Introduction to Adaptive Interventions

What are adaptive interventions (AI)?
What are the pieces that make up an AI?
Examples of AIs: Compare simple versus deeply-tailored AIs.
Discuss why AIs are needed
Utilizing theory to design an AI
How AIs can be used to inform clinical practice
<table>
<thead>
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<th>Module 1 Learning Goals</th>
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<tr>
<td>• To understand the components that make up an Adaptive Intervention (AI).</td>
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<td>• To understand settings in which AIs are needed</td>
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<td>• To understand the difference between a well-operationalized vs a poorly operationalized AI</td>
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<td>• To begin to identify critical scientific questions (gaps in your area of study) related to developing a high-quality AI</td>
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We will have practice exercises (leading to interesting discussions) at the end of this module aimed at helping to ensure you achieve these learning goals.
Outline

- What are Adaptive Interventions?
- Why use Adaptive Interventions?
- Adaptive Intervention Design Goals
- Summary & Discussion
AIs are individualized sequences of treatments

AIs operationalize clinical practice, and in fact it mimics how we make decisions in real-life.
Example

- Adaptive drug court program for drug abusing offenders
  - The goal: Minimize recidivism and drug use
  - Operationalized by graduating from the drug court program
  - Marlowe et al., 2008; 2009; 2012)
Adaptive Drug Court Program

Low risk
As-needed court hearings + standard counseling
Non-compliant
Non-responsive
As-needed court hearing + ICM
Non-compliant

High risk
Bi-weekly court hearings + standard counseling
Non-compliant
Non-responsive
Bi-weekly court hearing + ICM
Non-compliant

Jeopardy contract: “zero tolerance”
First Stage Decision Rule

At point of entry into the program:

If risk = low
Then, stage 1 intervention = \{As-needed + SC\}

Else if risk = high
Then, stage 1 intervention = \{Bi-weekly + SC\}

5. Outcomes:
Distal \rightarrow Long-term goal of intervention:
Program graduation (14 consecutive weekly negative drug urine specimens)
Proximal \rightarrow Short-term goal of decision rules:
Compliance and response in the course of intervention (mediator)

2. Tailoring Variable:
Patient information used to make treatment decisions

3. Intervention options:
Type/Dose

1. Decision Point:
A time in which treatment options should be considered based on patient information (Yoshino et al., 2009)
AI: 5 Elements

1. Decision Points ➔ Trigger
2. Tailoring Variable ➔ Monitoring
3. Decision rule ➔ Individualizing
4. Intervention Options ➔ Delivering
5. Proximal + Distal Outcomes ➔ Guide

Adaptation process
Various Types of AI

• Two dimensions:
  1. Adaptation Singular/Sequential
     • ***Singular***: for each participant, treatment is individualized at most once
     • ***Sequential***: for some (or all) of the participants, treatment may be individualized multiple times
  2. Adaptation Static/Dynamic
     • ***Static***: adaptation based on information that is unlikely to change over time as a result of treatment (e.g., personality, baseline)
     • ***Dynamic***: adaptation based on information that can change over time as a result of treatment (e.g., response status, engagement in treatment).
## Various Types of AI: Examples

<table>
<thead>
<tr>
<th>Adaptation</th>
<th>Dynamic</th>
<th>Static</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Singular</strong></td>
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</tbody>
</table>
**At program entry**
Stage 1 = As-needed + SC  
**Then, at week 4**
If program response = no
Then, stage 2 = {more SC}
Else if program response = yes
Then, stage 2 = {continue} | 
**At point of entry into the program**
If baseline risk = low
Then, stage 1 = {As-needed + SC}
Else if baseline risk = high
Then, stage 1 = {Bi-weekly + SC} |
| **Sequential** | 
**At point of entry into the program**
If baseline risk = low
Then, stage 1 = {As-needed + SC}
Else if baseline risk = high
Then, stage 1 = {Bi-weekly + SC}
**Then, at week 4**
If program response = no
Then, stage 2 = {more SC}
Else if program response = yes
Then, stage 2 = {continue} | 
**At point of entry into the program**
If baseline risk = low
Then, stage 1 = {As-needed + SC}
Else if baseline risk = high
Then, stage 1 = {Bi-weekly + SC}
**Then, at week 4**
If age < 18
Then, stage 2 = {maintenance prog. A}
Else if age ≥ 18
Then, stage 2 = {maintenance prog. B} |
About JITAIIs…

1. Decision Points ➔ Trigger
2. Tailoring Variable ➔ •Monitoring
3. Decision rule ➔ •Individualizing
4. Intervention Options ➔ •Delivering
5. Proximal + Distal Outcomes ➔ Guide

Any Time

Adaptation Process

Momentary
AIs provide a paradigm by which to improve clinical, policy, and public health practice which by its nature is often adaptive.

Individualization/personalization/tailoring is achieved by use of a decision rules at each decision point. Each decision rule takes accumulated, ongoing information about the unit (e.g., individual) including past response, adherence, burden, etc., and outputs a recommended, individualized treatment tailored to the circumstances of that unit.

A scientist first develops an AI. Later, they are used by clinicians to guide their thinking in actual clinical practice.

We use the term AI but others might use the terms: dynamic treatment regimes, treatment algorithms, stepped care models, expert systems, adaptive interventions, treatment protocols.
More Examples of Decisions

• About treatment **timing:**
  - How long should we use the first treatment
    - before transitioning to a maintenance/relapse prevention treatment? And which treatment should this be?
    - before declaring non-response and moving to another treatment? And which treatment should this be?
  
• About treatment **engagement:**
  - How do we re-engage patients who are non-adherent?
Other critical decisions: The individual’s participation in treatment (e.g., who should set health-related goals, the participant or the care provider?), the location of the intervention offered (e.g., is it...
**Even More Examples …**

• About intervention **tactics**
  
  − For people who do **not respond** well to treatment A
    - Should we enhance the intensity of A or add B
    - Should we enhance the intensity of A or switch to B
    - Should we continue with A or step-up to C
  
  − For people who **respond** well to treatment A
    - Should we continue or step-down
    - Should we stop immediately or gradually
    - Do we need a booster or not
More Examples of Tailoring Variables

- **Static:**
  age, gender, personality, SES, baseline severity of illness, comorbid conditions, past failed treatment, family background, baseline social support

- **Dynamic:**
  Adherence to present treatment, side effects while on present treatment, symptoms while on present treatment, social support during treatment

Other tailoring variables are genetics, family background, proteomics
Other Examples of Adaptive Interventions

- McKay (2005; 2009): AIs for alcohol and drug-use disorders
- Booner et al., (2004): Adaptive behavioral contingencies to enhance adherence to methadone treatment in opioid-dependent patients
- Rush et al. (2003) medication algorithms for treating depression, schizophrenia, and bipolar disorders


Adapt the intensity of family-based interventions to the needs and motivation of the family.
Aim: reduce substance use and antisocial behavior among students ages 11–17.


Adapt the types of engagement strategy to the engagement status of the patient in treatment
How to extend behavioral and pharmacotherapy interventions for alcohol and drug-use disorders


Population: opioid-dependent patients (n = 127) newly admitted to an ambulatory treatment program that provides methadone.

Two types of adaptation:
During the program, they adapted the type of behavioral contingencies to promote counseling attendance and drug negative urine specimens (e.g., latter medication time if you missed a session, discharge from the program if you missed too many sessions).
They also provided a rescue intervention if the participant was classified as a non-responder (defined as a 50% or higher rate of missed counseling sessions or a 50% or higher rate of drug-positive urine specimens (or both) over the first 90 days of randomized care).


Population: patienti with major depression, schizophrenia, bipolar disorders
Type of adaptation: mediation algorithms to guide clinical care. Clinicians could deviate from the algorithms.

Decision rules are wellspecified
Outline

- What are Adaptive Interventions?
- Why use Adaptive Interventions?
- Adaptive Intervention Design Goals
- Summary & Discussion
Why Adaptive Interventions?

1) High **heterogeneity** in need for or response to any one treatment
   - What works for one person may not work for another,
   - Thus, need to
     • Detect early signs of treatment failure
     • and modify the treatment
     • to prevent ultimate treatment failure

This is really “why do we need to consider a sequence of treatments?”
Why Adaptive Interventions?

2) Chronic or **waxing and waning** course of disorders
   - Improvement is not linear
   - Need to identify:
     - Intervals during which more intense treatment is required
     - Intervals in which less treatment is sufficient
     - Adapt treatment intensity accordingly

This is really “why do we need to consider a sequence of treatments?”
Why Adaptive Interventions?

3) When treatment is **burdensome**
   - Side effects
   - Patient required to invest Time/Effort
   - Burden leads to non-adherence
   - Non-adherence reduces positive intervention effect

   - Need to:
     - Identify signs of burden
     - Modify intensity based on signs of burden

Burden==exceeds personal resources
Why Adaptive Interventions?

4) Many treatments are **costly**
- Certain treatments can be very expensive
- Resources are often limited
- Difficulties in scalability
- Need to:
  - Try less expensive treatment first
  - Offer more costly treatments to people who need it
Why Adaptive Interventions?

5) Motivations for adapting mHealth
   - **Boredom**
     - Need to change delivery modalities
   - **Cognitive overload**
     - Sequence and adapt content to people’s attention capacity
   - **Habituation:** repetition → lower arousal
     - Stop intervention from time to time, introduce new content, change presentation.
Outline

- What are Adaptive Interventions?
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CLARIFICATION NOTE: Here we are discussing the design of the adaptive intervention (hence “treatment design”). We are not discussing the design of a trial to inform the development of an AI—that’s the next module on “trial design”.

Use behavioral/social/biological theory, clinical experience, expert opinion, consultation with clinical staff, review of extant literature to help select the tailoring variables and form the decision rules.

**Design Goals**

- Help me build a tech-based AI for at-risk drinkers:
  - Why at-risk drinking?
    - Exceeding gender-specific weekly/daily limits at least once in past 3 months
    - Associated with serious adverse consequences:
      - Subsequent alcohol use disorders, injuries, accidents etc.
  - Why tech-based (mobile + web)
    - Approach was found to be effective in reducing at-risk drinking
    - Require substantially lower delivery costs relative to in person alternatives.

Weekly limits: Men, > 14; Women, > 7 drinks per week
Daily limits: Men, ≥ 5; Women, ≥ 4 drinks per day
CLARIFICATION NOTE: Here we are discussing the design of the adaptive intervention (hence “treatment design”). We are not discussing the design of a trial to inform the development of an AI—that’s the next module on “trial design”.

Select intervention options that will affect my proximal outcome.

Use behavioral/social/biological theory, clinical experience, expert opinion, consultation with clinical staff, review of extant literature to help select the tailoring variables and form the decision rules.

**Design Goals**

1. Maximize the **strength** of the AI (not the trial)
   - This can be achieved by:
     - Well defined proximal and distal outcomes,
     - Select effective intervention options
     - Well chosen tailoring variables,
     - Well measured tailoring variables,
     - Well formulated decision rules,
     - Well implemented decision rules
Fidelity of implementation -- intervention is delivered in the way it was designed to be delivered.

Design Goals

2. Maximize replicability
   – in future experimental conditions, and
   – and real-world implementation conditions
   – We have confidence in an AI when its effects are replicable with different samples, clinical staff, locations, etc.
   – This can be achieved by
     • Clear articulation of the AI (make AI explicit)
     • Fidelity of implementation
     • Think carefully about and plan for non-standard scenarios that may arise
Recall: 5 Elements of AI

1. Decision Points ➔ Trigger
2. Tailoring Variable ➔ • Monitoring
3. Decision rule ➔ • Individualizing
4. Intervention Options ➔ • Delivering
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Adaptation process
I select this outcome because it is clinically meaningful

Often there are various ways to achieve the distal outcome. For, both stress reduction and reducing social norms for drinking are known as useful mechanisms to reduce heavy drinking.

I can choose to target both, or I can choose to target just one (given practical considerations).

Selecting a proximal outcome is important because it will guide the type of intervention you will offer, and/or the tailoring variable that you will select.

If my proximal outcome is stress reduction, my intervention options might be designed to reduce stress (e.g., stress-management intervention), and/or I will adapt the intervention based on the participant’s level of stress.
Response-based pathways are obvious short-term information that is part of the distal outcome: these are proximal measures that are part of the distal outcome, they form the distal outcome.

Performance-based: these are mechanisms (behaviors, experiences and feelings) that predict the distal outcome.

Engagement: these are indicators of engagement and adherence that predict the distal outcome.

Often– the distal outcome is a combination of all pathways.

Selecting a proximal outcome is important because it will guide the type of intervention you will offer, and/or the tailoring variable that you will select.

If my proximal outcome is stress reduction, my intervention options might be designed to reduce stress (e.g., stress-management intervention), and/or I will adapt the intervention based on the participant’s level of stress.
Here, we select intervention options based on the proximal outcomes we selected earlier.
Design Considerations: Decision Points

1. When do you need to make decisions/What kind

- What type of delivery modes
  - 1) Mobile-based
  - 2) Web-based

- What type of content:
  - 1) Stress Management
  - 2) PNF

- What type of augmentation tactics:
  - 1) With In-person sessions
  - 2) Continue

Program entry

End of week 4
Design Considerations:
Decision Points

2. Which decisions are critical and need to be guided (e.g. manualized, structured)?

- Not all decisions need to be guided.
  - But knowing which are and which are not is helpful.
- Need to guide decisions that likely influence the outcome
- My example:
  - **Guide:** delivery modality, content, augmentation tactic
  - **No need to guide:** timing of initial interview

variance: different staff would provide the same individual with different treatments

Non-systematic variance: this variance is due to issues unrelated to the individual (staff member is in a hurry, staff member is tired, last patient of the day, etc.)

Systematic variance: this variance is due to (unconscious) bias on the part of the staff member. One staff member connects to the individual whereas the other staff member does not. R
Design Considerations:
Tailoring Variables

How to select a tailoring variable?

- Select variables that are useful for making intervention decisions.

Useful how???
Design Considerations:
Tailoring Variables

Type 1: The Obvious
Useful in identifying a sub-group for whom specific options should not be considered for obvious practical/ethical/clinical reasons

Type 2: The Predictor
Useful in identifying a sub-group who need an intervention.

Type 3: The Moderator
Useful in identifying a sub-group of people who would benefit more from one type of intervention option over another
Design Considerations:
Tailoring Variables

Type 1: The Obvious

Useful in identifying sub-groups of people for whom different intervention options should not be considered for obvious practical, ethical, and/or clinical reasons.

Examples:

- Practically, its not reasonable to offer a mobile-based intervention to people who do not have a mobile device.
  - Owning a mobile device is a tailoring variable
- Practically, I will not consider an intervention that requires family support to a participant with poor family functioning
  - Family functioning is a tailoring variable
Design Considerations:  
Tailoring Variables

Type 2: The Predictor

Useful in identifying a sub-group of people who need an intervention (not clear what type) and a sub-group who do not need an intervention.

Example:

- Consider my tech-based intervention for at-risk drinkers.
- Empirical evidence and theories suggests that
  - People who remain at risk at week 4 (i.e., non-responders) are likely to fail in long-term (remain at-risk drinkers at week 12)
  - Hence, non-responders require an intervention.
In the next slide you will see why I call this the moderation: because I is guided by empirical evidence concerning how this variable moderates intervention effects.

**Design Considerations:**

**Tailoring Variables**

**Type 3: The Moderator**

Useful in identifying a sub-group of people who would benefit from one intervention option over another, and another sub-group

(a) for whom there is insufficient evidence to decide; or

(b) who would benefit from a different intervention option.
I used this moderated regression to determine whether and how response status can be used to tailor the tactic (i.e., to decide what tactic to offer and for who)

Moderation is used because via moderation I can determine whether the effect of the tactic varies depending on response status (my candidate tailoring variable)

Results: Tactic interacts with the response status in the following way:
Now you know why we call this type of tailoring variable the Moderator: because it is guided by empirical evidence concerning whether and how this variable moderates the intervention effect.

But its not a simple moderation that we are looking for in empirical evidence, it’s a special type of moderation that is informative for decision making.
<table>
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Response status is a moderator variable because the magnitude of the effect of tactic differs by response status.

Response status is not a tailoring variable:
Continue is better for all subjects.
However, what if for responders, the diff is zero?

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Response status is a Type 3a tailoring variable because it is useful for making an intervention decision for non-responders.

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Response Status is a Type 3b tailoring variable because the direction of the effect of tactic differs for responders vs. non-responders

Response status is useful for making different intervention decisions for different sub-groups
Design Considerations:
Tailoring Variables

Tailoring variables can be

- **Baseline variables:** gender, age, symptom severity

- **Proximal outcomes**
  - Short term representations of the distal outcome
    - Example: Monthly at-risk drinking days
  - Performance-based mechanisms
    - Example: Stress, social norms for drinking
  - Engagement/adherence–based mechanisms
    - Example: Weekly engagement in a web-based intervention
Assume that I want to use this instrument to define response and non-responders so that non-responders will receive augment and responders will receive continue.
I need to make sure is instrument is reliable and valid
Design Considerations:
Tailoring Variables

- **Reliability**: the degree to which an assessment tool produces stable and consistent results with repeated trials.
- **Unreliability**: Assume no black box
  - participants with the same level of drinking mark an answer depending on whatever they think a standard drink is
  - I’m capturing random variability (noise) in the testing method rather than actual differences in at-risk drinking (signal).
  - I might be making unsystematic assignment of people to subsequent interventions.
Assume that because of the way I framed the question, people consistently report that they had fewer at-risk drinking days than they actually did.

Design Considerations:
Tailoring Variables

- **Validity**: how well the test truly assesses the characteristic it is intended to study as judged by external criteria
- **Invalid (biased)**: assume I didn’t frame the question well, so
  - People consistently report that they had fewer at-risk drinking days than they actually did.
  - Instrument is reliable, but it is not valid because self-report is always lower than true drinking.
  - This will weaken intervention effect (assuming my theory is correct) as I will be systematically assigning people to the wrong subsequent intervention option
Empirical evidence suggests that in my population, change from at-risk to more heavy drinking patterns is unlikely to occur within a week, and I don’t want to burden my participants.
Design Considerations:
Decision Rules

How to derive decision rules?

- Articulate a theoretical model
  - For how treatment effect on key outcomes should differ across values of the tailoring variable.
  - For every value of the tailoring variable, state expected outcome associated with each intervention option.

- How?
  - Use prior clinical experience
  - Use prior experimental and observational studies
  - Discuss with research team / clinical staff, “What intervention option would be best for people with this value on the tailoring variable?”
Design Considerations: Decision Rules

- Good decision rules are objective, are operationalized.
- Strive for comprehensive rules, yet clear and specific
- Cover situations that can occur in real-life and practice
  - Including when tailoring variable is missing or unavailable.
Design Considerations:
Decision Rules

How to operationalize decision rules?

**Bad:** Individuals who drinking too much are non-responders and receive augment.

**Better:** Individuals who experience 2+ heavy drinking days (HDDs) in the past month are declared non-responders and receive in-person in addition to initial treatment.

**Awesome:** Individuals who experience 2+ HDDs in the past month are declared non-responders and receive in-person in addition to initial treatment; Whereas those with HDDs<2 in the past month continue with initial treatment.
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Questions?

More information:


