



HARVARD
T.H. CHAN
SCHOOL OF PUBLIC HEALTH

Biostatistics 258 Spring 2024 Syllabus
Causal Inference: Theory and Practice
credit hours: 4.0 (via FAS) or 5.0 (via HSPH)
lecture meets TuTh 02:00–03:30PM, FXB G12
laboratory meets F 09:45–11:15AM, Kresge LL6

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Office Hours: Tu 09:00–10:00AM

The instructional staff reserve the right to make changes to this syllabus at any time.

Course Description: Randomized experimentation is the gold standard for the measurement of the causal effect of an intervention (i.e., treatment, exposure) in the public health and biomedical sciences; however, randomization is often impossible, impractical, or unethical, leading to real-world scenarios in which causal inferences are drawn from observational studies. This course will review the foundations of causal inference in (bio)statistics, outlining causal analytic methods that help to extract as much evidence as imperfect observational studies carry about causal effects commonly of interest in applied health science settings. This doctoral-level survey of statistical causal inference will introduce a structured analytic roadmap for formulating causal (i.e., counterfactual) effect measures tied to clearly defined and well-articulated scientific queries. Such a roadmap begins with a formal model encoding the temporal ordering of variables in a system under study and the possibly *a priori*-known causal relationships between these variables. This is then followed by giving a clear mathematical formulation of the causal effect measure necessary to answer the scientific question of interest. Finally, state-of-the-art mathematical and statistical techniques must be applied to derive best-in-class estimators of the causal effect measures of interest, accompanied by valid statistical inference. Emphasis will be placed on understanding why a formal theory of causation is necessary and how intuition alone or the rote application of traditional statistical modeling frameworks can lead to logical mistakes that invalidate a data analysis and undermine its scientific conclusions.

This tour of statistical causal inference begins with foundational concepts: counterfactual random variables, the potential outcomes and graphical modeling frameworks (e.g., directed acyclic graphs), and necessary assumptions and common strategies for identification of the causal effects of static and dynamic interventions. Building on these foundations, this survey will introduce elements of semi-parametric efficiency theory necessary for the development of cutting-edge asymptotically efficient (e.g., augmented inverse probability weighted, targeted maximum likelihood) estimators of causal effect estimands. Methodological extensions for studying the causal effects of time-varying, longitudinal interventions (e.g., marginal structural models) will be touched upon as well. Further topics to be addressed include causal mediation analysis, heterogeneous treatment effects, optimal dynamic treatment regimes, the causal dose-response curve, and modified treatment policies. Time permitting, additional topics motivating current research will be introduced too. Wherever possible, this course will emphasize the application of modern regression (i.e., machine learning) tools for the estimation of causal effects, including an abbreviated applied introduction to this area.

Prerequisites and Recommendations:

This doctoral-level course is designed for students who are already equipped with a foundational understanding of probability theory and mathematical statistics, working fluency with scientific programming languages (e.g., R, numerical Python, Julia), and working proficiency with tools and best practices for scientific programming, including version control with git.

- *Pre-requisites:* Statistical theory/methods at the level of BST 231 (Inference I) and BST 232 (Methods) or equivalent, statistical computing/programming, and mathematical maturity.
- *Recommended:* EPI 207 (Advanced Epidemiologic Methods); BST 241 (Inference II).
- *Related:* STAT 286 (Causal Inference with Applications); STAT 293 (Design of Experimental and Non-experimental Studies); STAT 234 (Sequential Decision Making).

Acknowledging diversity of academic backgrounds, the instructional staff suggest that all students review key concepts and software tools in the initial weeks of instruction in a self-directed manner. While self-motivation and the continuous pursuit of learning are highly valued, we recognize the importance of support and collaboration. Each student is encouraged to actively engage in their own learning process, balancing independent growth with the readiness to seek *and offer* help.

Requirements and Materials:

Lecture notes, covering the topics discussed in class, will be distributed each week as the course progresses. A list of articles from the primary and secondary literature will also be provided. The course will not rely upon a single text, but several have been written on this topic, addressing it from a variety of angles. Below is a non-exhaustive list of well-written monographs, given in reverse chronological order of their publication. Students are *not required* to purchase any single text.

- [Hernán and Robins \(2024\)](#), *Causal Inference: What If*
- [van der Laan and Rose \(2018\)](#), *Targeted Learning in Data Science: Causal Inference for Complex Longitudinal Studies*
- [Peters et al. \(2017\)](#), *Elements of Causal Inference: Foundations and Learning Algorithms*
- [Pearl et al. \(2016\)](#), *Causal Inference in Statistics: A Primer*
- [VanderWeele \(2015\)](#), *Explanation in Causal Inference: Methods for Mediation and Interaction*
- [van der Laan and Rose \(2011\)](#), *Targeted Learning: Causal Inference for Observational and Experimental Data*
- [Pearl \(2009\)](#), *Causality: Models, Reasoning, and Inference*
- [Freedman \(2009\)](#), *Statistical Models: Theory and Practice*
- [Angrist and Pischke \(2009\)](#), *Mostly Harmless Econometrics: An Empiricist's Companion*
- [van der Laan and Robins \(2003\)](#), *Unified Methods for Censored Longitudinal Data and Causality*

In the first half of the course, you may also find it interesting to read [Pearl and Mackenzie \(2018\)](#)'s *The Book of Why*, a recently published book on the emerging science of causal inference.

Some elements of semi-parametric efficiency theory, especially the theory of influence functions, have become major tools for the formulation of asymptotically efficient estimators of causal effect estimands, and these will be introduced and reviewed with an eye towards their application in causal inference. For those inclined to dive deeper into this area, some relevant texts include

- [Kosorok \(2008\)](#), *Introduction to Empirical Processes and Semiparametric Inference*
- [Tsiatis \(2007\)](#), *Semiparametric Theory and Missing Data*
- [van der Vaart \(1998\)](#), *Asymptotic Statistics*

Pedagogic note: This is a doctoral-level course intended to equip students with the necessary background to begin pursuing research in causal inference. A critical aspect of what makes research challenging is that one does not know in advance the answer to a problem being worked on, or, much more frustratingly, that any satisfying answer even exists. A key skill is to learn to be at peace when working under uncertainty, and to be comfortable in making guesses and pursuing these to wherever they may lead. To build this skill, some of the problems assigned will pose conjectures without indicating whether one should pursue an answer or seek a counterexample. When stuck, try reversing your chosen strategy. While you probably will not find the answer to every question—and that’s alright!—you will develop a sense for what it means to conduct research in an area unfamiliar to you. This will prove to be a valuable, and highly transferable, skill. Educational research has shown that encountering challenges and feeling stuck is often when the deepest learning occurs, so embrace such moments as invaluable opportunities to grow and to sharpen understanding.

Laboratory section: In the laboratory section, students will actively apply the causal inference methodologies introduced in the lecture meetings. The aim is to go beyond abstract discussions, allowing students hands-on, practical opportunities to implement causal inference techniques *in a collaborative setting* to answer scientific questions while emphasizing transparency and reproducibility, as needed in real-world projects. The laboratory exercises are designed not only to supplement lecture meetings but to facilitate opportunities to explore select topics in depth and to facilitate guided practice in the application of the formal methodological framework of causal inference to scientific problems. The instructional staff strongly believe that proficiency in the use of open-source software tools for version control (e.g., `git`, GitHub) and literate computing (e.g., Quarto, Jupyter notebooks) is crucial for the modern applied statistician—that is, these tools constitute the applied statistician’s “workbench” and their proper setup a form of *mise en place*, helping to organize work in a manner that improves efficiency and enforces the “laboratory hygiene” necessary to ensure clear, reproducible results are obtained consistently. Laboratory exercises should be completed using such tools. Since competency in the use of these tools is expected from the course’s start, additional time and effort may be required to develop the expected skill set; we will provide references to tutorials and provide guidance to support this learning process. Hands-on experience in the laboratory section aims to enhance and reinforce understanding of causal inference concepts and to equip students with skills that are vital for the responsible practice of applied statistics.

Learning Outcomes and Objectives:

At the completion of this course, students will have learned...

- I To translate scientific questions of interest into causal inference questions (i.e., written in the language of counterfactuals) and to mathematically express counterfactual questions, including via causal diagrams expressing *a priori* subject matter knowledge and assumptions.
- II To assess when it is possible to learn a causal effect from experimental or observational studies and to state and evaluate common identification assumptions in appropriate scientific context.
- III To understand the inferential obstacles posed by intermediate and time-varying confounders and appreciate how formal frameworks, including for principal stratification, causal mediation analysis, and sequential adjustment or re-weighting, can help to address these issues.
- IV To apply concepts from semi-parametric efficiency theory to construct and evaluate state-of-the-art, asymptotically efficient estimators of target causal estimands (e.g., average treatment effect, average treatment effect on the treated, natural direct and indirect effects).
- V To implement both simple (e.g., inverse probability weighted) and robust and efficient (e.g., augmented inverse probability weighted) estimation approaches to compute a given target causal estimand (e.g., average treatment effect) with the data at hand.

- VI** To interpret the results of implementing causal analytic approaches in statistical data analysis and to understand when to give up on pursuing causal interpretations of study findings.

Grading Scheme:

- Course Project (40%): An in-depth exploration (or “deep dive”) into a single or closely related set of topics in statistical causal inference. Discoveries will be shared as a 10-page report and a 40-minute oral group presentation. We envision this as a collaborative endeavor in which small teams (of 2-4 learners) invest 3-4 weeks of dedicated effort into focused exploration. Guidance on expectations and a range of suggested topics will be shared at the semester’s midpoint. Please note that the presentation of previously conducted research—whether past or in-progress—falls strictly outside of the scope of this assignment.
- Assignments (20%): Four problem sets designed to highlight key concepts by including a range of conceptual, mathematical, and computational exercises will be distributed across the term. Any late submissions will be subjected to a 20% overall deduction per day late.
- Presentation (20%): In lieu of a mid-term examination, students will, in small groups (of 2–3 learners), have the opportunity to delve into a published research manuscript and to lead an in-depth discussion of it during a lecture meeting. Presenters should carefully and closely read the content and prepare presentation materials that summarize key ideas, stimulate discussion, and engage their peers in critical reflections.
- Participation (10%): Students’ active participation in class is highly valued. This encompasses regular attendance and substantive contributions to in-class discussions and activities. Engagement and understanding will be assessed occasionally via brief, open-note “concept checks” distributed at random during the lecture and/or laboratory meetings. Successful completion of the mid-term course evaluation is also expected.
- Journal Club (10%): Most weeks, students will read a manuscript assigned from the primary literature and distill their insights via brief write-ups that will guide in-class discussions. Specific expectations will be made available as the term progresses.

Course Policies and Expectations

Accommodations: Please make sure to speak with the Student Support Services staff (studentsupport@hsph.harvard.edu) as soon as possible if you may require any particular accommodations, and they will work out any necessary arrangements as best as possible. We are committed to making feasible adjustments to support educational success for all.

Scheduling Conflicts: Please notify the instructional staff by the second week of the term about any known or potential conflicts, such as religious observances or job interviews. If you foresee the possibility of missing the equivalent of two or more weeks of class, we recommend postponing enrollment in the course to a future term when your full engagement with the course material will be possible. Regular attendance and participation are vital for a complete learning experience.

Collaboration and Independence: Learning is a collective journey, so we encourage you to work together on homework assignments. That said, all homework assignment submissions should clearly list collaborators and references and should be written up independently. Submitted assignments will not be considered for credit if they are a replicate of another submission; further, such forms of academic misrepresentation may trigger disciplinary action. Use of ChatGPT and the like is strongly discouraged—*caveat emptor*—and we encourage you to practice forging your own insights and testing your own understanding. These guidelines are designed to support a constructive and inclusive learning experience for all course participants.

Important Dates

Unless otherwise stated, all deliverables are due by 6:00pm EST on the specified date.

Homework 1	Thursday, 8 th of February
Homework 2	Thursday, 22 nd of February
Homework 3	Thursday, 7 th of March
Midterm Feedback Survey	Thursday, 21 st of March
Homework 4	Thursday, 28 th of March
Homework 5	Thursday, 11 th of April
Final Project Report	Monday, 6 th of May
Final Project Presentations	Week of the 6 th of May

Class Session Structure

The primary class sessions focus on lecture-oriented *synchronous learning*. Each of the 90-minute learning sessions will be divided unevenly into an interactive, review component (Part I) and a lecture component (Part II), as elaborated upon below.

- Part I (20 minutes) begins with a brief 3-5 question, open-note “concept check” intended to review previously covered material and cover any assigned reading material. A random selection of students will present their answers, which will prompt a brief in-class discussion.
- Part II (70 minutes) is dedicated to a traditional lecture delivered by the faculty instructor, another member of the instructional staff (only sparingly) or, if appropriate, an invited guest lecturer. This will include time for questions from and discussion with the audience. Occasionally, student presentations will take 45 minutes of this period.

The laboratory sessions are a crucial part of the learning experience, providing an interactive environment to apply concepts introduced in the lectures through hands-on activities and exercises.

Course Outline

The course is divided into a series of modules. The weekly coverage of topics is subject to change, as it will depend on the progress of the class. Anticipated time for the completion of each module is indicated below. As the semester runs 16 weeks (n.b., Spring 2024 runs 22 January–10 May with Spring Break 11–15 March), we will cover only a selection of the modules listed. To strive for a reasonably comprehensive introduction to some core topics in statistical causal inference, part of the menu—the underlined modules—is served *prix fixe*. These will be supplemented by other modules to be selected based on the audiences’ indicated interests and at the instructor’s discretion.

1. **Introduction to and overview of causal inference.** Randomized controlled experiments, observational studies, and the pitfalls of trying to draw causal inferences by rote application of traditional statistical methods (i.e., regression); a roadmap for causal inference.
 - Time anticipated: 1 week (2 lectures)
 - Learning objectives: **I, II, VI**
 - Topics: Measures of association (risk difference, risk ratio, odds ratio, difference-in-means, regression coefficients); randomization as control (i.e., probability by fiat) and the design-based perspective; observational studies (i.e., probability “from nature”) and their shortcomings; the Yule-Simpson paradox and some real-life examples; perspectives on causality, statistics, and ontological commitments in applied statistical science.
 - Books and tutorials: **Hernán and Robins (2024, Ch. 1–3)**, **Freedman (2009, Ch. 1–2, 4)**, **Pearl (2009, Ch. 1)**, **Pearl et al. (2016, Ch. 1)**, **Angrist and Pischke (2009, Ch. 1–2, Sec. 3.1)**, **Pearl and Mackenzie (2018, Ch. 1–3)**, **Starmans (2018)**

- Primary literature: [Rubin \(1974\)](#), [Bickel et al. \(1975\)](#), [Holland \(1986\)](#), [Freedman \(1999\)](#), [Hernán and Taubman \(2008\)](#), [Petersen and van der Laan \(2014\)](#), [Vansteelandt \(2021\)](#)
2. **Potential outcomes, graphical models, and identification strategies.** Links between missing data and causal inference; structural causal models and graphical models; assumptions for identification of causal effects; g-computation and inverse probability weighting.
- Time anticipated: 3 weeks (6 lectures)
 - Learning objectives: **I, II, V, VI**
 - Topics: [Week 1](#): Intervention and outcome variables; counterfactual random variables; the Neyman-Rubin potential outcomes framework and the stable unit treatment value assumption; graphical modeling frameworks (i.e., DAGs, SWIGs) and basic properties. [Week 2](#): The positivity and overlap assumptions; the ignorability assumption and no unmeasured confounding; the propensity score; the g-computation algorithm. [Week 3](#): Estimation of causal effects using inverse probability weighting and outcome regression modeling; perils of model misspecification; influence functions and asymptotic linearity.
 - Books and tutorials: [Hernán and Robins \(2024, Ch. 6–8, 10, 12, 13, 15\)](#), [van der Laan and Rose \(2011, Ch. 2\)](#), [Pearl \(2009, Ch. 3, 6\)](#), [Pearl et al. \(2016, Ch. 2, Sec. 3.1–3.6, 4.1–4.4\)](#), [Angrist and Pischke \(2009, Sec. 3.2\)](#), [Pearl and Mackenzie \(2018, Ch. 4–8\)](#)
 - Primary literature: [Rosenbaum and Rubin \(1983\)](#), [Greenland and Robins \(1986\)](#), [Pearl \(1995\)](#), [Greenland et al. \(1999a\)](#), [Greenland et al. \(1999b\)](#), [Rubin \(2005\)](#), [Pearl \(2010\)](#), [Hubbard and van der Laan \(2008\)](#), [Robins et al. \(2007\)](#), [Petersen et al. \(2012\)](#)
3. **Semiparametric efficiency theory in causal inference and causal machine learning.** Infinite-dimensional or large statistical models; semi-parametric local efficiency; the efficient influence function and its key properties (e.g., double robustness); estimation strategies based on the efficient influence function; considering the role of machine learning in causal inference.
- Time anticipated: 3 weeks (6 lectures)
 - Learning objectives: **IV, V**
 - Topics: [Week 1](#): Nonparametric statistical models incorporating real-world knowledge; influence functions and asymptotic linearity (revisited); the efficient influence function and semi-parametric efficiency. [Week 2](#): Alleviating model misspecification via machine learning (cross-validation, loss-based estimation, and the super learner algorithm); cross-fitting and the role of regularity conditions. [Week 3](#): Asymptotic curse of dimensionality and asymptotic bias-correction; asymptotically efficient estimation based on the one-step correction, augmented inverse probability weighting, and targeted maximum likelihood.
 - Books and tutorials: [Kennedy \(2016\)](#), [Fisher and Kennedy \(2020\)](#), [Kennedy \(2022\)](#), [Hines et al. \(2022\)](#), [van der Laan and Rose \(2011, Ch. 4–6, Appx. A\)](#), [van der Vaart \(1998, Ch. 7–9, 19, 20\)](#), [Tsiatis \(2007, Ch. 2–3\)](#)
 - Primary literature: [Bang and Robins \(2005\)](#), [van der Laan and Rubin \(2006\)](#), [Rubin and van der Laan \(2007\)](#), [Tsiatis et al. \(2008\)](#), [Rubin and van der Laan \(2008\)](#), [Moore and van der Laan \(2009\)](#), [Rubin and van der Laan \(2011\)](#), [Wang et al. \(2019\)](#), [Kang and Schafer \(2007\)](#), [Vansteelandt et al. \(2012\)](#), [Gruber and van der Laan \(2015\)](#), [Schnitzer et al. \(2016\)](#), [Hahn \(1998\)](#), [Hirano et al. \(2003\)](#), [Hejazi and van der Laan \(2023\)](#), [Zheng and van der Laan \(2011\)](#), [Chernozhukov et al. \(2018\)](#), [Ju et al. \(2019\)](#), [van der Laan et al. \(2004\)](#), [Dudoit and van der Laan \(2005\)](#), [van der Laan et al. \(2007\)](#), [Wyss et al. \(2018\)](#), [Phillips et al. \(2023\)](#)

4. **Caught in the middle: Principal stratification and mediation analysis.** Issues that arise due to intermediate variables; principal strata; mediation as effect decomposition; well-known direct and indirect effect definitions and estimands; the interventionist perspective.
 - Time anticipated: 3 weeks (6 lectures)
 - Learning objectives: **II, III, V, VI**
 - Topics: **Week 1:** Post-treatment confounding due to intermediate variables; principal stratification and principal stratum causal effects; brief history of mediation analysis in statistics (e.g., path analysis). **Week 2:** Nonparametric identification of mediation effects (i.e., sequential ignorability, nested potential outcomes, “cross-world” counterfactuals); the controlled direct effect; the natural direct and indirect effects. **Week 3:** Estimation of direct and indirect effects; separability criteria and interventionist mediation analysis; intermediate confounding and the interventional direct and indirect effects.
 - Books and tutorials: [Hernán and Robins \(2024, Ch. 4–5, 23\)](#), [Freedman \(2009, Ch. 6\)](#), [VanderWeele \(2015, Ch. 1–2, 5–6, 8\)](#), [Pearl \(2009, Sec. 4.5\)](#), [Pearl et al. \(2016, Sec. 3.7, 4.5\)](#), [Pearl and Mackenzie \(2018, Ch. 9\)](#)
 - Primary literature: [Frangakis and Rubin \(2002\)](#), [Rubin \(2006\)](#), [Hudgens and Halloran \(2006\)](#), [Jemai et al. \(2007\)](#), [VanderWeele \(2011\)](#), [Pearl \(2011\)](#), [Gilbert et al. \(2011\)](#), [Dawid and Didelez \(2012\)](#), [Tchetgen Tchetgen \(2014\)](#), [VanderWeele \(2008\)](#), [Robins and Greenland \(1992\)](#), [Pearl \(2001\)](#), [Avin et al. \(2005\)](#), [Didelez et al. \(2006\)](#), [Petersen et al. \(2006\)](#), [van der Laan and Petersen \(2008\)](#), [VanderWeele and Vansteelandt \(2009\)](#), [Zheng and van der Laan \(2012\)](#), [VanderWeele and Vansteelandt \(2014\)](#), [Andrews and Didelez \(2020\)](#), [Díaz and Hejazi \(2020\)](#), [Robins et al. \(2022\)](#), [Miles \(2023\)](#), [Díaz \(2023\)](#)
5. **The same in a relative way: Time-varying interventions and confounding feedback.** Confounding due to dependencies between time-varying covariates and treatment schedules across time; causal effects of dynamic and time-varying intervention schemes; identification using the longitudinal g-computation algorithm and by inverse probability weighting; redux on asymptotically efficient estimation; brief overview of marginal structural models.
 - Time anticipated: 3 weeks (6 lectures)
 - Learning objectives: **II, III, IV, V, VI**
 - Topics: **Week 1:** Treatment-confounder feedback and the shortfall of “typical” methods; defining causal effects of time-varying interventions; extensions of g-computation and inverse probability weighting, and estimation based on these identification strategies. **Week 2:** Revisiting semi-parametric efficiency theory: the efficient influence function (e.g., for the counterfactual mean of a time-varying intervention), its emergent properties (i.e., sequential double robustness), and overview of the construction of efficient estimators. **Week 3:** Formulation of marginal structural models (MSMs) and longitudinal MSMs, MSMs as working projections, and efficient estimation of the parameters of an MSM.
 - Books and tutorials: [Hernán and Robins \(2024, Ch. 19–21\)](#), [VanderWeele \(2015, Ch. 6\)](#)
 - Primary literature: [Robins \(1986\)](#), [Tsiatis et al. \(2011\)](#), [Rotnitzky et al. \(2012\)](#), [van der Laan and Gruber \(2012\)](#), [Luedtke et al. \(2017\)](#), [Rotnitzky et al. \(2017\)](#), [Robins et al. \(2000\)](#), [Hernán et al. \(2000\)](#), [Neugebauer and van der Laan \(2007\)](#), [Cole and Hernán \(2008\)](#), [Rosenblum and van der Laan \(2010\)](#), [Petersen et al. \(2014\)](#), [Schnitzer et al. \(2014a\)](#), [Schnitzer et al. \(2014b\)](#)
6. **Born this way: Treatment effect heterogeneity and personalized interventions.** Causal effect heterogeneity and its connections to both effect modification and statistical interaction; the conditional average treatment effect and optimal dynamic treatment regimes.

- Time anticipated: 2 weeks (4 lectures)
 - Learning objectives: **II, IV, V**
 - Topics: **Week 1:** Measures of heterogeneity (i.e., interaction, effect modification) and differences between the associational and causal perspectives; the conditional average treatment effect (CATE)—challenges for identification and inference. **Week 2:** Optimal dynamic treatment regimes and tailoring rules based on expected benefit or harm (i.e., assignment based on the CATE); challenges posed by individualized treatment rules.
 - Books and tutorials: VanderWeele (2015, Ch. 9–10)
 - Primary literature: Rothwell (2005), Bland and Altman (2011), Moodie et al. (2007), Murphy (2003), Chakraborty et al. (2010), Zhang et al. (2012), Laber et al. (2014), Luedtke and van der Laan (2016), Luedtke and van der Laan (2017), Wager and Athey (2018), VanderWeele et al. (2019b), Nie and Wager (2021), van der Laan et al. (2024), Boileau et al. (2023), van der Laan and Petersen (2007), Bembom and van der Laan (2007), Qian and Murphy (2011), Zhao et al. (2012), Qiu et al. (2022)
7. **Dose makes the poison: The dose-response curve and modified treatment policies.** Defining causal effects suited to ordinal and continuous treatment variables; the causal dose-response curve; effects of interventions that would modify the treatment actually received.
- Time anticipated: 2 weeks (4 lectures)
 - Learning objectives: **II, IV, V**
 - Topics: **Week 1:** Defining and interpreting contrasts for continuous treatment variables; inferential perils of dichotomizing continuous treatment variables; on the definition and identification of the causal dose-response curve (CDRC) and some key challenges (e.g., structural positivity violations, pathwise differentiability). **Week 2:** Inference for the CDRC via (1) marginal structural models (as “working” projections) and (2) efficient estimation leveraging semi-parametric theory; definition and identification of the causal effects of modified treatment policies (MTPs); inference for the causal effects of MTPs.
 - Books and tutorials: Hernán and Robins (2024, Sec. 12.4)
 - Primary literature: Altman and Royston (2006), Imbens (2000), Hirano and Imbens (2004), Imai and Van Dyk (2004), Díaz and van der Laan (2012), Haneuse and Rotnitzky (2013), Young et al. (2014), Díaz et al. (2021), Kennedy et al. (2017), Westling et al. (2020), Westling (2022), van der Laan et al. (2023)
8. **Buying a stairway to heaven: Instrumental variables and non-identifiability.** Using an instrument for point- and set-identification; estimation of bounds in instrumental variables models; Mendelian randomization; negative controls and proximal causal inference.
- Time anticipated: 2 weeks (4 lectures)
 - Learning objectives: **II, VI**
 - Topics: **Week 1:** Brief history of instrumental variables; using instruments to address issues of measurement error and imperfect compliance; identification assumptions in the use of instruments (e.g., monotonicity); connections with principal stratification; the local average treatment effect curve and its nonparametric identification. **Week 2:** Biological phenomena as instrumental variables (i.e., Mendelian randomization)—some promises and pitfalls; negative controls as instrumental variables when some confounders may be unmeasured, and connections to the framework of proximal causal inference.
 - Books and tutorials: Hernán and Robins (2024, Ch. 16), Freedman (2009, Ch. 9), Pearl (2009, Ch. 8), Angrist and Pischke (2009, Ch. 4)

- Primary literature: Imbens and Angrist (1994), Angrist et al. (1996), Balke and Pearl (1997), Baiocchi et al. (2014), Small et al. (2017), Ogburn et al. (2015), Kennedy et al. (2017), Davey Smith and Ebrahim (2003), Didelez and Sheehan (2007), VanderWeele et al. (2014), Lipsitch et al. (2010), Miao et al. (2018)
9. **Where are your friends tonight? Interference, contagion, and spillover.** Violations of the stable unit treatment value assumption; between-unit dependence structures and their complications; identification of causal effects under common dependence structures.
- Time anticipated: 2 weeks (4 lectures)
 - Learning objectives: **II, VI**
 - Topics: **Week 1:** The no-interference part of the stable unit treatment value assumption and its plausibility; extensions of study designs and graphical models to accommodate interference; contagion versus interference; clustered treatment assignment and spillover causal effects. **Week 2:** Networks and network interference; relaxing the no-interference assumption in the identification of causal effects; overview of complications for inference on causal effect estimands when the no-interference assumption is weakened.
 - Books and tutorials: VanderWeele (2015, Ch. 14–15)
 - Primary literature: Rosenbaum (2007), Hudgens and Halloran (2008), Tchetgen Tchetgen and VanderWeele (2012), Ogburn and VanderWeele (2014), van der Laan (2014), Carnegie et al. (2016), Ogburn and VanderWeele (2017), Forastiere et al. (2021), Sävje et al. (2021), Zivich et al. (2022), Ogburn et al. (2024)
10. **Yeah, you wanted the truth: Sensibility and sensitivity analysis.** How randomization validates RCTs; epistemological uncertainty in drawing causal inferences from observational studies; sensitivity analysis in statistics and epidemiology; some assumption-lean approaches.
- Time anticipated: 1 week (2 lectures)
 - Learning objectives: **II, VI**
 - Topics: R.A. Fisher’s smoking–cancer controversy; when association really is causation; the Cornfield conditions in epidemiology; the “causal gap” and sensitivity analysis via its quantification; model-agnostic approaches to sensitivity analysis and the E-value.
 - Books and tutorials: N/A
 - Primary literature: Fisher (1957), Cornfield et al. (1959), Gilbert et al. (2003), Brumback et al. (2004), Shepherd et al. (2006), Díaz and van der Laan (2013), Ding and VanderWeele (2016), VanderWeele and Ding (2017), VanderWeele et al. (2019a), Haneuse et al. (2019), Zhao et al. (2019), Díaz et al. (2023)

Harvard Chan School Policies and Expectations

Inclusivity Statement

Diversity and inclusiveness are fundamental to public health education and practice. It is a requirement that you have an open mind and respect differences of all kinds. We share responsibility with you for creating a learning climate that is hospitable to all perspectives and cultures; please contact us if you have any concerns or suggestions.

Bias Related Incident Reporting

The Harvard Chan School believes all members of our community should be able to study and work in an environment where they feel safe and respected. As a mechanism to promote an inclusive

community, we have created an anonymous bias-related incident reporting system. If you have experienced bias, [please submit a report here](#) so that the administration can track and address concerns as they arise and to better support members of the Harvard Chan School community.

Title IX

For information on Harvard University policies and procedures and Title IX Resource Coordinators at the Harvard Chan School, please see:

- Harvard University Interim Title IX Sexual Harassment and Interim Other Sexual Misconduct policies and procedures: <https://titleix.harvard.edu/policies-procedures>
- Title IX Resource Coordinators: <https://titleix.harvard.edu/coordinators>
- Title IX Sexual Harassment and Other Sexual Misconduct resource guide: <https://titleix.harvard.edu/resource-guide>

Academic Integrity

You are expected to abide by the Harvard University and the Harvard T.H. Chan School of Public Health School's standards of Academic Integrity in conjunction with the expectations outlined in the Course Structure and Assessment of Learning section of this syllabus. All work submitted to meet course requirements is expected to be your own work. In the preparation of work submitted to meet course requirements, you should always take great care to distinguish your own ideas and knowledge from information derived from sources.

You must assume that collaboration in the completion of assignments is prohibited unless explicitly specified. You must acknowledge any collaboration and its extent in all submitted work. This requirement applies to collaboration on editing as well as collaboration on substance.

Should academic misconduct occur, you may be subject to disciplinary action as outlined in the Student Handbook. [See the Student Handbook](#) for additional policies related to academic integrity and disciplinary actions.

Accommodations for Students with Disabilities

Harvard University provides academic accommodations to students with disabilities. Any requests for academic accommodations should ideally be made before the first week of the semester, except for unusual circumstances, so arrangements can be made. You must register with a Local Disability Coordinator in the Office for Student Affairs to verify their eligibility for appropriate accommodations. Contact studentsupport@hsph.harvard.edu in all cases, including temporary disabilities.

Absence Due to Religious Holidays

According to Chapter 151c, Section 2B, of the General Laws of Massachusetts, any student in an educational or vocational training institution, other than a religious or denominational training institution, who is unable, because of his or her religious beliefs, to attend classes or to participate in any examination, study, or work requirement on a particular day shall be excused from any such examination or requirement which he or she may have missed because of such absence on any particular day, provided that such makeup examination or work shall not create an unreasonable burden upon the School. [See the Student Handbook](#) for more information.

Course Evaluation

Constructive feedback from students is a valuable resource for improving the teaching and learning experience. The feedback should be specific, focused, and respectful. It should address aspects of the course and teaching that are positive, as well as those which need improvement.

For registered students, submission of course evaluations is considered to be a School requirement because of their importance. The course evaluation system will open during the last week of the term and remain open for a three week period. You will gain access to your grades for the term after you have completed your course evaluations, and the course evaluation system has closed.

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