November 7, 2008

Colorado-Wyoming Chapter

Previous Up

Fall Meeting - November 7, 2008 - Anschutz Medical Center

The chapter fall meeting will be held on Friday November 7th on the Anschutz Medical Campus in the Education 2 North building, Room P28-1303. This is a wonderful opportunity to visit this amazing campus which has been created in the last decade. The selection of talks is biased towards topics in medical research. But everyone is encouraged to attend. Refreshments will be provided.

Directions are found below. More specific instructions will be forthcoming.
http://www.uchsc.edu/anschutzmedicalcampus/maps/

Tentative Fall meeting for the CO/WY Chapter of the ASA
Date: November 7, 2008
Location: Ed2 North, P28-1303, AMC Campus
Time: 1:00 to 3:30
Speakers:
Lorri Ogden A discussion of methods for statistical validation of intermediate endpoints
Miranda Grote Simplification of the Freedman method for statistical validation of intermediate endpoints
Matt Pocernich The History and Challenges of Statistics in the Field of Weather Modification
Brandie Wagner The Use of Averaged Expression Values for Gene Selection in Microarray Analysis
Xian Lu Use of Marginal Structural Models to Estimate the Causal Effect of Environmental Tobacco Smoke Exposure on Asthma Rescue Medication Use in Asthmatic Children
Loren Cobb Statistical Catastrophe Theory

Abstracts:
TITLE: A discussion of methods for statistical validation of intermediate endpoints
SPEAKER: **Lorri Ogden**
AUTHORS: Lorri Ogden, Miranda Grote
AFFILIATION: Colorado School of Public Health, University of Colorado Denver
A variety of methods have been proposed for testing and quantifying intermediate variable effects with a binary outcome measure. The statistical validation approach suggested by Freedman, et. al. (Stat. Med., 1992) compares coefficients from two models: Model 1 which estimates the effect of treatment on the outcome unadjusted for the intermediate variable, and Model 2 which estimates the effect of treatment on the outcome adjusted for the intermediate variable. The criticisms of this method for assessing intermediate endpoints are discussed and alternative strategies based on standardizing the coefficients from Model 1 and Model 2 (MacKinnon & Dwyer, Evaluation Review, 1993) or re-defining the total effect (Li, Meredith, & Hoseyni, Stat. Med., 2001) are described. We recommend a simpler method for testing the intermediate endpoint effect, along with an alternative method for calculating the total effect.

TITLE: Simplification of the Freedman method for statistical validation of intermediate endpoints
SPEAKER: **Miranda Grote**
AUTHORS: Miranda Grote, Lorri Ogden
AFFILIATION: Colorado School of Public Health, University of Colorado Denver
The use of an intermediate endpoint is commonly used in clinical research to assess treatment effects on an outcome through the intermediate variable. These endpoints, also called surrogate endpoints, are often used to evaluate the primary outcome of a study at the earliest time possible. One common method to validate the use of an intermediate

endpoint with a binary outcome is proposed by Freedman, et. al. (Stat. Med., 1992). His statistical validation approach compares beta coefficients for the treatment effect from two models: Model 1 is the effect of treatment on the outcome unadjusted for the intermediate variable, and Model 2 is the effect of treatment on the outcome adjusted for the intermediate variable. To estimate the covariance between model 1 and model 2 beta coefficients, Freedman provides a formula based on a first-order Taylor expansion, which has also been reported by Buyse and Molenberghs (Biometrics, 1998) using matrix notation. We provide a simplification of this formula and discuss its similarity to a method proposed by Greenland and Mickey (Appl. Statist., 1988) for testing strict collapsibility in contingency tables.

TITLE: The History and Challenges of Statistics in the Field of Weather Modification
SPEAKER: **Matt Pocernich**
AFFILIATION: National Center for Atmospheric Research
In the 1970's, John Tukey, Jerzy Neyman, William Kruskal and many other prominent statisticians were actively involved in the statistics supporting the field of weather modification. Debates on methods used by different projects were often contentious. This talk provides a brief overview the challenges that faced researchers of that period and why many of the same questions still remain unresolved nearly three decades later. Possibly surpising to some, weather modification projects still are an active area of research. This talk will also describe several active projects.

TITLE: The Use of Averaged Expression Values for Gene Selection in Microarray Analysis
SPEAKER: Brandie Wagner
AFFILIATION: Colorado School of Public Health, University of Colorado Denver
The commonly used microarray gene selection methods based on permutation theory are restricted to simple comparisons between groups and test genes individually, ignoring the opportunity to utilize the correlation that exists between some genes. The proposed method was aimed towards addressing this limitation by applying common testing and selection methods to the average expression of genes clustered together, rather than at the individual gene level. This approach lessens the multiplicity issue as well as reduces noise in the expression values. Genes were assigned to clusters based on their correlations or the observed similar expression patterns across subjects. These methods were applied to a microarray dataset investigating the association of gene expression with schizophrenia after accounting for smoking status, pH and age, which in previous studies have been determined to be potential confounders. The results from this method and from testing each gene separately are compared using information obtained from independent, previously published genetic association studies. This investigation suggested an improvement over testing genes individually.

TITLE: Use of Marginal Structural Models to Estimate the Causal Effect of Environmental Tobacco Smoke Exposure on Asthma Rescue Medication Use in Asthmatic Children
SPEAKER: **Xian Lu**
AFFILIATION: Nurse-Family Partnership (Denver, CO)
Marginal structural models (MSMs) are widely used to obtain causal effect estimates in observational studies with non-randomized exposure or treatment. Inverse probability of treatment weight (IPTW) estimation of an MSM was applied to observational data from an EPA funded study at National Jewish Medical and Research Center (2002-2003) involving children at the Kunsberg School. Effects of Environmental Tobacco Smoke (ETS) exposure on asthma rescue medication (albuterol) use for children were evaluated, and the results were compared with those obtained through traditional regression methods. We obtained an estimated causal albuterol use odds ratio of 3.1 (95% CI based on empirical standard errors: 0.94, 10.4, $p = 0.0636$) for ETS exposure versus non-exposure, whereas the traditional analysis yielded an odds ratio of 1.97 (95% CI: 0.81, 4.6, $p = 0.1240$). On the assumption that our models were correctly specified, these IPTW estimates will be consistent for the true marginal causal odds ratio as if data have been obtained from a randomized controlled trial, in which confounding effects are eliminated.

TITLE: Statistical Catastrophe Theory
SPEAKER: **Loren Cobb**
AFFILIATION: Visiting Professor, UCD
The so-called "catastrophe" models of differential topology exhibit a variety of useful but highly nonlinear behaviors: bifurcations, sudden transitions, hysteresis effects, etc. But the malleability of these topological models also makes them highly problematic for statistical analysis, because most statistical models are at best invariant only up to a linear transformation. However, recent research may have uncovered a way to introduce a lot more malleability into

statistical versions of these models. In this presentation I will show how to create stochastic differential equations for catastrophe models, and how to derive their corresponding equilibrium probability density functions. The results are multimodal exponential families which generalize many of the probability density functions of classical statistics. This extension of classical statistics opens up large domains of statistical models with multiple stable states and rich nonlinear dynamics. Finally, I will show how the recent work of Hartelman & Wagenmakers may make possible a form of statistical analysis that is invariant under smooth deformations of the underlying space. The implications for time series analysis are potentially large, if we can fully integrate these topological ideas into current statistical theory. There is plenty of material here for several enterprising and talented PhD students.