Friday 31th October at 10:00-11:00 in room 4.39:
Postdoc Søren Møller from the Biostatistics Unit at EBB will give a lecture on:

"Methods for studying heritability of cancer diagnosis using twins"

Abstract:

Brief Introduction: Different kinds of cancer are known to be quite heritable, although the extent to which variation in risk by age is explained by genetic factors remains uncertain. We address this question with respect to breast cancer by analyzing data on a large cohort of Nordic twins.

Materials and Methods: We study 21,055 monozygotic and 30,939 dizygotic same sex female twin pairs from the Nordic Twin Study of Cancer cohort the largest in the world, consisting of data from the Danish, Finish, Norwegian and Swedish Twin registries. We incorporate time-to-event analyses to estimate the concordance risk and heritability accounting for right-censoring due to individuals still alive or lost to follow-up and competing risks of death, essential sources of biases that have not been accounted for before. Hereby we extend the approach used by Lichtenstein et al. (NEJM, 2000).

We estimate the cumulative incidence using the non-parametric Aalen-Johansen estimator and taking account for left-censoring due to variable initiation of cancer registration. We determine the case wise concordance in MZ and DZ twins and its dependency on the age at diagnosis, weighting the sample by use of the additive Aalen model and the Kaplan-Meier method to handle censoring.

Moreover, we estimate the cumulative heritability using a time-varying biometric ACE-model both on the liability and on the risk scale.

Clinical Cases or Summary Results: We find a lifetime incidence of breast cancer of 8.8% taking account of the censoring, compared to 3.6% in the simpler model ignoring censoring. The case wise concordance with censoring is estimated to be 0.24 in monozygotic and 0.18 in dizygotic twins, compared to 0.19 in monozygotic and 0.11 in dizygotic twins if we ignore censoring. We find heritability explaining 24% of the variation while common environment explains 18%, both significantly higher than zero and different from the heritability of 38% and common environment of 7% one would get from the model ignoring censoring. We observe that the heritability is relatively stable over age while the common environment component slightly decreases. Moreover, we observe slightly higher heritability and lower common environment effects for pre-menopausal breast cancer compared to post-menopausal breast cancer.

Conclusions: We find significant heritability and common environment effects in the liability for breast cancer in Nordic Twins. Furthermore, we demonstrate that ignoring the censoring and competing risk, gives heavily biased and misleading results, substantiating the need for taking these factors into account.