SAMSI PMED Course
Introduction to Dynamic Treatment Regimes, Spring 2019

ST/MA 810 (NCSU), STOR 894/MATH 892 (UNC), STA 790/MATH 790 (Duke)

Course:

Lectures:	W, 4:30 pm - 7:00 pm, SAMSI, 4501 Research Commons, 79 T.W. Alexander Drive, Durham, NC
Website:	`https://dtrcoursespring2019.wordpress.ncsu.edu/`
Prerequisites:	PhD level background in probability theory and statistical inference, basic knowledge of statistical models, programming skills

Instructors:

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Goal: This course will provide a comprehensive introduction to methodology for data-based development and evaluation of dynamic treatment regimes. A dynamic treatment regime is a set of sequential decision rules, each corresponding to a key point in a disease or disorder process at which a decision on the next treatment action must be made. Each rule takes patient information to that point as input and returns the treatment s/he should receive from among the available options, thus tailoring treatment decisions to a patient's individual characteristics. Dynamic treatment regimes formalize how clinicians make decisions in practice by synthesizing evolving information on a patient and are thus of considerable importance in precision medicine. Dynamic treatment regimes are also relevant in other contexts in which sequential decisions on interventions or policies must be made, as in education, engineering, economics and finance, and resource management.

Methods for estimation of dynamic treatment regimes and in particular optimal treatment regimes from data will be motivated and developed through a formal time-dependent causal inference framework. The gold standard study design for developing and evaluating regimes is the sequential multiple assignment randomized trial (SMART), considerations for which will be discussed. Inference for optimal treatment regimes is a nonstandard statistical problem and is thus notoriously difficult; an introduction to this challenge will be presented. Examples throughout the course will be drawn from cancer and other chronic disease research and research in the behavioral, educational, and other sciences.

Students completing this course will have a foundation in causal inference and fundamental results and methods for dynamic treatment regimes that will provide the basis for study of the rapidly evolving literature on dynamic treatment regimes and precision medicine.

This course is being offered in conjunction with the SAMSI year-long research Program on Statistical,

Mathematical, and Computational Methods for Precision Medicine (PMED).

Text: Lecture notes prepared by the instructors. These will be available on the course website. The notes are based on a forthcoming book by the instructors and colleagues.

Grading: S/U (NCSU) or equivalent (UNC, Duke). Criteria for receiving a satisfactory grade are completion of the homework assignments and attendance at all lectures. Of course, if you must miss a lecture due to illness, job interview, family matter, etc, this if fine, but please inform the instructors in advance if possible. If you do miss a lecture, you are responsible for the material covered.

Homework: There will be four (4) homework assignments. Homeworks will involve a combination of analytical problems, data analyses, and simulation studies. Students are permitted and even encouraged to work together on homework; however, each student must turn in his/her own solutions.

Tentative assignments/due dates are as follows; definitive information will be posted on the course website.

Homework 1	Chapters 1-3, due Wednesday, February 6
Homework 2	Chapters 3-5, due Wednesday, March 6
Homework 3	Chapters 5-6, due Wednesday, April 3
Homework 4	Chapters 7-8, due Wednesday, April 24

Computing/Software: Students are free to program in the language of their choice. Basic familiarity with R is desirable, as we may use the `DynTxRegime` package to carry out some analyses.

Tentative Schedule: Spring Break for all three campuses is 03/11 - 03/15.

01/09 – 1. Introduction

- Motivation (precision medicine, clinical decision making)
- Meaning of "dynamic" (dynamic vs static regimes)
- Basic framework (K-decision regime, notation, optimal regime)
- Data (SMARTs, observational studies)

01/09 - 01/16 – 2. Preliminaries: Basic Causal Inference

- Statistical models
- Point exposure studies
- Potential outcomes and causal inference (causal effect, average causal effect, identifiability assumptions)
- Estimation of causal effects via outcome regression
- Review of M-estimation
- Estimation of causal effects via the propensity score (stratification, inverse probability weighted estimator)
- Doubly robust estimation of causal effects (augmented inverse probability weighted estimators, efficient AIPW estimator)

01/16 - 01/30 – 3. Single Decision Treatment Regimes: Fundamentals

- Treatment regimes for a single decision point (potential outcomes, value)
- Estimation of the value of a fixed regime (identifiability assumptions, outcome regression estimator, IPW/AIPW estimators)

- Characterization of an optimal regime (in terms of potential outcomes, observed data)
- Estimation of an optimal regime (regression, A-learning, direct search IPW/AIPW, nonregularity)

01/30 - 02/6 – 4. Single Decision Treatment Regimes: Additional Methods

- Optimal regimes from a classification perspective (IPW/AIPW estimators)
- Outcome weighted learning
- Interpretable regimes via decision lists
- Additional approaches

02/13 - 02/27 – 5. Multiple Decision Treatment Regimes: Fundamentals

- Treatment regimes for multiple decision points (definition, recursive representation)
- Statistical framework (potential outcomes, feasible set of treatments and classes of regimes, value, data and data sources, identifiability assumptions))
- The g-computation algorithm
- Estimation of of the value of a fixed regime (via g-computation, IPW/AIPW estimators, marginal structural models)

03/06, 03/20 - 03/27 – 6. Optimal Multiple Decision Treatment Regimes

- Characterization of an optimal regime ((in terms of potential outcomes, observed data)
- Estimation of an optimal regime (Q-learning, direct search IPW/AIPW, backward iterative implementation, backward outcome weighted learning, A-learning, marginal structural models)

04/03 - 04/10 – 7. Sequential Multiple Assignment Randomized Trials (SMARTs)

- Rationale and building blocks for a SMART
- Example SMARTs
- Primary analyses and power analyses
- Extensions and special topics

04/17 - 04/24 – 8. Statistical Inference for Treatment Regimes

- Nonsmooth functionals and inference
- Inference with Q-learning
- Inference for the conditional, unconditional, and average value

Class Evaluations for NCSU Students: Online class evaluations will be available for students to complete from 8:00 am on April 15, 2019 through 8:00 am on April 29, 2018. Students will receive an email message directing them to a website where they can login using their Unity ID and complete evaluations. All evaluations are confidential; instructors will not know how any one student responded to any question, and students will not know the ratings for any instructors.

Academic Integrity: The instructors expect that students will abide by their institution's policies on academic integrity. At NCSU, the University policy on academic integrity in the Code of Student Conduct Policy (POL 11.35.1) is available at `https://policies.ncsu.edu/policy/pol-11-35-01`. As noted above, students *may* consult with one another on the homework, similar to how real researchers

might consult with one another. However, students engaging in direct copying of the work or computer programs of fellow students will be considered in violation of policies on academic integrity.

Students with Disabilities: Reasonable accommodations will be made for students with verifiable disabilities. For NCSU students, to take advantage of available accommodations, students must register with Disability Services Office (DSO) at 2221 Student Health Services Building, Campus Box 7509, 515-7653; see `http://dso.dasa.ncsu.edu/`. For more information on NCSU's policy on working with students with disabilities, please see the Academic Accommodations for Students with Disabilities Regulation (REG02.20.01) (`https://policies.ncsu.edu/regulation/reg-02-20-01/`).