Wiener Biometrische Sektion
der Internationalen Biometrischen Gesellschaft
Region Österreich – Schweiz
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Einladung zum

BIOMETRISCHEN KOLLOQUIUM

am **Montag, 27. April 2015** um **16:00 Uhr** (s.t.)

Im Schulungsraum 512 des
Zentrums für Medizinische Statistik, Informatik und Intelligente Systeme (CeMSIIS)
der Medizinischen Universität Wien, Spitalgasse 23, 1090 Wien
(Plan siehe http://www.muw.ac.at/cemsiis/allgemeines/anschrift/)

Vortragender:

SØREN MÖLLER

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University of Southern Denmark, Odense

METHODS FOR CALCULATING HERITABILITY OF DISEASES ESTIMATED FROM LARGE TWIN STUDIES

Wir freuen uns auf zahlreichen Besuch.

Franz König
Präsident

Stephan Lehr
Sekretär

METHODS FOR CALCULATING HERITABILITY OF DISEASES ESTIMATED FROM LARGE TWIN STUDIES

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Abstract:

Aim

We model bivariate disease-free survival in twin pairs, and determine the association in twin pairs for the risk of getting certain diseases. This enables us to calculate different measures of heritability, taking account for censoring and competing risk of death.

Methods

The risk of an event in a twin given the occurrence of the event in the co-twin, the casewise concordance, is the measure reported in a large number of twin studies of dichotomous traits. We review the classical concordance model and extend it to the cases in which multiple discrete outcomes and events over time are present.
The casewise concordance is suitable for studying how within pair dependence might change over time and we present a novel method that allows for estimating the risk of an event in a twin up to a certain time given that the co-twin experienced the event before that time. This enables us to estimate heritability of a disease on the risk scale.
On the other hand we can estimate heritability on the liability scale, by applying liability threshold models to determine a variance partition which models the twin structure by biometric ADCE-models, which describe additive (A) and dominant (D) genetic components as well as shared (C) and individual (E) environment components. Doing this we use improved methodology to take account for censoring and competing risk, which enables us to avoid biases inherent in earlier studies of these settings.

Applications

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 casewise

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.

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. Moreover, we present similar results for other traits.