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Familial risks of breast, ovarian and prostate cancers and the influence of diagnostic and screening methods.

Geboren am 19.03.1976 in Ahmedabad, Indien
Diplom der Fachrichtung Genetic Epidemiologie am 10.06.2002 an der Erasmus Universität, Rotterdam, The Netherlands

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The main objective of this thesis was to study the influence of screening and diagnostic practices on the familial risk of breast, ovarian and prostate cancer. Diverse aspects of possible influence of screening were addressed: the changes in the age incidences, the risk of subsequent invasive carcinoma and the likely bias in the estimation of familial risks due to family history.

Screening is able to identify asymptomatic early stage carcinomas. Breast and prostate cancer screening modifies their incidences as more asymptomatic premalignant lesions are identified. This study found a dramatic shift in the age incidence relationship for breast cancer: the maximal age shifted from 75 years in 1976-1985 to 60-64 years in 1996-2000. The age specific incidence of prostate cancer showed similar trends: between 1961 to 1995, the highest incidence was in the age group 70+ years, from 1995 onwards the highest incidence occurred in the age group 60 to 64 years. Thus, screening has resulted in the diagnosis of cancer at younger ages. In future, breast and prostate cancers are likely to be diseases of middle aged persons in screened populations.

The present dissertation permits to conclude that the incidence of in situ carcinoma of the breast has increased in the last decade. The introduction of screening in Sweden and new treatments seem to have modified the pattern of risk of invasive breast cancer after in situ carcinoma. The

risk of invasive cancer in the ipsilateral breast has increased. Women affected by LCIS are at higher risk of invasive breast cancer than women with DCIS. The risks estimated in this study may help in the clinical counselling.

Risks for ovarian cancer were high for women with a maternal history of breast, endometrial, ovarian and laryngeal cancers and for daughters with a sister history of liver, breast, endometrial, ovarian and thyroid cancers. The proportion of the familial clustering which can be ascribed to environmental and genetic components – known genes or described syndromes – should be analyzed in future studies. Epithelial ovarian cancer was related with ovarian, endometrial and skin cancer and with melanoma and myeloma; papillary serous cystadenocarcinoma was associated with ovarian and skin cancers and with myeloma. Endometrioid carcinoma was related with endometrial, ovarian and prostate cancers and with melanoma. Endometrioid carcinoma was associated with prostate cancer and serous carcinoma was associated with Hodgkin's disease. The familial association of histology specific ovarian cancers with specific cancer sites and the variation in the strength of the associations may guide future search for etiological differences between histologies. Higher familial risk of ovarian cancer in the offspring can also be attributed to the opportunistic screening because of a known familial history of a breast or ovarian cancer or associated cancer sites.

Some risk excess in brother of men affected with prostate cancer is probably due to overdiagnosis of prostate cancer. The magnitude of this bias will add a future uncertainty to clinical genetic counseling. This will be an increased problem in all population for whom modern screening techniques are offered.