Module 1: Adaptive Interventions

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Outline

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

Group Practicum Preview

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

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

Definition of an Adaptive Intervention

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!
- These interventions are known by many different names: adaptive health interventions, adaptive treatment strategies, dynamic treatment regimes, treatment algorithms, stepped care models, treatment protocols, individualized interventions...

Adaptive Intervention: 5 Elements

1. Decision Points ⇢ Trigger
2. Tailoring Variable ⇢ Monitoring
3. Decision Rule ⇢ Individualizing
4. Intervention Options ⇢ Delivering

Adaptation Process

5. Proximal + Distal Outcomes ⇢ Guide

Example AI: Substance Use Treatment

PI: Jim McKay, UPenn

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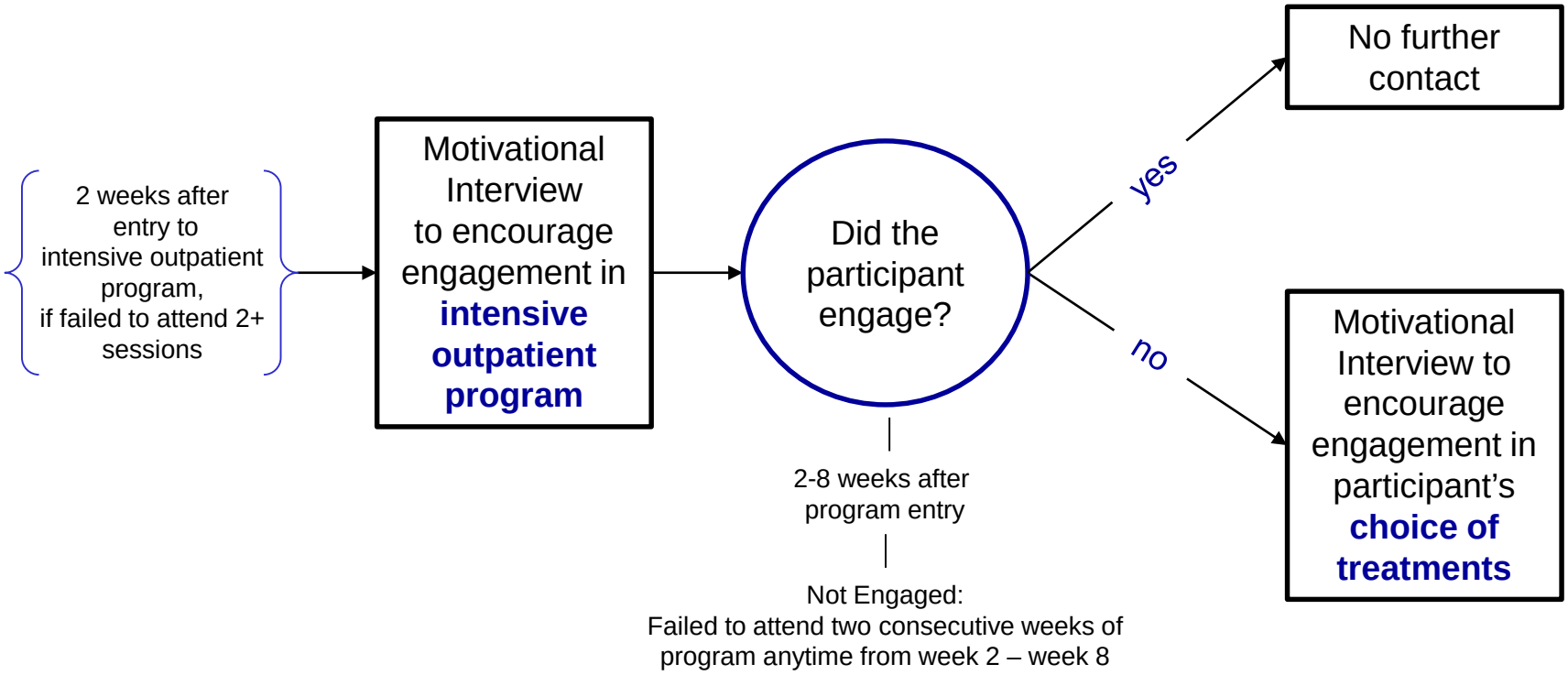

Example AI: Substance Use Treatment

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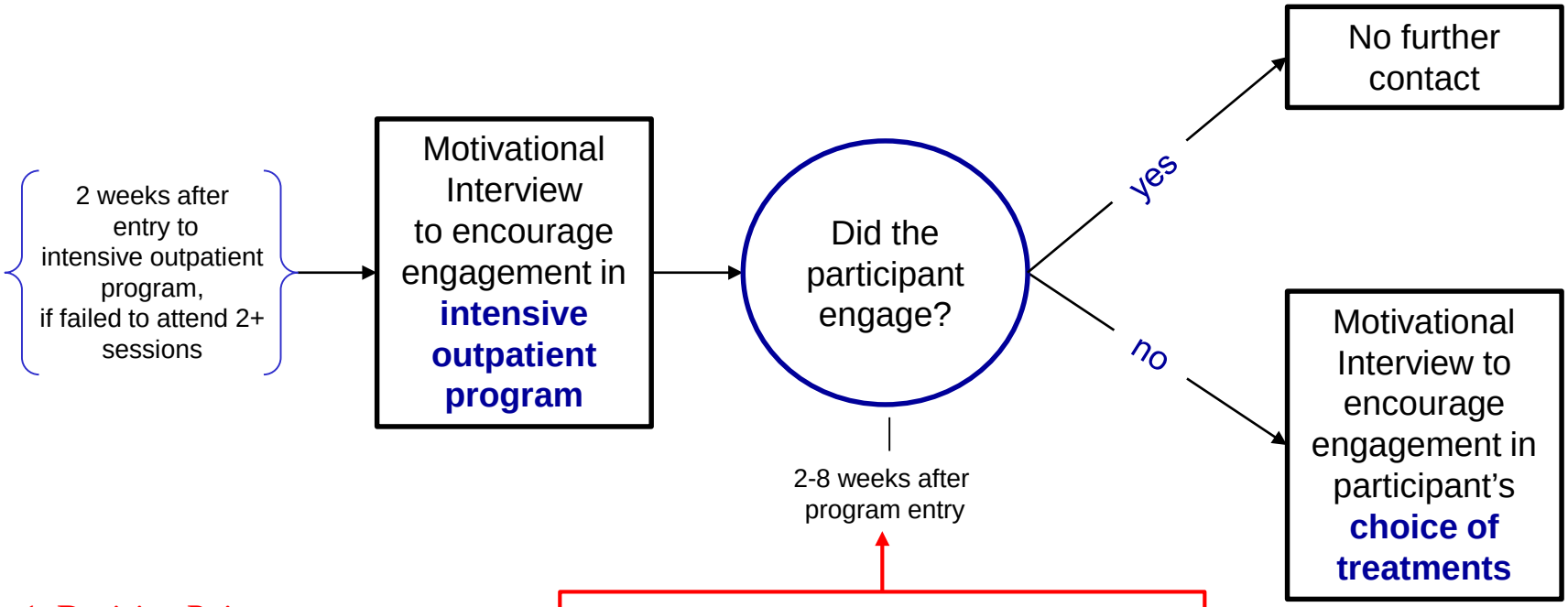

1. Decision Points
2. Tailoring Variable
3. Decision Rule
4. Intervention Options
5. Proximal + Distal Outcomes

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

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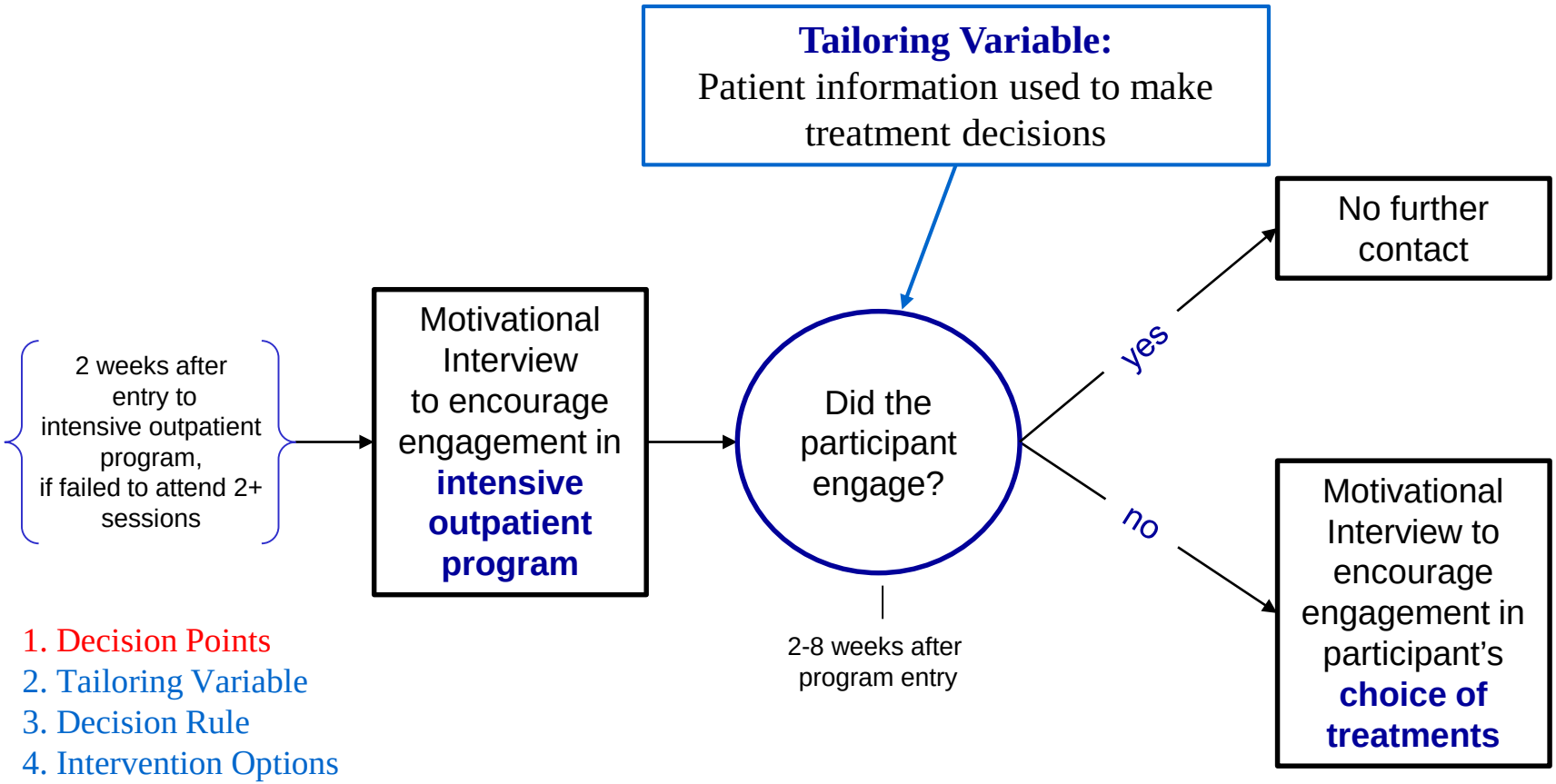

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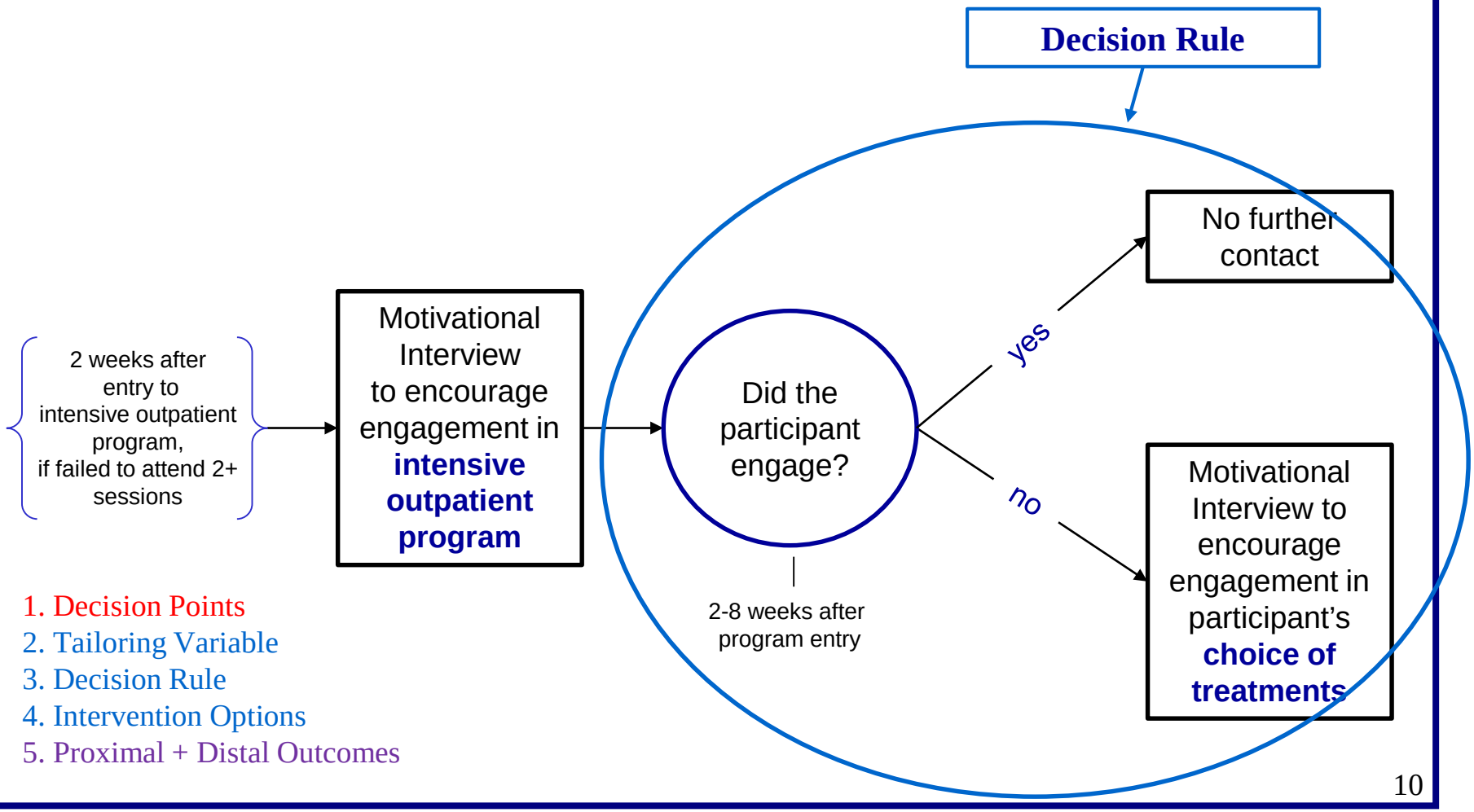

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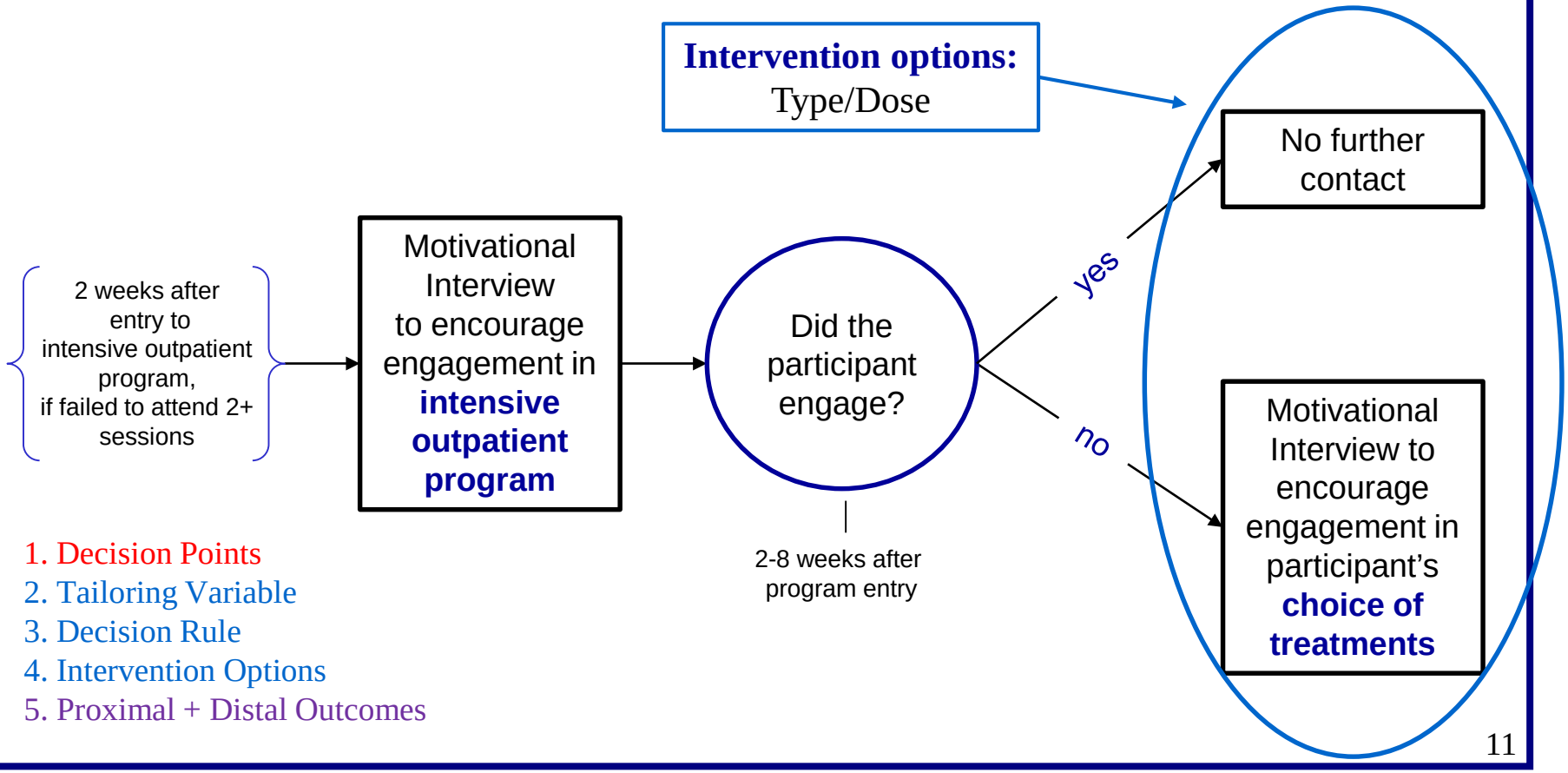

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Example AI: Substance Use Treatment

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Outcomes Guiding the Adaptive Intervention

Distal → Long-term goal of the adaptive intervention

- *Reduced substance use*

Proximal → Short-term goal of the adaptive intervention

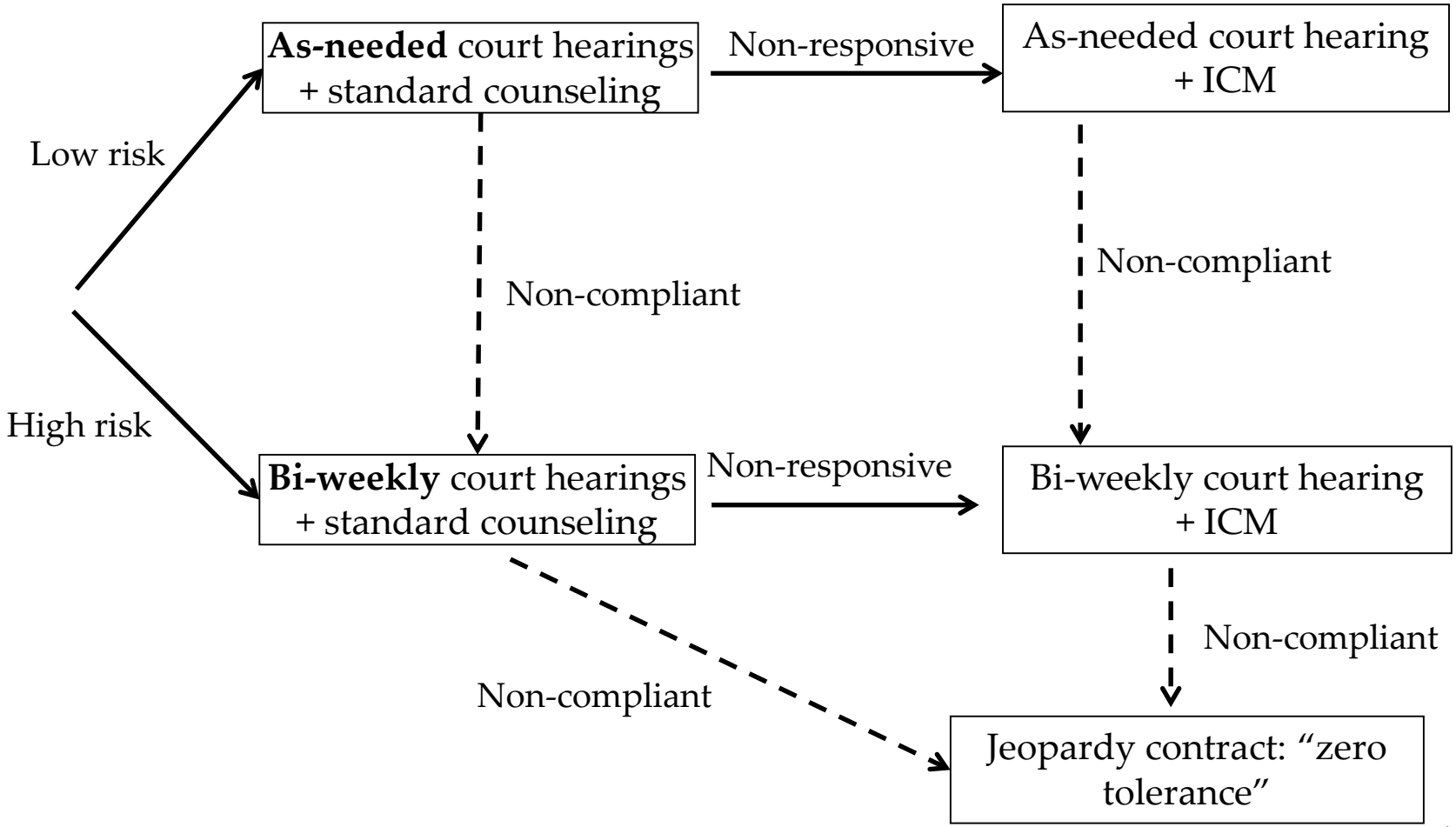
- *Engagement in treatment*

Example AI: Adaptive Drug Court Program

- Adaptive drug court program for drug abusing offenders
- The goal was to minimize recidivism and drug use, operationalized by completion of the drug court program.

(Marlowe et al., 2008; 2009; 2012)

Example AI: Adaptive Drug Court Program



Example AI: Adaptive Drug Court Program

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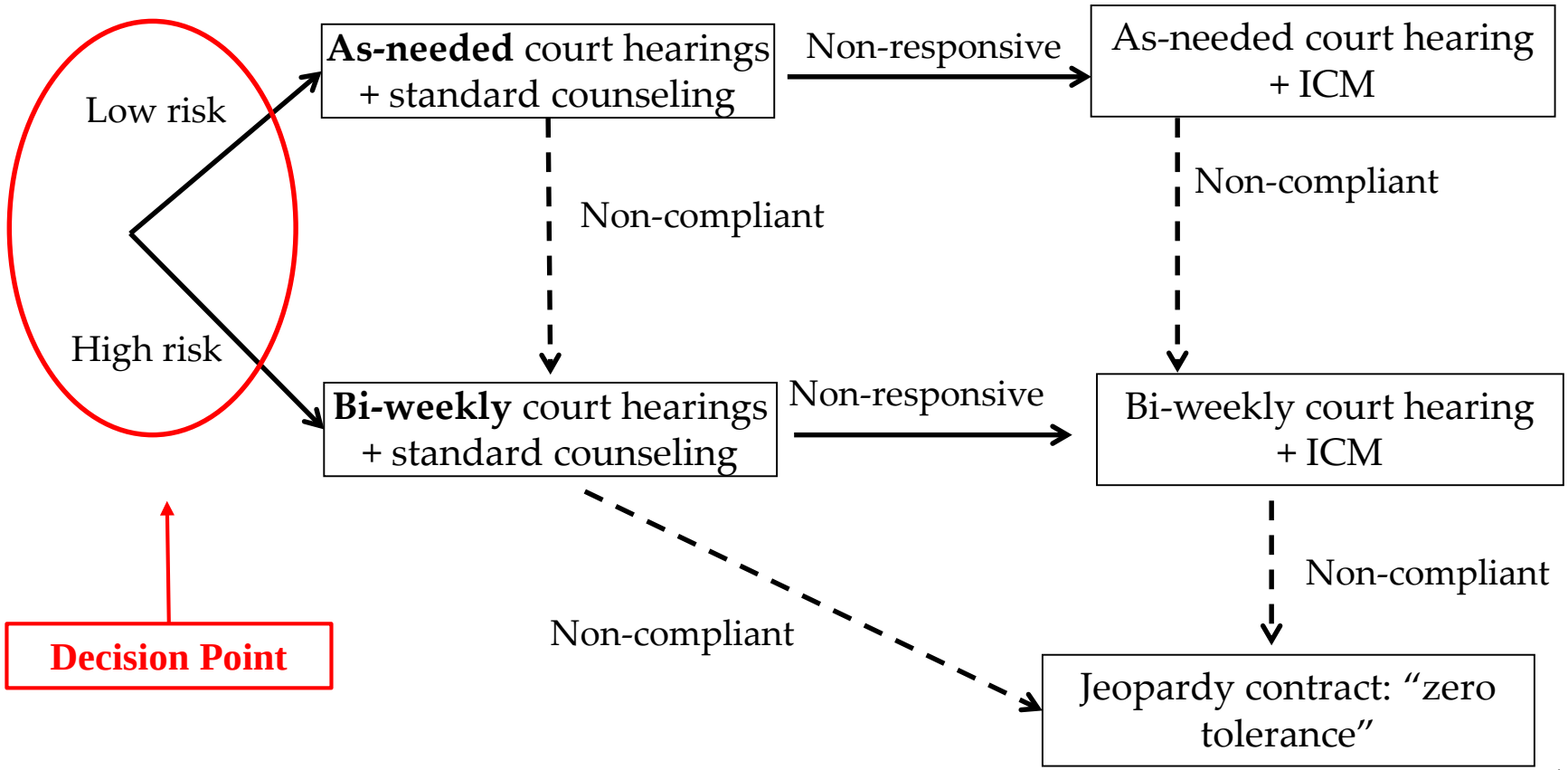

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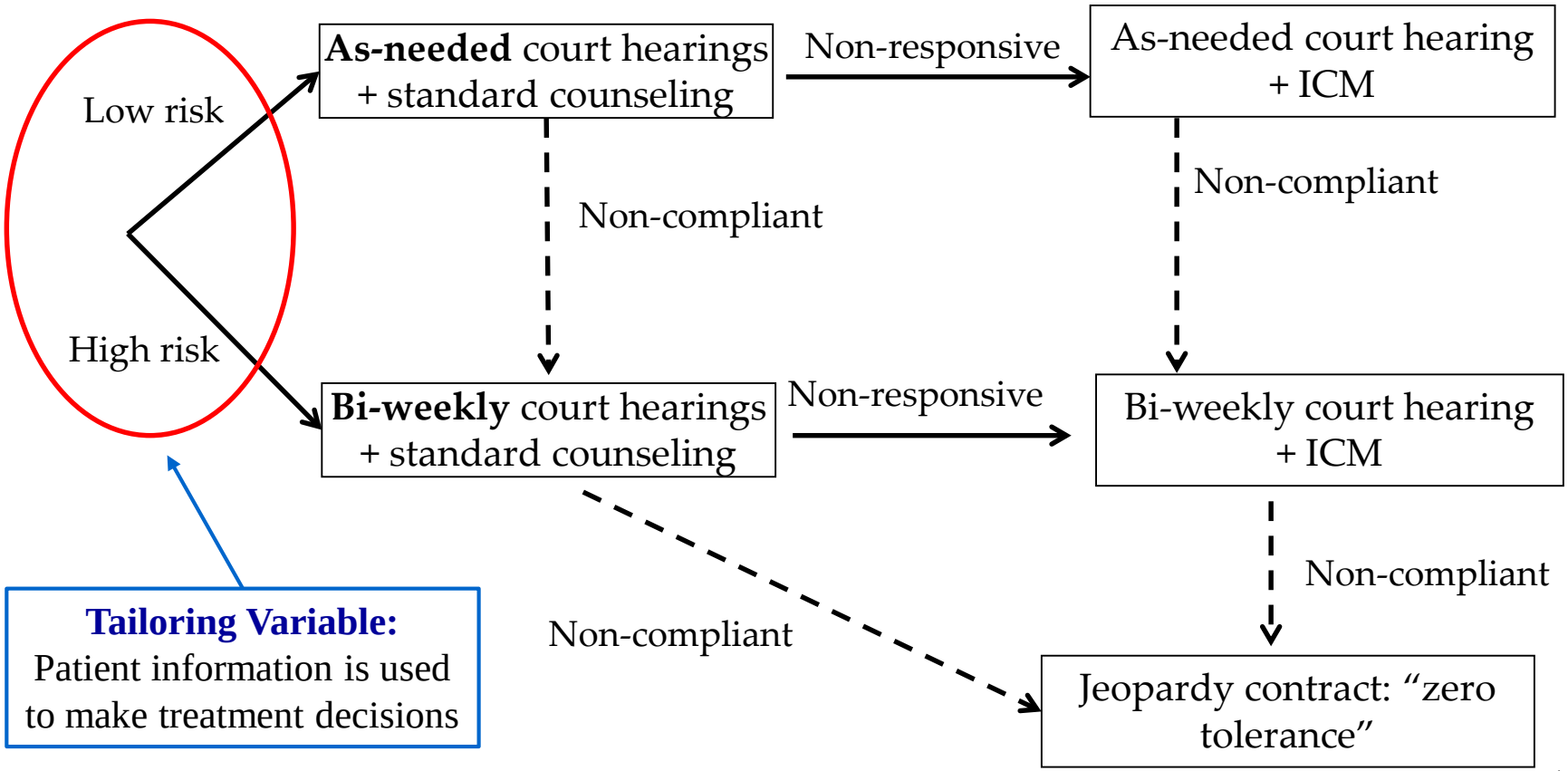

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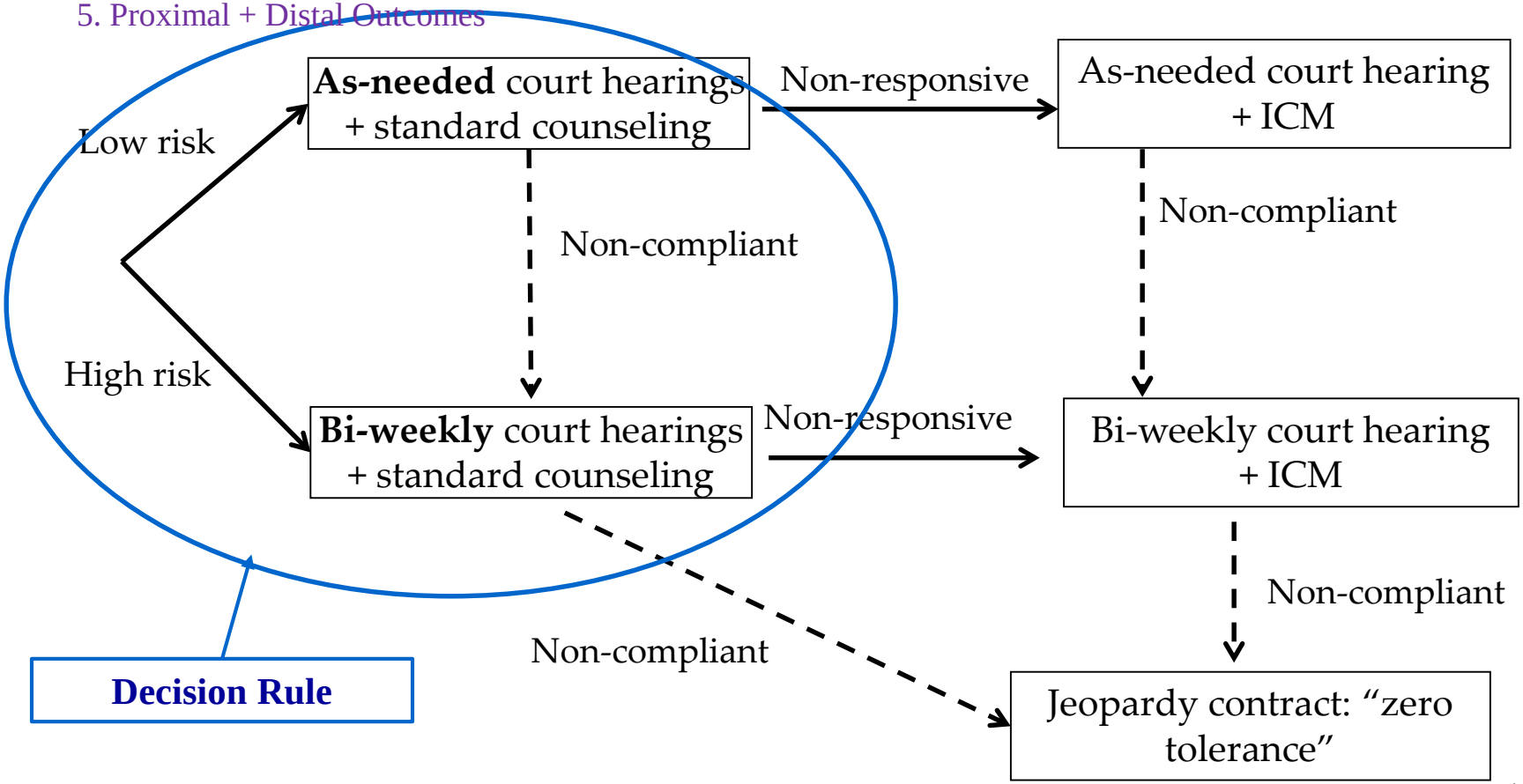

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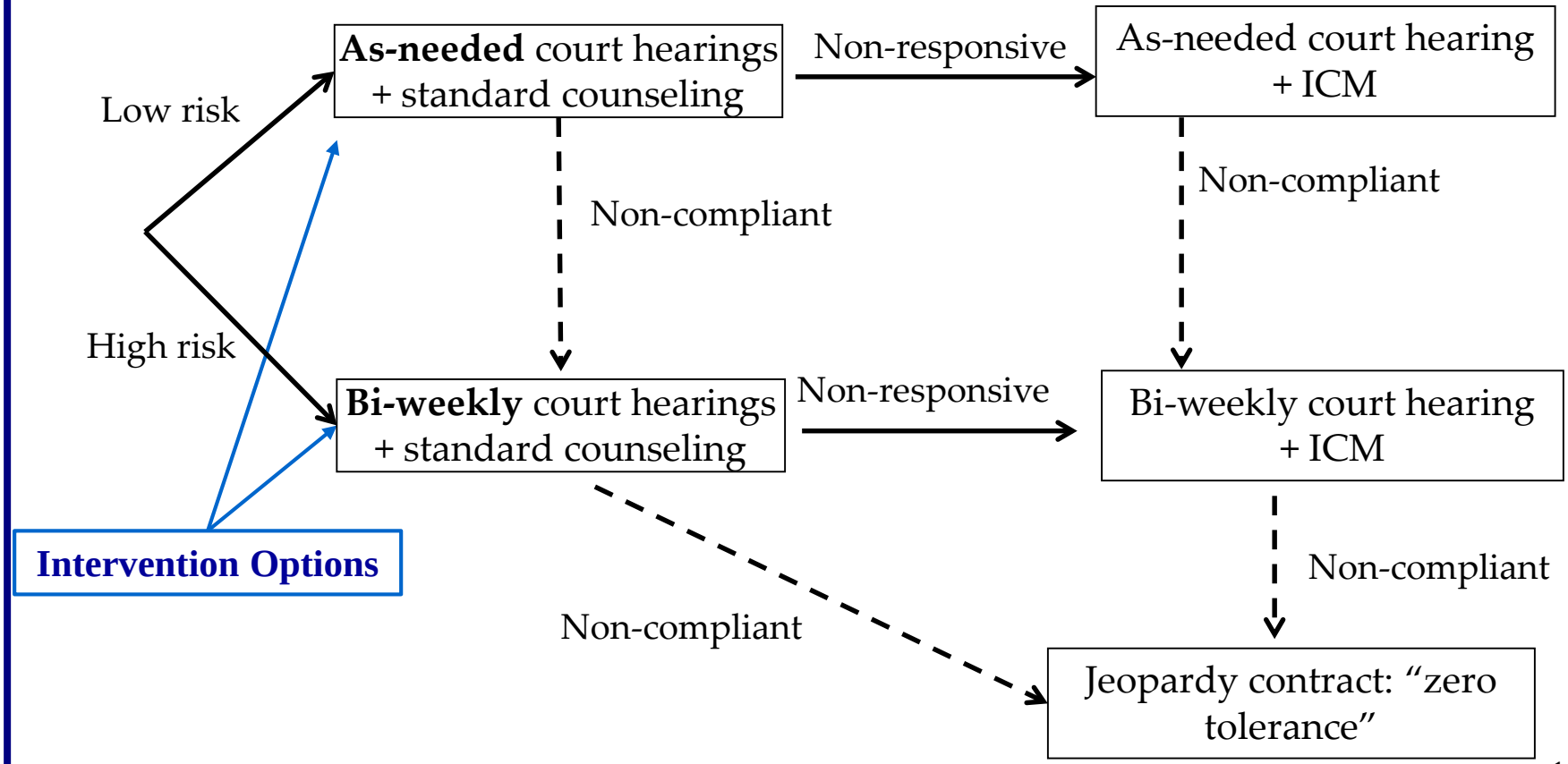

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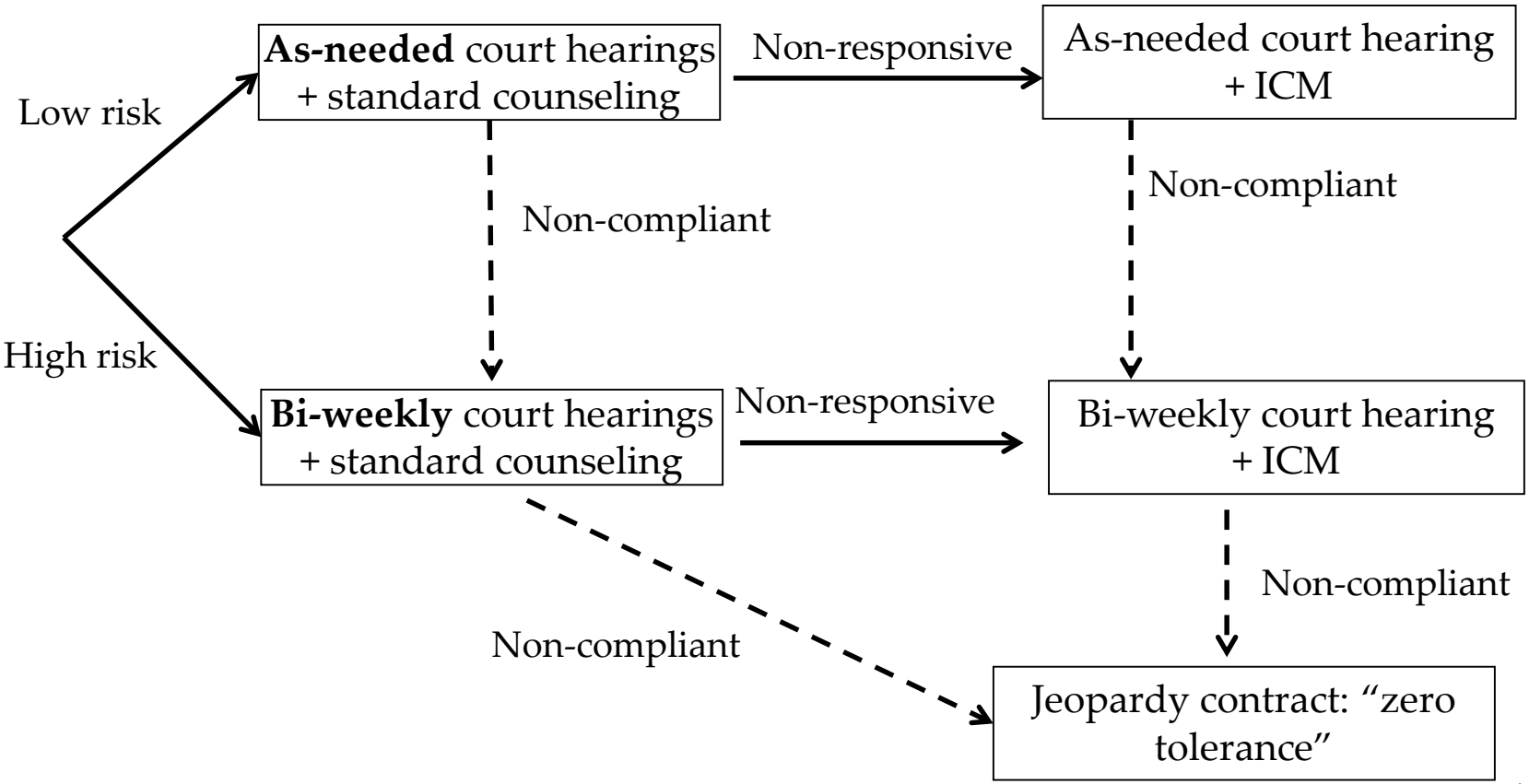


Example AI: Adaptive Drug Court Program

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

Outcomes Guiding the Adaptive Intervention

Distal → Long-term goal of the adaptive intervention
- *Program graduation*

Proximal → Short-term goal of the adaptive intervention
- *Compliance*
- *Response*

Two Dimensions of Adaptive Interventions

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.

Dimension 2: Information Used to Individualize

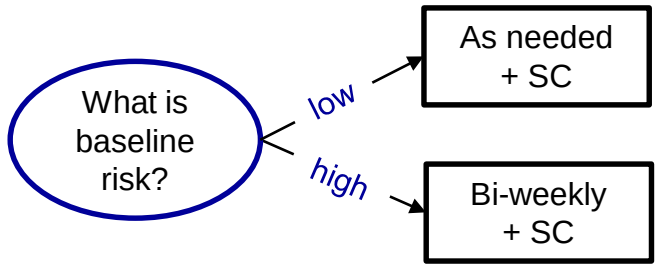
Static: Individualization based on information that is unlikely to change over time as a result of treatment (e.g., personality, baseline).

Dynamic: Individualization based on information that can change over time as a result of treatment (e.g., response status, engagement in treatment).

Two Dimensions of Adaptive Interventions

INFORMATION USED TO INDIVIDUALIZE

POINT OF INDIVIDUALIZATION

	Static Information	Dynamic Information
Singular	**At program entry:** 	
Sequential		

Two Dimensions of Adaptive Interventions

INFORMATION USED TO INDIVIDUALIZE

POINT OF INDIVIDUALIZATION

	Static Information	Dynamic Information
Singular		**At program entry:** As needed + SC **Then, at week 4:** What is response? — no → more SC; yes → stay the course
Sequential		

Two Dimensions of Adaptive Interventions

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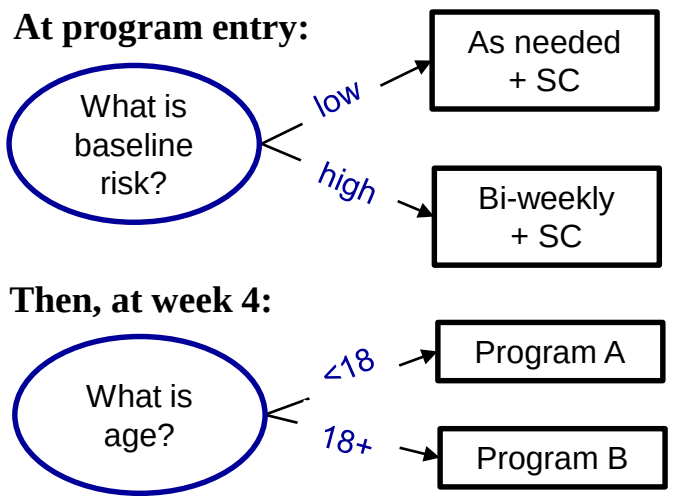
Sequential		

Two Dimensions of Adaptive Interventions

INFORMATION USED TO INDIVIDUALIZE

POINT OF INDIVIDUALIZATION

	Static Information	Dynamic Information
Singular		
Sequential		**At program entry:** What is baseline risk? — low → As needed + SC; high → Bi-weekly + SC **Then, at week 4:** What is response? — no → more SC; yes → stay the course

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

Examples of Decisions

- About intervention **timing**:
  - How long should we implement the first treatment?
    - Before transitioning to a maintenance/relapse prevention treatment?
    - Before declaring non-response and moving to another treatment?
- About intervention **engagement**:
  - Do we try to re-engage participants who are non-adherent, or who are showing early signs of non-adherence/disengagement? If so, how?

More Examples of Decisions

- About intervention **delivery**:
  - Location of delivery?
    - Home vs. clinic
    - In-class vs. out-of-class
  - Mode of delivery?
    - Internet vs. in-person vs. mobile device vs. telephone

Even More Examples of Decisions

- 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 C?
    - Should we continue with A or step-up to D?
  - For people who **do respond** well to treatment A
    - Should we continue or step-down?
    - Should we stop immediately or gradually?
    - Do we need a booster or not?

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 **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.

Outline

- What are Adaptive Interventions?
- Why use Adaptive Interventions?
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Why Use Adaptive Interventions?

1) High **heterogeneity** in need for, or response to, a particular treatment

   – What works for one person may not work for another.

   – Thus, need to:

     • detect early signs of treatment failure

     • modify the treatment

     • work to prevent ultimate treatment failure

Why Use 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 Use Adaptive Interventions?

3) Treatment is **burdensome** when
   - Side effects
   - Patient required to invest significant time/effort
   - Burden leads to non-adherence
   - Non-adherence reduces positive intervention effect
   - Need to identify:
     - signs of burden
     - how to modify intervention intensity based on signs of burden

Why Use Adaptive Interventions?

4) Treatment is **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 most costly treatment up front and step down treatment

Outline

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Motivating Example

Let's 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 for Adaptive Interventions

1. Maximize the ***strength*** of the Adaptive Intervention
2. Maximize ***replicability*** of the Adaptive Intervention

Design Goals: Strength

Goal 1: Maximize the ***strength*** of the AI

This can be achieved by:

- Well-defined proximal and distal outcomes
- Effective intervention options
- Well-chosen tailoring variables
- Well-measured tailoring variables
- Well-formulated decision rules
- Well-implemented decision rules

Design Goals: Replicability

Goal 2: Maximize ***replicability*** of the AI

- in future ***experimental*** conditions, and
- in 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
- Fidelity of implementation
- Thinking carefully about, and planning for, non-standard scenarios that may arise

Design Considerations

Recall the 5 elements of Adaptive Interventions:

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

We can maximize the strength and replicability of an AI by carefully designing each element.

Design Considerations: Distal Outcome

Clearly define the ultimate goal of the intervention.

Examples:

- Increased number of social communicative utterances outside of therapy
- Enhanced treatment engagement (session participation)
- Prevention of relapse
- Improved school performance

Design Considerations: Proximal Outcome

Proximal outcomes are pathways through which you want the intervention to achieve its ultimate goal.

1. Response-based pathways (direct) are proximal measures that are part of the distal outcome.
   Example: Social communicative utterances during therapy

2. Performance-based pathways (indirect) are mechanisms that predict the distal outcome.
   Example: Play, not just about the words

3. Engagement/adherence-based pathways are indicators of engagement and adherence that predict the distal outcome.
   Example: Receive intervention at least once per week

Design Considerations

Recall the 5 elements of Adaptive Interventions:

1. Decision Points
2. Tailoring Variable
3. Decision Rule
4. Intervention Options
   - ✓ Proximal + Distal Outcomes

We can maximize the strength and replicability of an AI by carefully designing each element.

Design Considerations: Intervention Options

Possible Intervention Options

Type of Proximal Outcome	JASPER (2x weekly)	JASPER + (3x weekly)	SGD	Parent training	Parent observes session	Treatment at clinic	Treatment at home	Treatment via Tele-Health
Direct (utterances)	✓	✓	✓					
Indirect (play)	✓	✓	✓	✓	✓			
Engagement (attendance)			✓			✓	✓	✓

Design Considerations

Recall the 5 elements of Adaptive Interventions:

1. Decision Points
2. Tailoring Variable
3. Decision Rule
✓ Intervention Options
✓ Proximal + Distal Outcomes

We can maximize the strength and replicability of an AI by carefully designing each element.

Design Considerations: Decision Points & Intervention Options

- When do you need to make decisions?
- What kind of intervention options are feasible at each decision point?

Design Considerations: Decision Points & Intervention Options

When	Feasible Intervention Options
Program entry →	1) Treatment at clinic 2) SG Device 3) JASPER (2x/week) 4) Parent observes clinic treatment 5) Treatment via tele-health
Weekly →	1) Continue JASPER 2) Increase dose of JASPER (3x/week) 3) SG Device 4) Parent Training 5) Treatment at home 6) Treatment via Tele-health

Design Considerations: Decision Points & Intervention Options

Which decisions are *critical* and need to be guided via manual or other structured guide?

- Not all decisions need to be guided, but thinking about which are and which are not is helpful.
- May be important to guide decisions that are likely to influence the outcomes.

Design Considerations

Recall the 5 elements of Adaptive Interventions:

- ✓ Decision Points
- 2. Tailoring Variable
- 3. Decision Rule
- ✓ Intervention Options
- ✓ Proximal + Distal Outcomes

We can maximize the strength and replicability of an AI by carefully designing each element.

Design Considerations: Selection of Tailoring Variables

Which tailoring variables will be *useful* for making intervention decisions?

Useful how?

Design Considerations: Selection of Tailoring Variables

Approach 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, or clinical reasons

Examples:

- We may not want to offer an intervention that requires parent support to a child who lacks strong parental involvement.
  - Strong parent involvement is a tailoring variable
- It may not be reasonable to offer a mobile-based intervention to people who do not have a mobile device.
  - Owning a mobile device is a tailoring variable

Design Considerations: Selection of Tailoring Variables

Approach 2: **Based on a Predictors Data Analysis**

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

Example:

- In the Autism example, 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 the long-term (i.e., will not be socially communicative at weeks 24-36)
  - Social communication progress is a tailoring variable

Design Considerations: Selection of Tailoring Variables

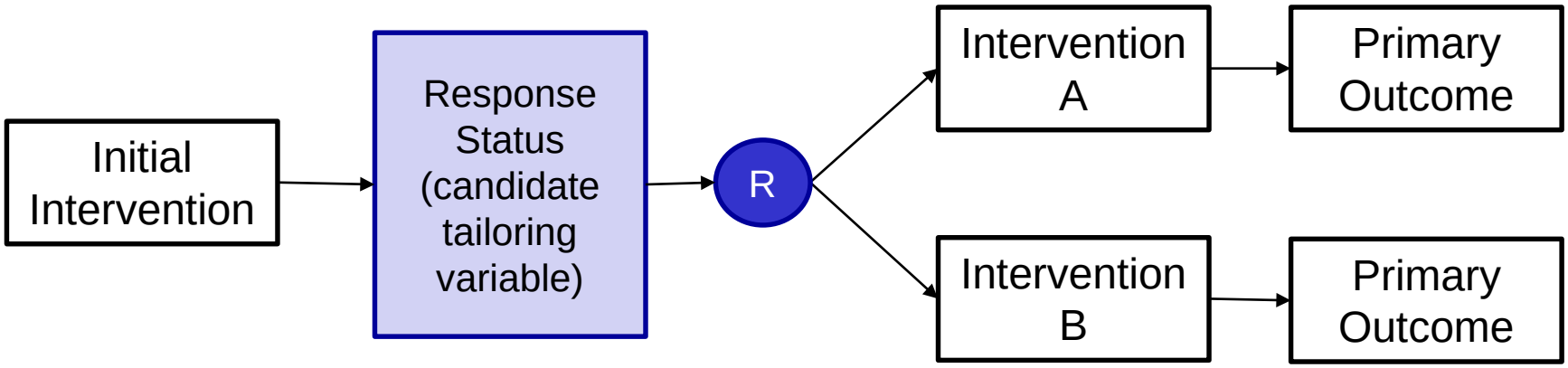
Approach 3: **Based on a Moderators Data Analysis**

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

This is a sub-group:

- for whom there is insufficient evidence to decide; or
- who would clearly benefit from a different intervention option.

Hypothetical Moderation Analysis

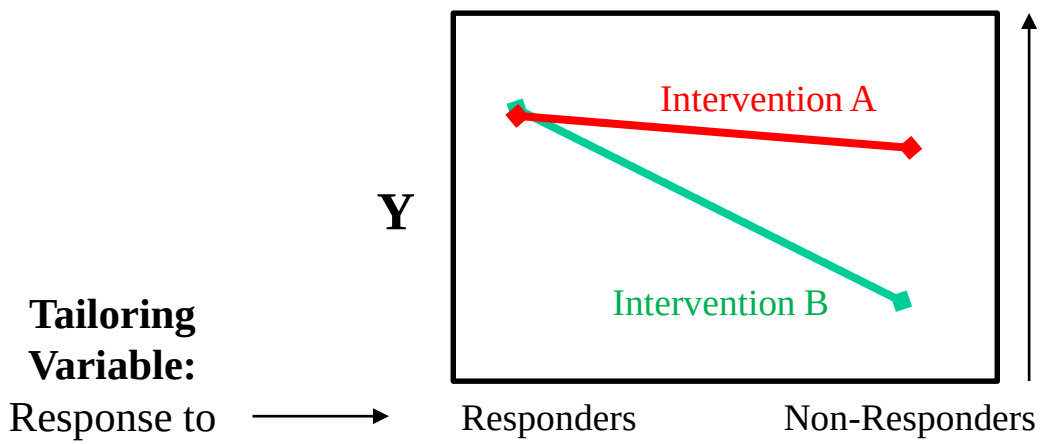


$$\boldsymbol{Y = \beta_0 + \beta_1(Response) + \beta_2(Intervention) + \beta_3(R * I) + e}$$

There are 3 types of moderator tailoring variables.

Design Considerations: Selection of Tailoring Variables

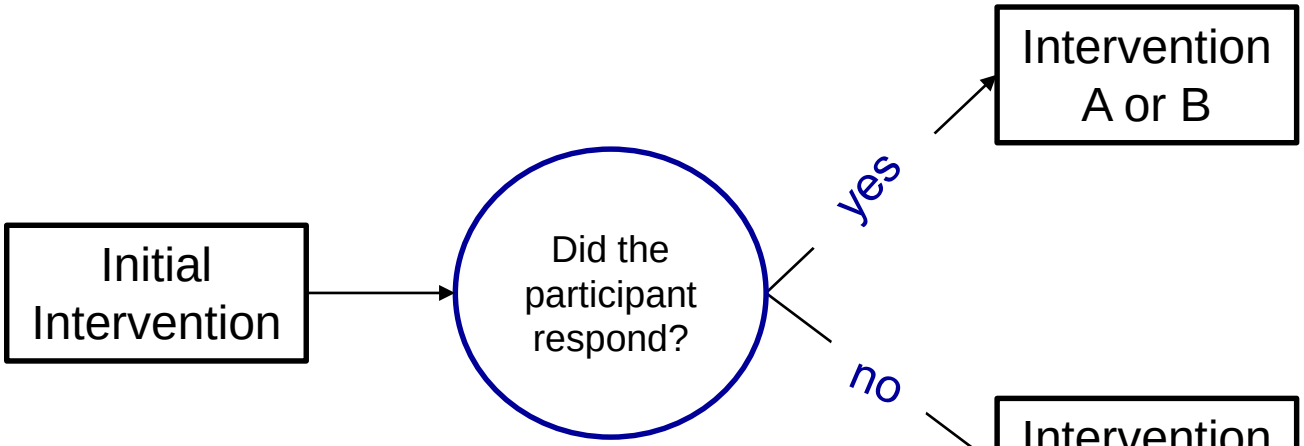
Type 3a:	Evidence suggests that subgroup 1 benefits from one intervention over another, but the evidence is unclear for subgroup 2

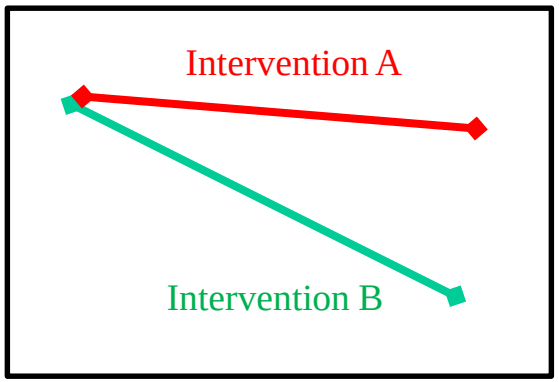


Response status is a Type 3a tailoring variable because it is useful for making an intervention decision for non-responders.

*There *is evidence* for the use of response status as a tailoring variable:*
A *for non-responders.*
B *or* ***A*** *for responders.*

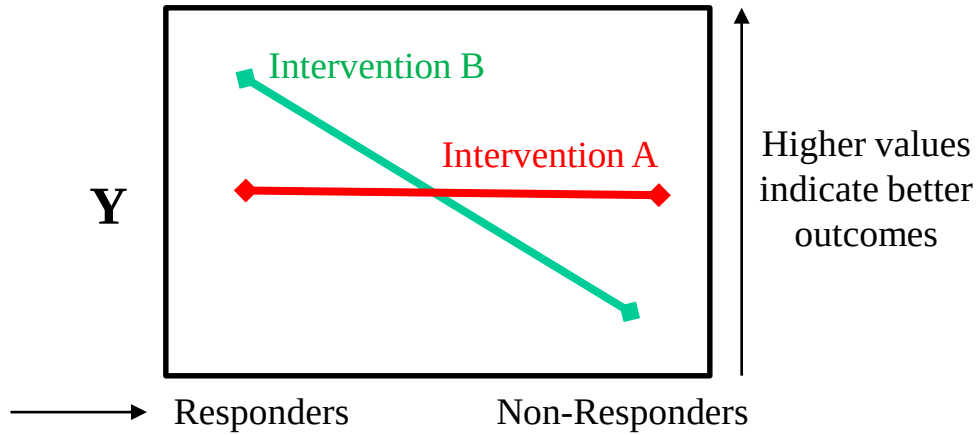
AI for Tailoring Variable 3a





Design Considerations: Selection of Tailoring Variables

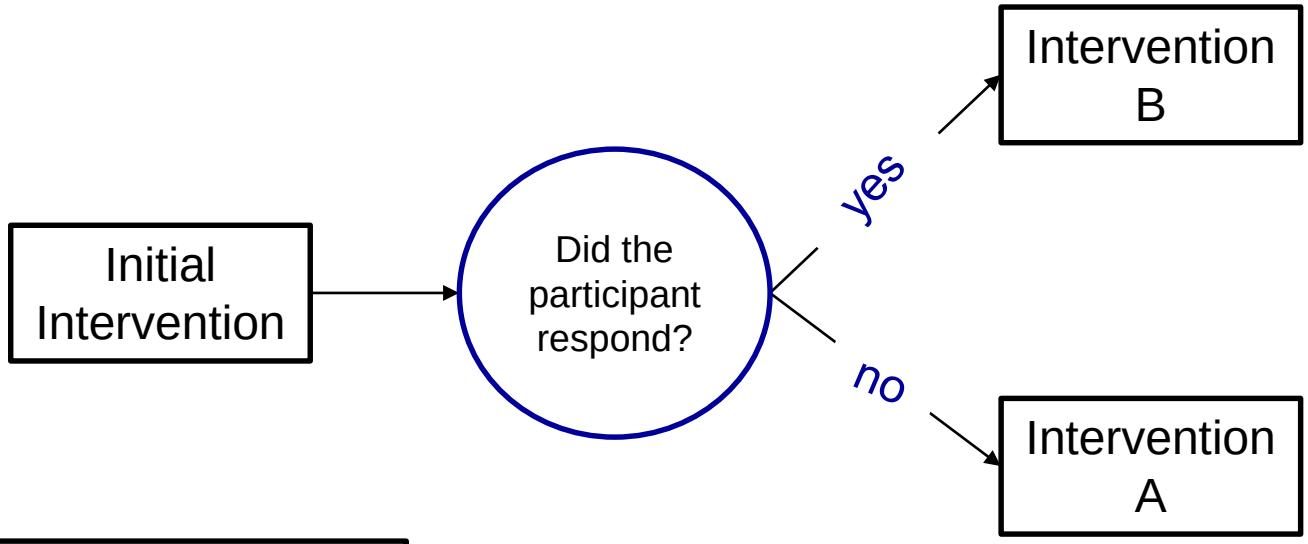
Type 3b:	Evidence suggests that subgroup 1 benefits from one intervention over another, while subgroup 2 benefits from the alternate intervention

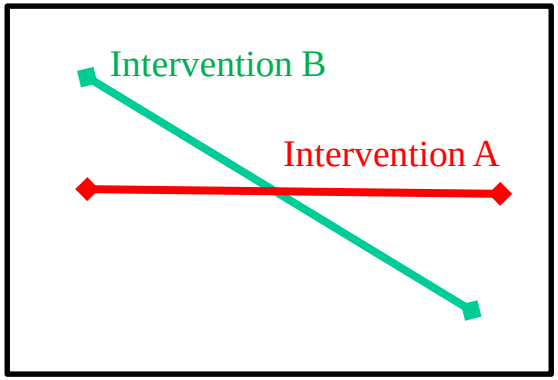


Response status is a Type 3b tailoring variable because the direction of the intervention approach differs for responders vs. non-responders.

*There *is evidence* for the use of response status as a tailoring variable:*
***A** for non-responders.*
***B** for responders.*

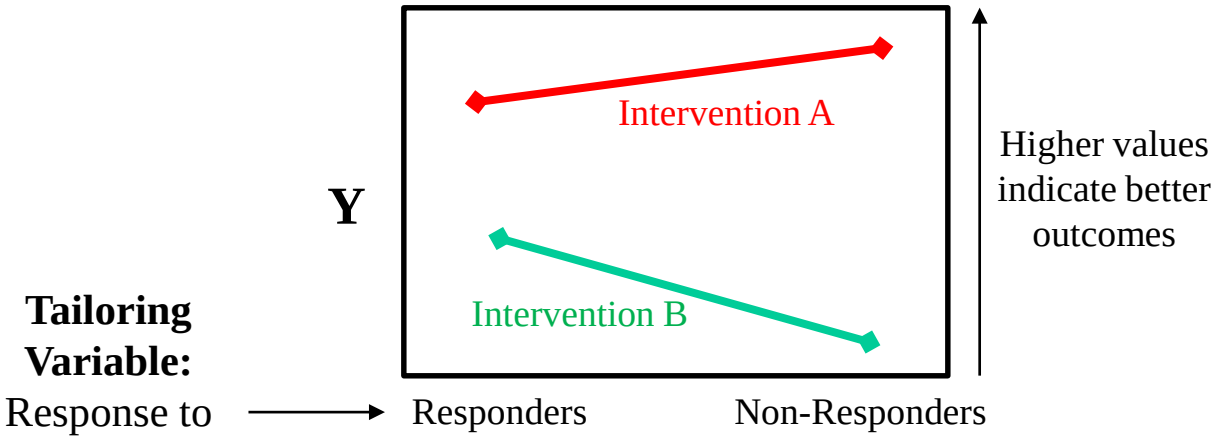
AI for Tailoring Variable 3b





Design Considerations: Selection of Tailoring Variables

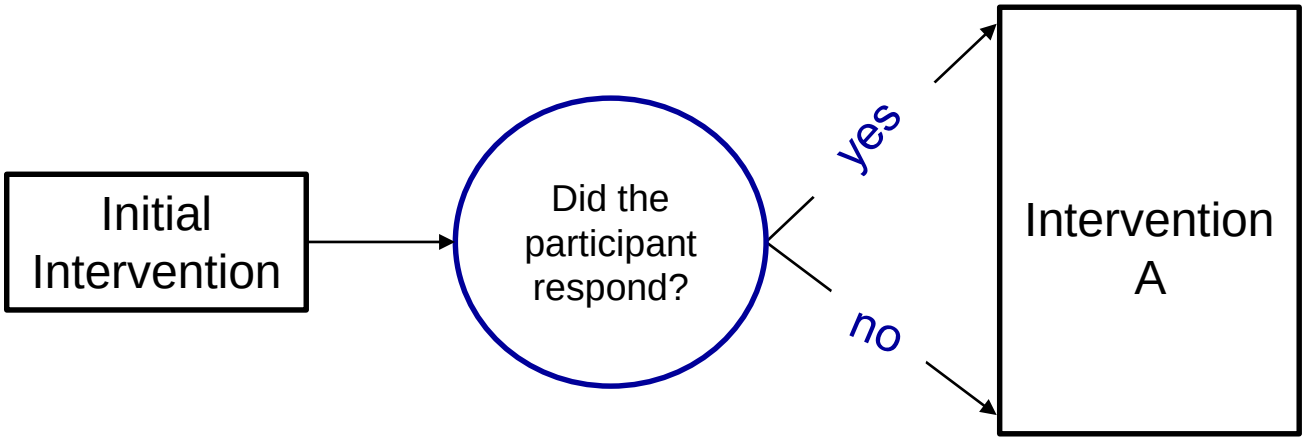
Type 3c:	Evidence suggests that one intervention is better for both subgroups, but the magnitude of the effect differs by subgroup.

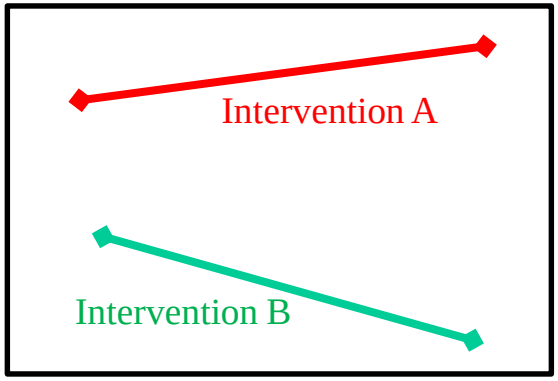


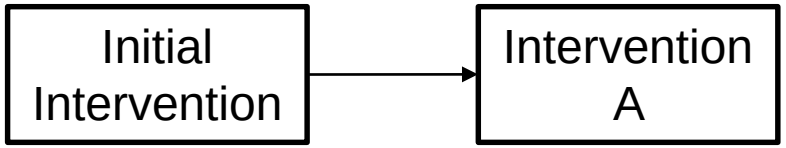
Response status is a Type 3c tailoring variable because both responders and non-responders do better under Intervention A.

*There *is NO evidence* for the use of response status as a tailoring variable:*
A *for non-responders and responders*

AI for Tailoring Variable 3c



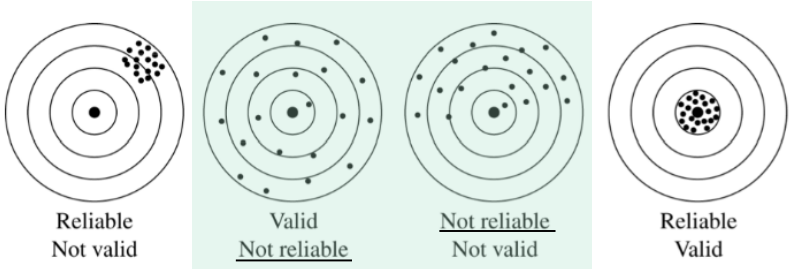




Design Considerations: Selection of Tailoring Variables

- Baseline variables: gender, age, symptom severity
- Proximal outcomes:
  - Short term representations of the distal outcome
    - Example: Change in communicative utterances during therapy since last visit
  - Performance-based mechanisms
    - Example: Child is using toys during and playing during treatment
  - Engagement/adherence–based mechanisms
    - Example: Weekly attendance to clinic treatment

Design Considerations: Measurement of Tailoring Variables

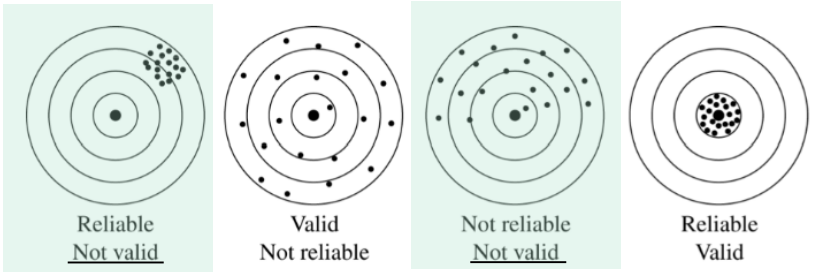


- **Reliability:** The degree to which an assessment tool produces stable and consistent results with repeated trials (under the *same conditions*).

- Tailoring variables that are not measured with high reliability are capturing random variability (noise) rather than actual differences in social communication.

  Impact: assignment to intervention may be unsystematic

Design Considerations: Measurement of Tailoring Variables



- **Validity:** how well the measurement assesses the characteristic it is intended to measure as judged by external criteria.
- A measure with low validity may result in a clinician who consistently scores lower than the "true" value.

  Impact: intervention effect is weakened because participants are systematically assigned to the wrong intervention.

Design Considerations: Measurement of Tailoring Variables

Timing: Tailoring variables 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 communicative utterances weekly or every 2 weeks?

Design Considerations

Recall the 5 elements of Adaptive Interventions:

- ✓ Decision Points
- ✓ Tailoring Variable
- 3. Decision Rule
- ✓ Intervention Options
- ✓ Proximal + Distal Outcomes

We can maximize the strength and replicability of an AI by carefully designing each element.

Design Considerations: Decision Rules

How do we derive decision rules?

Design a theoretical model that:

- Articulates how treatment effects on key outcomes are expected to differ across values of the tailoring variable.
- States expected outcome associated with each intervention option for every value of the tailoring variable.

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

Strong decision rules:

- are objective and clearly operationalized
- are comprehensive, clear and specific
- cover situations that can occur in real-life and practice
  - including when the tailoring variable is missing or unavailable!

Design Considerations: Decision Rules

Poor: 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% (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 attend assessment at week 12, use change in SCU up to previous visit.

Outline

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

Summary

- The objective of an AI is to guide clinical or educational practice, or public health policy (which are adaptive in nature).
- Individualization is achieved through the use of decision rules at each decision point.
- Scientists develop adaptive interventions, and clinicians use them to guide clinical practice.

Summary

- There are a number of experimental designs that can be used to develop and evaluate Adaptive Interventions.
  - Pilot Studies can be used to determine the acceptability and feasibility of implementing an Adaptive Intervention in practice.
  - Enhanced Non-Responder Trials or **Sequential Multiple Assignment Randomized Trials** can be used to optimize an Adaptive Intervention (e.g., to identify the best decision rules in an Adaptive Intervention).
  - Randomized Clinical Trials can be used to evaluate an already developed AI relative to a suitable control condition.

Practicum

Goal: Develop one simple example adaptive intervention in your research area.

10 minutes: break, gather group

30 minutes: small group work to develop a shared idea

20 minutes: large group discussion/brainstorm