

Marianne Weires

Dr. sc. hum.

**Estimating environmental effects in cancer development and mortality:  
methods and applications**

Geboren am 18.01.1981 in Tarnobrzeg (Polen)

Diplom der Fachrichtung Medizinische Informatik am 25.07.2007 an der Universität  
Heidelberg

Promotionsfach: DKFZ (Deutsches Krebsforschungszentrum)

Doktorvater: Prof. Dr. med. Dr. Kari Hemminki

The overall aim of this thesis was to identify and quantify the effect of shared environmental factors on cancer risks and cause-specific mortality risks based on the Swedish Family-Cancer Database.

The study on socio-economic status and mortality showed that in Sweden, a country with in principal universal access to health care, socio-economic status is significantly associated with overall and cause-specific mortality risk and social inequalities exist. Using the Swedish Family-Cancer Database, I was able to investigate more specific causes of death than have been typically reported. The results might reflect different behavioral and lifestyle aspects and different expo-sure to occupational and environmental factors among socio-economic groups with elevated overall and cause-specific mortality. Comparison of overall and cause-specific mortality among female and male socio-economic groups may provide helpful insights into the underlying causes of socio-economic inequalities in mortality. In addition, further research is needed to confirm my results and to identify specific factors related to increased mortality in specific socio-economic groups. These factors will help to prevent higher mortality among more deprived socio-economic groups in Sweden.

Although decades of cohabitation of spouses result in a common lifestyle and health behavior, my findings showed only small increased risks for cancer among spouses. I analyzed systematically the risk for all concordant and discordant cancers and, in addition, I created an etiological map of cancer aggregation among spouses. The results suggest that only strong environmental risk factors such as smoking modify cancer risk in adulthood. In general, the lifestyle shared by spouses seems to play a minor role in cancer development. The proposed etiological map based on a comprehensive summary of 24 cancer types identifies some

clusters - for example, non-Hodgkin lymphoma and leukemia, bone cancer and myeloma – that are likely related to exposure to yet unidentified environmental risk factors during adulthood.

It is reasonable to assume that husbands and wives, who share environmental factors in their adulthood, may have also related times of cancer diagnosis. The most important contribution of this thesis consisted in the extension of previous analysis to age-of-onset traits in order to quantify to which extent shared environment accounts for possible dependencies between husbands' and wives' time until diagnosis of cancer. This included the analysis of correlated time-to-event data with frailty models. I used lung cancer data to illustrate the usefulness and practical application of frailty models. The correlation of spousal susceptibility to lung cancer was around 9%, which means that approximately 9% of the variance in time until lung cancer is explained by shared marital environmental factors. Although the theory of frailty models is relatively well developed, standard software packages are still lacking. Therefore, I investigated and compared available packages for frailty models to create an overview. I also demonstrated and discussed how frailty models can be used to estimate heritabilities of age-of-onset traits based on family data from the Swedish Family-Cancer Database.