



Presented by
Daniel Almirall, PhD

Primary Aim Analyses in a SMART

Part II

Module 5

 60 min

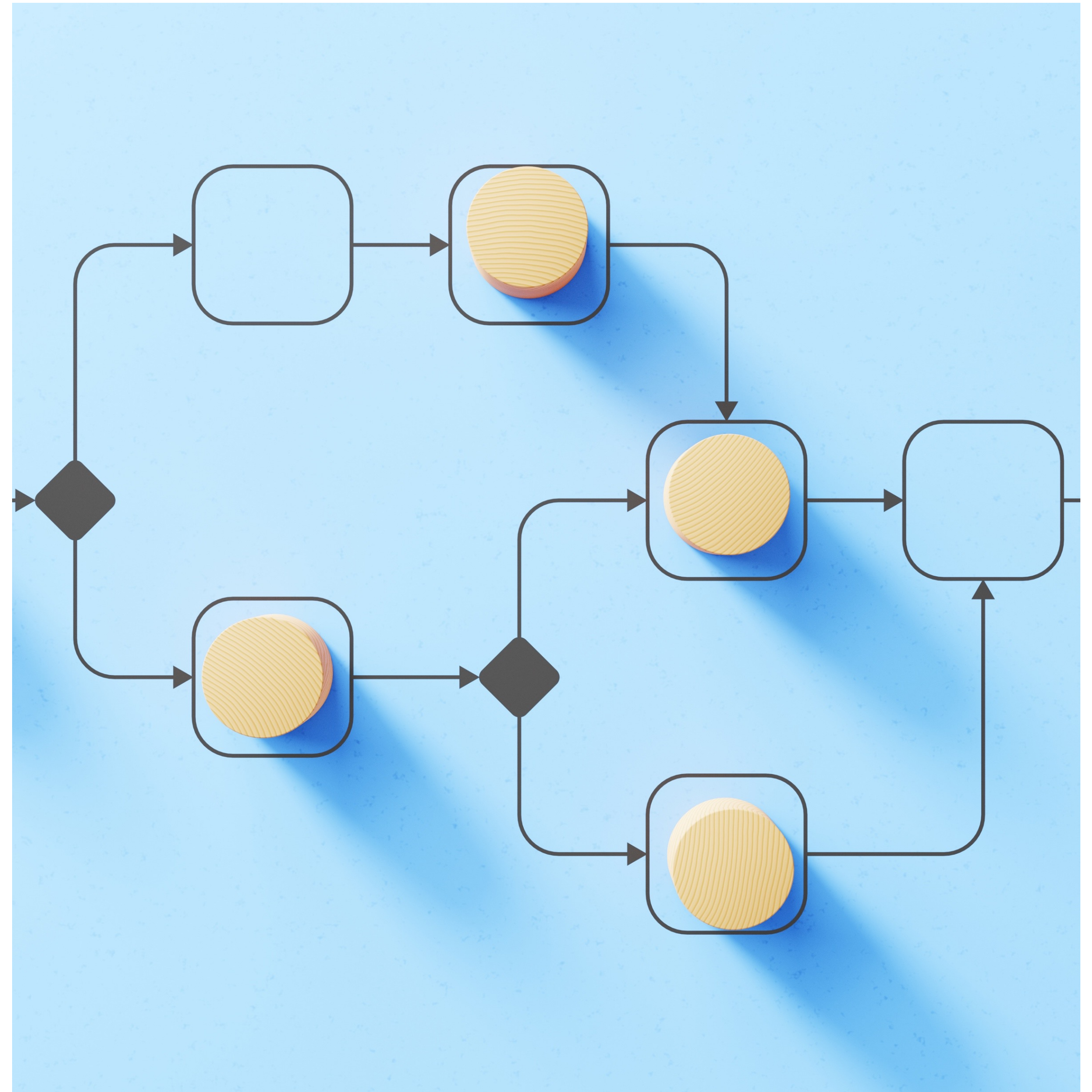


Learning Objectives

You will have a better understanding, and will continue learning how to frame, the typical Primary Aims in a SMART

You will learn about key statistical considerations in Primary Aim analyses in a SMART

You will learn how to interpret the output for the different Primary Aim Analyses in a SMART



Outline

Illustrative Example: ADHD SMART Study (PI: Pelham)

Prepare (again) for a third primary aim analysis by

(d): Estimate and compare the mean outcome under two of the embedded AIs using weighted least squares

Use a single weighted-and-replicated least squares regression approach capable of address any/all three primary aims in a SMART



Outline

Illustrative Example: ADHD SMART Study (PI: Pelham)

Prepare (again) for a third primary aim analysis by

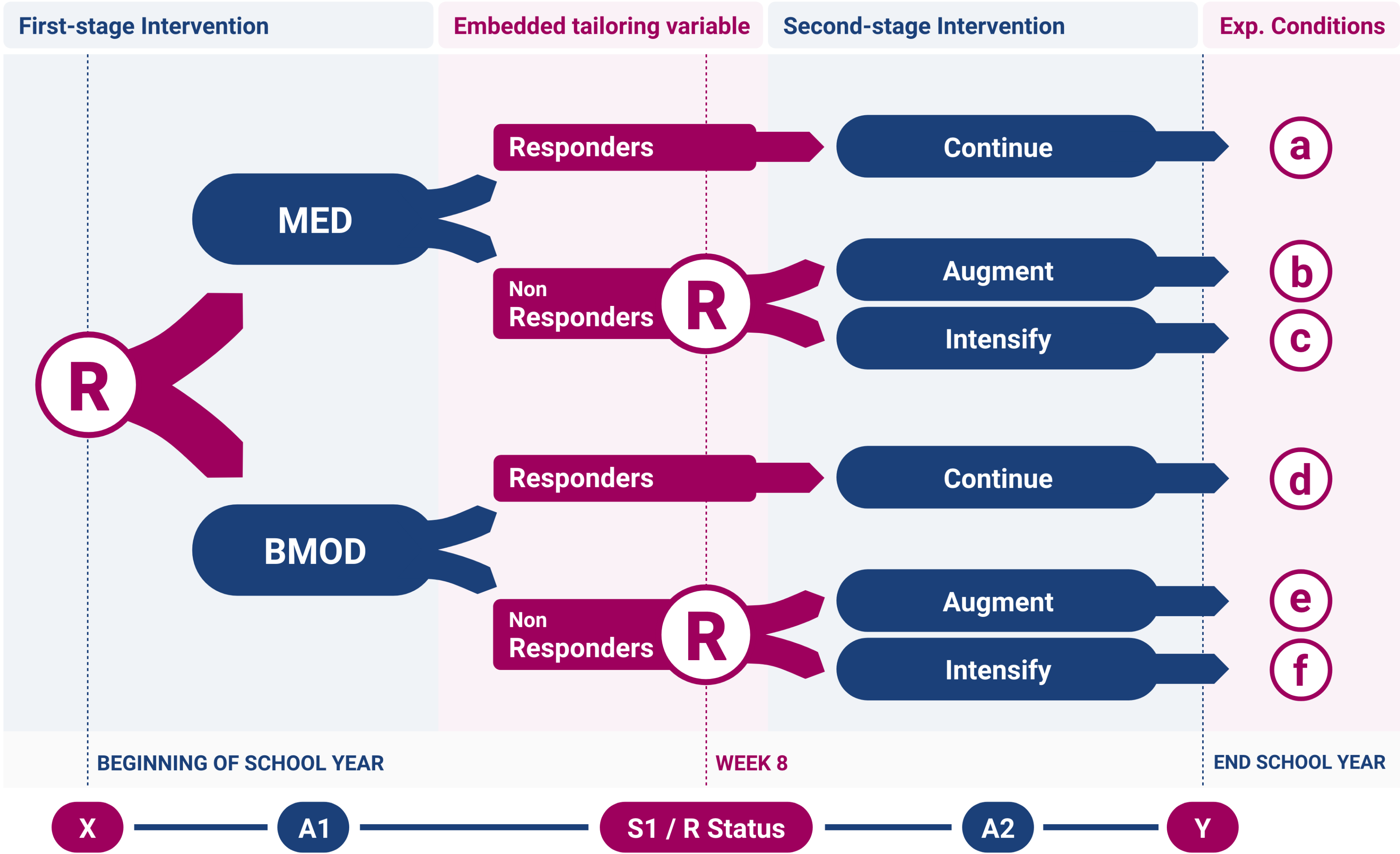
(d): Estimate and compare the mean outcome under two of the embedded AIs using weighted least squares

Use a single weighted-and-replicated least squares regression approach capable of address any/all three primary aims in a SMART



SMART Example ADHD Study

PI: Pelham



SMART Example 4 Embedded Adaptive Interventions

PI: Pelham

Adaptive Intervention 1

At the beginning of the school year **Stage 1 = {MED}**;
then, every month, starting week 8
if response status = {NR},
then, Stage 2 = {AUGMENT};
else if response status = {R},
then, Continue Stage 1

Adaptive Intervention 3

At the beginning of the school year **Stage 1 = {MED}**;
then, every month, starting week 8
if response status = {NR},
then, Stage 2 = {INTENSIFY};
else if response status = {R},
then, Continue Stage 1

Adaptive Intervention 2

At the beginning of the school year **Stage 1 = {BMOD}**;
then, every month, starting week 8
if response status = {NR},
then, Stage 2 = {AUGMENT};
else if response status = {R},
then, Continue Stage 1

Adaptive Intervention 4

At the beginning of the school year **Stage 1 = {BMOD}**;
then, every month, starting week 8
if response status = {NR},
then, Stage 2 = {INTENSIFY};
else if response status = {R},
then, Continue Stage 1

Adaptive Intervention 1

At the beginning of the school year

Stage 1 = {MED};

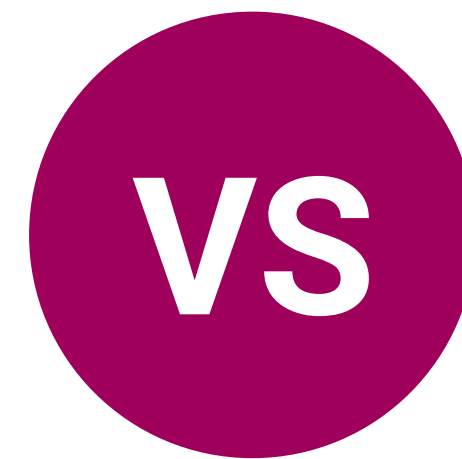
then, every month, starting week 8

if response status = {NR},

then, Stage 2 = {AUGMENT};

else if response status = {R},

then, Continue Stage 1



Adaptive Intervention 2

At the beginning of the school year

Stage 1 = {BMOD};

then, every month, starting week 8

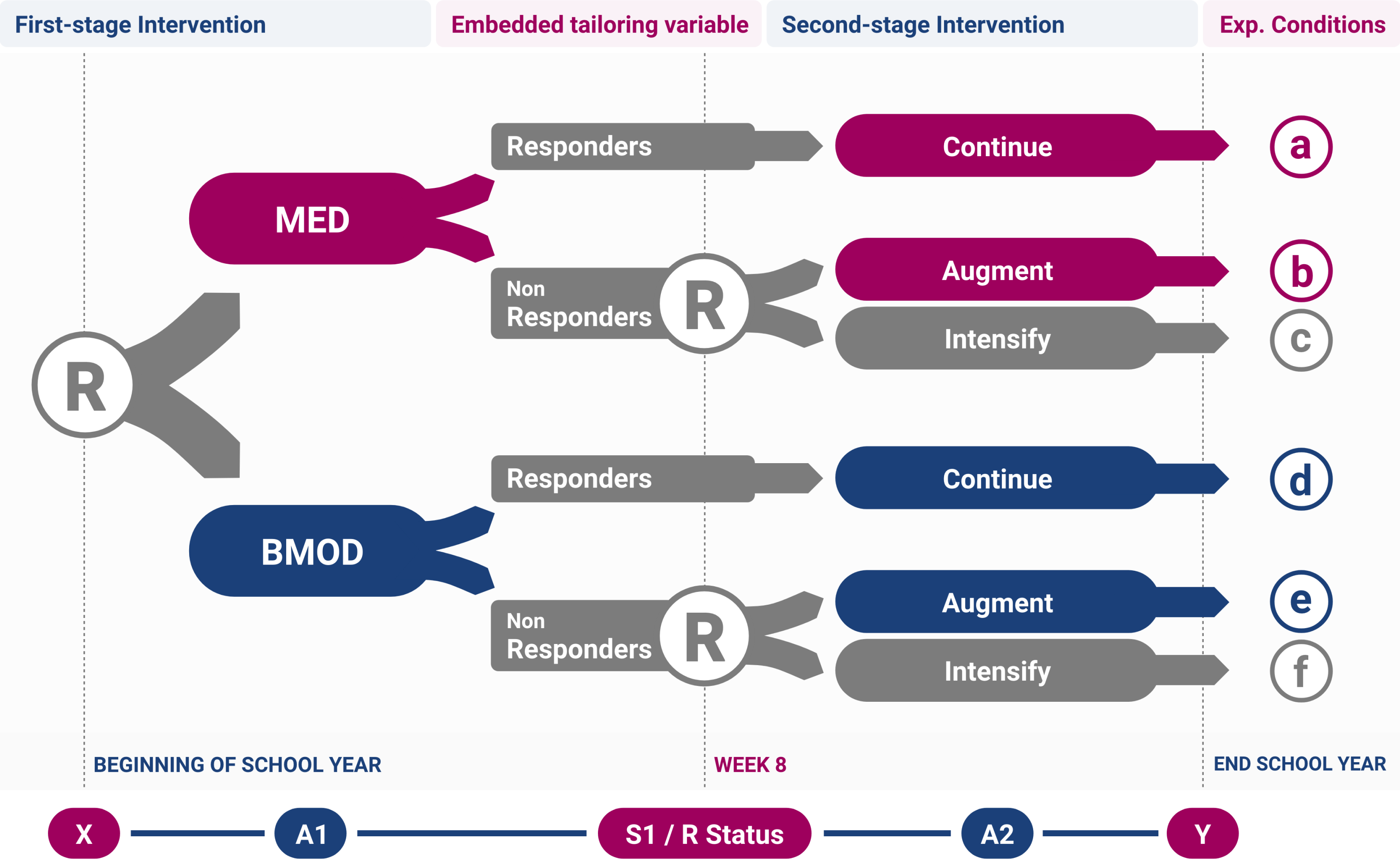
if response status = {NR},

then, Stage 2 = {AUGMENT};

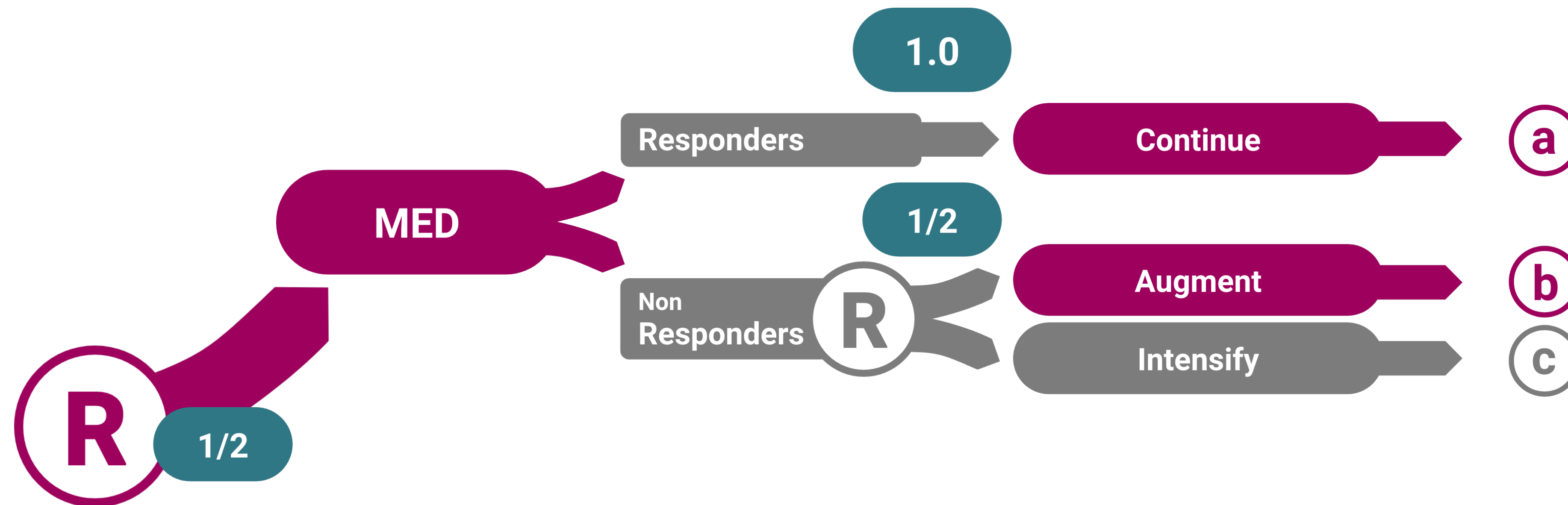
else if response status = {R},

then, Continue Stage 1

This Aim is a Comparison of the Mean Outcome under AI#1 vs. the Mean Outcome of AI#2

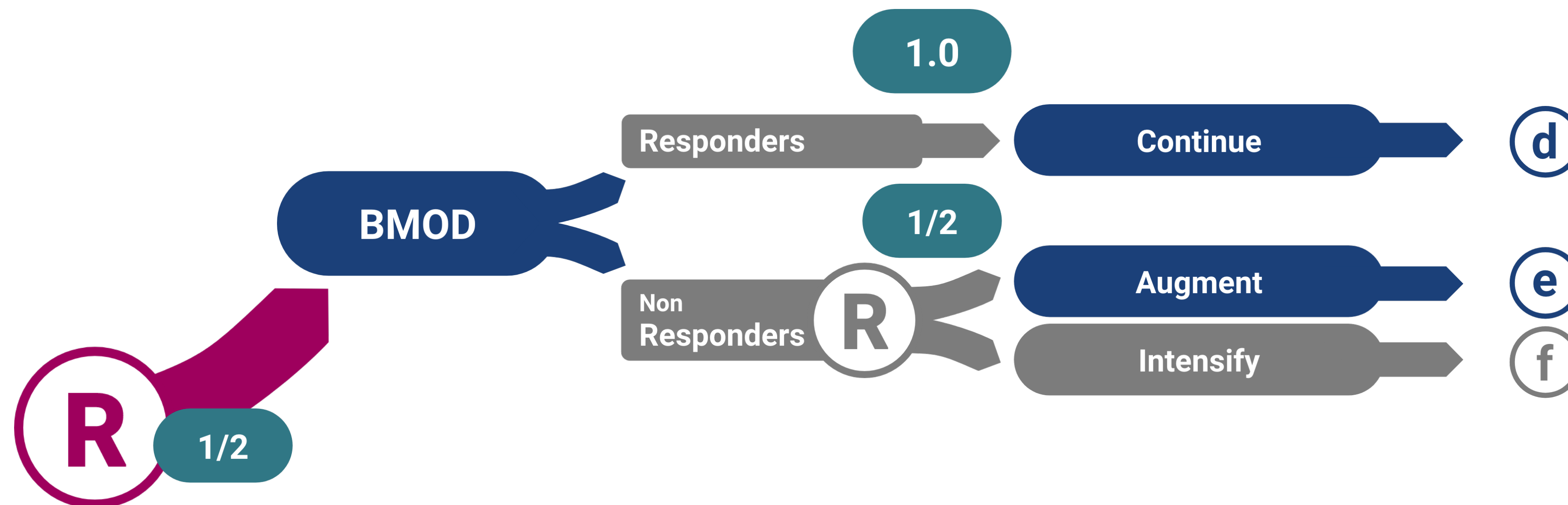


We Know How to Account for Imbalance in Non-Responders Following AI#1



- Assign $W = \text{weight} = 2$ to responders to MED $\rightarrow 2 * \frac{1}{2} = 1$
- Assign $W = \text{weight} = 4$ to non-responders to MED $\rightarrow 4 * \frac{1}{4} = 1$
- Then we take W -weighted mean of sample who ended up in circles A+B.

A Similar Approach (and SAS Code) Can be Used to Obtain Mean Under AI #2



- Assign $W = \text{weight} = 2$ to responders to BMOD $\rightarrow 2 * \frac{1}{2} = 1$
- Assign $W = \text{weight} = 4$ to non-responders to BMOD $\rightarrow 4 * \frac{1}{4} = 1$
- Then we take W -weighted mean of sample who ended up in circles D+E.

Results for Estimated Mean Outcome had All Participants Followed AI#2 (BMOD, AUGMENT)

Results are from simulated data.

| Analysis Of GEE Parameter Estimates | | | |
|-------------------------------------|----------|----------------|---------|
| Parameter | Estimate | Standard Error | Pr > Z |
| Intercept | 3.149 | 0.1477 | <.0001 |
| Z1 | 0.6836 | 0.1477 | 0.0001 |

| Contrast Estimate Results | | | | | |
|------------------------------------|---------------|-----------------------|-------|----------------|------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error | Pr > ChiSq |
| | | Lower | Upper | | |
| Mean Y under AI #2 (BMOD, AUGMENT) | 3.833 | 3.363 | 4.303 | 0.24 | <.0001 |

Interpretation: The estimated mean school performance score for children consistent with AI #2 is ~3.83 (95% CI: (3.36, 4.30)).



Outline

Illustrative Example: ADHD SMART Study (PI: Pelham)

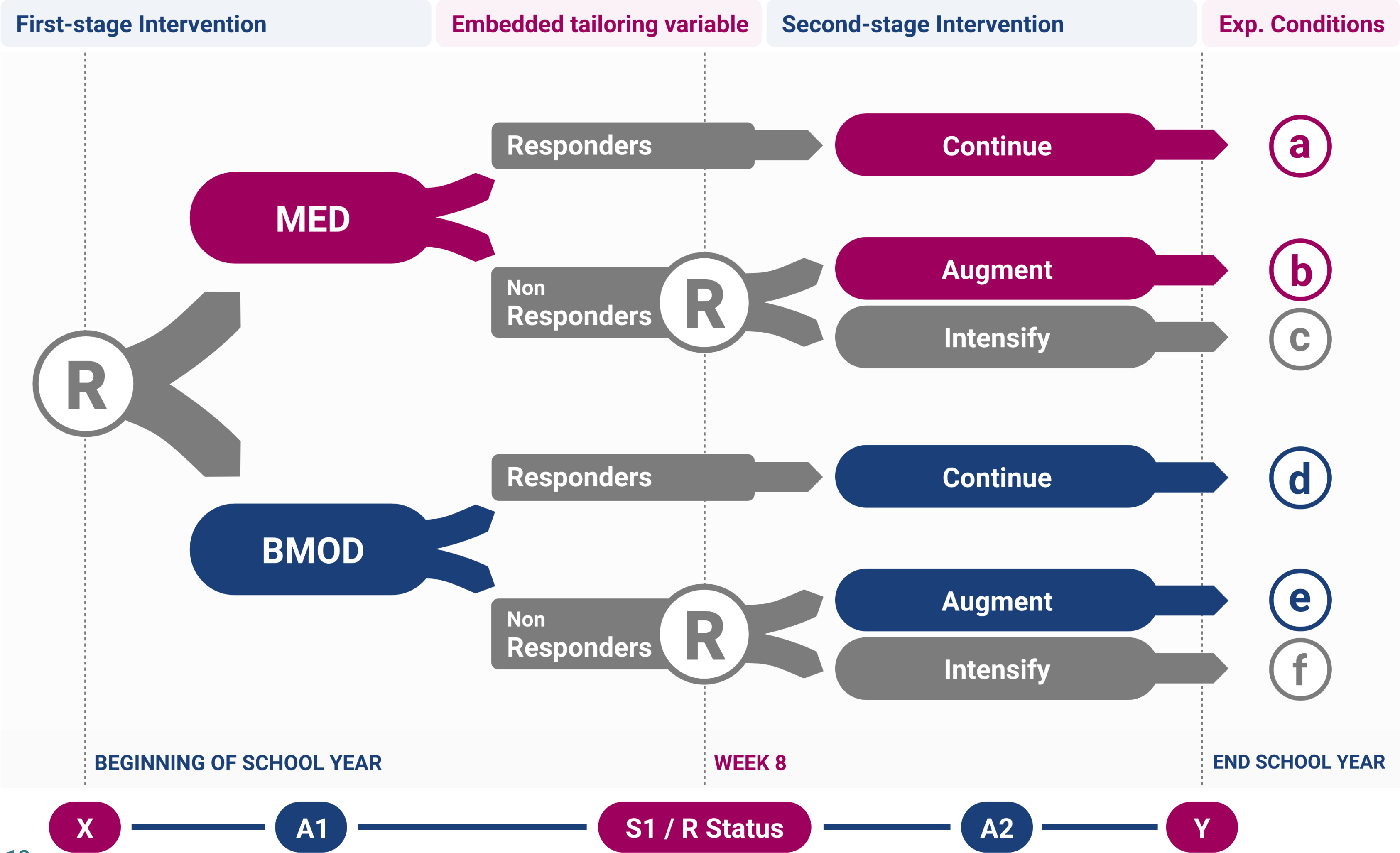
Prepare (again) for a third primary aim analysis by

(d): Estimate and compare the mean outcome under two of the embedded AIs using weighted least squares

Use a single weighted-and-replicated least squares regression approach capable of address any/all three primary aims in a SMART



An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2



An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

```
data dat7; set dat1;
```

```
Z1=-1; ←
```

```
    if A1*R=-1 then Z1=1;
```

```
    if (1-A1)*(1-R)*A2=-2 then Z1=1;
```

```
Z2=-1;
```

```
    if A1*R= 1 then Z2=1;
```

```
    if (1+A1)*(1-R)*A2=-2 then Z2=1;
```

```
W=2*R + 4*(1-R);
```

```
run;
```

Create Z1 → indicator for whether or not the person is consistent with AI#1

```
data dat8;
```

```
    set dat7; if Z1=1 or Z2=1;
```

```
run;
```


An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

```
data dat7; set dat1;  
  Z1=-1;  
    if A1*R=-1 then Z1=1;  
    if (1-A1)*(1-R)*A2=-2 then Z1=1;  
  Z2=-1; ←  
    if A1*R= 1 then Z2=1;  
    if (1+A1)*(1-R)*A2=-2 then Z2=1;  
  W=2*R + 4*(1-R);  
run;
```

Create Z2 → indicator for whether or not the person is consistent with AI#2

```
data dat8;  
  set dat7; if Z1=1 or Z2=1;  
run;
```

An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

```
data dat7; set dat1;  
  Z1=-1;  
    if A1*R=-1 then Z1=1;  
    if (1-A1)*(1-R)*A2=-2 then Z1=1;  
  Z2=-1;  
    if A1*R= 1 then Z2=1;  
    if (1+A1)*(1-R)*A2=-2 then Z2=1;  
  W=2*R + 4*(1-R);  
run;
```

Assigned Weights

```
data dat8;  
  set dat7; if Z1=1 or Z2=1;  
run;
```


An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

```
data dat7; set dat1;  
  Z1=-1;  
    if A1*R=-1 then Z1=1;  
    if (1-A1)*(1-R)*A2=-2 then Z1=1;  
  Z2=-1;  
    if A1*R= 1 then Z2=1;  
    if (1+A1)*(1-R)*A2=-2 then Z2=1;  
  W=2*R + 4*(1-R);  
run;
```

```
data dat8;  
  set dat7; if Z1=1 or Z2=1;  
run;
```

← Delete data from participants not consistent with either AI#1 or AI#2

An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

The Regression and Contrast Coding Logic:

Recall:

Z_1 is now an indicator for whether the person is consistent with AI#1 or with AI#2:

→ $Z_1 = 1 = \text{AI\#1}$

→ $Z_1 = -1 = \text{AI\#2}$

To compare the 2 AIs, we can fit the Model:

$$Y = \beta_0 + \beta_1 Z_1 + e$$

Overall Mean Y under AI#1 = $\beta_0 + \beta_1 \times 1$

Overall Mean Y under AI#2 = $\beta_0 + \beta_1 \times -1$

Diff Between AIs = $\beta_0 + \beta_1 - (\beta_0 - \beta_1) = 2\beta_1$

An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

```
proc genmod data = dat8;  
  class id;  
  model Y = Z1;  
  scwgt W;  
  repeated subject = id / type = ind;  
  estimate 'Mean Y AI#1(MED, Add BMOD)' intercept 1 Z1 1;  
  estimate 'Mean Y AI#2(BMOD, Add MED)' intercept 1 Z1 -1;  
  estimate 'Diff: AI#1 - AI#2' Z1 2;  
run;
```

$$\begin{aligned}\text{Mean Y under AI\#1} &= \beta_0 + \beta_1 \times 1 \\ \text{Mean Y under AI\#2} &= \beta_0 + \beta_1 \times -1 \\ \text{Diff Between AIs} &= 2\beta_1\end{aligned}$$

An Intuitive [Yet Less Efficient] Approach to Comparing AI#1 vs. AI#2

| Analysis Of GEE Parameter Estimates | | | | | |
|-------------------------------------|----------|----------------|--|---------|--|
| Parameter | Estimate | Standard Error | | Pr > Z | |
| Intercept | 3.25 | 0.1613 | | <.0001 | |
| Z1 | -0.583 | 0.1613 | | 0.0003 | |

| Contrast Estimate Results | | | | | |
|---------------------------------------|---------------|-----------------------|---------|----------------|------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error | Pr > ChiSq |
| | | Lower | Upper | | |
| Mean Y under AI #1 (MED, AUGMENT) | 2.666 | 2.242 | 3.0892 | 0.216 | <.0001 |
| Mean Y under AI #2 (BMOD, AUGMENT) | 3.833 | 3.363 | 4.3028 | 0.240 | <.0001 |
| Diff: AI#1 – AI#2 | -1.167 | -1.799 | -0.5347 | 0.323 | 0.0003 |

↑
Notice SE



An Intuitive Approach to Comparing AI#1 vs. AI#2

```
proc genmod data = dat8;
```

```
class id;
```

```
model Y = Z1 Y0c oddc;
```

```
scwgt w;
```

```
repeated subject = id / type = ind;
```

```
estimate 'Mean Y AI#1(MED, AUGMENT)' intercept 1 Z1 1;
```

```
estimate 'Mean Y AI#2(BMOD,AUGMENT)' intercept 1 Z1 -1;
```

```
estimate 'Diff: AI#1 - AI#2' Z1 2;
```

```
run;
```

Adding baseline control
covariates (mean centered)



An Intuitive Approach to Comparing AI#1 vs. AI#2

| Analysis Of GEE Parameter Estimates | | | | | |
|-------------------------------------|----------|----------------|--|---------|--|
| Parameter | Estimate | Standard Error | | Pr > Z | |
| Intercept | 3.26 | 0.1148 | | <.0001 | |
| Z1 | -0.45 | 0.1160 | | <.0001 | |
| Y0 | 2.13 | 0.2464 | | <.0001 | |
| oddc | 0.09 | 0.2511 | | 0.715 | |

| Contrast Estimate Results | | | | | |
|---------------------------|---------------|-----------------------|---------|----------------|------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error | Pr > ChiSq |
| | | Lower | Upper | | |
| Mean Y under AI #1 | 2.806 | 2.5198 | 3.0927 | 0.146 | <.0001 |
| Mean Y under AI #2 | 3.713 | 3.3491 | 4.0787 | 0.186 | <.0001 |
| Diff: AI#1 – AI#2 | -0.907 | -1.3776 | -0.4376 | 0.240 | 0.0001 |

Notice SE: Slightly smaller compared to the analysis without control covariates



Outline

Illustrative Example: ADHD SMART Study (PI: Pelham)

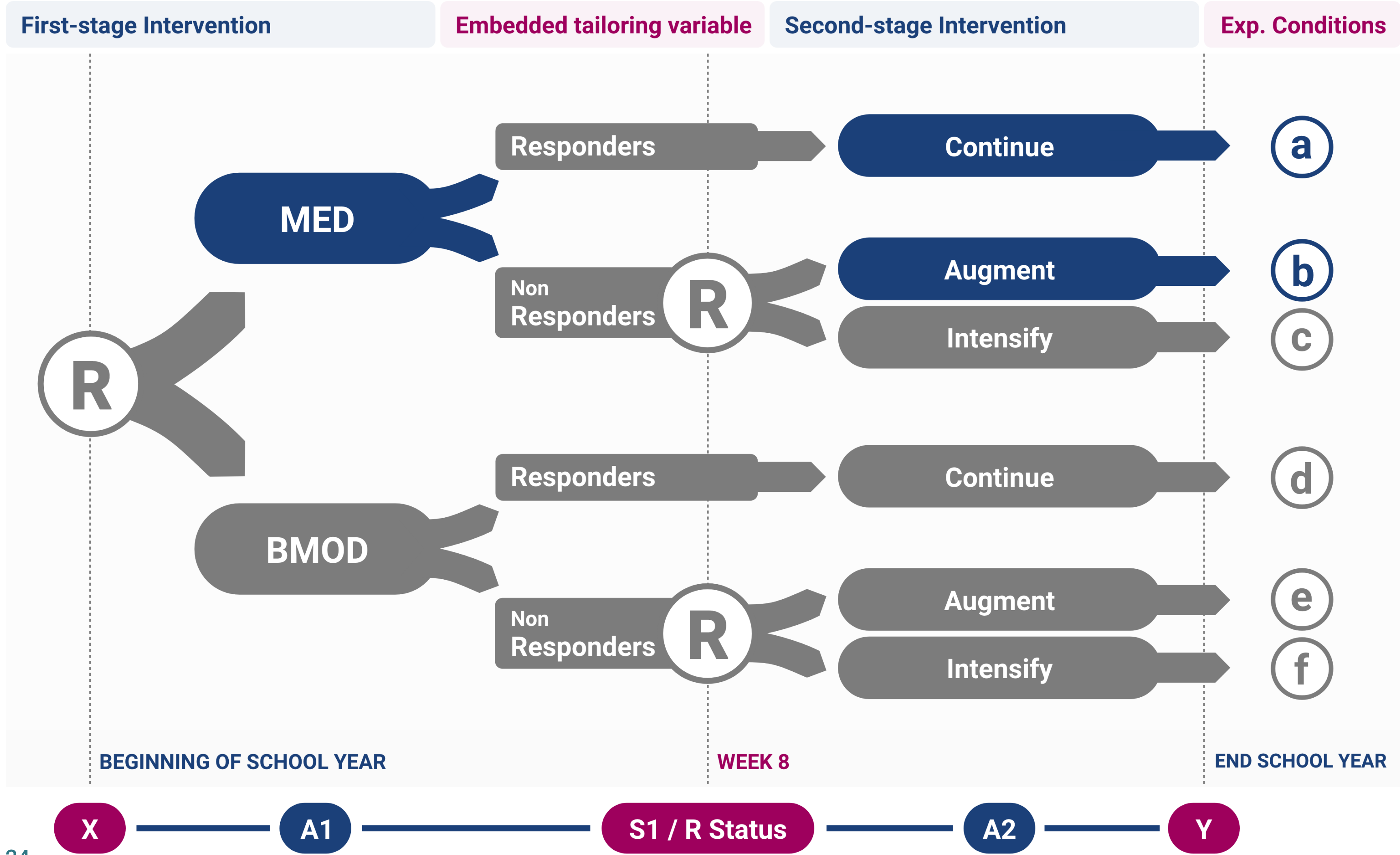
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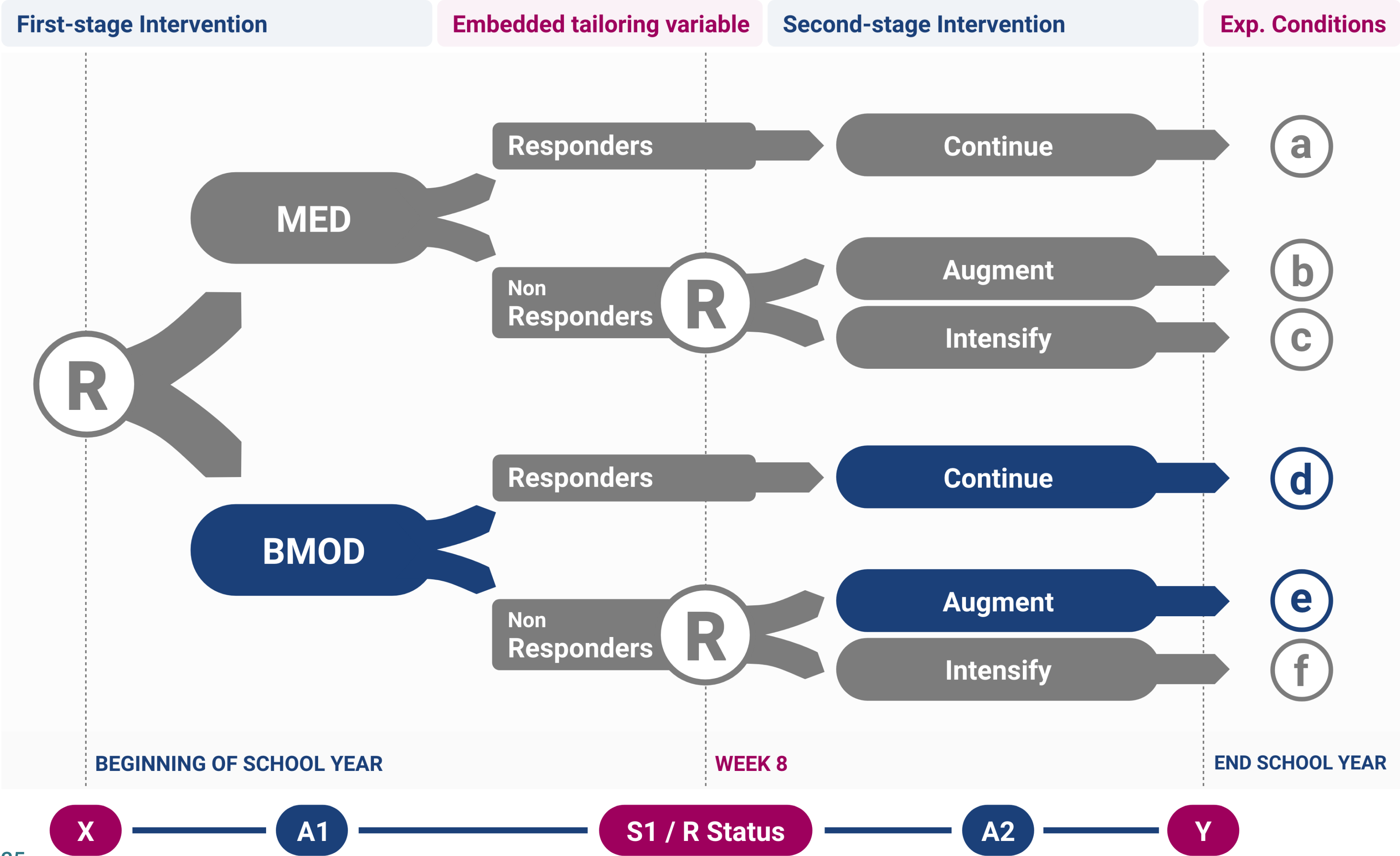
Use a single weighted-and-replicated least squares regression approach capable of address any/all three primary aims in a SMART



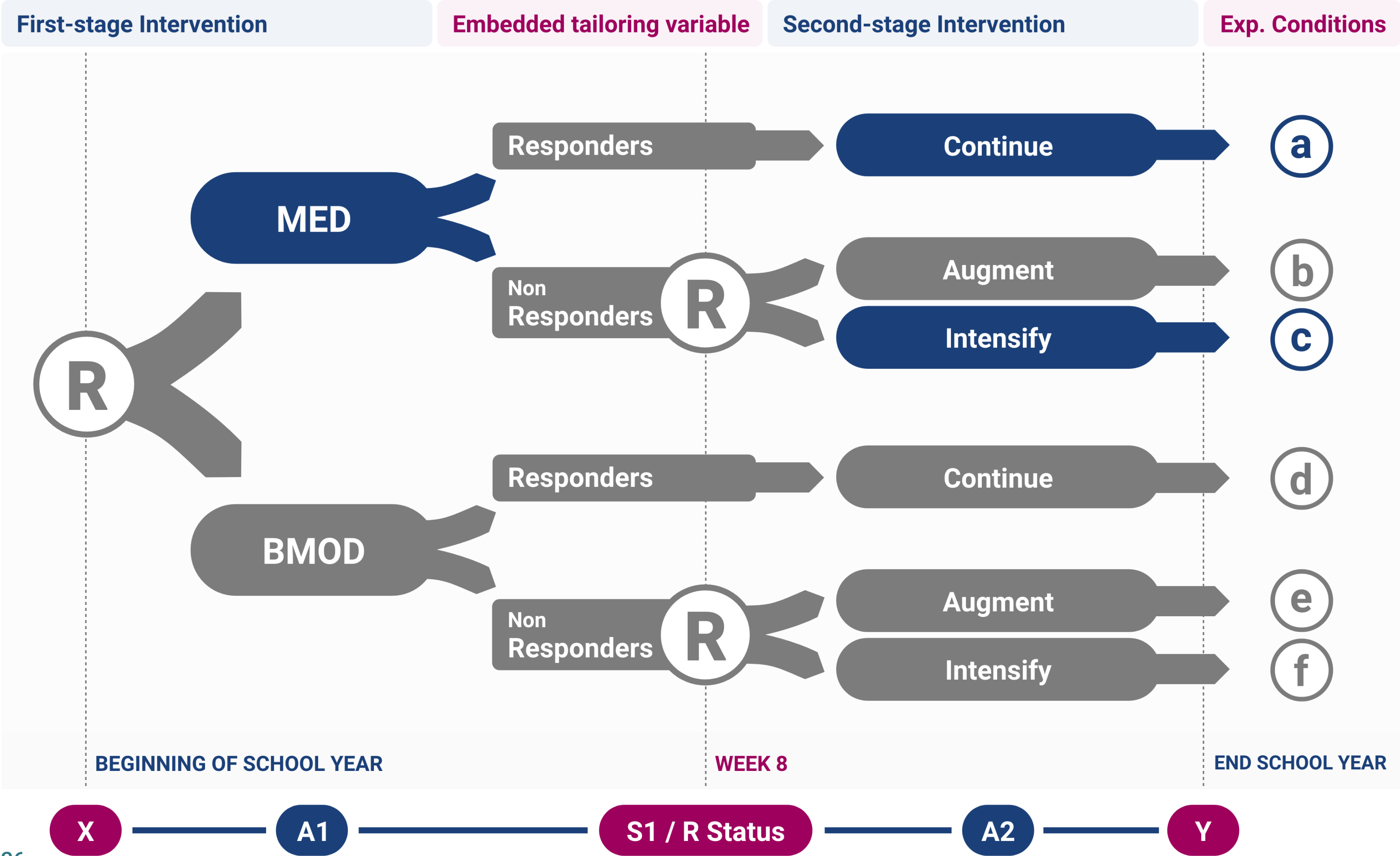
What about a regression to compare AI#1 (MED, add BMOD) vs...



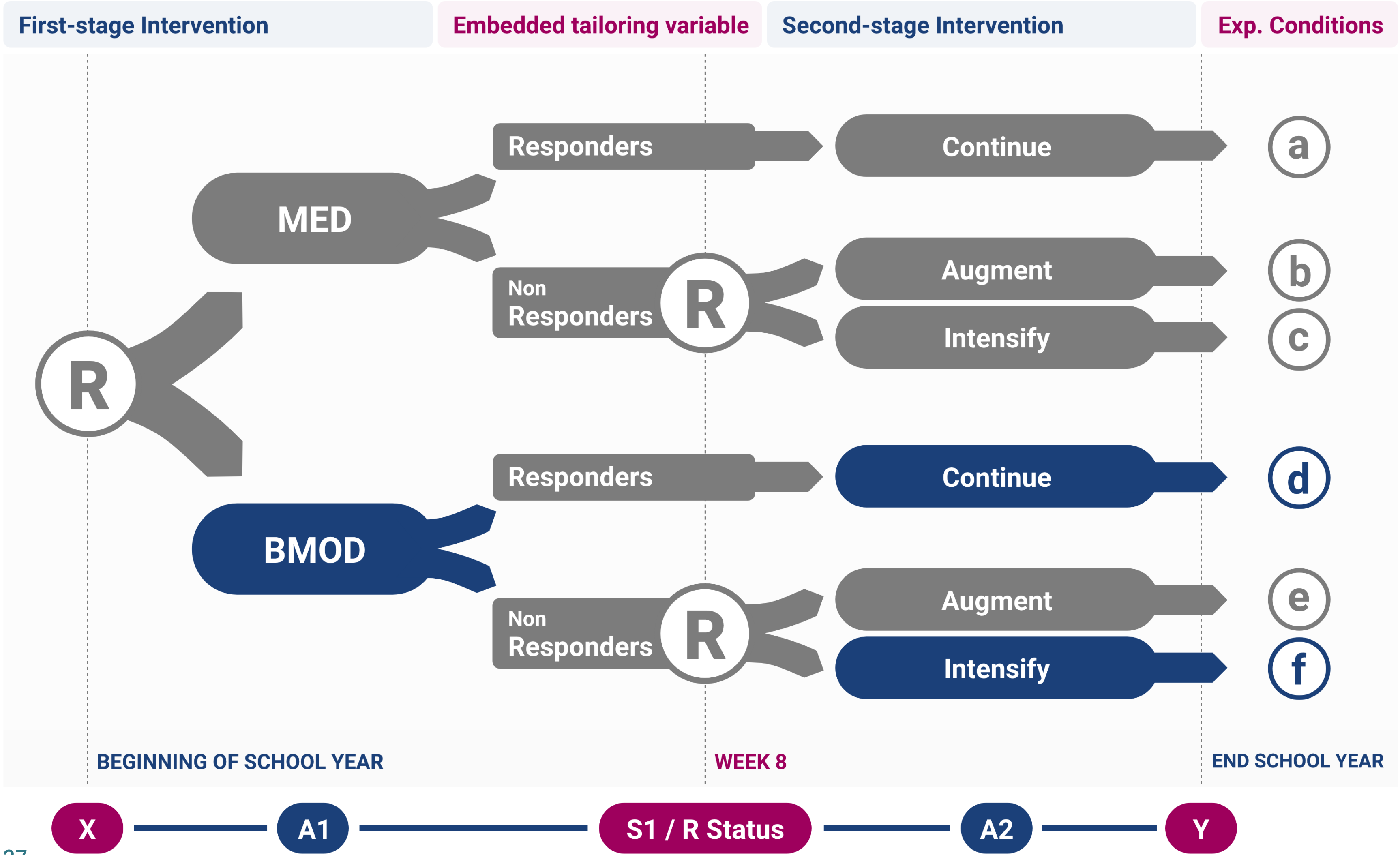
...AI #2 (BMOD, Add MED) vs...



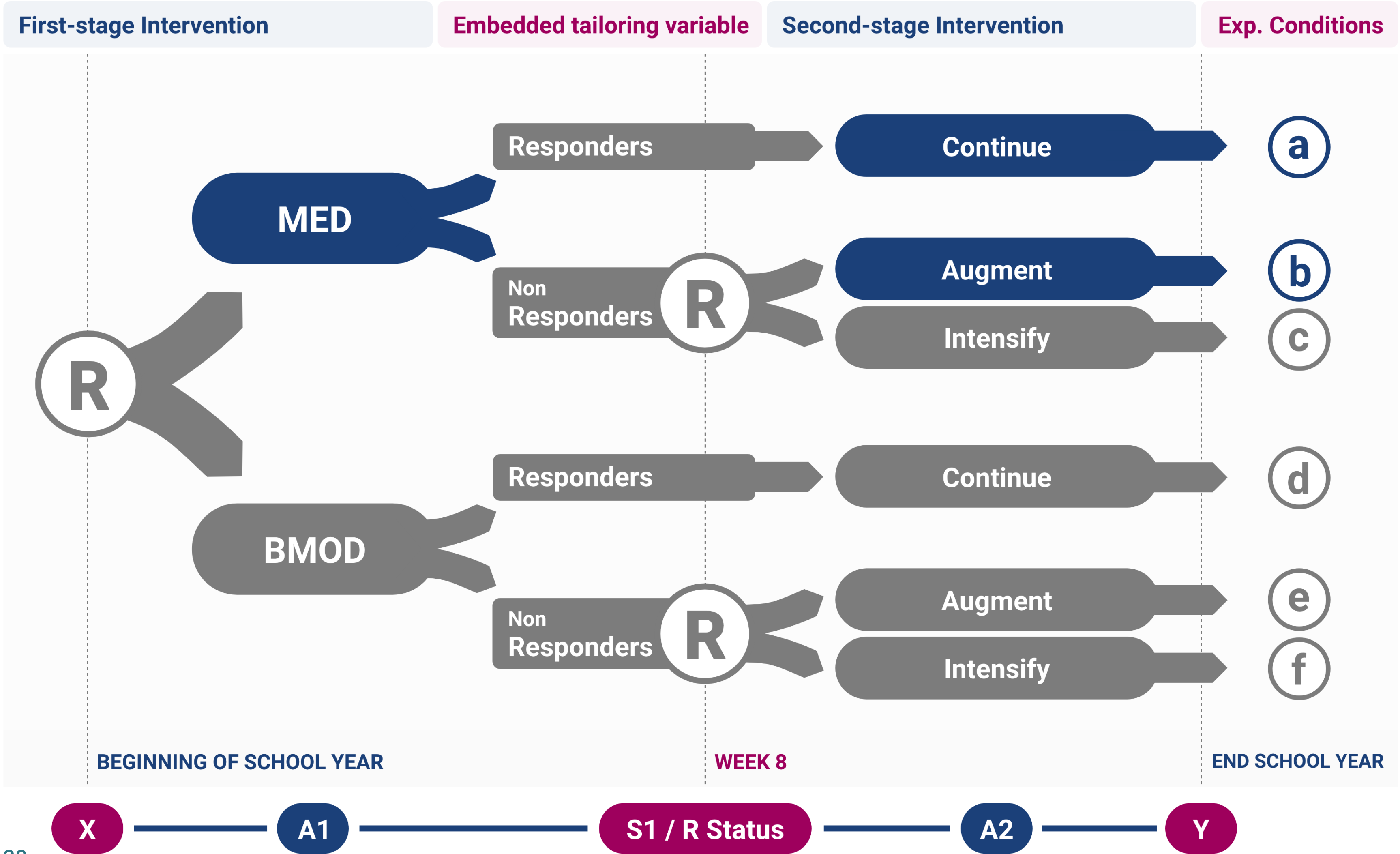
...AI #3 (MED, INTENSIFY) vs...



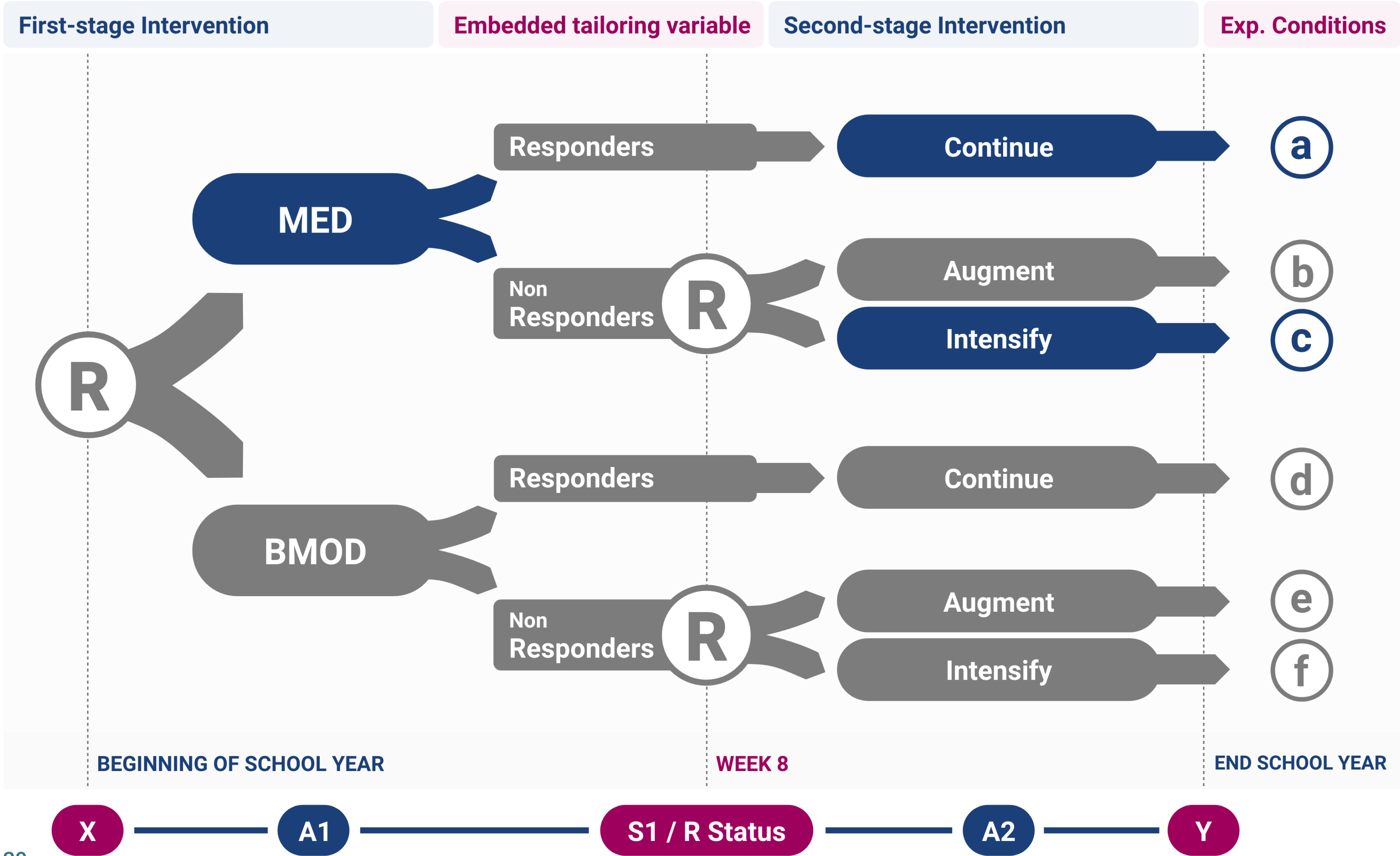
...AI#4 (BMOD, INTENSIFY), all in one swoop!



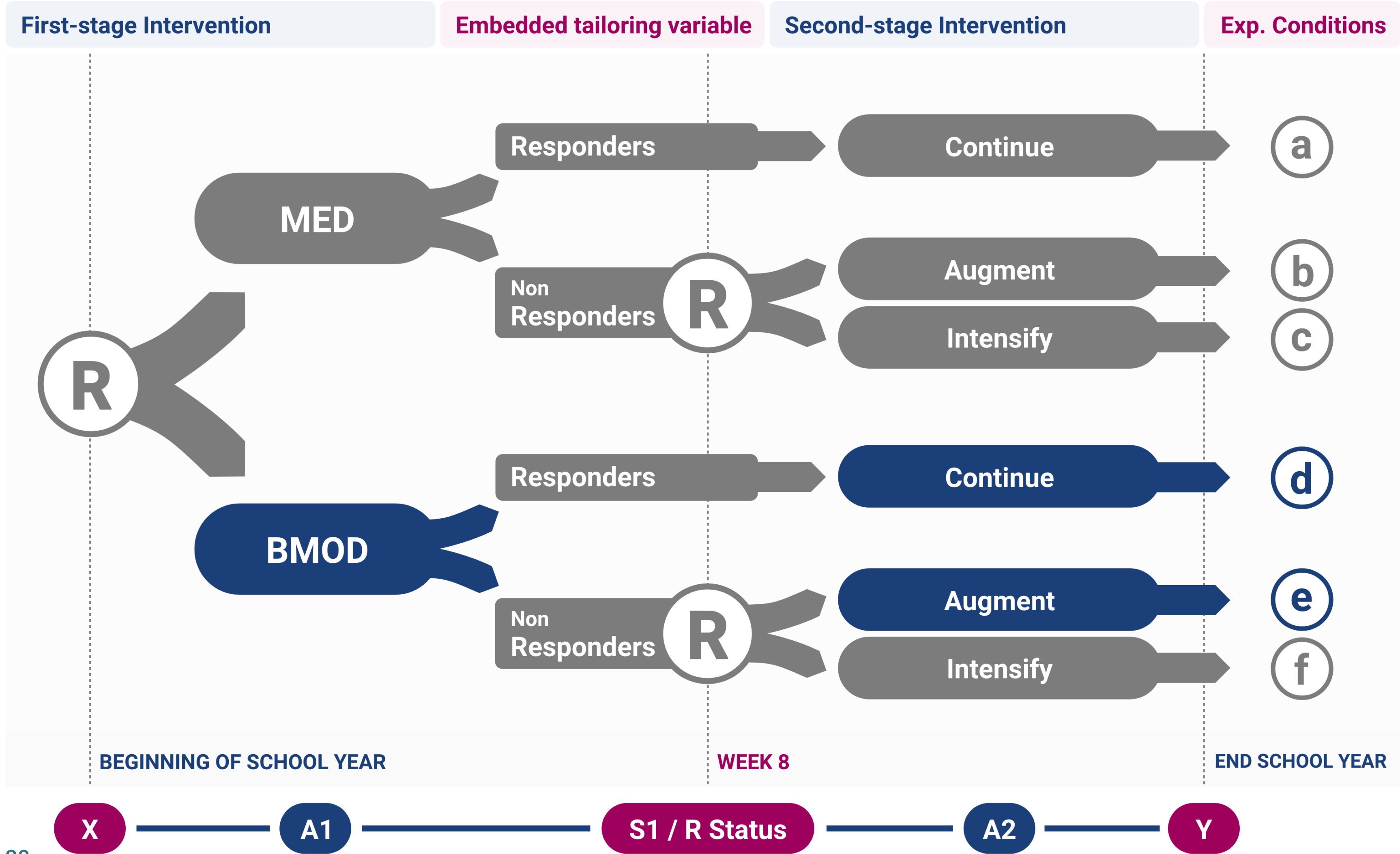
Notice that AI#1 and AI#3 (start MED) share responders (box A)



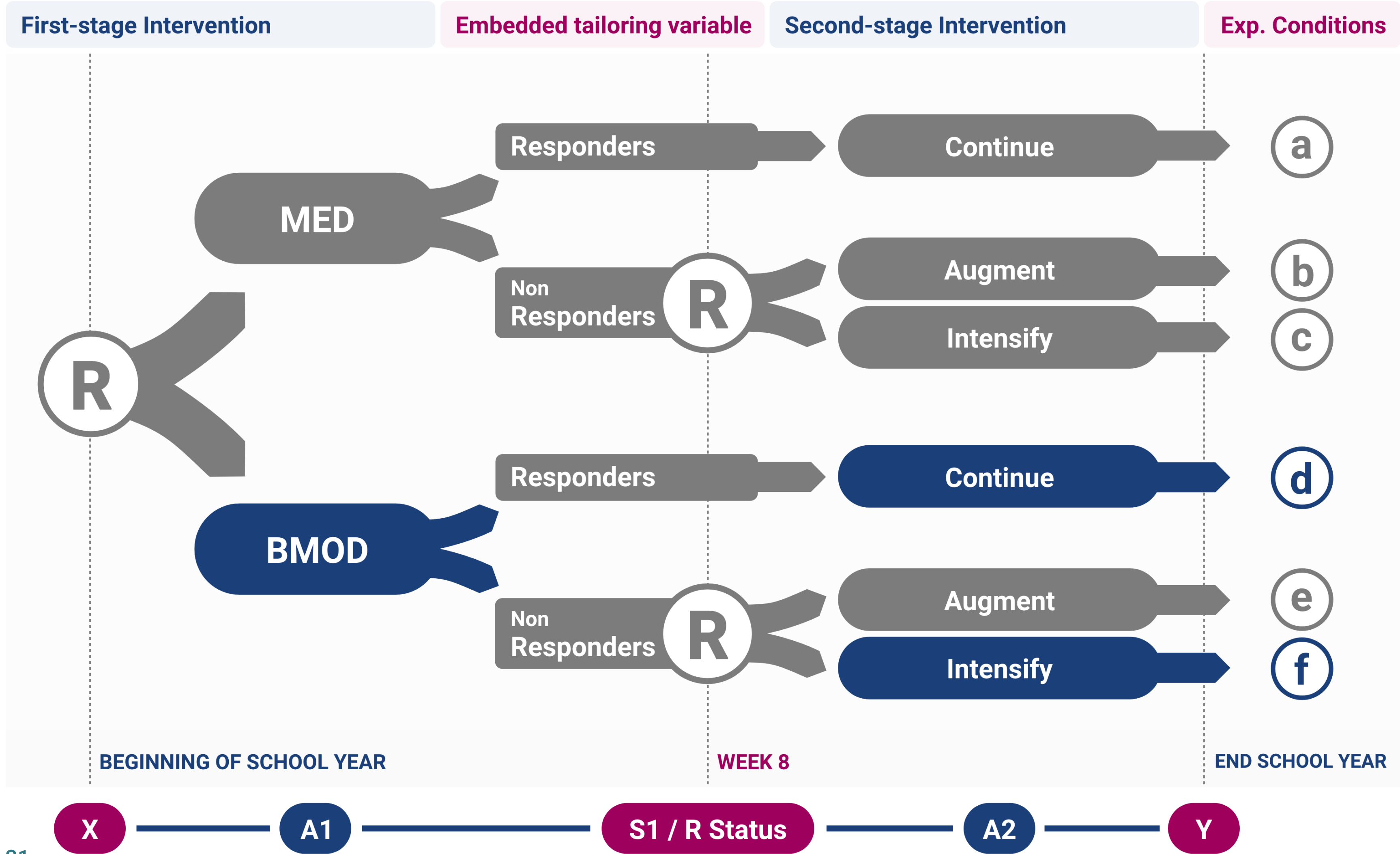
Notice that AI#1 and AI#3 (start MED) share responders (box A)



Similarly: Notice that AI#2 and AI#4 (start BMOD) share responders (box D)



Similarly: Notice that AI#2 and AI#4 (start BMOD) share responders (box D)



So, what's going on?

In the ADHD SMART, all responders are consistent with two AIs

- Responders to MED are part of AI#1 and AI#3
- Responders to BMOD are part of AI#2 and AI#4

If our goal is to estimate the mean outcome under all AIs simultaneously, we must share responders somehow.

- But how?

What do we do?

- We “trick” the software into using the responders twice
- We do this by replicating responders:
 - Create 2 observations for each responder
 - We assign $\frac{1}{2}$ of them $A2 = 1$, the other $\frac{1}{2}$ $A2 = -1$
- $W=2$ to responders and $W=4$ to non-responders
- Robust standard errors account for weighting and the fact that responders are “re-used”. No cheating here!

Weighting and Replicating Serve Different Purposes

Weighting

- Accounts for over/underrepresentation of responders or non-responders
- Because of the randomization scheme

Replicating

- Allows us to use standard software to do simultaneous estimation and comparison
- Because participants are consistent with more than one AI

SAS code for Replication-and-Weighting to Compare Means Under All Four Als

```
data dat9; set dat1;  
  if R=1 then do;  
    ob = 1; A2 = -1; weight = 2; output;  
    ob = 2; A2 = 1; weight = 2; output;  
  end;  
  else if R=0 then do;  
    ob = 1; weight = 4; output;  
  end;  
run;
```

Replicated Data

| Obs | ID | A1 | R | A2 | Y | o11c | o12c | o13c | o14c | ob | weight |
|-----|----|----|---|----|---|----------|----------|----------|----------|----|--------|
| 45 | 32 | 1 | 1 | -1 | 5 | -0.35333 | -2.73889 | -0.31333 | 0.19333 | 1 | 2 |
| 46 | 32 | 1 | 1 | 1 | 5 | -0.35333 | -2.73889 | -0.31333 | 0.19333 | 2 | 2 |
| 47 | 33 | 1 | 0 | 1 | 3 | 0.64667 | -1.07820 | 0.68667 | 0.19333 | 1 | 4 |
| 48 | 34 | 1 | 0 | 1 | 2 | -0.35333 | 0.21667 | -0.31333 | 0.19333 | 1 | 4 |
| 49 | 35 | 1 | 0 | -1 | 5 | -0.35333 | -0.31333 | -0.31333 | 0.19333 | 1 | 4 |
| 50 | 36 | -1 | 0 | 1 | 1 | -0.35333 | -0.31333 | -0.31333 | 0.19333 | 1 | 4 |
| 51 | 37 | -1 | 1 | -1 | 1 | -0.35333 | 0.99556 | -0.31333 | 0.19333 | 1 | 2 |
| 52 | 37 | -1 | 1 | 1 | 1 | -0.35333 | 0.99556 | -0.31333 | 0.19333 | 2 | 2 |
| 53 | 38 | -1 | 0 | -1 | 3 | -0.35333 | 0.14034 | 0.68667 | -0.80667 | 1 | 4 |
| 54 | 39 | -1 | 1 | -1 | 3 | 0.64667 | 1.64983 | 0.68667 | 0.19333 | 1 | 2 |
| 55 | 39 | -1 | 1 | 1 | 3 | 0.64667 | 1.64983 | 0.68667 | 0.19333 | 2 | 2 |

Responders are replicated!

Non-Responders aren't!

After Replication-and-Weighting, the SAS code for the weighted regression

The Regression and Contrast Coding Logic:

Recall:

- Our goal is to compare all 4 embedded Als
- We have 2 indicators: A_1, A_2

$A_1 = 1 \rightarrow \text{BMOD}$

$A_1 = -1 \rightarrow \text{MED}$

$A_2 = 1 \rightarrow \text{INTENSIFY}$

$A_2 = -1 \rightarrow \text{AUGMENT}$

To compare all 4 Als, we can fit the following Model:

$$Y = \beta_0 + \beta_1 A_1 + \beta_2 A_2 + \beta_3 A_1 A_2 + e$$

After Replication-and-Weighting, the SAS code for the weighted regression

The Regression and Contrast Coding Logic:

$$Y = \beta_0 + \beta_1 A_1 + \beta_2 A_2 + \beta_3 A_1 A_2 + e$$

Mean Y under AI#1 (MED, AUGMENT) = $\beta_0 + \beta_1(-1) + \beta_2(-1) + \beta_3(-1)(-1)$

Mean Y under AI#2 (BMOD, AUGMENT) = $\beta_0 + \beta_1(1) + \beta_2(-1) + \beta_3(1)(-1)$

Mean Y under AI#3 (MED, INTENSIFY) = $\beta_0 + \beta_1(-1) + \beta_2(1) + \beta_3(-1)(1)$

Mean Y under AI#4 (BMOD, INTENSIFY) = $\beta_0 + \beta_1(1) + \beta_2(1) + \beta_3(1)(1)$

$A_1 = 1 \rightarrow$ BMOD

$A_1 = -1 \rightarrow$ MED

$A_2 = 1 \rightarrow$ INTENSIFY

$A_2 = -1 \rightarrow$ AUGMENT

After Replication-and-Weighting, the SAS code for the weighted regression

The Regression and Contrast Coding Logic:

$$Y = \beta_0 + \beta_1 A_1 + \beta_2 A_2 + \beta_3 A_1 A_2 + e$$

Mean Y under AI#1 (-1, -1) = $\beta_0 + \beta_1(-1) + \beta_2(-1) + \beta_3(-1)(-1)$

Mean Y under AI#2 (1, -1) = $\beta_0 + \beta_1(1) + \beta_2(-1) + \beta_3(1)(-1)$

Mean Y under AI#3 (-1, 1) = $\beta_0 + \beta_1(-1) + \beta_2(1) + \beta_3(-1)(1)$

Mean Y under AI#4 (1, 1) = $\beta_0 + \beta_1(1) + \beta_2(1) + \beta_3(1)(1)$

$A_1 = 1 \rightarrow$ BMOD

$A_1 = -1 \rightarrow$ MED

$A_2 = 1 \rightarrow$ INTENSIFY

$A_2 = -1 \rightarrow$ AUGMENT

After Replication-and-Weighting, the SAS code for the weighted regression

The Regression and Contrast Coding Logic:

$$Y = \beta_0 + \beta_1 A_1 + \beta_2 A_2 + \beta_3 A_1 A_2 + e$$

$$\text{Mean Y under AI\#1 } (-1, -1) = \beta_0 + \beta_1(-1) + \beta_2(-1) + \beta_3(-1)(-1)$$

$$\text{Mean Y under AI\#2 } (1, -1) = \beta_0 + \beta_1(1) + \beta_2(-1) + \beta_3(1)(-1)$$

$$\text{Mean Y under AI\#3 } (-1, 1) = \beta_0 + \beta_1(-1) + \beta_2(1) + \beta_3(-1)(1)$$

$$\text{Mean Y under AI\#4 } (1, 1) = \beta_0 + \beta_1(1) + \beta_2(1) + \beta_3(1)(1)$$

$$\text{Diff AI\#1} - \text{AI\#2} = (\beta_0 - \beta_1 - \beta_2 + \beta_3) - (\beta_0 + \beta_1 - \beta_2 - \beta_3) = -2\beta_1 + 2\beta_3$$

After Replication-and-Weighting, the SAS code for the weighted regression

```
proc genmod data = dat9;  
class id;  
model Y = A1 A2 A1*A2;  
scwgt weight;  
repeated subject = id / type = ind;  
estimate 'MeanY:AI#1(MED,AUGMENT)' int 1 A1 -1 A2 -1 A1*A2 1;  
estimate 'MeanY:AI#2(BMOD,AUGMENT)' int 1 A1 1 A2 -1 A1*A2 -1;  
estimate 'MeanY:AI#3(MED,INTNSFY)' int 1 A1 -1 A2 1 A1*A2 -1;  
estimate 'MeanY:AI#4(BMOD,INTNSFY)' int 1 A1 1 A2 1 A1*A2 1;  
estimate 'Diff: AI#1 - AI#2' int 0 A1 -2 A2 0 A1*A2 2;  
estimate 'Diff: AI#1 - AI#3' int 0 A1 0 A2 -2 A1*A2 2;  
estimate 'Diff: AI#1 - AI#4' int 0 A1 -2 A2 -2 A1*A2 0; *etc...;  
run;
```

After Replication-and-Weighting, the SAS code for the weighted regression

```
proc genmod data = dat9;
class id;
model Y = A1 A2 A1*A2;
scwgt weight;
repeated subject = id / type = ind;
estimate 'MeanY:AI#1(MED,AUGMENT)' int 1 A1 -1 A2 -1 A1*A2 1;
estimate 'MeanY:AI#2(BMOD,AUGMENT)' int 1 A1 1 A2 -1 A1*A2 -1;
estimate 'MeanY:AI#3(MED,INTENSFY)' int 1 A1 -1 A2 1 A1*A2 -1;
estimate 'MeanY:AI#4(BMOD,INTNSEV)' int 1 A1 1 A2 1 A1*A2 1;
estimate 'Diff: AI#1 - AI#2' int 0 A1 -2 A2 0 A1*A2 2;
estimate 'Diff: AI#1 - AI#3' int 0 A1 0 A2 -2 A1*A2 2;
estimate 'Diff: AI#1 - AI#4' int 0 A1 -2 A2 -2 A1*A2 0; *etc...;
run;
```

$$\text{Diff AI\#1} - \text{AI\#2} = -2\beta_1 + 2\beta_3$$

Comparing Mean Outcomes for All AIs Simultaneously

| Contrast Estimate Results | | | | |
|--------------------------------------|---------------|-----------------------|---------|----------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error |
| | | Lower | Upper | |
| Mean Y under AI #1 (MED, AUGMENT) | 2.643 | 2.5305 | 3.1992 | 0.1706 |
| Mean Y under AI #2 (BMOD, AUGMENT) | 3.798 | 3.1643 | 3.8490 | 0.1747 |
| Mean Y under AI #3 (MED, INTENSIFY) | 2.342 | 2.4644 | 3.1145 | 0.1658 |
| Mean Y under AI #4 (BMOD, INTENSIFY) | 3.208 | 2.2515 | 3.0552 | 0.2050 |
| Diff: AI#1 – AI#2 | -1.16 | -1.799 | -0.5347 | 0.323 |
| Diff: AI#1 – AI#3 | 0.0754 | -0.3106 | 0.4614 | 0.1969 |

NOTE: We get the exact same results as before when we compared AI#1 vs AI#2, but now we can simultaneously make inference for all the comparisons.

This analysis is with simulated data.



But wait, there's more...

Weighted-and-replicated regression can improve statistical precision (power)!

Replicated-and-Weighted Regression is More Efficient Statistically

```
proc genmod data = dat9;
class id;
model Y = A1 A2 A1*A2 Y0c oddc;
scwgt weight;
repeated subject = id / type = ind;
estimate 'MeanY:AI#1(MED,AUGMENT)' int 1 A1 -1 A2 -1 A1*A2 1;
estimate 'MeanY:AI#2(BMOD,AUGMENT)' int 1 A1 1 A2 -1 A1*A2 -1;
estimate 'MeanY:AI#3(MED,INTENSFY)' int 1 A1 -1 A2 1 A1*A2 -1;
estimate 'MeanY:AI#4(BMOD,INTNSFY)' int 1 A1 1 A2 1 A1*A2 1;
estimate 'Diff: AI#1 - AI#2' int 0 A1 -2 A2 0 A1*A2 2;
estimate 'Diff: AI#1 - AI#3' int 0 A1 0 A2 -2 A1*A2 2;
estimate 'Diff: AI#1 - AI#4' int 0 A1 -2 A2 -2 A1*A2 0; *etc...;
run;
```

Improve power: Adjusting for baseline covariates that are associated with outcome leads to more efficient estimates (lower standard error = more power = smaller p-value).

Results for Weighted-and-Replicated Regression: Comparing Mean Outcome for all AIs Simultaneously

Improved efficiency: Adjusting for baseline covariates resulted in lower standard error and tighter confidence intervals. Point estimates remained about the same, as expected.

| Contrast Estimate Results | | | | |
|--------------------------------------|---------------|-----------------------|---------|----------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error |
| | | Lower | Upper | |
| Mean Y under AI #1 (MED, AUGMENT) | 2.780 | 2.5869 | 3.1733 | 0.1496 |
| Mean Y under AI #2 (BMOD, AUGMENT) | 3.750 | 3.0689 | 3.7018 | 0.1614 |
| Mean Y under AI #3 (MED, INTENSIFY) | 2.311 | 2.5163 | 3.1135 | 0.1524 |
| Mean Y under AI #4 (BMOD, INTENSIFY) | 3.212 | 2.3596 | 3.1081 | 0.1909 |
| Diff: AI#1 – AI#2 | -0.97 | -0.9401 | -0.0704 | 0.2219 |
| Diff: AI#1 – AI#3 | 0.469 | 0.2811 | 0.4115 | 0.1767 |

SE in unadjusted model was **0.323**



Results for Weighted-and-Replicated Regression: Comparing Mean Outcome for all AIs Simultaneously

Improved efficiency: Adjusting for baseline covariates resulted in lower standard error and tighter confidence intervals. Point estimates remained about the same, as expected.

| Contrast Estimate Results | | | | |
|--------------------------------------|---------------|-----------------------|---------|----------------|
| Label | Mean Estimate | 95% Confidence Limits | | Standard Error |
| | | Lower | Upper | |
| Mean Y under AI #1 (MED, AUGMENT) | 2.8801 | 2.5869 | 3.1733 | 0.1496 |
| Mean Y under AI #2 (BMOD, AUGMENT) | 3.3854 | 3.0689 | 3.7018 | 0.1614 |
| Mean Y under AI #3 (MED, INTENSIFY) | 2.8149 | 2.5163 | 3.1135 | 0.1524 |
| Mean Y under AI #4 (BMOD, INTENSIFY) | 2.7338 | 2.3596 | 3.1081 | 0.1909 |
| Diff: AI#1 – AI#2 | -0.5053 | -0.9401 | -0.0704 | 0.2219 |
| Diff: AI#1 – AI#3 | 0.0652 | 0.2811 | 0.4115 | 0.1767 |

SE in unadjusted model was **0.2442**

SE in adjusted model but including only data from participants in AI#1 and AI#2 was **0.2244**

This analysis is with simulated data.



Citations

- Murphy, S. A. (2005). An experimental design for the development of adaptive intervention. *Statistics in Medicine*, 24, 455-1481.
- Nahum-Shani, I., Qian, M., Almirall, D., Pelham, W. E., Gnagy, B., Fabiano, G. A., ... & Murphy, S. A. (2012). Experimental design and primary data analysis methods for comparing adaptive interventions. *Psychological methods*, 17(4), 457.

Q&A



10 min