

## 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  $\geq 50\%$  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