Adaptive Treatment Strategies

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Adaptive Treatment Strategies

- "...are individually tailored sequences of treatments, with treatment type and dosage adapted to the patient."

- "Adaptive"
  - Decisions are tailored to individual patients at the time of treatment

- "Strategy"
  - A sequence of treatment decisions unfolding over time
Adaptive Treatment Strategies?

- Sounds like “Clinical Practice”
  - Doctors tailor treatments to individual patients, and often have a long-range strategy in mind.
- We want to operationalize this
  - We can then construct adaptive treatment strategies from data.
Why Adaptive Treatment Strategies?

- When do doctors use them? Chronic illness.
- Adaptive (tailoring)
  - What works for one patient may not work for another.
- Strategy (sequencing)
  - What works now may not work later.
  - There may be cycles of remission/relapse.
  - **Treatments provide both therapeutic and diagnostic benefit.**
Example: Depression*

- Provide Citalopram for up to 12 weeks.
  - If the patient **remit**, defined by a QIDS-SR depression rating score $\leq 5$, continue to provide Citalopram and **monitor**.
  - Otherwise if the patient **does not remit**, 
    - If the patient’s QIDS-SR score is $> 15$, switch treatment to **Bupropion**.
    - If the patient’s QIDS-SR score is $\leq 15$, switch treatment to **Venlafaxine**.

- Here, treatments are *adapted* using QIDS-SR as a tailoring variable, and the *strategy* has up to two treatments

*I am not a psychiatrist! This is a made-up example. Don’t try this at home.*
- Provide **CIT**alopram for up to 12 weeks.
  - If the patient **remits**, defined by a QIDS-SR depression rating score $\leq 5$, continue to provide **CIT**alopram and monitor.
  - Otherwise if the patient **does not remit**,
    - If the patient’s QIDS-SR score is $> 15$, switch treatment to **BUP**ropion.
    - If the patient’s QIDS-SR score is $\leq 15$, switch treatment to **VEN**lafaxine.
How would we develop such a treatment strategy?

- **From Data**
  - Longitudinal data collected from patients as they follow different paths through a proposed set of possible treatment strategies

- **Sequenced Multiple Assignment Randomized Trials**
  - Pinpoint a *small number* of critical decisions per patient to investigate
  - A randomization takes place at each critical decision (multiple randomizations for each patient)
  - Goal is to inform the construction of an adaptive treatment strategy.
SMART Design Principles

- At each stage, restrict class of treatments only by ethical, feasibility or strong scientific considerations. **Use a summary instead of complicated intermediate outcomes** to restrict class of next treatments.

- **But collect intermediate outcomes** that might be useful in ascertaining for whom each treatment works best. This information might enter into the adaptive treatment strategy.
How might we arrive at this strategy?
Run a randomized trial
Start at the end of the study
Identify the best final treatment
Work backwards in time toward the beginning of the study
Analyses can use patient characteristics/outcomes to provide evidence for a more sophisticated adaptive treatment strategy.

How might we arrive at this strategy?
CIT

Remission

WebDM
Monitor

No Remission

BUP
VEN

SER

Remission

WebDM
Monitor

No Remission

BUP
VEN
CIT

Remission → Monitor

No Remission → BUP

VEN

SER

Remission → Monitor

No Remission → BUP

VEN
CIT
Remission
No Remission
SER
Remission
No Remission

QIDS > 15
BUP
QIDS <= 15
VEN

Monitor

Monitor

QIDS > 15
BUP
QIDS <= 15
VEN
CIT

Remission

No Remission

QIDS > 15 → Monitor
QIDS <= 15 → BUP

VEN
- Run a randomized trial
- Start at the end of the study
- Identify the best final treatment
- Work backwards in time toward the beginning of the study
- Analyses can use patient characteristics/outcomes to provide evidence for a more sophisticated adaptive treatment strategy.
Analyses To Date

- **STAR*D**: Sequenced Treatment Alternatives to Relive Depression
  - NIMH-funded, ~4000 patients, ~4 stages of treatment
- **CATIE**: Clinical Antipsychotic Trials of Intervention Effectiveness
  - NIMH-funded, ~1600 patients, ~3 phases of treatment
- Both of these predate SMART, and are quite complicated.
- We have done preliminary analyses of these studies.
Ongoing Research

- How do we know if we’ve really constructed a good strategy?
  - Eric Laber and I are working on measures of confidence for strategy quality.
- Can the data inform us about which quantities are useful for selecting treatments?
  - Peng Zhang is working on selecting covariates for decision points.
- What if we are interested in an objective that is censored?
  - Zhiguo Li is working on incorporating survival analysis techniques.
Thank You

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