Adaptive Interventions

Module 1

Experimental Design and Analysis Methods for Developing Adaptive Interventions: Getting SMART

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Outline

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

• Goal: Develop one simple example adaptive intervention in your educational/clinical area.
  1. Rationale for the AI
  2. Distal outcome(s)? Proximal outcome(s)?
  3. First- and second-stage intervention options?
  4. Tailoring variables?
  5. Decision rules?
Definition of AI

An intervention design, not an experimental design…

…in which intervention options are individualized to accommodate the specific and changing needs of individuals.

• Sounds much like actual educational, clinical, policy or public health practice? Yes!

• Go by many different names: adaptive health interventions, adaptive treatment strategies, dynamic treatment regimes, treatment algorithms, stepped care models, treatment protocols, individualized interventions...
Example of a School-based Adaptive Intervention for Children with Autism

PI: Connie Kasari, UCLA
Example of a School-based Adaptive Intervention for Children with Autism

1. Decision Point:
A time in which treatment options should be considered based on patient information (Yoshino et al., 2009)
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Example of a School-based Adaptive Intervention for Children with Autism

2. Tailoring Variable: Patient information used to make treatment decisions
Example of a School-based Adaptive Intervention for Children with Autism

3. Intervention options:
   Type/Dose
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3. Intervention options:
   Type/Dose
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4. Decision rule
Example of a School-based Adaptive Intervention for Children with Autism

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Example of a School-based Adaptive Intervention for Children with Autism

5. Outcomes Guiding the Adaptive Intervention:
Distal → Long-term goal of intervention: *Improved Academic Outcomes*

Proximal → Short-term goal of decision rules:
*Improved Social Communication (in class and playground) and Creating an Environment to Facilitate Social Communication*
AI: 5 Elements

1. Decision Points → Trigger
2. Tailoring Variable → •Monitoring
3. Decision rule → •Individualizing
4. Intervention Options → •Delivering
5. Proximal + Distal Outcomes → Guide
Example of an AI in Substance Use

- 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-responsive
  - Non-compliant

High risk

- Bi-weekly court hearings + standard counseling
  - Non-responsive
  - Non-compliant

- As-needed court hearing + ICM
  - Non-responsive
  - Non-compliant

Non-responsive

- Bi-weekly court hearing + ICM
  - Non-responsive
  - 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}

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

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

3. Intervention options:
Type/Dose

4. Decision rule

5. Outcomes:
Distal → Long-term goal of intervention:
Program graduation (14 consecutive weekly negative drug urine specimens)

Proximal → Short-term goal of decision rules:
Compliance and response in the course of intervention (mediator)
AI: 5 Elements

1. Decision Points  ➔ Trigger
2. Tailoring Variable  ➔ Monitoring
3. Decision rule  ➔ Individualizing
4. Intervention Options  ➔ Delivering
5. Proximal + Distal Outcomes  ➔ Guide
Adaptive Interventions Fall Into Four Categories

• AIs can vary along two dimensions (with 2 levels each):

  1. **Dimension 1: Points of Individualization**
     • **Singular**: for each participant, treatment is individualized at most once (might still be offered a sequence)
     • **Sequential**: treatment may be individualized multiple times

  2. **Dimension 2: Information Used to Individualize**
     • **Static**: individualization based on information that is unlikely to change over time as a result of treatment (e.g., personality, baseline)
     • **Dynamic**: individualization based on information that can change over time as a result of treatment (e.g., response status, engagement in treatment).
## Adaptive Interventions Fall Into Four Categories

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

• The objective of an AI is to guide clinical or educational practice, or public health policy.
  – Which are adaptive in nature.

• From the individual/student/patient’s point of view:
  – AI is a sequence of (individualized) treatments

• From the educator/clinician’s point of view:
  – AI is a sequence of decision rules that recommend one or more treatments/intervention options at each critical decision point.
More Examples of Decisions

• About intervention **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 intervention **engagement**:  
  – How do we re-engage participants who are non-adherent?  
  – Or showing early signs of non-adherence/disengagement?
Some More Examples …

• About intervention delivery:
  – Location of delivery?
    ▪ home vs. school
    ▪ in-class vs. out-of-class
  – Mode of delivery?
    ▪ internet vs. in-person
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
Example of a School-based Adaptive Intervention for Children with Autism

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Another Example AI in Education
RTI: Identify/Support Students’ Learning and Behavior Needs

**Tier 1**
- Academic or behavioral concerns are noted.

**Parent/Teacher Meeting**
- Initiate Tier 1 Intervention

**SUCCESSFUL**
- Document intervention and continue as long as necessary

**UNSUCCESSFUL**
- Informal request for assistance from Consultant

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**Tier 2**
- Consultant, Parent, & Teacher meet to assess the problem.
  - Initiate Tier 2 intervention

**Consultant, Parent, & Teacher Follow-Up**
- To evaluate Tier 2 intervention

**SUCCESSFUL**
- Document intervention and continue as long as necessary

**UNSUCCESSFUL**
- Continue to Tier 3 Student Support Team Meeting.

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**Tier 3**
- Prepare for formal Student Support Team (SST) meeting.

**Convene SST**
- Implement Intervention

**SST Review Meeting**
- Include specific program screening instruments when appropriate

**SUCCESSFUL**
- Document intervention and continue as long as necessary

**UNSUCCESSFUL**
- Should the student be referred to another program?

**NO**
- Continue the plan for a predetermined time period or try a different intervention.

**YES**
- Refer for other Programs or Services
  - Refer to Dyslexia
  - Refer to Special Education
  - Refer to Section 504
Another Example AI in Education
RTI: Identify/Support Students’ Learning and Behavior Needs

8-10 weeks following initiation of Tier 1

If success = yes

Then, intervention = \{document and continue\}

Else if success = no

Then, intervention = \{move to Tier 2\}

Proximal outcome: Improve ongoing progress in a given area (e.g., reading, math, social behavior).

Distal outcome: obtain successful outcomes for students
Another Example AI in Education

• Individualizing Student Instruction (ISI) intervention
  (Carol Connor; Fred Morrison et al…2011)
  
  • **Goal:**
    – Improve first graders’ word reading achievement.
  
  • **Adaptation:**
    – Amounts of reading instructions individualized based on initial levels and progress in the student’s vocabulary and reading skills
Other Example AIs that Education Scientists Might Be Familiar With

• **Fast Track** *(Conduct Problems Prevention Research Group, 1992)*
  • **Goal:**
    – Prevent conduct problems among high-risk children.
  • **Adaptation:**
    – # of home-visits individualized based on family functioning
    – Reading tutoring assigned only to children showing academic difficulties

• **Adolescent Transitions Program (ATP)** *(Dishion & Kavanagh, 2003)*
  • **Goal:**
    – Reduce substance use / antisocial behavior, students ages 11–17.
  • **Adaptation:**
    – Intensity of family-based interventions adapted based on family motivation and needs.
Other Interesting Example Adaptive Interventions Outside Education

- 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
- Connell et al. (2007): An adaptive approach to family intervention targeting problem behaviors
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
Why Adaptive Interventions?

2) Changing, chronic, or *waxing and waning* course of disorders
   - Improvement or decline 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
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
Why Adaptive Interventions?

4) Many treatments are costly
   – Certain treatments can be very expensive
   – Resources are often limited
   – Difficulties in scalability
   – Perhaps need to:
     – Try less expensive treatment first
     – Offer more costly treatments to people who need it
     – Try costliest treatment up front and step down treatment
Outline

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

• Help me build a non-traditional, tech-based AI for children with autism who are minimally verbal:
  – Why older children w/ASD who are minimally verbal?
    • Interventions have overlooked older children with ASD
    • >50% of children with ASD who receive traditional interventions at age 2 are minimally verbal at age 9
    • Failure to develop language by age 5 = poor prognosis
  – What interventions options are available?
    • One option is Joint Attention, Symbolic Play, Engagement and Regulation (JASPER) intervention
    • One tech-based option is the use of speech-generating devices (think iPad)
Design Goals

1. Maximize the *strength* of the AI

   *(remember: we are not talking about the experimental trial or study here!)*

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
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
5. Proximal + Distal Outcomes ➞ Guide

Adaptation process
Design Considerations: Distal Outcome

• Define the ultimate goal of the intervention
  – What you want the AI to achieve at the end
    • Example: Increased number of social communicative utterances outside of therapy ("generalization")

  – Other examples:
    • Enhance treatment engagement (session participation)
    • Prevent relapse
    • Improve school performance
Design Considerations: Proximal Outcome

- Select and clearly define proximal outcomes
  - Pathways through which you want the intervention to achieve its ultimate goal
  - Three types of pathways:
    - Response-based pathways (direct)
      - Example: Social communicative utterances during therapy
    - Performance-based pathways (indirect)
      - Example: Play, engagement, not just about the words
    - Engagement/adherence–based pathways
      - Example: Receive intervention at least once per week
Design Considerations: Intervention Options

- Engagement/adherence–based pathways
  - Receive intervention at least once per week
- Performance-based pathways
  - Play, engagement, not just about the words
- Response-based pathways
  - Social communicative utterances during therapy

Select intervention options in light of the proximal outcomes
Design Considerations:
Decision Points

1. When do you need to make decisions/What kind of intervention options are feasible at each decision point

Program entry

- 1) Tx at clinic
- 2) SGD
- 3) JASPER (2x/week)
- 4) Parent view tx at clinic
- 5) Tx via tele-health (??rural??)

Weekly

- 1) Continue JASPER
- 2) JASPER+ (3x/week)
- 3) SGD
- 4) Parent Training
- 5) Tx at home
- 6) Tx via Tele-health
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.
- May be important to guide decisions that are likely to influence the outcome.
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: Based on Clinical, Practical or Ethical Considerations

Useful in identifying a sub-group for whom specific options should not be considered for clear practical/ethical/clinical reasons

Type 2: Based on a Predictors Data Analysis

Useful in identifying a sub-group who needs an intervention or a change from the current intervention

Type 3: Based on a Moderators Data Analysis

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: Based on Clinical, Practical, Ethical Considerations

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:

– We may not want to offer an intervention that requires parent support to a child who lacks strong parental involvement.
  • Parent involvement is a tailoring variable

– In other examples, practically, it’s 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
Type 2: Based on a Predictors Data Analysis

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.

Examples:

- Consider our example for children with ASD.
- Empirical evidence and theories suggests that:
  - Children who have not made progress in social communication between weeks 6 and 12 are likely to fail in long-term (i.e., will not be socially communicative at weeks 24-36)
Design Considerations:
Tailoring Variables

Type 3: Based on a Moderators Data Analysis

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.
**Design Considerations:**

**Tailoring Variables**

**Type 3a:** one sub-group would benefit from one intervention option over another, and another for whom there is insufficient evidence to decide.

Data from a randomized trial in which:

- Children started with JASPER (2x/week) [no SGD]
- At week 12 everyone randomized to JASPER+ (3x/week) vs add SGD

\[ Y = \beta_0 + \beta_1 R + \beta_2 T + \beta_3 T \times R + e \]

- \( Y \) = # SCU at week 36
- \( R \) = Response status at week 4
- \( T \) = JASPER+ (3x/week) vs add SGD

Design Considerations:

- Tailoring Variables
Design Considerations: Tailoring Variables

**Type 3b:** one sub-group would benefit from one intervention option over another, whereas another sub-group would benefit from a different intervention option

Data from a randomized trial in which:

- Children started with JASPER (2x/week) [no SGD]
- At week 12 everyone randomized to JASPER+ (3x/week) vs add SGD

\[ Y = \beta_0 + \beta_1 R + \beta_2 T + \beta_3 R \times T + e \]

- Y = \# SCU at week 36
- R = Response status at week 4
- T = JASPER+ (3x/week) vs add SGD
Response status is a moderator variable because the magnitude of the effect of tactic differs by response status.

*Interesting, but there is *no evidence* for the use of response status as a tailoring variable: *Add SGD* is better for all subjects.*

---

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

*There *is evidence* for the use of response status as a tailoring variable: *Add SGD* for non-responders. JASPER+ or *Add SGD* for 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

*There *is evidence* for the use of response status as a tailoring variable: *Add SGD* is for non-responders. JASPER+ for responders.*
Design Considerations:
Tailoring Variables

Tailoring variables can be

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

- **Proximal outcomes**
  - Short term representations of the distal outcome
    - Example: Change in SCU during therapy since last visit
  - Performance-based mechanisms
    - Example: Child is using toys during and playing during txt
  - Engagement/adherence–based mechanisms
    - Example: Weekly attendance to clinic txt
Design Considerations: Tailoring Variables

- **Reliability**: the degree to which an assessment tool produces stable and consistent results with repeated trials (under the same conditions).

- **Unreliability**: Assume no black box
  - Capturing random variability (noise) in the measuring method rather than actual differences in social communication (signal).
  - Impact: I might be making unsystematic assignment of people to subsequent interventions.
Design Considerations: Tailoring Variables

- **Validity**: how well the measurement assesses the characteristic it is intended to measure as judged by external criteria

- **Invalid (biased)**:
  - Instrument is reliable, but it is not valid because the clinician’s quick checklist of SCU during therapy is always lower than “true” SCU (i.e., assume there is some clinician-rated gold standard).
  - Impact: This could weaken intervention effect (assuming my theory is correct) as I will be systematically assigning people to the wrong subsequent intervention option
How to Time Assessments of Tailoring variable?

- Tailoring variable should be assessed at sufficiently frequent intervals so that non-response is detected in a timely manner.
  - Too infrequent → condition may deteriorate so much that you might not be able to rescue with available options.
  - Too frequent → disengagement or non-adherence
  - Example: should I measure change in SCU weekly or every 2 weeks?
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:** Children who make poor progress in social communication should be offered SGD.

**Better:** Children who do not show improvement in clinician-rated SCU during therapy should be offered SGD.

**Awesome:** Children who, at week 12 following JASPER, improve by more than 25% change (since baseline) on clinician-rated SCU should remain on JASPER; otherwise, the child should be offered JASPER with SGD starting at the next clinic visit. If the child does not show at week 12, use change in SCU up to previous visit.
Outline

• What are Adaptive Interventions?
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• Summary & Discussion
Questions?

More information:


Backup Slides
About JITAIIs…

1. Decision Points
2. Tailoring Variable
3. Decision rule
4. Intervention Options
5. Proximal + Distal Outcomes

Any Time

Trigger

• Monitoring
• Individualizing
• Delivering

Guide

Adaptation Process

Momentary
Practicum

• Goal: Develop one simple example adaptive intervention in your educational/clinical area.

1. Rationale for the AI
2. Distal outcome(s)? Proximal outcome(s)?
3. First- and second-stage intervention options?
4. Tailoring variables?
5. Decision rules?