Clinical epidemiology

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Risk of second primary cancer in hereditary and non-hereditary retinoblastoma: Results from a population based study with more than 40 years follow-up

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Purpose: To determine the risk of second primary cancer in retinoblastoma survivors, we have identified and followed the 240 patients diagnosed with the disease in Denmark between 1943 and 1995.

Methods: Data on treatment, heredity, mortality and observed/expected numbers of second primary cancers have been extracted from the Danish Cancer Registry, primary records from the clinical departments, the Danish Population Registry, and church records. Median follow-up of the 210 retinoblastoma survivors is 25.2 years of age.

Results: At 40 years of age, the cumulative incidence (3%) and mortality (3%) of second primary cancer in the non-hereditary group is similar to the population at large. In contrast, the corresponding values for the hereditary group is significantly higher at 19% and 11%, respectively. Among the hereditary patients, the increased risk is the same for patients treated with or without radiation therapy for their primary disease. None of the patients have received chemotherapy. Except for a higher incidence (particularly of malignant melanomas), the second primary cancers are of the same type as the time- and age-specific cancers observed in the population.

Conclusions: Associated with hereditary retinoblastoma is an increased risk for second primary cancer. This is not linked to the use of radiation therapy but strictly to the genetic status of the patient.

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Cancer in twins

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Purpose: To assess the importance of the heritable and environmental components in the aetiology of the common cancer sites, a follow-up study was carried out on incident cancer cases in the Finnish Twin Cohort.

Methods: The entire cohort (13,888 twin pairs in a prospective follow-up since 1975) was linked to the Finnish Cancer Registry. The data are analyzed by calculating site-specific standardized incidence ratios based on national rates, and by concordance analysis in monozygotic (MZ) and dizygotic (DZ) twin pairs. The comparison of MZ and DZ give the magnitude of the genetic effect.

Results: A total of 2355 new cancer cases were identified (630 in MZ, 1289 in DZ twins and 436 in twins of unknown zygosity). The most common cancer types include cancers in breast (328 cases), lung (307), stomach (178), prostate (150) and colon (104). 222 pairs were concordant for having cancer. Of them, 79 were diagnosed in MZ and 97 in DZ twins. The probandwise concordance rates for breast cancer were 8% in MZ vs. 6% in DZ twins. As to other sites, the comparative figures were 15% vs. 3% for lung, 11% vs. 8% for stomach, 18% vs. 8% for prostate, and 9% vs 6% for colorectum.

Conclusions: The heritable component appears to be rather small in breast cancer. Coinciding smoking habits of MZ twins may explain lung cancer result. Detailed analyses with extended follow-up period are conducted to ascertain the findings.

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Cancer registries for quality assurance: Experience in Southeastern Netherlands

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Of the population of the EU 40% is served by population-based cancer registries. According to the Eurocare study, patterns of care and survival rates were quite different. To reduce discrepancies between evidence-based guidelines and true practice of care, registries can be involved in quality assurance, provided they collect data from clinical records. The 9 comprehensive cancer centres (CCC) in Holland are involved in the multidisciplinary process of implementing (inter)national guidelines with tumour-study groups and facilitating clinical research, observational & experimental.

Purpose: describe the contribution of Eindhoven Cancer Registry to quality assurance within CCC South that serves 2.1 million people treated in 17 general hospitals, 6 regional pathology laboratories and 2 radiotherapy institutes.

Methods: guided by multidisciplinary tumour-study groups, receiving feedback on their practice from the registry, and with clinical epidemiological support, extra data on prognostic factors e.g. co-morbidity, histology and staging process are collected for retro- and prospective studies of adherence to guidelines, recurrence and survival.

Results: multidisciplinary involvement across the board and 'good' survival rates, which has been documented for e.g. patients with lymphomas, female breast and genital cancer and rectal carcinoma. Furthermore, a high participation rate in recognised clinical trials.

Conclusion: 'bottom-up' involvement can be enhanced by a common database with clinical epidemiological studies.

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Cancer research priorities: The discrepancy between research needs and research output

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Purpose: Are research efforts in balance with the needs of research? Thereto we defined measures for (1) cancer research priority, and (2) *research output.*

Methods: (1) Cancer research priority (CaRP) is defined by a linear relationship between cancer incidence, mortality rate and fraction of non-preventable deaths, expressed as the number of inevitable US 'cancer deaths' in 1997. (2) Research effort per cancer site is assumed to be proportional to the number of articles in Medline™ 1995. The CaRP-per-Article (CaRP/A) is an indicator of research effort relative to the number of cancer deaths. The Cancer Research Adjustment Factor (CaRAF) is defined as the CaRP/A divided by the average CaRP/A The CaRAF is a magnitude of imbalance between research priority and effort.

Results: The CaRP ranged from 1,000 (larynx) to 43,000 (colorectal) cancer deaths. The CaRP/A ranged from 0.25 (childhood) to 24 (pancreas) cancer-deaths per article, suggesting an almost 100-fold discrepancy in research efforts. To meet the average research effort for all cancer sites (CaRAF = 1), research efforts would need to be intensified ≥50% for colorectal, pancreas, prostate, ovary and non-hodgkin lymphoma and could be diminished >50% for childhood, Hodgkin's disease, melanoma, larynx, oral/pharynx and cervix uteri.

Conclusion: The underrepresentation of research on important cancer problems in the literature suggests that cancer research policies need to be reassessed.

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Cancer reviews need to be systematic if they are to be reliable

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Purpose: Reviews (Rs) prepared by experts have become important. Clinicians cannot find, let alone read, all reports. It is, therefore, very important that such reviews are unbiased.

Methods and Results: An analysis of Rs published in JCO from Jan 1983 to Sept 1995 (CW & VB, ASCO Proc. 15: 929, 1996) showed that <10% of 106 Rs reported using methods designed to avoid bias (data identification and selection, validity assessment, quantitative synthesis). An analysis (CW & ML) of Rs of chemotherapy for advanced ovarian cancer confirms these data and find further weaknesses. A MEDLINE search found 68 Rs. 49 were eligible and have been obtained. Only 2 included a search strategy, 0 gave selection criteria, 1 assessed validity of the data extracted and 0 used quantitative synthesis of the data. Only 4 reported raw data from referenced papers, the rest give minimal or no data. Papers quoted were not representative (mean number refs to RCTs 5.7 [0–30], >60 RCTs published) Most first authors only appeared once, one wrote 10 reviews. Conclusions quoted in the R were not always substantiated by the original paper. Rs tried to answer many questions. Recommendations were made in most Rs, though none were substantiated.

Conclusions: Systematic Rs are needed to reduce potential bias.

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Determination of DNA damage in uranium miners

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Purpose: In this presentation we present the data obtained in former German uranium miners (Wismut AG) who were exposed during the years 1945 to 1955 to excessive doses of radon decay products. Furthermore they had an elevated continuous radiation exposure between these wild years and today due to the fact that radioactive lead was deposited in the skeletal bones. We analysed whether it is possible to demonstrate today's evidence of this chronic low level radiation exposure in leukocytes seen as effets on the DNA level.

Methods: The alkaline comet assay was used to determine the initial DNA damage as well as the DNA repair capacity of the cells as a parameter of the functional status. For this purpose blood cells were subjected to an *in vitro* irradiation of 100 cGy and DNA damage was determined directly and at different time intervals after *in vitro* irradiation. Patients: 106 former uranium miners were compared to an appropriate control group.

Results: There was no statistically significant difference of DNA damage and DNA repair capacity between the radiation exposed uranium miners and the non-exposed control population.

Conclusions: Our results indicate that the level of chronic radiation exposure during the past 50 years did not result in a significant DNA damage or in an impaired DNA repair capacity of the leukocytes and their progenitors.

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Cancer publication trends, 1966–1995

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Purpose: Description of publication trends on cancer in the medical literature.

Methods: A Medline™ subject-heading and keyword search was used to count articles on cancer and related topics from 1966 through 1995. USA Cancer Statistics were used to correlate publication numbers to cancer incidences.

Results: (1) Between 1966 and 1995, the number of publications on cancer per year tripled from 16,398 to 47,572. (2) The contribution of publications per cancer site showed little changes in 30 years, e.g. on childhood cancer from 18% to 15%, on leukaemia from 8% to 9%, on breast cancer from 5% to 9%, and on prostate cancer from 1% to 3%. (3) In 1995, the number of cancer articles per new USA cancer case was 28.6 for all neoplasms, ranging between 193.0 for prostate and 0.9 for childhood cancer. (4) The contribution of publications by treatment modality remained stable for radiotherapy and surgical oncology papers at 5% and 11%, and showed an increase for chemotherapy papers from 26% in 1966 to 37% in 1974, remaining stable thereafter. (5) For 1992–1995, most radiotherapy papers originated from the USA; Sweden, The Netherlands and Canada had most publications per number of citizens.

Conclusion: Despite a tripled cancer research output since 1966, there is a major and consistent misbalance in research topics, both with regards to tumour site and treatment modality. Therefore, research objectives have to be redefined.

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Factors encouraging or discouraging women undergo clinical breast examination

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Purpose: To evaluate the factors influencing female immigrants from the former USSR & veteran Israeli women to undergo breast clinical examination (CBE) in order to develop an efficient intervention program.

Study Population: Immigrants from the former USSR living in Israel 5 years or less & Israeli women born in Israel or living there for at least 20 years. A total of 196 women were sampled. Excluded: 4 due to breast cancer & 10 who could not be traced. Refusal to participate was 19%, mainly for fear and reluctance to discuss cancer. The final samples were 97 immigrants & 89 veteran Israelis.

Methods: Cross sectional study using a self report questionnaire based on the Health Belief Model (HBM). Data were processed in three stages. 1st: the differences between the two groups were described using *t* test or $\chi 2$. 2nd: the HBM factors were examined by Principal Component Analysis. 3rd: logistic regression on CBE with demographic variables, HBM components & group assignment in the model.

Results: Greater use of CBE was associated with older age and higher education level and less barriers involving timing and attending the service. No difference between immigrants & veteran women was found.

Conclusions: Intervention should take into consideration.fears & suspicious related to cancer, barriers of the service, age and education level of women.

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Knowledge and beliefs about cancer prevention in a Northeast Italian population

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Purpose: We made an self administered questionnaire to explore the people knowledge and beliefs about cancer prevention modalities.

Methods: We distributed this questionnaire to people coming in several units of hospitals in Italy

Results: Until now we collected 2480 questionnaires assessing 73% females and 27% males. In the sample 76% of people aged from 20 to 59 ys, up 70% had a medium-high educational level, 35% were houseworking, 21% were smokers, 45% drank wine and 51% had almost one relative affected by a neoplastic disease. The information about prevention modalities was assessed as good in 40% questionnaires but the prevention was really performed in low percentage: in the last five years 81% never performed occult blood test, 87% rectoscopy, 65% oral cavity exploration; among the 49% of the women performing breast self-examination, only 24% do it monthly. In the last five years 46% of the women never underwent mammography and 26% PAP-test. The main obstacle in performing cancer prevention examinations was showed in the indolence by 28%, in the fear by 21%, in the economic charges by 8% and in the lack of quick benefit by 5%. About 47% of the people think that the health authorities advertise the prevention little and 81% that the main part in the education for preventing cancer would be represented by health authorities (39% by school).

Conclusions: More enterprise is need by health authorities for increasing the cancer prevention.

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Physicians' attitudes toward rectal cancer: Results of a French survey

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Purpose: Our survey is focused on therapeutic attitudes face to rectal cancer, related to specialities and physicians' very factors influencing therapeutic decision.

Methods: In spring 1996, a questionnaire was sent to a sample of 720 french physicians, stratified in 4 specialities: gastroenterology, digestive surgery, radiotherapy, medical oncology. This questionnaire included 3 clinical cases of rectal cancer at different stage, a T3N0 tumor, an advanced cancer with recto-vaginal fistula and a relapsed rectal cancer.

Results: 352/622 exploitable answers were returned (57%). The decision modality was pluridisciplinary (versus not) for 52% of physicians for the 1st case, 64% for the 2nd case and 61% for the 3rd case. This decision modality was significantly different according to speciality, type of practice, public or private practice, and proximity of radiotherapy department. Two main attitudes emerged for the 1st clinical case: an exclusive radiotherapy-surgery (RT-SU) (44%) (consensual choice) and a RT-SU with optionnal or systematic chemotherapy (CT) (51%). This latter choice appeared to be closely dependent on medical speciality and background. For the second clinical case, 70% of physicians have chosen an association RT-SU-CT while 18% have chosen a RT-SU and 4% an exclusive medical treatment. For the 3rd one, 63% have recommended a RT-SU-CT, 18% a RT-SU and 13% an exclusive RT-CT.