Presented by
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Secondary Aim Analyses in a SMART: Using moderators to build a more deeply-tailored AI

Workflows and Code

This module was developed in collaboration with Jamie Yap, Mason Ferlic, Daniel Almirall, and Billie Nahum-Shani at the University of Michigan, John J. Dziak at the University of Illinois, and Susan Murphy at Harvard

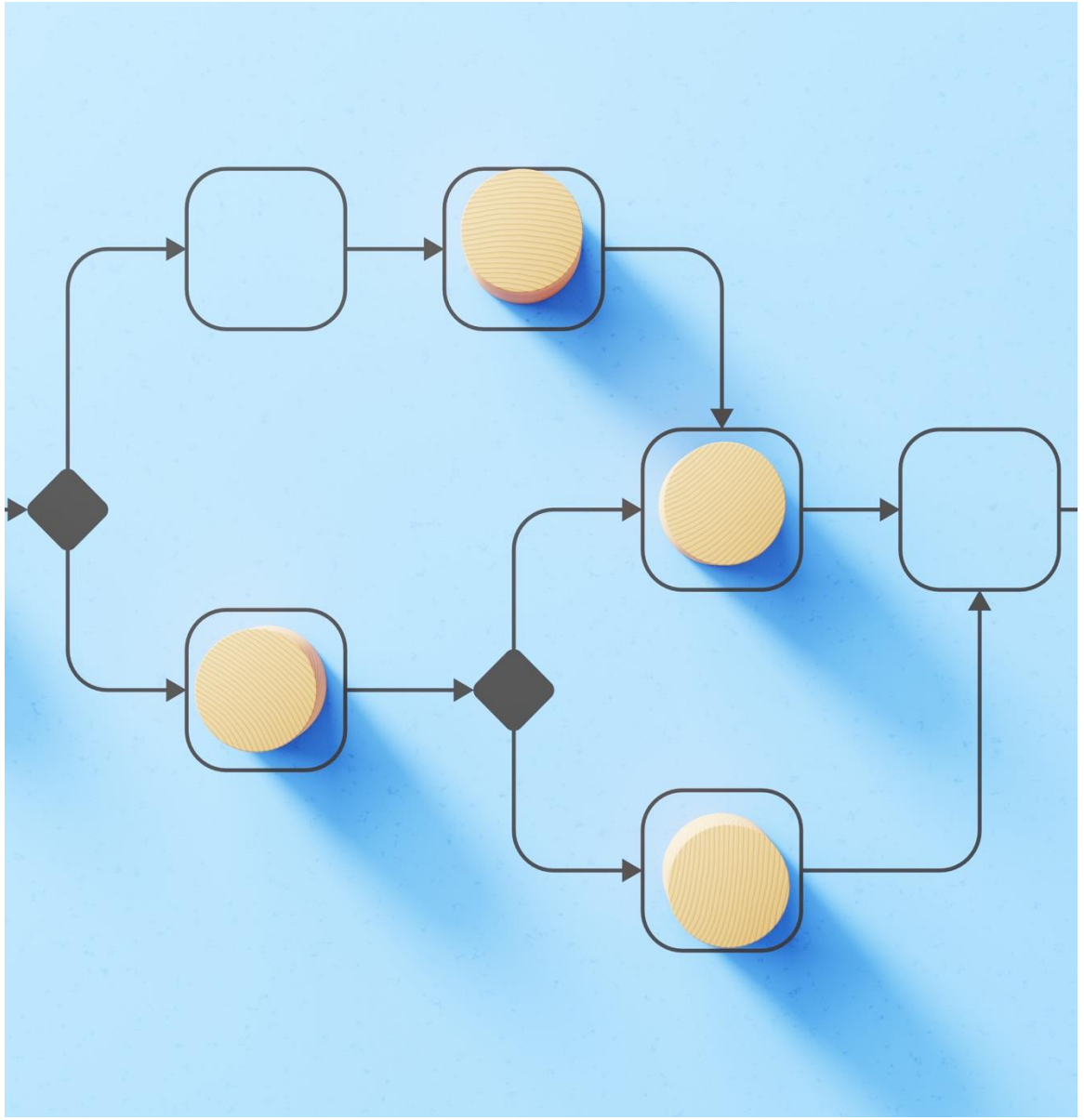
Virtual Module 3 100 min

Learning Goals

Review how moderators can be used to build an optimal adaptive intervention using Q-learning

Learn how to implement Q-learning

- Fit and interpret moderated regression models
- R package qlaci



Outline of module

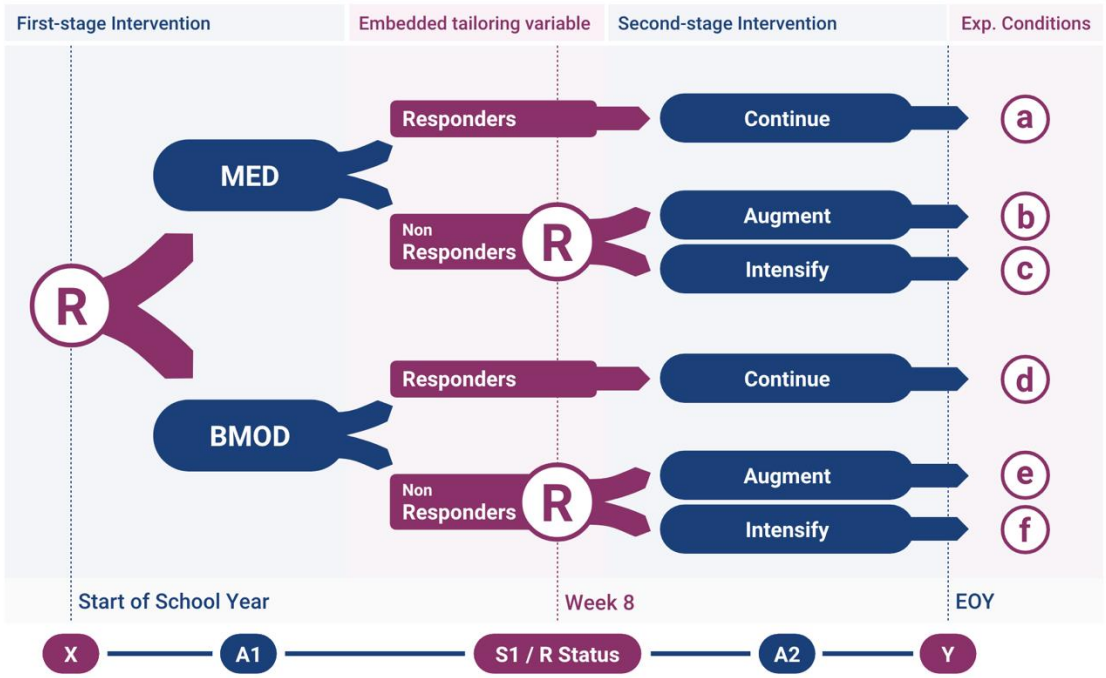
- Review (30 min)
- Break (10 min)
- Follow-Along (60 min)
- Q&A (20 min)

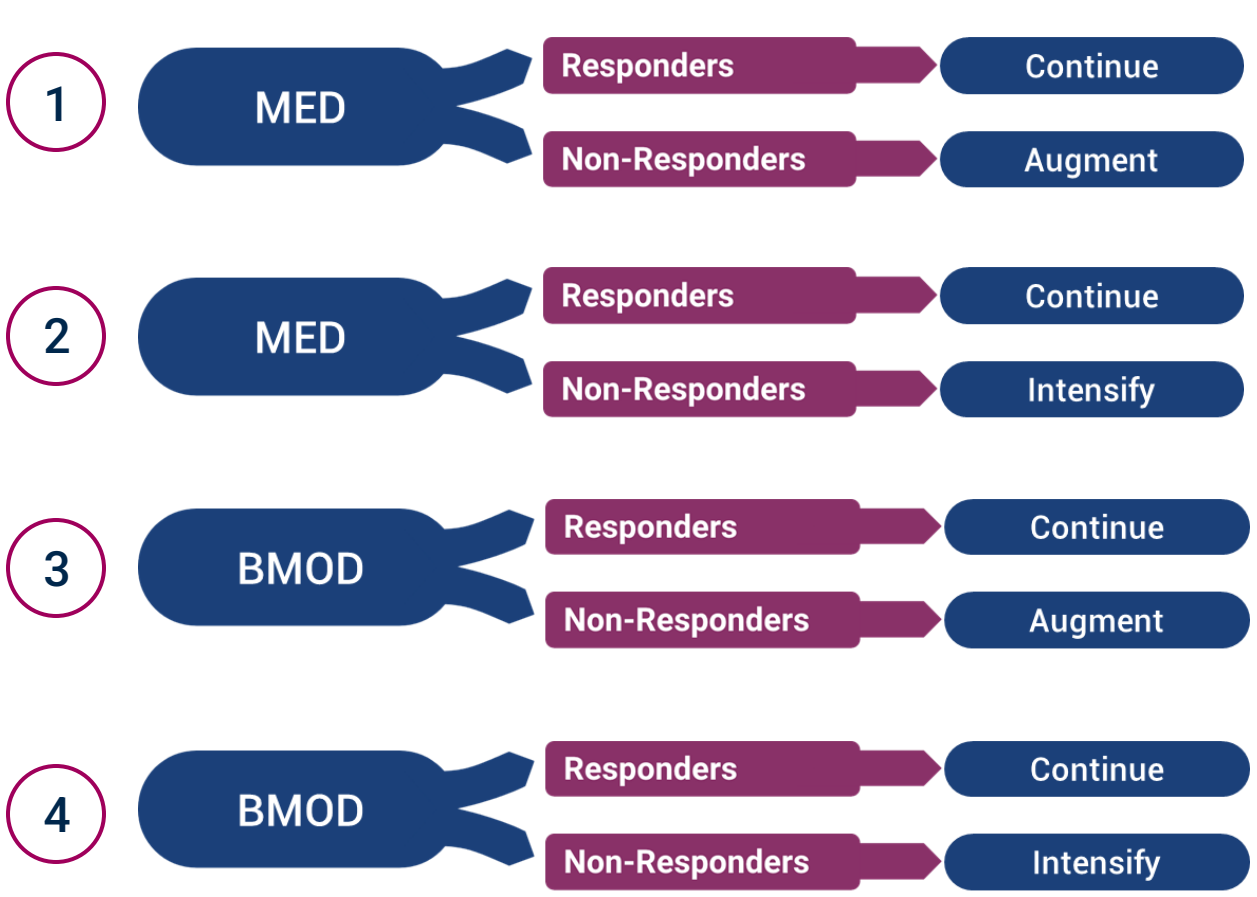
Review

🕒 30 min

Example ADHD SMART with 4 Embedded Adaptive Interventions (AIs)

PI: Pelham



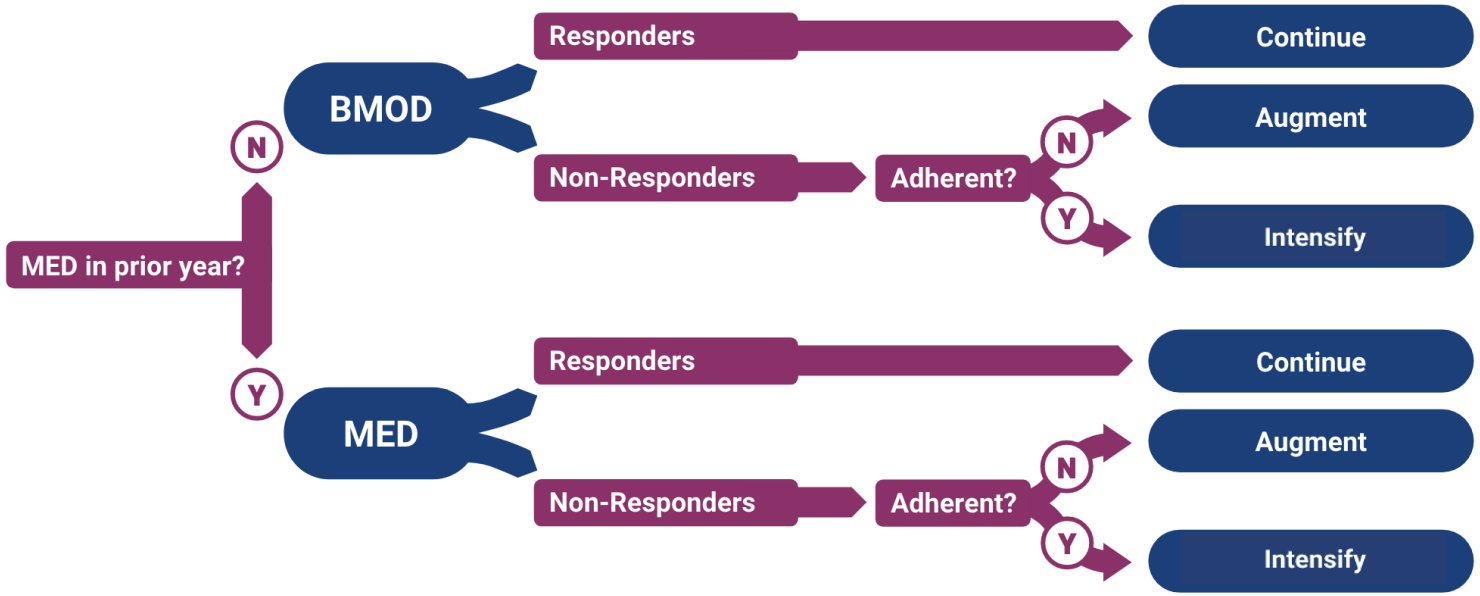


What is a more deeply-tailored AI?

- A **more deeply-tailored AI** is an adaptive intervention that
  - includes additional tailoring variables or decision rules relative to the adaptive interventions embedded in the SMART (e.g., response status=embedded)
  - and has the potential to lead to better outcomes by increasing personalization

Embedded AI: tailor based on 1 variable

More deeply tailored AI: tailor based on 3 variables



A typical secondary aim in a SMART is to better understand the utility of candidate tailoring variables

A typical secondary aim

Secondary Aim: *To construct a more deeply*-tailored adaptive intervention that maximizes [outcome] by examining:

1. Whether [baseline variable] is useful for tailoring first-stage intervention options; **AND**
2. Whether [baseline variable], first-stage intervention, and [intermediate variable] are useful for tailoring second-stage intervention options.

Example secondary in the ADHD SMART

Secondary Aim: *"To construct a more deeply*-tailored adaptive intervention that maximizes end-of-year school performance by examining…":

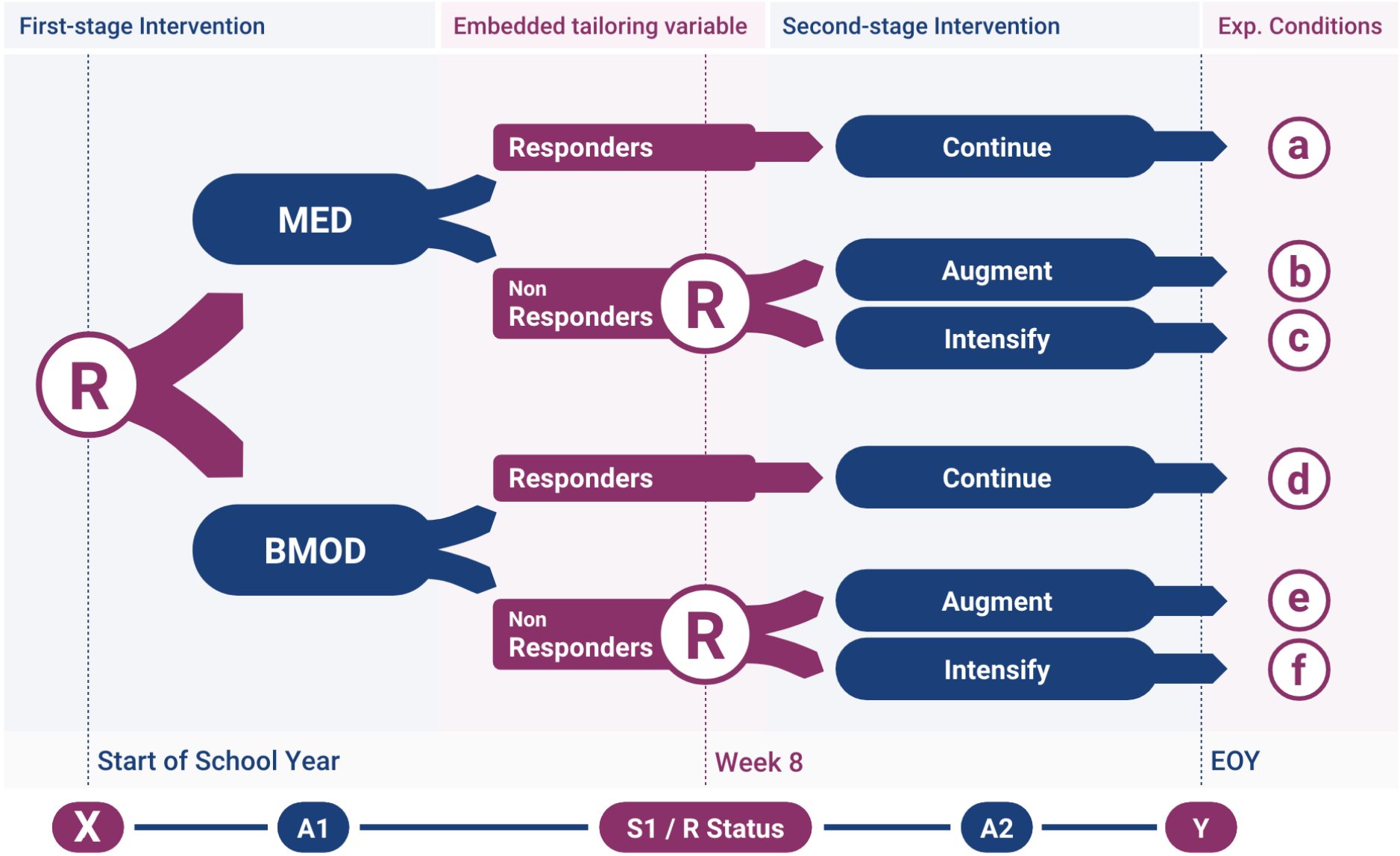
1. Whether prior med is useful for tailoring first-stage intervention options; AND
2. Whether first-stage intervention, and adherence are useful for tailoring second-stage intervention options among non-responders

Q-learning can be used to address this type of Secondary Aim

Q-learning

- Provides evidence for the utility of candidate tailoring variables
- Leads to a proposal for a more deeply-tailored AI
- **Similar to moderators analysis, which you know how to do. So let's review that first ☺**

Measures collected in a SMART



X

Baseline Covariates

- Prior MED
- Demographics
- Baseline ADHD scores
- Baseline school performance
- ODD
- etc.

S1

Intermediate Covariates

- Adherence to stage 1 intervention
- Month of non-response
- Parent function during stage 1

Review

What is a moderator variable in a standard 2-arm RCT?

- Typical to examine the causal effect of an intervention (**A**) on an outcome (**Y**)
  - E.g., **A** = BMOD (1) or MED (-1)
  - E.g., **Y** = school performance (higher is better)
- A **moderator** is a third variable (**X**) that influences the **causal effect** (strength/direction) of an intervention (**A**) on an outcome (**Y**).
- Temporal ordering is important!
  - E.g., **X = moderator variable = prior medication use**

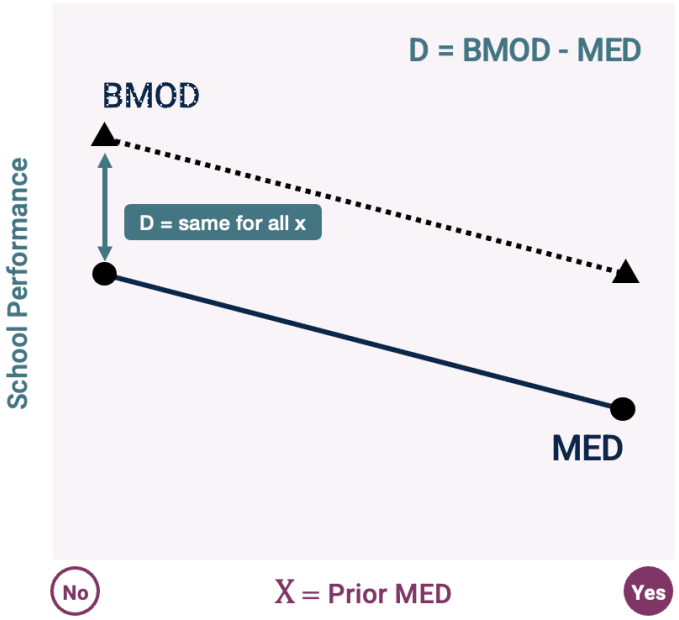
Moderator analysis is useful for informing the design of an adaptive intervention because…

X = moderator
A = Intervention
Y = outcome

- Reveals under which context(s) or circumstance(s) an intervention is most effective (“who/where/when”)
- Can lead to a proposal for useful tailoring variables
- Enhances our theoretical understanding of why and how an intervention works/fails

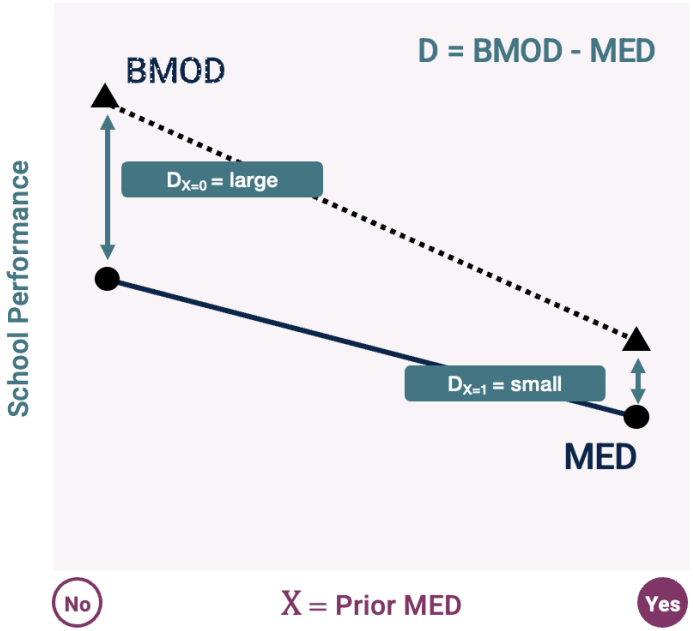
Review: Not all moderators make good tailoring variables

Hypothetical results examining whether X moderates the effect of A on Y



No, X is not a moderator

No, X is not useful for tailoring



Yes, X is a moderator

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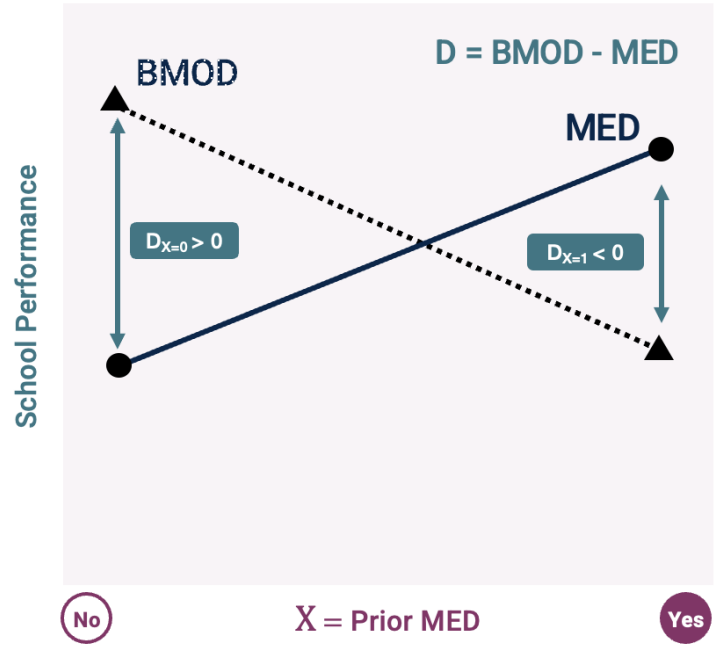


Yes, X is a moderator

Yes, X is useful for tailoring

Moderator analyses in a SMART can be conducted at each decision point…

Baseline covariates as moderators of the effect of first stage intervention on Y, <u>among all participants</u>

First-stage:

Moderator analyses in a SMART can be conducted at each decision point…

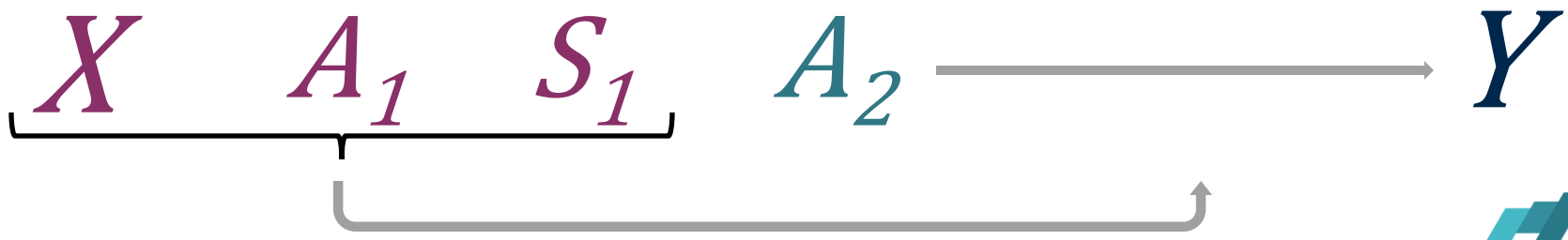
Baseline covariates as moderators of the effect of first stage intervention on Y, among all participants

First-stage:

Baseline, first-stage treatment, and intermediate covariates as moderators of the effect of the second-stage intervention on Y, among non-responders

Second-stage:

$R=0$



Q-learning extends moderator analysis to sequential interventions

- This leads to a proposal for an AI that uses baseline AND time-varying covariates to tailor treatment
- How?
- Links moderated regressions for second-stage and then first-stage interventions!
  - Analysis moves *backwards* in time
    - **Q-learning ensures the proposed adaptive intervention incorporates *synergy* between the first and second-stage decision rules**

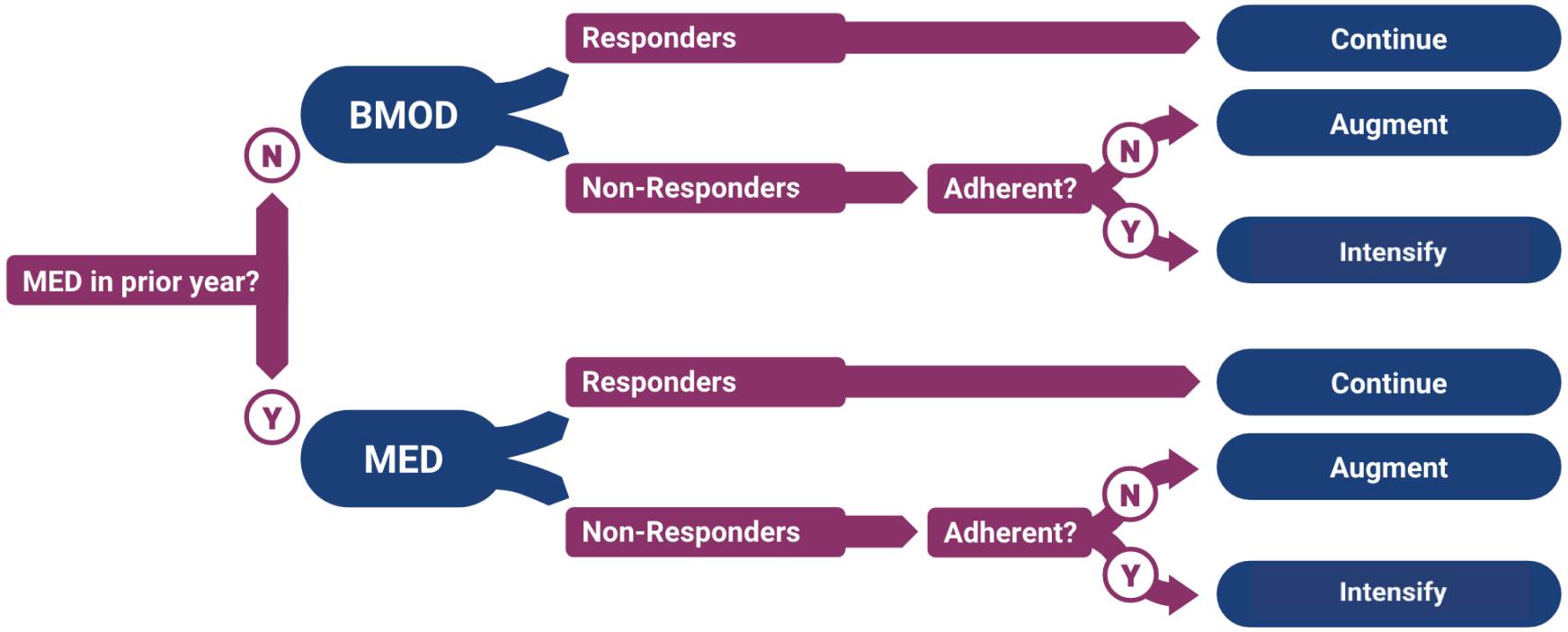
The 3 steps of Q-learning

1. **Fit moderated regression** model to obtain optimal stage 2 decision rule

2. **Calculate** the expected outcome if the individual had received optimal 2nd stage intervention

3. **Fit moderated regression** model using expected outcomes (from step 2) to obtain optimal stage 1 decision rule

This is the adaptive intervention you get from Q-Learning!



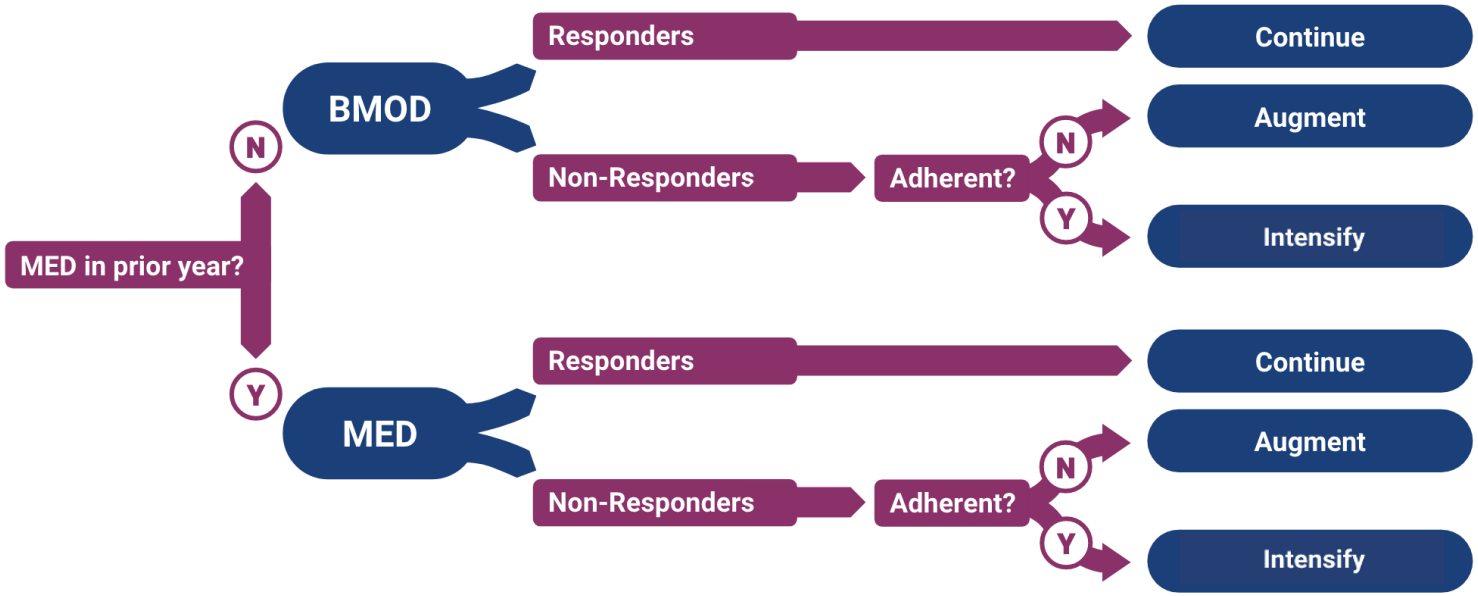
What is the benefit of Q-Learning?

- To get a better sense of the benefit of Q-Learning, estimate the mean outcome under the more deeply tailored adaptive intervention

Embedded AI

Mean Y = 3.83

More deeply tailored AI



Mean Y = 4.70

Estimated mean of more deeply-tailored AI using Q-Learning

Means of embedded AIs and Proposed More Deeply Tailored AI

	Estimate	95% LCL	95% UCL
BMOD, INT	2.97	2.46	3.48
BMOD, AUG	3.83	3.36	4.30
MED, INT	2.17	1.63	2.71
MED, AUG	2.67	2.24	3.09
QL More Deeply Tailored AI	4.70		

Questions?

Break

🕒 10 min