**St. Pölten, 2015 OeGEpi Session**

Vortrag 1

**The use of routinely collected health examination data for medical research: The VHM&PP**

**Hans Concin, Gabriele Nagel, Hanno Ulmer**

In 1976, the general practitioner Leopold Bischof wrote an article in Methods of Information in Medicine entitled "Die Datenverarbeitung für die Gesundheitsvorsorge in Vorarlberg". In this work, Bischof laid the visionary foundation of a system of population-based, data-driven health examinations in Vorarlberg, the westernmost province of Austria. The Agency for Preventive- and Social Medicine began to routinely document health examinations, from 1985 onwards with an IT system that functions to this day. In the beginning, contrarily to Bischof's intent, the data-recording was mainly used for accounting purposes. It was only in 2003, that the data started to be applied for medical research under the name of "Vorarlberg Health Monitoring & Promotion Programme" (VHM&PP).

During the last decade, the research output from analyses of the VHM&PP database was considerable. Original publications on how risk factors track over time, on the way patterns of heart diseases vary by season, and on gender differences and secular trends in chronic disease have all made important contributions to medical literature. The research has provided a novel understanding of how gamma-glutamyltransferase and uric acid are associated with both cardiovascular and cancer outcomes. Recently VHM&PP contributed to several international pooled analyses which enhanced the understanding on how metabolic factors are involved in the risk of chronic diseases.

Vortrag 2

**Motivating regression analysis: confounding, moderation and mediation**

**Hanno Ulmer**

The primary biostatistical tools in epidemiologic and clinical research are single-outcome, multiple predictor methods, shortly called regression analyses. The most common forms are (1) multiple linear regression for continuous outcomes, (2) logistic regression for binary outcomes, and the (3) Cox proportional hazards regression models for time-to-event outcomes. The presence of confounding, moderation (effect modification), and mediation motivates the application of regression analysis.

In this paper, these three important concepts - confounding, moderation and mediation - will be illustrated with the use of direct acyclic graphs and examples from the VHM&PP. The examples are drawn from the context of cardiovascular epidemiology but generalize to other areas of application.

An Hand von Beispielen CVD Risikofaktoren würde ich schrittweise erklären

Uni vs multivariate Analyse

Regressionsanalyse wieso

Welche: lineare Regression, logistische Regression, Cox PH

DAG Graphen

Interpretation, siehe oben

Vermeidung von Regressionsanalysen Randomisierung Matching

Propensity Score Matching

Vortrag 3

**Metabolic mediators of body mass index: Are published results reliable?**

**Josef Fritz, Hanno Ulmer**

In clinical research and epidemiology, there is increasing interest to quantify effects of a given treatment or risk exposure into different causal pathways via the so called mediation analysis. Traditionally, an approach introduced in 1986 by Baron and Kenny was used to decompose the total effect of a given treatment or exposure into a direct and an indirect effect through one or more mediators. Recently, Lange et al. have presented a new framework for mediation analysis based on marginal structural models that is also applicable in the case of survival data. It has been shown that the Baron and Kenny method works well in the special case of linear models without interactions, but is mathematically inconsistent otherwise.

We applied both approaches, Baron and Kenny versus Lange et al., in the field of cardiovascular epidemiology to investigate the relationship between body mass index and coronary heart disease, mediated by metabolic risk factors. We found substantial different results between the two statistical methods, leading to serious concerns regarding recently published results. It appears that the effect of body mass index is mediated to a larger extent by risk factors such as systolic blood pressure, total cholesterol, fasting glucose, and smoking than previously assumed.

Vortrag 4

**Metabolic mediators of sex/gender: Do risk factors explain the gender gap in coronary heart disease?**

**Josef Fritz, Michael Edlinger, Gabriele Nagel, Hans Concin, Margarethe Hochleitner, Hanno Ulmer**

There is overwhelming evidence of a strong sex/gender gap in coronary heart disease (CHD). However, little is known regarding the contribution of cardiovascular risk factors to this sex/gender effect. With the use of a recently developed mediation technique for survival analysis we aimed to assess the specific contribution of risk factors to the difference between males and females regarding CHD outcomes. The sex/gender-specific CHD mortality was examined in the Vorarlberg cohort consisting of more than 170,000 individuals with 3,892 deaths due to CHD during a median follow-up of 14.6 years. The total effect of sex/gender on the risk was decomposed into direct and indirect effects mediated by the four major cardiovascular risk factors systolic blood pressure, total cholesterol (TC), fasting blood glucose, and smoking status. The extent to which these risk factors contribute to the difference between males and females regarding CHD mortality decreases strongly with age. Over the ages of 50 years, the persisting survival advantage of females can be explained in an unexpectedly small part through the pathway of known modifiable risk factors.

Vortrag 5

**The Metabolic Syndrome and Cancer Project (Me-Can): the rationale and ambitions**

Michael Edlinger, Tanja Stocks, Tone Bjørge, Gabriele Nagel, Jonas Manjer, Hans Concin, Pär Stattin, Hanno Ulmer

The metabolic syndrome includes several metabolic risk factors, which have, separately and jointly, been associated with an increased risk of cardiovascular diseases. About the association with cancer risk little is known to date. Therefore, in 2006 the Metabolic syndrome and Cancer project (Me-Can) was initiated to create a large pooled cohort of existing cohorts in Norway, Austria, and Sweden, that is: the Oslo study I (Oslo), the Norwegian Counties Study (NCS), the Cohort of Norway (CONOR), the Age 40-programme (40-year cohort), the Vorarlberg Health Monitoring and Prevention Programme (VHM&PP), the Västerbotten Intervention Project (VIP), and the Malmö Preventive Project (MPP).

Measurements of height, weight and systolic and diastolic blood pressure were available, as well as levels of glucose, total cholesterol and triglycerides. Besides, additional data concerned age, sex, smoking and fasting status, relevant dates, diagnoses and follow-up status including death.

Various statistical methods were to be applied to get the most out of the data and to assure valid results. Among others, in the Cox proportional hazard regression analyses reverse causation and regression dilution bias were dealt with. Also, the exposure variables were studied in quintiles and as standardised variables to ascertain the combined effect of metabolic factors.

The strength of this pooled approach is particularly the large amount of subjects in population-based surveys and a nearly complete coverage of data. Also, there was information on repeated measurements and a high-quality follow-up. As for the weaknesses, unfortunately data on several potential confounders, tumour characteristics, and treatment are lacking.

Vortrag 6

**The Metabolic Syndrome and Cancer Project (Me-Can): results on incident risks of main cancer types**

Michael Edlinger, Tanja Stocks, Tone Bjørge, Jonas Manjer, Gabriele Nagel, Hans Concin, Pär Stattin, Hanno Ulmer

Background:

Little has been reported about the joint influence of metabolic factors on the risk of various types of cancer. The aim of this study was to evaluate the association between metabolic syndrome and the most common types of cancer.

Methods:

Data on body mass index, blood pressure and plasma levels of glucose, total cholesterol and triglycerides from seven European cohorts were analysed. Altogether the project contained 564,596 men and women with a mean age of 44 years available for analyses. The metabolic factors were weighted equally into a standardised metabolic risk score (MRS) with a mean of 0 and a standard deviation (SD) of 1. Cancer risks (HRs) were estimated by Cox regression with age as the timescale and relevant adjustments, including smoking status.

Results:

During a mean follow-up of 12 years, 21,593 men and 14,348 women were diagnosed with cancer. MRS was linearly and positively associated with incident cancer in total and at sites (p < 0.05). In men, risk per SD of MRS was increased by 43% (95% confidence interval (CI) 27 to 61) for renal cell cancer, 43% (CI 16 to 76) for liver cancer, 29% (CI 20 to 38) for colon cancer, 27% (CI 5 to 54) for oesophageal cancer, 20% (CI 9 to 31) for rectal cancer, 19% (CI 4 to 37) for leukaemia, 15% (CI 1 to 30) for oral cancer, and 10% (CI 2 to 19) for bladder cancer. In women, risk increases per SD of MRS were 56% (CI 42 to 70) for endometrial cancer, 53% (CI 29 to 81) for pancreatic cancer, 40% (CI 16 to 67) for renal cell cancer, 27% (CI 9 to 47) for cervical cancer and 17% (CI 3 to 32) for rectal cancer.

Conclusion:

This largest study to date, regarding the influence of combined metabolic factors on risk of separate cancers, showed increased risks for several cancers, including some relatively common types with rather large risks, in particular renal cell and endometrial cancer.