Causal Inference in Statistics and the Quantitative Sciences  
May 3-8, 2009

MEALS

*Breakfast (Buffet): 7:00–9:30 am, Sally Borden Building, Monday–Friday  
*Lunch (Buffet): 11:30 am–1:30 pm, Sally Borden Building, Monday–Friday  
*Dinner (Buffet): 5:30–7:30 pm, Sally Borden Building, Sunday–Thursday  

Coffee Breaks: As per daily schedule, 2nd floor lounge, Corbett Hall

*Please remember to scan your meal card at the host/hostess station in the dining room for each meal.

MEETING ROOMS

All lectures will be held in Max Bell 159 (Max Bell Building accessible by walkway on 2nd floor of Corbett Hall). LCD projector, overhead projectors and blackboards are available for presentations. Please note that the meeting space designated for BIRS is the lower level of Max Bell, Rooms 155–159. Please respect that all other space has been contracted to other Banff Centre guests, including any Food and Beverage in those areas.

SCHEDULE

Sunday, May 3
16:00  Check-in begins (Front Desk, Professional Development Centre: open 24 hours)
17:30–19:30  Buffet Dinner, Sally Borden Building
20:00  Poster session and social gathering on 2nd floor lounge, Corbett Hall


Beverages and snacks available on a cash honour-system.

Monday, May 4
7:00–8:45  Breakfast
8:45–9:00  Introduction and Welcome by BIRS Station Manager, Max Bell 159
9:00–9:10  Welcome to workshop by David Stephens and Erica Moodie
9:10–10:00  Seminar: Judea Pearl
10:10–10:30  Coffee Break, 2nd floor lounge, Corbett Hall
10:30–11:45  Seminar, continued: Judea Pearl
11:45–13:00  Lunch
13:00–14:00  Guided tour of The Banff Centre; meet in the 2nd floor lounge, Corbett Hall
14:00–14:20  Group photo; meet on the front steps of Corbett Hall
14:20–16:15  Seminars: Mark van der Laan, Sara Geneletti, Eric Neufeld
17:30–19:30  Dinner
<table>
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<tr>
<th>Time</th>
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<tr>
<td>Tuesday, May 5</td>
<td>Breakfast</td>
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<tr>
<td>7:00–8:45</td>
<td>Seminars: Dylan Small, Tyler VanderWeele</td>
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<td>8:45–10:00</td>
<td>Coffee, 2nd floor lounge, Corbett Hall</td>
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<td>10:00–10:30</td>
<td>Seminars: Douglas Schaubel, Robin Henderson</td>
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<td>11:45–13:15</td>
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<td>13:15–14:30</td>
<td>Seminars: Siamak Noorbaloochi, Sander Greenland</td>
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<td>17:30–19:30</td>
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<td>Wednesday, May 6</td>
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<td>7:00–8:45</td>
<td>Seminars: Erin Strumpf, Thomas Richardson</td>
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<td>8:45–10:00</td>
<td>Coffee Break, 2nd floor lounge, Corbett Hall</td>
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<td>10:00–10:30</td>
<td>Seminars: Els Goetghebeur, Keisuke Hirano</td>
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<td>12:15–13:15</td>
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<td>Thursday, May 7</td>
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<td>7:00–8:45</td>
<td>Seminars: Andrea Rotnitzky (presented by Jamie Robins), Elja Arjas</td>
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<td>8:45–10:00</td>
<td>Coffee Break, 2nd floor lounge, Corbett Hall</td>
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<td>10:00–10:30</td>
<td>Seminars: Miguel Hernan, Marshall Joffe</td>
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<td>13:15–14:30</td>
<td>Seminars: Susan Murphy, Jamie Robins</td>
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<td>Coffee Break, 2nd floor lounge, Corbett Hall</td>
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<td>15:00–16:15</td>
<td>Seminar: Alberto Abadie, Michael Rosenblum</td>
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<td>Friday, May 8</td>
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<td>7:00–8:45</td>
<td>Seminars: Jasjeet Sekhon, Lawrence McCandless</td>
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<td>8:45–10:00</td>
<td>Coffee Break, 2nd floor lounge, Corbett Hall</td>
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<td>10:00–10:30</td>
<td>Seminars: Adam Glynn, Paul Gustafson</td>
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<td>11:45–13:30</td>
<td>Lunch</td>
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** Participants are required to checkout of the guest rooms by 12 noon on Friday. **
Causal Inference in Statistics and the Quantitative Sciences
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POSTERS

Speaker: Chakraborty, Bibhas (University of Michigan)
Title: Dealing with nonregularity in optimal dynamic treatment regimes: An Empirical Bayes approach
Abstract: Dynamic treatment regimes are individually tailored treatments. They offer a way to operationalize the adaptive multistage decision making in clinical practice, thus providing an opportunity to improve such decision making. However, when using longitudinal data on patients to construct these treatment regimes, hypotheses concerning the choice of the optimal treatment at each stage may involve nonregular parameters. The nonregularity stems from the fact that parameters are functions of maxima. As a result, the parameter estimates can be biased, and traditional methods of constructing confidence intervals can have poor frequentist properties. Here we present and evaluate a method that adapts to this nonregularity by the use of an empirical Bayes approach.

Joint work with Susan Murphy.

Speaker: Ertefaie, Ashkan (McGill University)
Title: Generalized Propensity Score vs Inverse Probability Weighting
Abstract: Robins OYee”P has developed a set of causal or counterfactual models, the marginal structural models (MSMs) using Inverse Probability Weighting (IPW). We describe an alternative approach based on Generalized Propensity Score (GPS). We then compare the strengths and weaknesses of IPW versus GPS for causal inference from two interval simulated longitudinal data.

Joint work with David A. Stephens.

Speaker: Geneletti, Sara (Imperial College London)
Title: Causal evaluation of lifestyle intervention trials: The Counterweight Project
Abstract: The Counterweight project (CWP) is a Lifestyle intervention trial (LIT) recently completed in the UK aimed at assessing the effectiveness of a weight-loss management programme for obese people. Briefly, the CWP team invited a random sample of UK practices to participate in the programme. Of those who responded, 80 were recruited and audited to determine what weight-management programmes were in place. Subsequently, 18 were randomised to controls and the remainder were administered the intervention. This consisted in training the general practitioners (GPs) to refer patients into the programme and training the practice nurses (PNs) to deliver 1-on-1 or group weight-loss sessions. The aim was to achieve and maintain a 5% weight-loss as this has been shown to be beneficial in particular w.r.t co-morbidities such as diabetes. The results of the CWP were encouraging, showing that the intervention practices achieved a higher weight-loss amongst their obese patients than the control practices. How effective would the CWP be if it became policy and were rolled out to all practices in the UK? In order to answer this question we propose using the Decision theoretic approach to causal inference (DT). DT is based on statistical decision theory and is designed to directly answer the question of interest to the policy maker “given what we know about the CWP, would applying this intervention to an average UK practice result in desired weight-loss and subsequent burden to the National Health Service?” . The DT approach will have to take account of bias and will be combined with methods to deal with missing data and Bayesian Hierarchical models. The analysis is still in its initial phase and we present here an overview of the problems and possible solutions.

Joint work with Gary Frost.
Speaker: **Kaufman, Jay** (McGill University)
Title: *Reducing bound width using structural assumptions in directed acyclic graphs involving three observed binary variables*

Abstract: The causal risk difference (RD<sub>C</sub>) has minimum and maximum values that can achieved under any set of linear constraints on the potential response type distribution. For binary exposure X, covariate Z and outcome Y, I consider two DAGs, one in which Z is not affected by X, and is a potential confounder of the causal effect of X on Y, and a second in which Z is affected by X and intermediate in the causal pathway between X and Y. For each situation I consider various linear constraints corresponding to the presence or absence of arcs in the DAG, monotonicity assumptions, and presence or absence of additive-scale interactions. The effects of interest, all in the risk difference scale, include the Z-stratum-specific bounds when Z is a potential effect measure modifier, and bounds for both controlled and natural direct effects when Z is affected by X. Without additional constraints, bounds on the average causal risk difference have unit width, and are therefore largely uninformative. But these bounds can be narrowed substantially with background knowledge-based assumptions. I show bound widths for various combinations of assumptions in the two scenarios and apply these bounds to real data from two studies.

Speaker: **Rich, Benjamin** (McGill University)
Title: *Optimal dynamic regimes: practical considerations for the application of g-estimation*

Abstract: G-estimation was proposed by Robins (2004) as a method for estimating the optimal dynamic regime from observational data in a longitudinal setting with time-varying endogenous covariates. As for any general method, its application requires careful consideration of the targets of inference of modeling strategies. First, in a simulation study we consider the relative merits of basing standard error estimates on asymptotic results or bootstrap resampling. Then, we consider real data from a study of breastfeeding to which this method has already been applied by Moodie et al. (2009). We extend their analysis by considering two alternative reward function, as well as blip function models that include covariate information.

Joint work with E.E.M. Moodie and D.A. Stephens.

Speaker: **Shortreed, Susan** (McGill University)
Title: *Marginal structural models and missing data in the exposure of interest: A simulation study based on the Framingham Heart Study*

Abstract: Missing data is common in longitudinal studies and can occur in the exposure of interest. We design a series of simulations based on the Framingham Heart Study dataset in order to investigate the impact of missing data in the primary exposure of interest in a complex, realistic setting. We use marginal structural models to estimate the marginal causal odds ratio of outcome comparing if everyone in the FHS population were physically active their whole adult life compared if everyone in the FHS population were physically inactive their whole adult life. We report and discuss the results of four commonly used missing data methods in four different missing data scenarios. In all four scenarios a complete case analysis introduces little bias, we discuss why this is so as well as potential pitfalls of all the missing data methods.

Joint work with Andrew Forbes.

Speaker: **Stuart, Elizabeth** (Johns Hopkins School of Public Health)
Title: *Combining experimental and population data: Moving towards external validity*

Abstract: While the immediate question in any randomized trial is the efficacy of the program among the study participants, the broader question is generally one of external validity: What are the effects of the program among a broader population? Little work has been done in thinking about how to make these kinds of generalizations from randomized trials to broader populations. We propose a new method to determine when and how such generalizations can be made that takes advantage of situations with a randomized trial as well as data on the population of interest. The
work is related to methods such as research synthesis and meta-analysis, but is tailored for settings where only one experiment is available. The methods are illustrated and explored using a group randomized trial of Positive Behavior Interventions and Supports (PBIS), a school-wide violence prevention program, embedded within the broader statewide implementation of the PBIS program in schools across Maryland. We address the question of how the randomized trial of PBIS can inform policymakers about the broader effectiveness of the program statewide. Using the rich set of school characteristics available, we use propensity scores to examine how similar the randomized trial schools are to schools statewide and then weight the trial schools to represent the full set of schools in the state. We lay out the assumptions underlying this approach, being particularly clear about the types of schools to which we can and cannot generalize the findings from the randomized trial. In addition to assisting policymakers in assessing the broader effectiveness of the PBIS program, this work helps to provide a framework for considering the role of randomized trials within questions of broader program effectiveness.

Speaker: Xiao, Yongling (McGill University)
Title: Simulation study of time-dependent confounding/mediating effects in Cox's regression
Abstract: In many longitudinal clinical settings, the adjustment of a treatment depends on the value of a marker of disease progression, which makes the marker a potential confounder for the treatment effect. Yet, if such marker is affected by the previous treatment, it may also act as a mediating variable. In such situations, standard regression models will yield a biased estimate of the treatment effect. Marginal structural models (MSM) provide a powerful tool to separate confounding effect of a time-dependent covariate from its mediating effect (see, for e.g., Hernan et al 2000). Yet, most applications of MSM to such time-to-event data relied on pooled logistic regression, rather than on models specifically for time-to-event analyses, such as Cox’s PH model. We use simulations to investigate these issues in the context of Cox’s regression. We simulate a prospective study of a hypothetical cohort of HIV-positive subjects, with repeated measurements of CD4 count. We assume that, at each visit, i) decision to treat a patient with HAART depends on the current CD4 count; ii) CD4 count is an important determinant of the outcome (opportunistic infection); iii) individual patients’ CD4 counts decrease when not treated, but increase when treated; iv) both ‘current’ and previous treatments lower the hazard in current interval. The simulated data are first analyzed with two versions of the conventional Cox’s time-dependent model. Both versions include binary indicators of being treated in previous and ‘current’ intervals, but they differ in whether the most recent CD4 count is adjusted for or not. Both models yield, as predicted, biased estimates of the effect of, respectively, either previous or current treatment effects. We then investigate to what extent fitting a MSM to a Cox model can eliminate or reduce these biases.

Joint work with Michal Abrahamowicz and Erica E.M. Moodie.
SEMINARY ABSTRACTS

Speaker: **Abadie, Alberto** (Harvard University)
Title: *New results on the properties of matching estimators*
Abstract: Matching estimators are often used in statistical data analysis. However, the distribution of matching estimators has been derived only for particular cases (Abadie and Imbens, 2006). This article develops methods that can be used to calculate the asymptotic distribution of a broad class of matching estimators. As an illustration of the theory, we derive the asymptotic distribution of matching estimators under different matching schemes.

Speaker: **Arjas, Elja** (University of Helsinki and National Institute for Health and Welfare)
Title: *Predictive Bayesian inference and dynamic treatment regimes: the MACS data revisited*
Abstract: Dynamic treatment regime is a decision rule in which the choice of a treatment at any given time can depend on the known past history of an individual, including baseline covariates, earlier treatments, and their measured responses. In this talk it is argued that finding an optimal regime can, at least in moderately simple cases, be accomplished by a straightforward application of nonparametric Bayesian modeling and predictive inference. As an illustration we consider the well-known Multicenter AIDS Cohort Study (MACS) data set, studying the effect of AZT initiation on CD4 cell counts during a 12-month follow-up.

Speaker: **Geneletti, Sara** (Imperial College London)
Title: *The decision theoretic approach to causal inference*
Abstract: The aim of this presentation is to give an overview of the decision theoretic (DT) framework for causal inference introduced by Dawid (2002, 2007). The approach is based on statistical decision theory and supplies a formal language by means of which causal questions can be rigorously posed and analysed, using clear and meaningful assumptions. We argue that DT requires fewer assumptions than other approaches such as the counterfactual or potential responses approaches. In the DT framework, causal assumptions are expressed in terms of conditional independence statements, that can, in principle if not always in practice, be tested, something that cannot be done for assumptions based on counterfactuals. Thus we believe that the DT framework provides a more concise, economical and justifiable approach to inference on treatment effects.

Joint work with A.P. Dawid.

Speaker: **Glynn, Adam** (Harvard University)
Title: *What can be learned from a post-treatment variable? Bayesian sensitivity analysis for total causal effects with an informative post-treatment variable and non-ignorable (and perhaps unobserved) treatment*
Abstract: What can one learn about total causal effects from the observation of a post treatment variable? Using a Bayesian model, this paper demonstrates that the observation of a post-treatment variable can improve our knowledge about total causal effects when treatment assignment is non-ignorable and the assumptions necessary for the front-door technique do not hold. Furthermore, the Bayesian model provides a framework for sensitivity analysis when the treatment is unobserved but a post-treatment (i.e. proxy variable) is observed. We illustrate this methodology with social science examples.
Speaker: **Goetghebeur, Els** (Ghent University)
Title: *Comparing instrumental variable estimators for the causal effect of an exposure on a dichotomous outcome*
Abstract: Inference for causal effects can benefit greatly from the availability of an instrumental variable (IV) which, by definition, is associated with the given exposure, but not with the outcome of interest in the absence of a causal effect. Estimation methods for instrumental variables are now well established for continuous outcomes. The case of dichotomous outcomes turns out much more difficult and has received much less attention so far. In this talk, we review both exact and approximate IV-estimators (popular with Mendelian randomization) that have been proposed for the causal odds ratio in the biostatistical, epidemiological and econometric literature. Methods comparisons are made, both formally and via simulation, and new insights are developed into the assumptions underlying their validity. The different estimators will be used to assess the risk of gastrointestinal (GI) complications attributable to Cox-2 inhibitors rather than other non-steroidal anti-inflammatory drugs.

Joint work with Manoochehr Babanezhad and Stijn Vansteelandt.

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Speaker: **Gustafson, Paul** (University of British Columbia)
Title: *What are the limits of posterior distributions arising from nonidentified models, and why should we care?*
Abstract: In causal inference settings, and in other settings where available data are much coarser than one would wish, methods often rely on plausible but unverifiable assumptions. One use of Bayesian analysis is to move such assumptions from exact to approximate. For instance, one might replace an assumption that an instrumental variable is exactly independent of the outcome given exposure with an assumption that the extent of any conditional dependence is not likely large. Or one might replace an assumption that the magnitude of exposure measurement error is exactly known with an assumption that the value is likely in a given range. While such relaxations are often honest and realistic, they may change the statistical model from identified to nonidentified (or perhaps from nonidentified to even more nonidentified). Consequently, the posterior distribution on an interest parameter may no longer concentrate to a single point as the sample size grows. Thus it seems important to study the width (particularly the support) of such large-sample limiting posteriors, and their sensitivity to the choice of prior distribution. It will be seen that sometimes determining the limiting posterior is easy, and sometimes it is computationally challenging. Connections will be drawn with the literature on bounding methodologies. Examples involving instrumental variables will be emphasized.

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Speaker: **Henderson, Robin** (University of Newcastle)
Title: *Regret-regression for optimal dynamic treatment regimes*
Abstract: We consider the problem of deriving optimal dynamic treatment regimes from observational data. Model building, checking and comparison have had little or no attention so far in this literature. Motivated by an application on optimal dosage of anticoagulants, we propose a modelling and estimation strategy which incorporates the regret functions of Murphy (2003) into a regression model for observed responses. Estimation is quick and diagnostics are available, meaning a variety of candidate models can be compared.

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Speaker: **Hernan, Miguel** (Harvard University)
Title: *Survival analysis with dynamic treatment regimes*
Abstract: When estimating the effect of time-varying treatments, inverse probability (IP) weighting can appropriately adjust for confounding due to time-varying covariates that are affected by prior treatment. Most applications of IP weighting of marginal structural Cox models have focused on static treatment regimes. For example, several articles compared the AIDS-free survival of HIV-infected patients under the static regimes “initiate highly active antiretroviral therapy (HAART)
at baseline” vs “never initiate HAART during the follow-up.” However, the comparison of dynamic treatment regimes is often more interesting. IP weighting can be used to compare dynamic regimes by combining it with artificial censoring (an inefficient approach), or with a structural dose-response model as described by Orellana et al (2007) for mean models. This talk describes an application of a dynamic marginal structural model to the failure time setting.

Speaker: **Hirano, Keisuke** (University of Arizona)
Title: *Impossibility results for moment inequality models*
Abstract: Recent work in economics has used moment inequalities to identify bounds on structural and causal parameters. Much of this has focused on inference, which is complicated by discontinuities in limit distributions. We focus on estimation when a boundary is identified by two (or more) moment inequalities, and examine difficulties with defining optimal estimators. This problem is closely related to the problem of estimating the smaller of two normal means.

Joint work with Jack Porter.

Speaker: **Joffe, Marshall** (University of Pennsylvania)
Title: *Selective ignorability assumptions in causal inference*
Abstract: Most attempts at causal inference in observational studies are based on assumptions that treatment assignment is ignorable (Rosenbaum and Rubin 1983); ignorability involves conditional independence of treatment and the potential outcomes. Such assumptions are usually made casually, largely because they justify the use of available statistical methods and not because they are truly believed. It will often be the case that it is plausible that conditional independence holds at least approximately for a subset but not all of the experience giving rise to one’s data. Such selective ignorability assumptions may be used to derive valid causal inferences in conjunction with structural nested models, whereas methods based on assuming full ignorability are biased in this setting. In this paper, we outline selective ignorability assumptions mathematically, discuss various variants of it, and sketch how it may be used along with otherwise standard G-estimation methods to obtain inference on structural nested models. We motivate and illustrate our development by considering an analysis of an observational database to estimate the effect of erythropoetin use on mortality among hemodialysis patients. We discuss the close connection between selective ignorability assumptions and G-estimation with instrumental variables assumptions and estimation.

Speaker: **McCandless, Lawrence** (Simon Fraser University)
Title: *Hierarchical priors for bias parameters in Bayesian adjustment for unmeasured confounding*
Abstract: Recent years have witnessed new innovation in Bayesian techniques to adjust for unmeasured confounding. A challenge with existing methods is that the user is often required to elicit prior distributions for high dimensional parameters that model competing bias scenarios. This can render the methods unwieldy. In this paper we introduce a novel methodology to adjust for unmeasured confounding that assigns default priors for bias parameters for observational studies with binary covariates. The confounding effects of measured and unmeasured confounders are modelled as exchangeable within a Bayesian framework. We model the joint distribution of covariates using a loglinear model with pairwise interaction terms. Hierarchical priors constrain the magnitude and direction of bias parameters. An appealing property of the method is that the conditional distribution of the unmeasured confounder follows a logistic model, giving a simple equivalence with previously proposed methods.

Speaker: **Murphy, Susan** (University of Michigan)
Title: *A prediction interval for the misclassification rate*
Abstract: The misclassification rate of a classifier is a non-smooth function of the classifier. The estimated rate suffers from bias due to over-fitting and the misclassification rate is a “minimized” quantity. For both of these reasons the construction of measures of confidence such as estimates of
variance and confidence/prediction intervals are challenging. We discuss this problem and propose a method based on the use of a smooth upper bound combined with the bootstrap. This upper bound utilizes the surrogate loss that is used in the construction of the classifier.

Joint work with Eric Laber.

Speaker: Neufeld, Eric (University of Saskatchewan)
Title: Causality and data visualization
Abstract: Some proponents of information visualization advocate that a complete visualization of a dataset should contain a visual representation of all the data values, and leave it to the eye/brain of the observer to generate hypotheses about relationships in the data that might subsequently be tested formally. This ensures that important, but perhaps statistically insignificant data points or variables are not summed out.

This is a good goal, but runs into dimensionality problems. Graphical models, in particular, causal models provide visualizations that do not summarize variables out of the data. Introductory exploratory research on a variety of methods for visualizing both random and causally related data suggests that causality offers a meaningful way of increasing the dimensionality of what can be represented in traditional (paper or LCD) displays, and moreover formalizes the assumptions underlying the visualized structure. Moreover, differences regarding some of the assumptions underlying the definitions of causality can be used to allow the user to modify the structure accordingly.

The visualizations we have developed offer an interesting pedagogical tool for explaining the ideas of causation, intervention, and confounding.

Speaker: Noorbaloochi, Siamak (Center for Chronic Disease Outcome Research)
Title: Sufficiency, ancilarity and bias reduction for high dimensional predictor spaces
Abstract: We show how sufficiency and ancilarity concepts can be used to understand and construct a host of methods to reduce bias due to (large number of) imbalance baseline predictors. As an example we show how the effective dimension reduction summaries of the Regression Graphics provide alternative summaries to the propensity based analyses.

Joint work with David Nelson and Masoud Asgharian.

Speaker: Pearl, Judea (University of California, Los Angeles)
Title: The mathematics of causes and counterfactuals
Abstract: The questions that motivate most studies in the health, social and behavioral sciences are not statistical but causal in nature. For example, what is the efficacy of a given drug in a given population? Whether data can prove an employer guilty of hiring discrimination? What fraction of past crimes could have been prevented by a given policy?

Remarkably, although much of the conceptual and algorithmic tools needed for tackling such problems are now well established, they are hardly known to empirical researchers. The barrier has been cultural; formulating causal problems mathematically requires certain extensions to the standard mathematical language of statistics, and these extensions are not generally emphasized in the mainstream literature and education. (Traditionalists are invited to write down a mathematical formula for the claim: ‘The rooster crow does not cause the sun to rise.’)

In this talk, I will introduce a few basic principles that are sufficient for solving most (if not all) problems involving causal relationships. The principles are based on non-parametric structural equation models, a natural generalization of those used by econometricians in the 1950-60s, yet cast in new mathematical underpinnings. This semantical framework, enriched with a few ideas from logic and graph theory, gives rise to a formal yet friendly calculus of counterfactuals that unifies all existing approaches to causation and resolves long-standing problems in several of the sciences. These include questions of confounding, causal effect estimation, covariate selection, policy analysis, legal responsibility, effect decomposition, instrumental variables, and the integration of data from diverse studies.

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Speaker: **Richardson, Thomas** (University of Washington)
Title: *Analysis of the binary instrumental variable model*
Abstract: In this talk I consider an instrumental variable potential outcomes model in which the instrument \((Z)\), treatment \((X)\) and response \((Y)\) are all binary. It is well known that this model is not identified by the observed joint distribution \(p(x,y,z)\). Consequently many statistical analyses impose additional untestable assumptions or change the causal estimand of interest.

Here we take a different approach, directly characterizing and graphically displaying the set of distributions over potential outcomes that correspond to a given population distribution \(p(x,y,z)\). This provides insights into the variation dependence between the partially identified average causal effects for various compliance groups. The analysis also leads directly to re-parametrization that may be used for Bayesian inference and the development of models that incorporate baseline covariates.

Joint work with James Robins.

Speaker: **Robins, James** (Harvard University)
Title: *A bold vision of artificial intelligence and philosophy: Finding causal effects without background knowledge or statistical independences*
Abstract: I describe a statistical methodology based on philosophy, causal directed acyclic graphs, and a pinch of magic and miracle that holds the promise of making a silk purse of causal knowledge out of the sow’s ear of an observational data set with no obvious structure. In 10 years or so, for better or worse, this methodology may become part of mainstream genomics.

Joint with Thomas Richardson, Ilya Shpitser, and Steffen Lauritzen.

Speaker: **Rosenblum, Michael** (University of California, San Francisco)
Title: *Targeted maximum likelihood estimation for the parameter of a marginal structural model, and a related method for diagnosing bias due to violation of experimental treatment assignment*
Abstract: The targeted maximum likelihood estimator (van der Laan and Rubin, 2006) is a general tool that can be used to estimate a wide variety of parameters, and is of particular use in causal inference. Here, we present the targeted maximum likelihood estimator for the parameter of a marginal structural model, discussing advantageous properties of the estimator. We discuss an interesting property of this estimator, related to diagnosing bias due to violation of experimental treatment assignment. These methods are applied to estimate the effect of medication adherence on viral suppression in a cohort of HIV positive, homeless individuals in San Francisco.

Joint work with Mark van der Laan, Steve Deeks, and David Bangsberg.

Speaker: **Rotnitzky, Andrea** (Harvard University)
Title: *Estimation and extrapolation of optimal dynamic treatment and testing strategies from observational longitudinal data*
Abstract: We review recent developments in the estimation of an optimal treatment strategy or regime from longitudinal data collected in an observational study. We propose novel methods for using the data obtained from an observational database in one health care system to determine the optimal treatment regime for biologically similar subjects in a second health care system when, for cultural, logistical, and financial reasons, the two health care systems differ (and will continue to differ) in the frequency of, and reasons for, both laboratory tests and physician visits. Finally, we propose a novel method for estimating the optimal timing of expensive and/or painful diagnostic or prognostic tests. Diagnostic or prognostic tests are only useful in so far as they help a physician to determine the optimal dosing strategy, by providing information on both the current health state and the prognosis of a patient because, in contrast to drug therapies, these tests have no direct causal effect on disease progression. Our new method explicitly incorporates this no direct effect restriction.

Joint work with James Robins and Liliana Orellana.
Speaker: **Schaubel, Douglas** (University of Michigan)
Title: *Estimating the effect of an experimental time-dependent therapy on residual mean lifetime*
Abstract: We develop semiparametric methods to estimate the effect on restricted mean lifetime of a time-dependent treatment. In the data structure of interest, both an experimental and established form of treatment are available; pre- and post-treatment hazards are non-proportional; subjects may experience periods of treatment ineligibility; treatment assignment is not randomized. The proposed methods involve weighting results from stratified proportional hazards models fitted using a generalization of case-cohort sampling. Asymptotic and finite-sample properties of the proposed estimators are evaluated. The proposed methods are applied to data from a national organ transplant registry.

Joint work with John D. Kalbfleisch.

Speaker: **Sekhon, Jasjeet** (University of California, Berkeley)
Title: *Matching methods for causal inference and their limitations: Evaluating medical interventions*
Abstract: In recent years there has been a burst of innovative work on methods for estimating causal effects using matching methods. There is, however, little consensus on the effectiveness of matching methods. Policy-makers worldwide are making use of health economic evaluations, which generally use observational data because of the paucity of randomized trials that compare appropriate treatment options and measure long-term costs and outcomes. Here the key concern is the adjustment for confounders; traditional approaches in this literature have focused on propensity score and standard regression methods. Even if the selection on observables assumption holds, cost-effectiveness analyses poses specific challenges for the matching method to address: non-linear response surfaces; and observed confounders often have wide baseline imbalances between treatment groups and non-ellipsoidal distributions. We apply a non-parametric matching method, Genetic Matching (GenMatch), to a variety of cost effectiveness examples, including the prominent case of Pulmonary Artery Catheterization. GenMatch uses an evolutionary search algorithm to optimize covariate balance. Both propensity score matching and Mahalanobis distance matching are special limiting cases of this method. We present theoretical results and examples. In our examples, GenMatch is able to replicate the experimental results using observational data while propensity score matching does not. However, although our algorithm helps researchers obtain better balance for observed covariates, many problems remain. Even if the selection on observables assumption holds, in finite samples, assumptions about the response surface must be made either implicitly or explicitly. If we did not have experimental benchmarks to validate our results, much debate would remain: which covariates to adjust, how much adjustment is enough, etc. No amount of statistical modeling or algorithmic wizardry can resolve these questions.

Speaker: **Small, Dylan** (University of Pennsylvania)
Title: *The Malaria Attributable Fraction: Definition, inference and sensitivity analysis*
Abstract: Malaria is an infectious disease caused by a parasite that is an important public health problem in many countries. A major symptom of malaria is fever. An important epidemiological quantity for measuring the burden of malaria is the proportion of children that have fevers that are attributable to malaria, called the malaria attributable fraction (MAF). A difficulty in estimating the MAF is that it is difficult to diagnose a fever as being due to malaria parasites as opposed to other illnesses such as influenza, pneumonia, viral hepatitis or typhoid fever. Microscopic examination of blood for malaria parasites helps to diagnose a fever as being due to malaria, but children living in areas of high malaria endemicity often tolerate malaria parasites without developing any signs of disease; consequently, a fever may not be attributable to malaria even if the child has malaria parasites in his or her blood. We consider estimation of the MAF based on data on fever incidence and parasite density in the blood. We present a potential outcomes framework for defining the MAF, and analyze previously proposed estimators in this framework. We show that the classical estimator depends on an assumption that parasite densities among children are effectively randomly
assigned, and present evidence that this assumption does not hold. We develop a sensitivity analysis that assesses the sensitivity of inferences to departures from the assumption of random assignment of parasite densities.

Speaker: **Strumpf, Erin** (McGill University)
Title: *Inside an applied economists toolkit for causal inference: instrumental variables and regression discontinuity methods*
Abstract: Applied economists generally use natural experiments and policy changes, combined with econometric methods, to identify causal effects of interest. I will provide an overview of two widely-used methods: instrumental variables and regression discontinuity. In addition to providing a brief description of the statistical assumptions and method implementation, I will discuss how these methods have been used to address health-related questions and their relative strengths and weaknesses in this context.

Speaker: **van der Laan, Mark** (University of California, Berkeley)
Title: *Towards robust black-box algorithms for causal effects that preserve meaningful statistical inference*
Abstract: Current statistical practice to assess an effect of an intervention or exposure on an outcome of interest often involves either maximum likelihood estimation for a priori specified regression model, or, manual and/or data adaptive interventions to fine tune a choice of model. In both cases, bias in the point estimates and the estimate of the signal to noise ratio are rampant, causing an epidemic of false claims based on data analyses.

In this talk we present our efforts to construct machine learning algorithms for estimating a causal effect that take away the need for specifying regression models, while still providing maximum likelihood based estimators and inference. Two fundamental concepts underlying this methodology are the very aggressive use of cross-validation to select optimal combinations of many model fits, and subsequent targeted maximum likelihood estimation to target the fit towards the causal effect of interest.

We illustrate this method in observational studies for assessing the effect of an intervention on adherence to drug regimen in HIV infected patients, and for discovery of mutations in the HIV virus that cause resistance to a particular drug regimen. We also illustrate the performance on FDA approved clinical trials, simulated data imitating postmarket safety analysis, and the analysis of single nucleotide polymorphisms.

Speaker: **VanderWeele, Tyler** (University of Chicago)
Title: *Marginal structural models for sufficient cause interactions*
Abstract: Sufficient cause interactions concern cases in which a particular causal mechanism for some outcome will operate only if two or more specific causes are present. Empirical conditions have been derived to test for sufficient cause interactions. However, when regression outcome models are used to control for confounding variables in tests for sufficient cause interactions, the outcome models impose restrictions on the relationship between the confounding variables and certain unidentified background causes within the sufficient cause framework; often these assumptions are implausible. By using marginal structural models to test for sufficient cause interactions, assumptions are instead made on the relationship between the causes of interest and the confounding variables; these assumptions will often be more plausible. The use of marginal structural models also allows for testing for sufficient cause interactions in the presence of time-dependent confounding. Such time-dependent confounding may arise in cases in which a genetic factor of interest may affect both an environmental factor of interest and the outcome. It is furthermore shown that marginal structural models can be used not only to test for sufficient cause interactions but to give lower bounds on the prevalence of such sufficient cause interactions.