



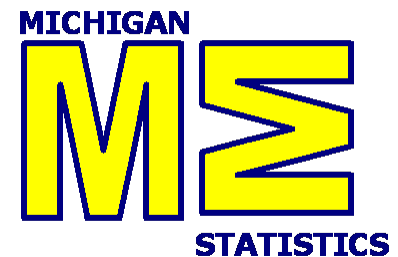
# *Adaptive Health Interventions*

## Module 1

Getting SMART About Developing Individualized  
Adaptive Health Interventions

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# Before We Begin...Throughout This Module, Keep in Mind the End-of-Module Practice Exercise and Discussion Question

**Exercise:** *Write/draw one simple AHI to address a disorder in your field.*

**Discussion Question:** *How are AHIs similar/different to the types of behavioral interventions we typically think about?*



# Outline

- What are Adaptive Health Interventions?
- Why use Adaptive Health Interventions?
- Adaptive Health Intervention Design Goals
- What does an Adaptive Health Intervention include?
- Summary & Discussion



# Adaptive Health Interventions

- Are individually-tailored time-varying treatments composed of
  - a sequence of critical treatment decisions
  - tailoring variables
  - decision rules, one per critical decision; decision rules input tailoring variables and output individualized treatment recommendation(s).
- Operationalized guides for clinical practice.



## Example: Adaptive Aftercare for Alcohol Dependent Individuals

- **Population:** alcohol dependent individuals who have graduated from an intensive outpatient program
- **Overall goal:** prevent relapse to alcohol abuse
- **Critical treatment decisions:** which treatment to provide first?; which treatment to provide second?
- **Tailoring variable:** heavy drinking days



## Decision Rules

All alcohol dependent individuals are provided Naltrexone along with Medical Management upon graduation.

**IF** an individual experiences 3 or more heavy drinking days prior to 8 weeks

**THEN** the individual's Naltrexone treatment is augmented with Combine Behavioral Intervention.

**ELSE IF** the individual successfully completes 8 weeks with fewer than 3 heavy drinking days

**THEN** the individual is provided a prescription to Naltrexone along with Telephone Disease Management.



# Adaptive Health Interventions

- From the individual/patient/client's point of view: a sequence of (individualized) treatments
- From the clinician's point of view: a sequence of decision rules that recommend one or more treatments at each critical decision.



# More examples of critical treatment decisions

- How long should we use the first treatment before transitioning to a maintenance/relapse prevention treatment? And which treatment should this be?
- How long should we try the first treatment before declaring non-response and moving to another treatment? And which treatment should this be?
- How should a treatment be delivered?
- How do we re-engage patients who are non-adherent?





# More examples of tailoring variables

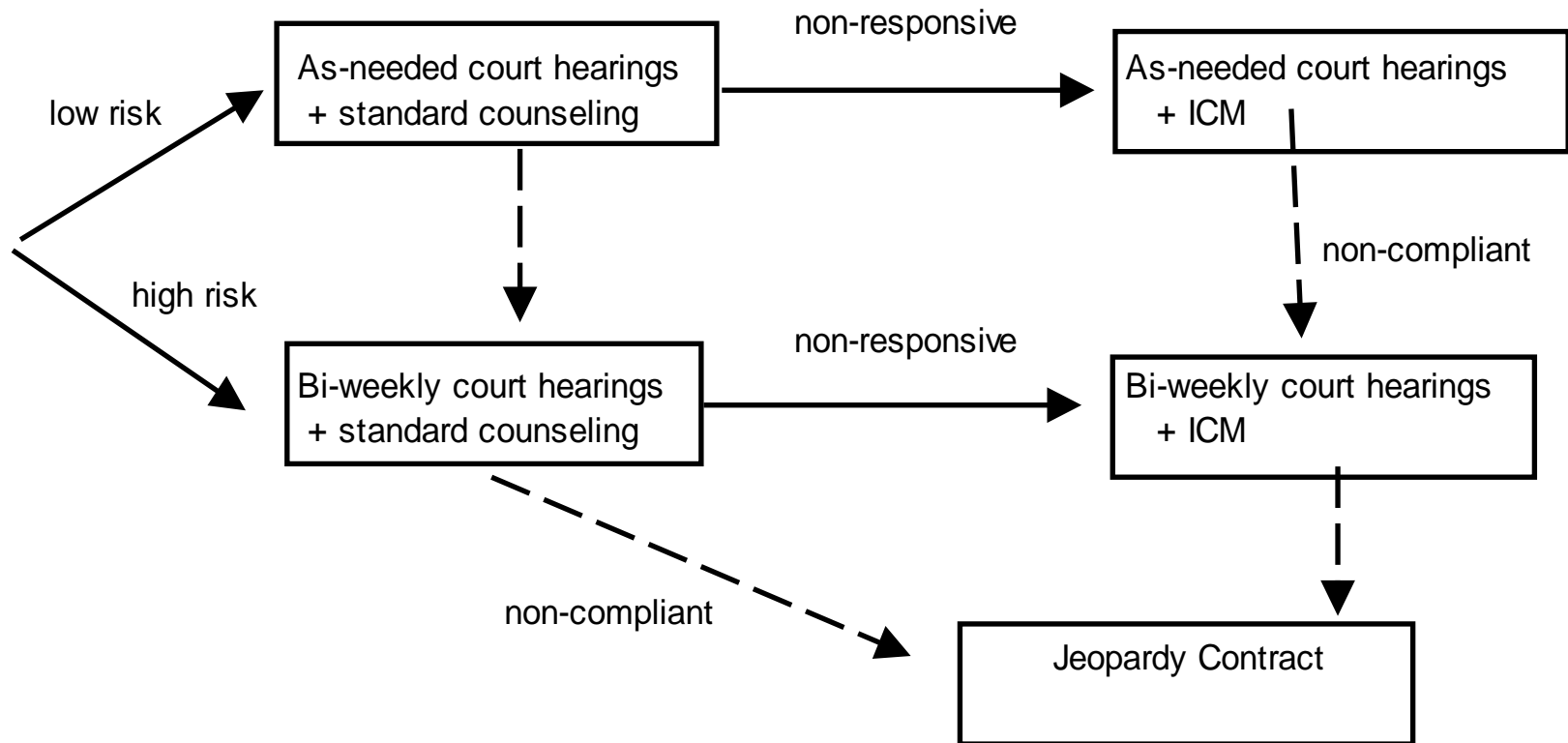
- Age, Severity of illness, Presence of comorbid mental or physical conditions, Quality of family support, Past failed treatments
- Adherence to present treatment, Side effects while on present treatment, Symptoms while on present treatment
- Candidate tailoring variables include moderators, mediators or short-term outcomes or even proximal measures of the ultimate outcome of interest



# Example: Adaptive Drug Court Program

- **Population:** drug abusing offenders assigned to drug court
- **Overall goal:** minimize recidivism and drug use
- **Critical treatment decisions:** which treatment to provide first?; which treatment to provide second?
- Marlowe et al. (2008, 2009, 2012)

# Adaptive Drug Court Program



# Adaptive Drug Court Program

## Tailoring Variables

- Stage 1 Tailoring Variables: ASPD, Prior formal drug abuse treatment
- Stage 2 Tailoring Variables: Attendance at counseling sessions, Infractions, Providing scheduled urine screens, Positive urine specimens



# Adaptive Drug Court Program

## Decision Rules

- Stage 1 Decision Rule: Provide group-based drug abuse counseling to all. **If** ASPD or Prior formal drug abuse treatment **then** provide bi-weekly court hearings. **Else** provide as-needed court hearings.
- Stage 2 Decision Rule: **If** committed an infraction or missed 2 or more counseling sessions or missed 2 or more urine screens **then** step up court supervision. **Else if** 2 or more positive urine specimens **then** step up treatment to ICM. **Else** continue on stage 1.



# Other Examples of Adaptive Health Interventions

- Brooner et al. (2002, 2007) Treatment of Opioid Addiction
- McKay (2009) Treatment of Substance Use Disorders
- HIV-Causal Collaboration (2011) Treatment of HIV
- Rush et al. (2003) Treatment of Depression



# Outline

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# Why Adaptive Health Interventions?

---or, better put---

## Why Do We Need to Consider a Sequence of Treatments?

- 1) High heterogeneity in need for or response to any one treatment

What works for one person may not work for another, thus often need a sequence of treatments just to obtain an acute response





# Why Adaptive Health Interventions?

## 2) Chronic or Waxing and Waning Course

Improvement often marred by relapse

Intervals during which more intense treatment is required alternate with intervals in which less treatment is sufficient




# Why Adaptive Health Interventions?

## 3) Treatment is burdensome

Treatment required over long time periods is burdensome

Non-adherence leads to relapse or loss of positive effect



## Why not combine all possible efficacious therapies and provide all of these to the patient now and in the future?

- Treatment incurs side effects and substantial burden, particularly over longer time periods.
- Problems with adherence:
  - Variations of treatment or different delivery mechanisms may increase adherence
  - Excessive treatment may lead to non-adherence
- Treatment is costly (Would like to devote additional resources to patients with more severe problems)

More is not always better!



# Outline

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# Main Adaptive Health Intervention Design Goal is to Improve Outcomes

- Maximize the strength of the Adaptive Health Intervention
  - by well chosen and measured tailoring variables, and
  - by well conceived and implemented decision rules



# Another Important Adaptive Health Intervention Design Goal is to...

- Maximize replicability in future real-world implementation conditions (primary) and experiments/research studies (secondary)
  - by clearly defining the treatment strategy &
  - by high quality fidelity of implementation



# Recall the definition of an AHI

- **Adaptive Health Interventions** are individually tailored time-varying treatments composed of
  - a sequence of critical treatment decisions
  - tailoring variables
  - decision rules, one per critical decision; decision rules input tailoring variables and output individualized treatment recommendation(s).



# Considerations re Critical Decisions

- Which treatment decisions are critical and need to be guided (e.g. manualized, structured) ?
- Which decisions are likely influenced by non-systematic variance (due to issues unrelated to individual)?
- Which decisions are likely influenced by systematic variance (due to issues related to individual)? (may lead to bias)





# Adaptive Health Intervention Design Considerations

- Choice of the Tailoring Variable
- Measurement of the Tailoring Variable
- Decision Rules linking Tailoring Variables to Treatment Decisions
- Implementation of the Decision Rules



# Primary Consideration re Choice of Tailoring Variables

- Significant differences in effect sizes in a comparison of fixed treatments as a function of the candidate tailoring variable.
  - That is, some values of the tailoring variable should indicate a particular treatment decision is best while other values of the tailoring variable should indicate that a different treatment decision is best.



# Adaptive Aftercare for Alcohol Dependent Individuals

- Hypothetical Study (do this study in your head): Alcohol dependent individuals on NTX; after 8 weeks randomize individuals to continue on NTX or to an augment of NTX with CBI
- Result of hypothetical study: Among individuals who had returned to heavy drinking, NTX+CBI performs better than NTX only. However there is little or no difference for individuals who were maintaining a more sober lifestyle.



# Adaptive Aftercare for Alcohol Dependent Individuals

- Individuals who return to heavy drinking while on Naltrexone (NTX) need additional help to maintain a non-drinking lifestyle.
- This suggests the tailoring variable is heavy drinking
- Providing CBI to non-heavy drinkers is costly (and no better than continuing NTX alone).
- Implication: Provide NTX+CBI to individuals who are drinking heavily. NTX only is sufficient for individuals who are maintaining a non-heavy drinking lifestyle.



# Technical Interlude!

$S$  = tailoring variable (heavy drinking)

$Tx$  = treatment type (NTX vs NTX+CBI)

$Y$  = primary outcome (days abstinent, high is preferred)

$$Y = \beta_0 + \beta_1 S + \beta_2 Tx + \beta_3 S Tx + error$$

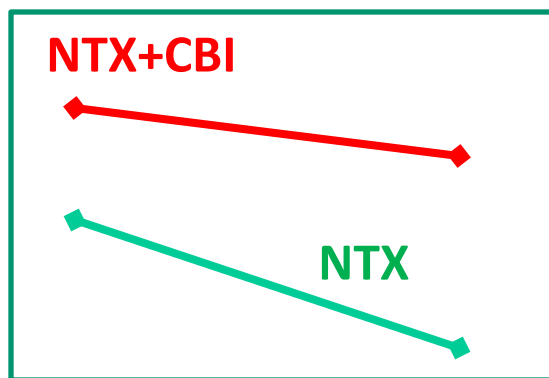
$$= \beta_0 + \beta_1 S + (\beta_2 + \beta_3 S)Tx + error$$

If  $(\beta_2 + \beta_3 S)$  is zero or negative for some  $S$  and positive for others, then  $S$  is a tailoring variable.

Y

Future Days Abstinent  
(High is better)

S=0                      S=1  
no heavy drinking      returned to heavy  
drinking



**S is a moderator variable** because the magnitude of the effect of Tx=NTX+CBI versus Tx=NTX differs by levels of S.

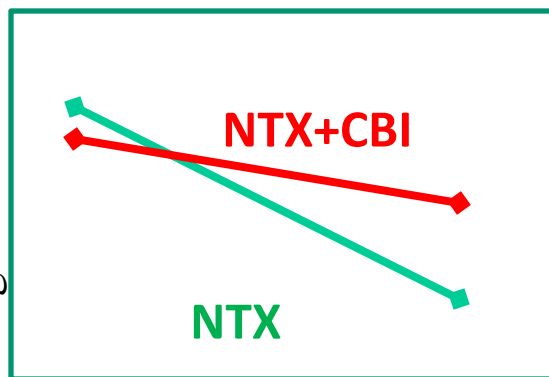
**However, S is not a tailoring variable:** Tx=NTX+CBI is better for all subjects.

BETTER

Y

High is better

S=0                      S=1



**S is a weak tailoring variable** because the direction of the effect of Tx=NTX+CBI versus Tx=NTX differs by levels of S but magnitude is small.

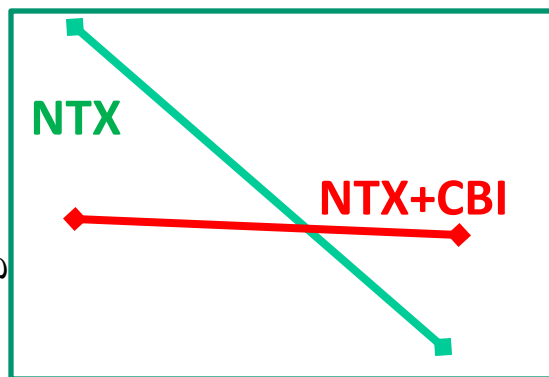
**S is somewhat prescriptive:** Offer Tx=NTX+CBI to S=1 subjects; the difference in effects is not substantial for S=0 subjects.

BEST

Y

High is better

S=0                      S=1



**S is a strong tailoring variable** because the direction of the effect of Tx=NTX+CBI versus Tx=NTX differs by levels of S.

**S is very prescriptive:** Offer Tx=NTX to S=0 subjects; offer Tx=NTX+CBI to S=1 subjects. Large magnitudes of clinical significance.



# Tailoring variables

- Tailoring variables include baseline tailoring variables and time-varying tailoring variables
- Tailoring variables are moderators of subsequent treatment; they may also be
  - Baseline variables
  - Mediators
  - Short-term outcomes
  - Proximal measures of the ultimate outcome of interest.
  - Time-varying versions of all of the above



# Measurement of Tailoring Variables

**SKIP  
SLIDE**

- Reliability -- high signal to noise ratio
- Validity -- unbiased





# Measurement: Timing of Tailoring Variable Collection

- Tailoring variable should be assessed at sufficiently frequent intervals so that (non) response is detected in a timely manner.
- Too infrequent and an individual's condition may deteriorate so much that readily available rescue options are ineffective.
- Too frequent assessment may result in dependence or non-adherence

# Adaptive Aftercare for Alcohol Dependent Individuals

- Example:** The tailoring variable is heavy drinking days. Should we measure this variable weekly or twice a week?



# Derivation of Decision Rules

- Articulate a theoretical model for how treatment effect on key outcomes should differ across values of the tailoring variable.
- Use prior clinical experience.
- Use prior experimental and observational studies.
- Discuss with research team and clinical staff, “What dosage would be best for people with this value on the tailoring variable?”



# Derivation of Decision Rules

- Good decision rules are objective, are operationalized.
- Strive for comprehensive rules (this is hard!) – cover situations that can occur in practice, including when the tailoring variable is missing or unavailable.

# Operationalize the Decision Rules

- Bad:** Individuals who are drinking excessively are switched to NTX+MM+CBI
- Better:** Individuals who experience 3 or more heavy drinking days are non-responders and are switched to NTX+MM+CBI.
- Best:** As soon as 3 or more heavy drinking days occur within weeks 3-8 while on NTX+MM, the person is declared a non-responder and switched to NTX+MM+CBI. Otherwise, remain on NTX+MM.



# Adaptive Aftercare for Alcohol Dependent Individuals

- **Example:** Suppose an individual misses his weekly clinic visit. Then the number of heavy drinking days in the prior week is missing.
- Should we wait until the following week to decide if the individual is a non-responder or should we call the individual a non-responder immediately?
  - This is a clinical (treatment design) issue.

# Summary & Discussion

- Adaptive Health Interventions are attractive alternatives to fixed treatments

if in a comparable fixed treatment, significant variation in treatment effect would be expected as a function of identifiable tailoring variables, across participants and/or within participants over time

# Summary & Discussion

Adaptive Health Interventions enhance the potency of the treatment if

- by increasing salience and negative effects, they improve adherence
- by reducing waste it becomes possible to devote additional resources to higher-risk individuals who can benefit from them.



# Summary & Discussion

- Research is needed to build a theoretical literature that can provide guidance:
  - in identifying tailoring variables,
  - in the development of reliable and valid indices of the tailoring variables that can be used in the course of repeated clinical assessments
  - on the important role of clinical judgment.

# Questions?

## More information

L.M Collins, S.A. Murphy and K.A. Bierman (2004), A Conceptual Framework for Adaptive Preventive Interventions, *Prevention Science* 5:185-196.

S.A. Murphy & J.R. McKay (2004), Adaptive Treatment Strategies: an Emerging Approach for Improving Treatment Effectiveness. Clinical Science (Newsletter of the American Psychological Association Division 12, section III: The Society for the Science of Clinical Psychology) Winter 2003/Spring 2004

L.M. Collins, S.A. Murphy, V. Nair & V. Strecher (2005), A Strategy for Optimizing and Evaluating Behavioral Interventions, *Annals of Behavioral Medicine*. 30:65-73.

S.A. Murphy, L.M. Collins, A.J. Rush (2007). Customizing Treatment to the Patient: Adaptive Treatment Strategies. *Drug and Alcohol Dependence*,. 88(2):S1-S72.

# Discussion & Practice Exercise

**Exercise:** *Write/draw one simple AHI to address a disorder in your field. How to do this: a) Identify two sequenced critical decision points. b) Identify a tailoring variable for each decision point. c) Identify a treatment option for each value/level of the tailoring variable.*

**Discussion Question:** *How are AHIs similar/different to the types of behavioral interventions we typically think about?*

# Extra Slides



# Another Important Adaptive Health Intervention Design Goal is to...

- Maximize replicability in future experimental and real-world implementation conditions
  - by clearly defining the treatment strategy & by fidelity of implementation



# Implementation of the AHI in a Trial

- Try to implement decision rules universally, applying them consistently across subjects, time, site & staff members.
- We want to avoid treating some subjects differently from others due to factors that are not in the decision rules.
  - The non-systematic component introduces random error and increases variance.
  - The systematic component harms replicability by increasing the plausibility of alternative explanations for the (in)effectiveness of the Adaptive Health Intervention.



# Implementation of the AHI in a Trial


- Try to implement rules universally, applying them consistently across subjects, time, site & staff members.
- Staff may be resistant to implementing the rules universally because
  - Missing but needed tailoring variables
  - Measured tailoring variable lacks validity
  - The way the tailoring variable weighs different criteria may be questioned.
  - Decision rules are ambiguous
  - Insufficient training



# Implementation of the AHI in a Trial

- Exceptions to the rules should be made only after group discussions and with group agreement.
- If it is necessary to make an exception, document this so you can describe the implemented treatment.
- Document the value of the tailoring variable.





# Role of Clinical Judgment in Derivation of the Decision Rules

How should the decision rules include clinical judgment? How should clinical judgment be structured?

- Via structured measurements that enter into tailoring variable?
- Via a choice among a restricted set of options?