving any seretype among 831 evaluable vaccine recipients and 800 avaluable placebo recipients, respectively rate reduction: 82.2% (95% confidence interval: 15.1%). In the per protocal analysis, all 8 GI to G4 rotavirus attributable events that occurred >2 weeks after dose 3 were in the placebo group (rate reduction 100% (95% confidence interval. 40.9%-100%). Of the 1802 subjects

included in the safety analyses, intussusception was confirmed for 1 vaccine receipient (115 days after the third doses) and 3 placebo recipients. One vaccine recipient and 3 placebo recipients died during the follow-up period, but none of the deaths was considered to be vaccine-related.

Conclusions: In this posthoc subgroup analysis, the vaccine reduced health care resource utilization attributable to rotavirus gastroenteritis without increased risk of intussusceptions or other serious adverse events among infants in a resource- limited country.

Distinguishing between bacterial and aseptic meningitis in children: European comparison of two clinical decision rules

F Dubos, B Korczowski, DA Aygun et al
ADC 2010; 95 : 963-967

Background: Clinical decision rules (CDRs) could be helpful to safely distinguishing between bacterial and aseptic meningitis (AM).

Objective: To compare the performance of two these CDRs for children; the Bacterial Meningitis Score (BMS) and the Meningitest.

Design: Six paediatric emergency or intensive care units of tertiary care centres in five European countries.

Patients: Consecutive children aged 29 days to 18 years presenting with acute meningitis and procalcitonin (PCT) measurement.

Intervention: None

Main outcome measures: The sensitivity and specificity of the BMS (start antibiotic in case of seizure positive cerebrospinal fluid (CSF) Gram staining, blood reutrophil count >10 x 102/1, CFS protein level >80 mg/dl or CSF neutrophil count >1000x105/1) and the Meningitest (start antibiotics in case of seizure, purpura, toxic appearance, PCT level >05ng/ml, positive CFS Gram staining or CSF protein level >50 mg/dl) were compared using a McNemar test.

Results: 198 patients (mean age 4.8 years) from six countries in five European countries were included; 96 had bacterial menititis. The BMS and Meningitiest both showed 100% sensitivity (95% CI 96% to 100%). The BMS had a significantly higher specificity (62%, 95% CI 42% to 62% vs 36%, 95% CI 27% to 46%; p<10-8)

Conclusions: The Meningitest and the BMS were both 100% sensitive. The result provides level II evidence for the sensitivity of both rules, which can be used cautiously. However, use of BMS could safely avoid significantly more unnecessary antibiotic treatments for children with AM than can the Meningitest in this population.

Scoring system to identify patients at high risk of oesophageal cancer

E Rhatigan, I Tympus, G Murray et al.
British Journal of Surgery 2010; 97: 1831-1837

Background: Identification of a patient cohort at high risk of developing oesophageal cancer might enable a greater proportion of patients with curable disease stages to be identified and permit better use of investigative resources. The aim of this study was to develop a scoring system that identifies patients with dysphagia at greatest risk of having oesophageal cancer.

Methods: Data on 435 patients with dysphagia were recorded. Univariable and multivariable analyses were performed to identify parameters predictive of cancer. These were used to create the Edinburgh Dysphagia Score (EDS), which was then validated in a second cohort of patients.

Results: The EDS contained six parameters: age, sex, weight loss, duration of symptoms, localization of dysphagia and acid reflux. It stratified the development cohort into a group at higher risk, containing 39 of 40 patients with cancer, and a group at lower risk, comprising 36.0 per cent of referrals (sensitivity 97.5 per cent, negative predictive value 99-3 per cent). On validation, the EDS divided the referrals into a higher-risk group identifying all 26 cancers and a lower-risk group comprising 30.0 per cent of referrals.

Conclusion: From 574 referrals, the EDS correctly classified as higher risk all but one patient with cancer. Some 34 per cent of patients identified as lower risk could have been investigated less urgently. This simple scoring system permits sensitive prioritization of patients referred with dysphagia, and enables more efficient use of investigative resources.

Management of blunt injuries to the spleen

P Renzulli, T Gross, B Schnuriger et al
British Journal of Surgery 2010; 97: 1696-1703

Background: Non-operative management (NOM) of blunt splenic injuries is nowadays considered the standard treatment. The present study identified selection criteria for primary operative management (OM) and planned NOM.

Methods: All adult patients with blunt splenic injuries treated at Berne University Hospital, Switzerland, between 2000 and 2008 were reviewed.

Results: There were 206 patients (146 men) with a mean(s.d.) age of 38.2(19. 1) years and an Injury Severity Score of 30.9(11.6). The American Association for the Surgery of Trauma classification of the splenic injury was grade 1 in 43 patients (20.9 per cent), grade

2 in 52 (25.2 per cent), grade 3 in 60 (29.1 per cent), grade 4 in 42 (20.4 per cent) and grade 5 in nine (4-4 per cent). Forty-seven patients (22.8 per cent) required immediate surgery. Transfusion of at least 5 units of red cells (odds ratio (OR) 13-72, 95 per cent confidence interval 5.08 to 37-01), Glasgow Coma Scale score below 11 (OR 9.88, 1.77 to 55-16) and age 55 years or more (OR 3.29, 1.07 to 10-08) were associated with primary OM. The rate of primary OM decreased from 33.3 to 11 .9 per cent after the introduction of transcatheter arterial embolization in 2005. Overall, 159 patients (77.2 per cent) qualified for NOM, which was successful in 143 (89.9 per cent). The splenic salvage rate was 69.4 per cent. In multivariable analysis age at least 40 years was the only factor independently related to failure of NOM (OR 13.58, 2.76 to 66.71).

Conclusion: NOM of blunt splenic injuries has a low failure rate. Advanced age is independently associated with an increased failure rate.

The role of lymph node resection in ovarian cancer: analysis of the surveillance, epidemiology, and end results (SEER) database

R Rouzier, C Bergzoil, JL Burn et al
BJOG 2010; 117: 1451-1458

Objective: The therapeutic role of lymphadenectomy on the survival in patients with ovarian cancer is controversial. The aim of this study was to evaluate the survival impact of lymphadenectomy, depending on the disease stage and extent of the surgery.

Design: The surveillance, epidemiology, and end results (SEER) registry provided ovarian cancer data from 17 registries.

Setting: Surveillance, Epidemiology, and End Results database.

Population: The study population comprised 49 783 patients.

Methods: Survival was studied according to the number of lymph nodes removed, with stratifications on disease stage and extent of surgery.

Main outcome measure: The 5-year cause-specific survival rate.

Results: The median follow up for patients alive at the last follow-up visit was 39 months. The five-year cause specific survival rates were 37, 62, and 71 % for the groups in which no lymph nodes were examined, in which between one and nine nodes were examined, and in which ten or more nodes were examined, respectively ($P < 0.001$). Avoiding lymphadenectomy was deleterious in all stages of the disease. It was maximal for International Federation of Gynecology and Obstetrics (FIGO) stage-II patients, but there was no significant interaction between stage and extent of lymphadenectomy. The cause-specific survival was found to significantly increase when more nodes were resected, even if the surgical procedure consisted of debulking surgery or a pelvic exenteration.

Conclusion: Our study suggests a beneficial effect of lymphadenectomy in epithelial ovarian tumours, regardless of the stage of disease and extent of surgery. However, potential biases inherent to this retrospective methodology, such as staging migration, defining the extent of residual disease, and the possibility that thorough lymphadenectomy may reflect the quality of cytoreductive surgery, preclude any formal conclusions on the therapeutic role of lymphadenectomy.

Maternal vitamin D status in pregnancy and adverse pregnancy outcomes in a group at high risk for pre-eclampsia

AW Shand, N Nassar, PV Dadeiszen et al
BJOG: 2010; 117 : 1593-1598

Objective: To determine in a group of pregnant women if vitamin D status, based on serum 25-hydroxyvitamin D (250HD) concentration, was associated with a subsequent risk of pre-eclampsia or adverse pregnancy outcomes.

Design: Prospective cohort study.

Setting: Vancouver, British Columbia, Canada (49°N).

Population: Women attending a specialist antenatal clinic because of clinical or biochemical risk factors for preeclampsia (n = 221).

Methods: Serum 250H D concentration measured between 10 and 20 weeks of gestation.

Main outcome measures: Pre-eclampsia and composite adverse pregnancy outcomes.

Results: Of the women, 78% were vitamin D insufficient (250HD <75 nmoUl) and 53% were vitamin D deficient (250HD <50 nmol/I). There was no difference in the rates of pre-eclampsia, gestational hypertension, preterm birth or composite adverse pregnancy outcomes by 250HD concentration.

Conclusions: Vitamin D deficiency and insufficiency were common in a group of women at high risk of pre-eclampsia; however, it was not associated with subsequent risk of an adverse pregnancy outcome.