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Development, Validation, and Application of Risk Prediction Models - Course Syllabus 2011-2012

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M19-527 Development, Validation, and Application of Risk Prediction Models

Spring 1 and 2 (1/23-4/30/12) G. Colditz, E. Liu & others 2.0 credits

This course will present detailed discussion of the methods of predictive modeling, with applications to clinical and population health settings. When does adding another variable to prediction improve classification? At what trade-off to implementation in real world settings? The philosophy of the course is that learning should move away from the dictionary definition, "to receive instruction, to be informed, to commit to memory" to one that works for how computers learn, where committing to memory is a trivial task: things (students in a course like this?) learn when they change their behavior in a way that makes them perform better in the future. A performance based definition. We explore how prediction models fit into this concept of learning focusing on their development and implementation to improving health outcomes.

Building from traditional risk factor identification to model refinement and validation of prediction, a number of statistical approaches will be reviewed. Each method is motivated by clinical examples. Basic concepts and philosophy of supervised and unsupervised data mining as well as appropriate applications will be discussed. Topics covered will include model development and validation; regression approaches, model selection, inference, averaging; classification and regression trees (CART), multivariate adaptive splines (MARS), neural networks, random forests, and bagging and boosting. Approaches to validation will be discussed and strategies for estimation of added value with expanded variable lists will be a key focus of this applied quantitative methods course.

Course note: Biostatistics I and II (M21-560 and M21-570) are required prerequisites. Meets Mondays 2 p.m. to 4 p.m.

Text: (available on reserve at the library)

Data mining Practical Machine Learning Tools and Techniques. Witten IH, Frank E, Hall MA. MorganKaufman, Burlington Mass, 2011. (from Waikato University, New Zealand; has Weka web based software).

A more statistical theory based text for reference is

The Elements of statistical learning. Data mining, inference, and prediction. Hastie T, Tibshirani R, Friedman J. Springer, 2011.

Course Activities:

Lectures, discuss assigned papers, critique manuscripts, and computer labs.

Evaluation:

Students will outline a formal strategy to develop, validate and evaluate performance of a clinically relevant model, including strategies to evaluate the benefit of adding new markers to a model and the clinical and public health utility of an extended model for risk prediction and classification.

Competencies:

Develop the knowledge and skills to design, implement, and evaluate epidemiologyrelated, health services or clinical research projects of clinical or public health significance including:

- Develop the knowledge and skills with biostatistical methods and computer software for performing appropriate analyses of public health services or clinical outcomes data.
- Develop the knowledge and skills with the definitions in basic issues involved in the clinical prediction rules including, design, development, validation, implementation, and interpretation of results for their application in clinical or public health settings.
- Apply the principles of dissemination and implementation science to the evaluation of evidence for use of risk prediction models in clinical and public health programs. Design and implement strategies with appropriate integration of evaluation to inform the refinement of clinical and public health programs that will lead to improved health and wellness of the population.
- To achieve this competency, students will: Understand the development, implementation, evaluation and refinement of guidelines as they relate to risk prediction models.
- Apply principles of study design and evaluation to T2 research and implementation projects.

Topics from list above

Clinical risk prediction: 1. Overview of clinical and public health risk prediction

Wald N. When can a risk factor be used as a worthwhile screening test? BMJ 1999; 319:1562-5

Lloyd-Jones et al., Narrative review: Assessment of C-reactive protein in risk prediction for cardiovascular disease. Ann intern Med 2006; 145:35-42

Kim HC, et al. Multimarker prediction of coronary heart disease risk. The Women's Health Initiative. J Am Coll Cardiol 2010; 55: 2080-91

Wang TJ, et al. Multiple biomarkers for prediction of first major cardiovascular events and death. NEJM 2006; 355:2631-9

Pencina, D'Agostino et al...Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Statistics in Medicine 2008; 30;27(2):157-72 and discussion 207-12

Steyerberg et al Assessing the performance of prediction models, A framework for traditional and novel measures. Epidemiology 2010; 21:128-138

Steyerberg et al Assessing the incremental value of diagnostic and prognostic markers: a review and illustration. Eur J Clin Invest 2011

Rosner B, Colditz GA, Iglehart JD, Hankinson SE. Risk prediction models with incomplete data with application to prediction of estrogen receptor-positive breast cancer: prospective data from the Nurses' Health Study. Breast Cancer Res. 2008; 10(4):R55.

2. Stats approaches and issues... Logistic regression

Olsen MA, et al Developing a risk stratification model for surgical site infection after abdominal hysterectomy. Infect Control Hosp Epidemiol 2009; 30:1077-83

Huang, ... Olsen et al. Use of Medicare claims to rank hospitals by surgical site infection risk following coronary artery bypass graft surgery. Infect control Hosp Epidemiol 2011:32:775-83

3. Stats approaches and issues... ROC analysis

OBGYN example Esplin and Macones commentary

Cook NR: Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation* 2007, **115**:928-935.

4. Stats approaches and issues... Sample size

e.g. Rosner and Glynn Power and sample size estimation for the Wilcoxon rank sum test with application to comparisons of C statistics from alternative prediction models. *Biometrics.* 2009 Mar; 65(1): 188-97.

(Rosner and other examples)

5. Stats approaches and issues...

Data mining techniques in propensity score estimation (Schneeweiss examples)

Setoguchi, Schneeweiss, et al. Evaluating uses of data mining techniques in propsensity score estimation: a simulation study. Pharmacoepdemiol Drug Saf 2008; 17:546-55.

Schneeweiss et al. High-dimensional propensity score adjustment in studies of treatment effects using health care claims data. Epidemiol 2009; 20:512-22

6. Stats approaches and issues... Instrumental variables

Rassen et al. Instrumental variables I: instrumental variables exploit natural variation in nonexperimental data to estimate causal relationships. J Clin Epi 2009; 62:1226-32

Rassen et al. Instrumental Variables II: Instrumental variable application in 25 variations, the physician prescribing preference generally was strong and reduced covariate imbalance J Clin Epidemiol 2009;62:1233-41

7. Applications Development and validation in urology practice

Kattan M et al – prostate develop and validate...

Nam et al Prospective multi-institutional study evaluating the performance of prostate cancer risk calculators J Clin Oncol 2011; 29:2959-64

8. Applications CVD

Nancy Cook references

Incremental role of novel and emerging risk factors Curr Cardiovasc Risk Rep 2010; 4:112-119

Performance of reclassification statistics in comparing risk prediction models. Biom J 2011; 53:237-58

Cardiovascular risk prediction in diabetic men and women using HbA1c vs diabetes as a high-risk equivalent. Arch intern med 2011:

9. Applications Pharmaco-epidemiology

Schneeweiss references

10. Applications breast cancer models and comparisons

Colditz GA, Atwood KA, Emmons K, Monson RR, Willett WC, Trichopoulos D, Hunter DJ. Colon cancer prevention. Volume 4: Harvard Cancer Risk Index Working Group, Harvard Center for Cancer Prevention. Cancer Causes Control 2000; 11:477-488.

Kim DJ, Rockhill B, Colditz GA. Validation of the Harvard Cancer Risk Index: A prediction tool for individual cancer risk. J Clin Epi 2004;57(4):332-40.

Rosner B, Colditz GA. Nurses' Health Study: Log-incidence mathematical model of breast cancer incidence. J Natl Cancer Inst 1996;88:359-364.

Colditz GA, Rosner BA. Cumulative risk of breast cancer to age 70 years according to risk factor status: Data from the Nurses' Health Study. Am J Epidemiol 2000; 152(10): 950-64.

Colditz GA, Rosner BA, Chen WY, Holmes MD, Hankinson SE. Risk factors for breast cancer according to estrogen and progesterone receptor status. J Natl Cancer Inst 2004; 96(3):218-28.

Rosner B, Colditz GA, Iglehart JD, Hankinson SE. Risk prediction models with incomplete data with application to prediction of estrogen receptor-positive breast cancer: prospective data from the Nurses' Health Study. Breast Cancer Res. 2008; 10(4):R55.

Tamimi RM, Rosner B, Colditz GA. Evaluation of a Breast Cancer Risk Prediction Model Expanded to Include Category of Prior Benign Breast Disease Lesions. Cancer 2010; 116(21): 4944-53.

11. Applications Stepwise regression:

Odibo et al Prediction of intrauterine fetal death (IUFD) associated with small for gestational age: impact of including ultrasound biometry in the customized models. *Ultrasound Obstet Gynecol.* 2011 Apr 28. doi: 10.1002/uog.9036

12. Applications Multivariate pattern analysis (MVPS) using machine learning algorithms (Schlaggar lab)

Doesenbach et al Prediction of individual brain maturity using fMRI. Science 2010; 329:1358-61

13. Applications.. RPART

Thiel SW, et al (Shannon) Early Prediction of Septic Shock in Hospitalized Patients. Journal of Hospital Medicine 2010; 5:19–25.

14. Applications with other methods

From development to implementation and improved outcomes

Dubberke E, et al. Development and validation of a Clostridium difficile infection risk prediction model. Infection control hospital epidemiol 2011; 32: 360-6

Additional examples ...

Examples drawn from, Random forests, MCMC modeling, Bayesian approaches, MARS, Bagging and boosting