Presented by
Ahnalee Brincks, PhD

SMART Case Studies

Module 3

50 min

catie d3c

Outline

Four SMART case studies

Summary comparison of the four SMARTs

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Summary comparison of the four SMARTs

SMART Case Studies

ExTENd: Treatment of Alcohol Dependence
PI: Oslin

RBT: Treatment for Pregnant Women who are Drug Dependent
PI: Jones

SMART Weight Loss: Integrating mHealth in Obesity Treatment
PI: Nahum-Shani & Spring

ASIC: School-based Implementation of Cognitive Behavioral Therapy
PI: Kilbourne

ExTENd

PI: Oslin

Population

Alcohol-dependent adults completing an intensive outpatient program [IOP].

Rationale

Naltrexone [NTX, an opiate antagonist] is efficacious, but

- ~1/3 of patients relapse while on NTX
- Need strategies for non-responders
- Need long-term maintenance strategies for responders
- Relapse because of various barriers: physiological / social / psychological

Outcome

Drinking behavior [% days abstinent]

ExTENd

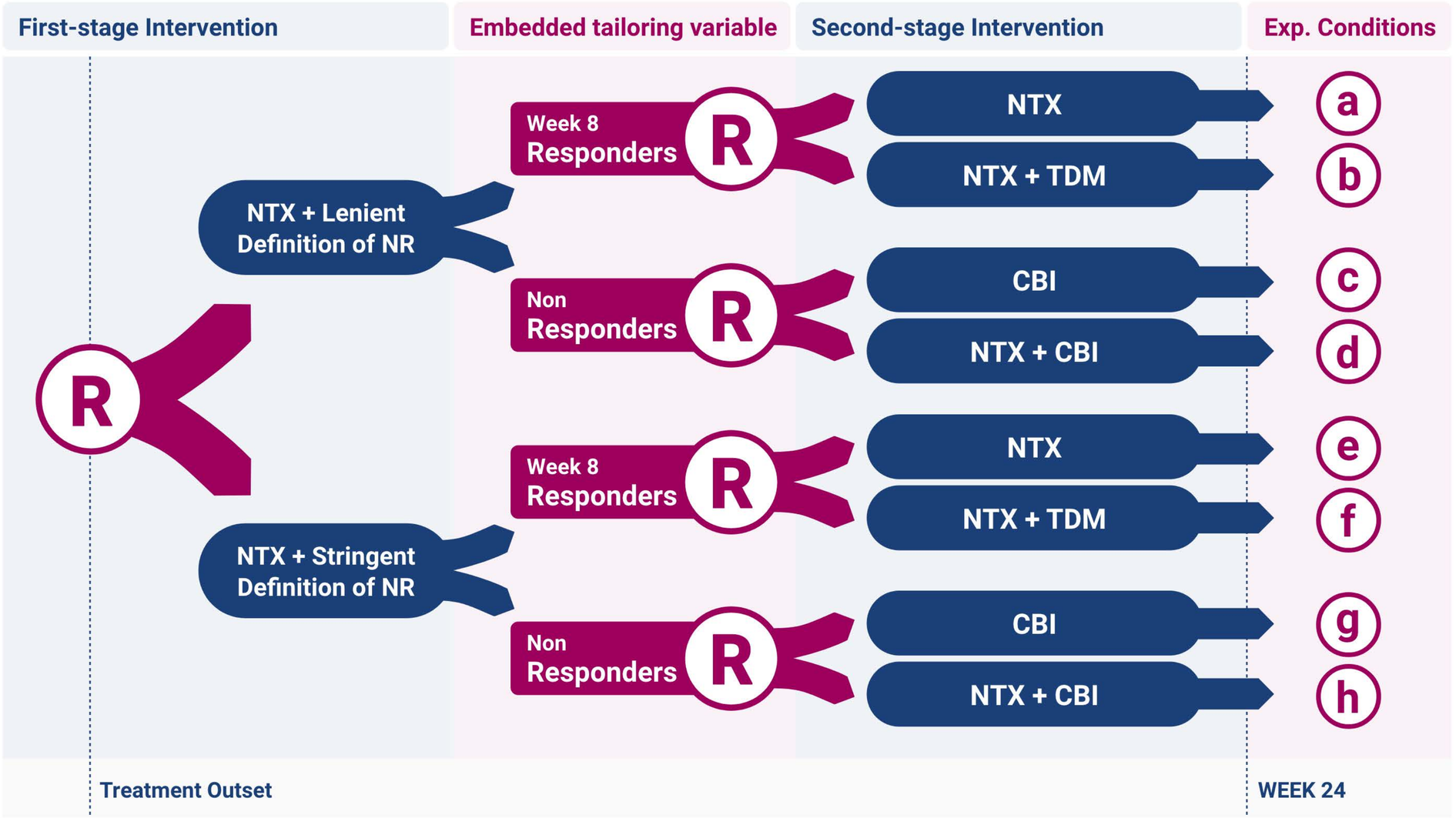
PI: Oslin

Scientific Questions

- What measure of drinking behavior best reflects non-response to NTX?
- What intervention strategy would be useful among non-responders to NTX?
- What maintenance strategy would be useful among responders to NTX?

SMART Example ExTENd

PI: Oslin N=302



NTX →

Naltrexone (opioid antagonist)

TDM →

Telephone disease management

CBI →

Combined Behavioral Intervention

Lenient Definition →

5+ heavy drinking days in one week

Stringent Definition →

2+ heavy drinking days in one week

SMART Example ExTENd

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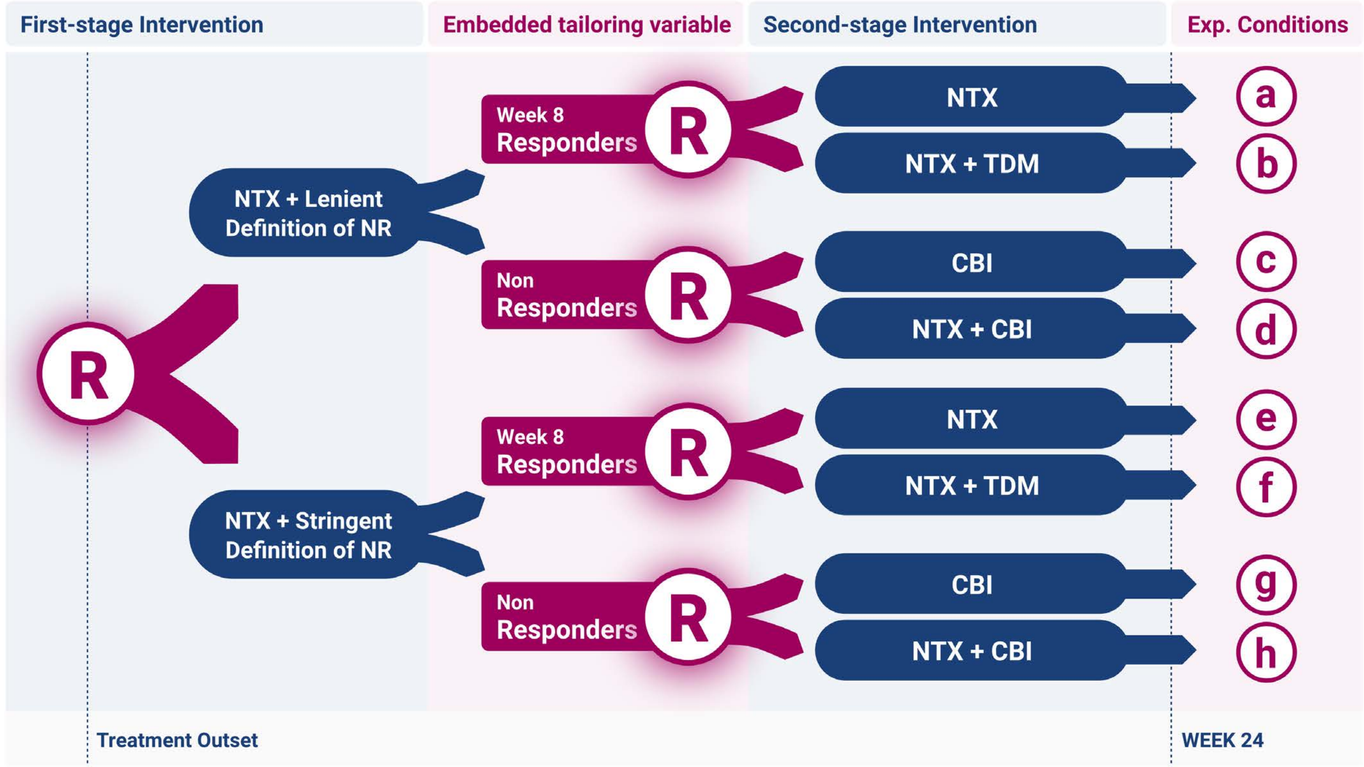


NTX → Naltrexone (opioid antagonist)

SMART Example ExTENd

PI: Oslin N=302

Intervention Options:

First-stage

NTX

Second-stage non-responders

Switch to CBI

Add CBI to NTX

Second stage responders

Continue NTX

Add TDM to NTX

Why CBI?

A prior study found that participants who took NTX and had 2-5 days of heavy drinking in the first 60 days were not likely to reduce their drinking if they just continued with NTX and medical management (minimal clinical support).

SMART Example ExTENd

PI: Oslin N=302

Embedded Tailoring Variable:

Response/non-response status

Measured based on weekly self-reported heavy drinking days [HDDs]

Males: > 5 Drinks / Day

Females: > 4 Drinks / Day

Non-response if during first 8 weeks of NTX

Lenient: 5+ HDDs

Stringent: 2+ HDDs

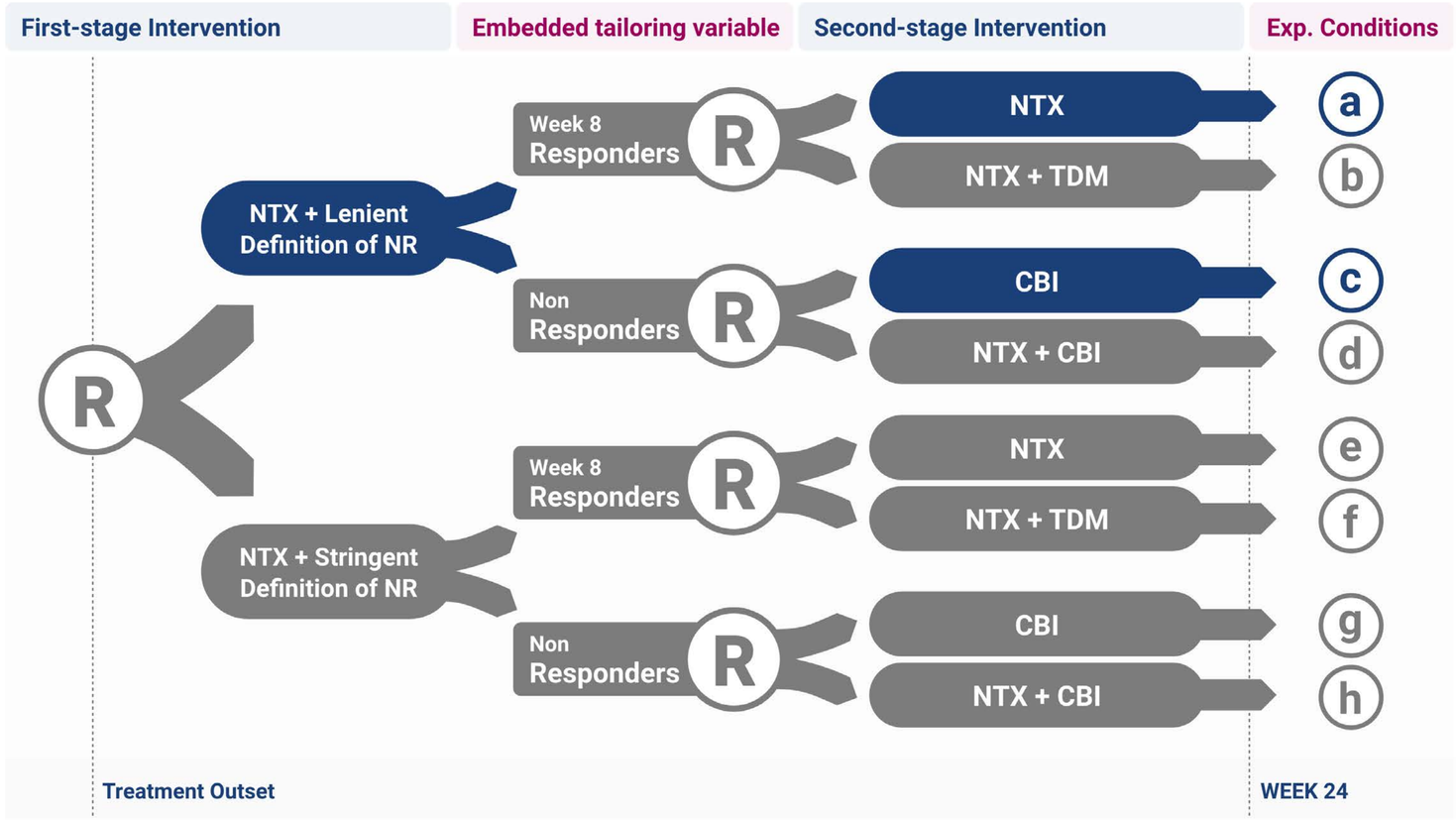
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 1

Start on **NTX**;
if **5+ HDDs prior to week 8**, **switch to CBI**;
else at week 8 **continue NTX**



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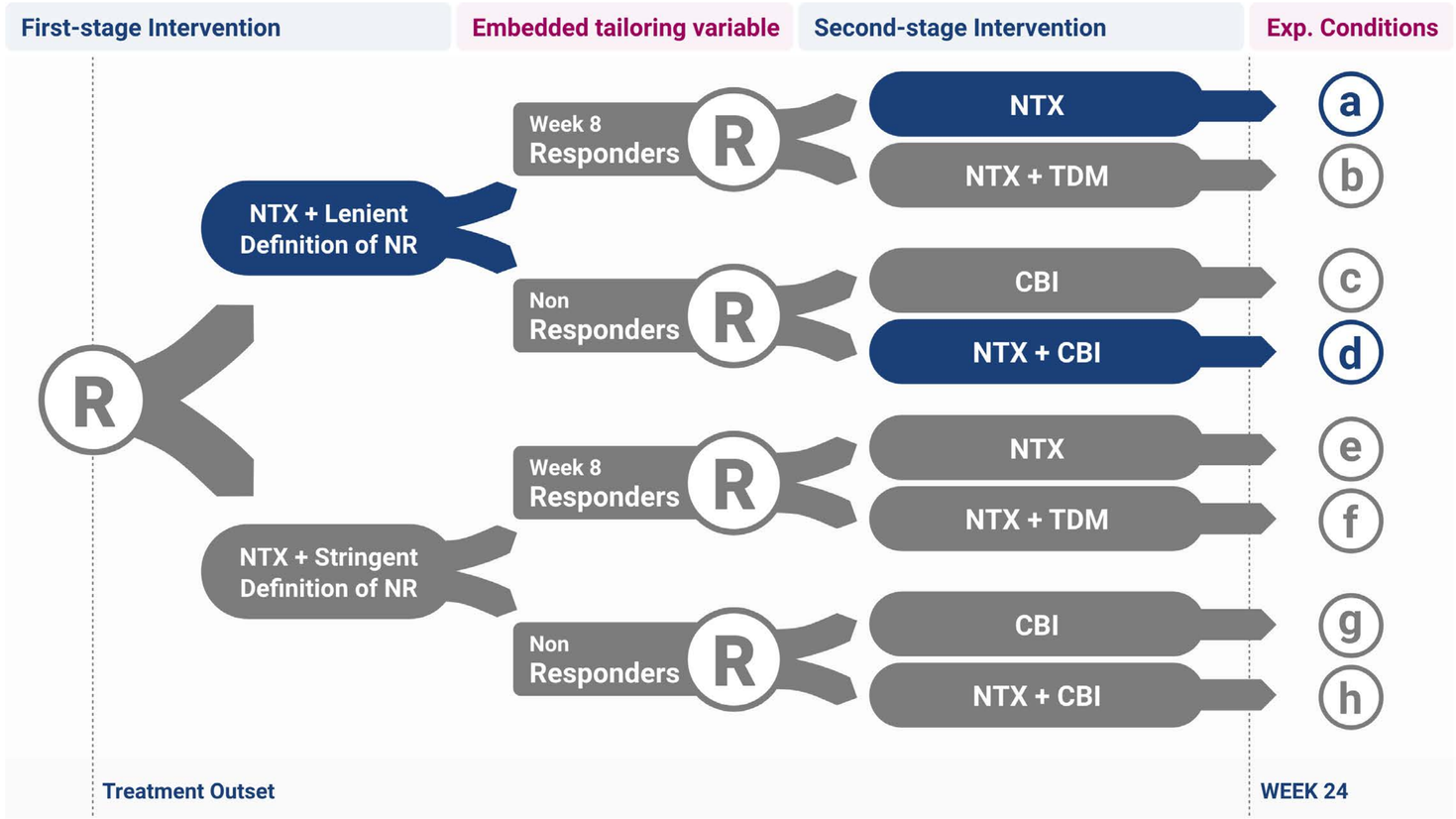
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 2

Start on **NTX**;
if **5+ HDDs prior to week 8**,
switch to NTX + CBI;
else at week 8 **continue NTX**



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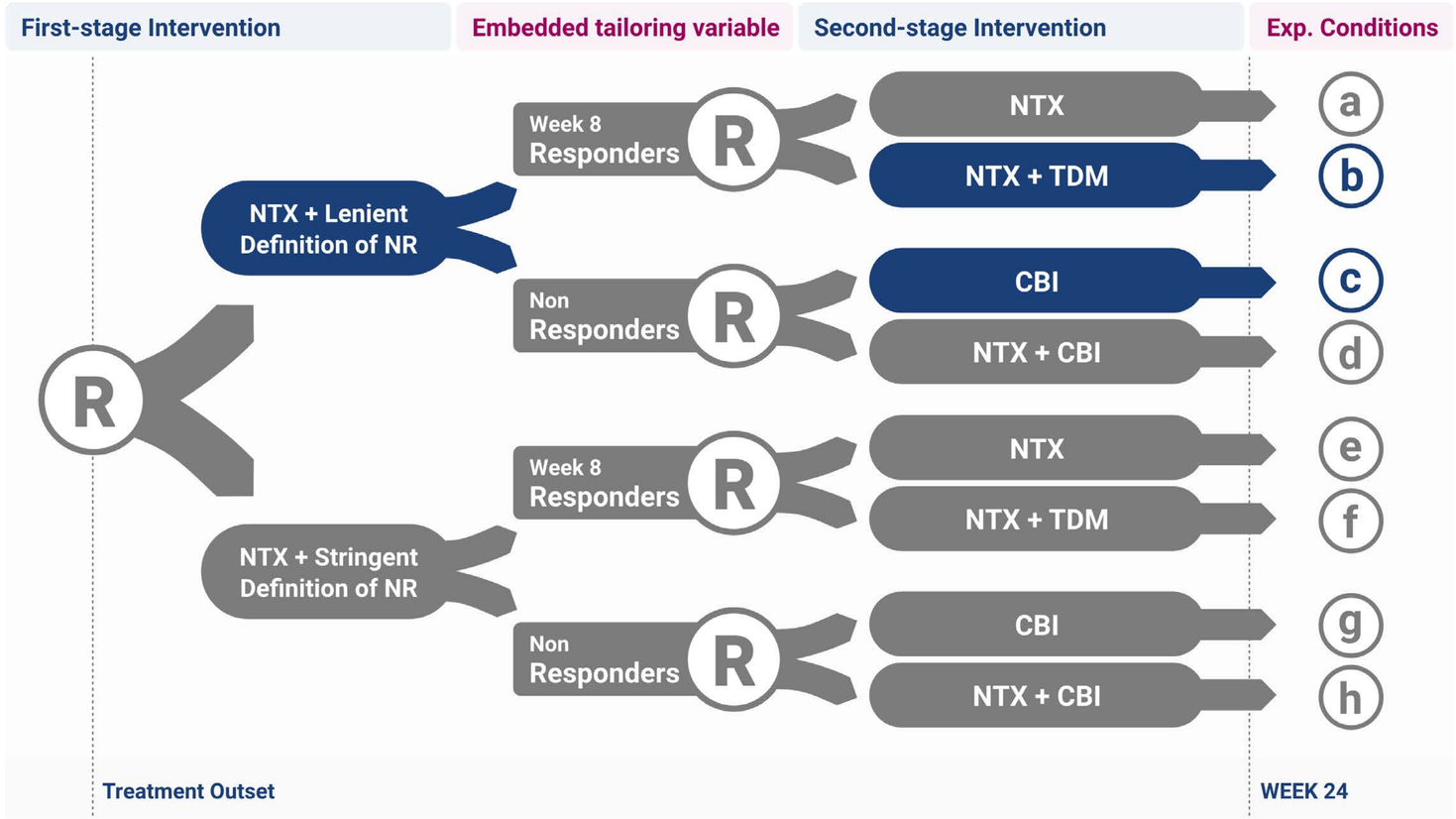
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 3

Start on **NTX**;
if **5+ HDDs prior to week 8**, **switch to CBI**;
else at week 8 **continue NTX + TDM**



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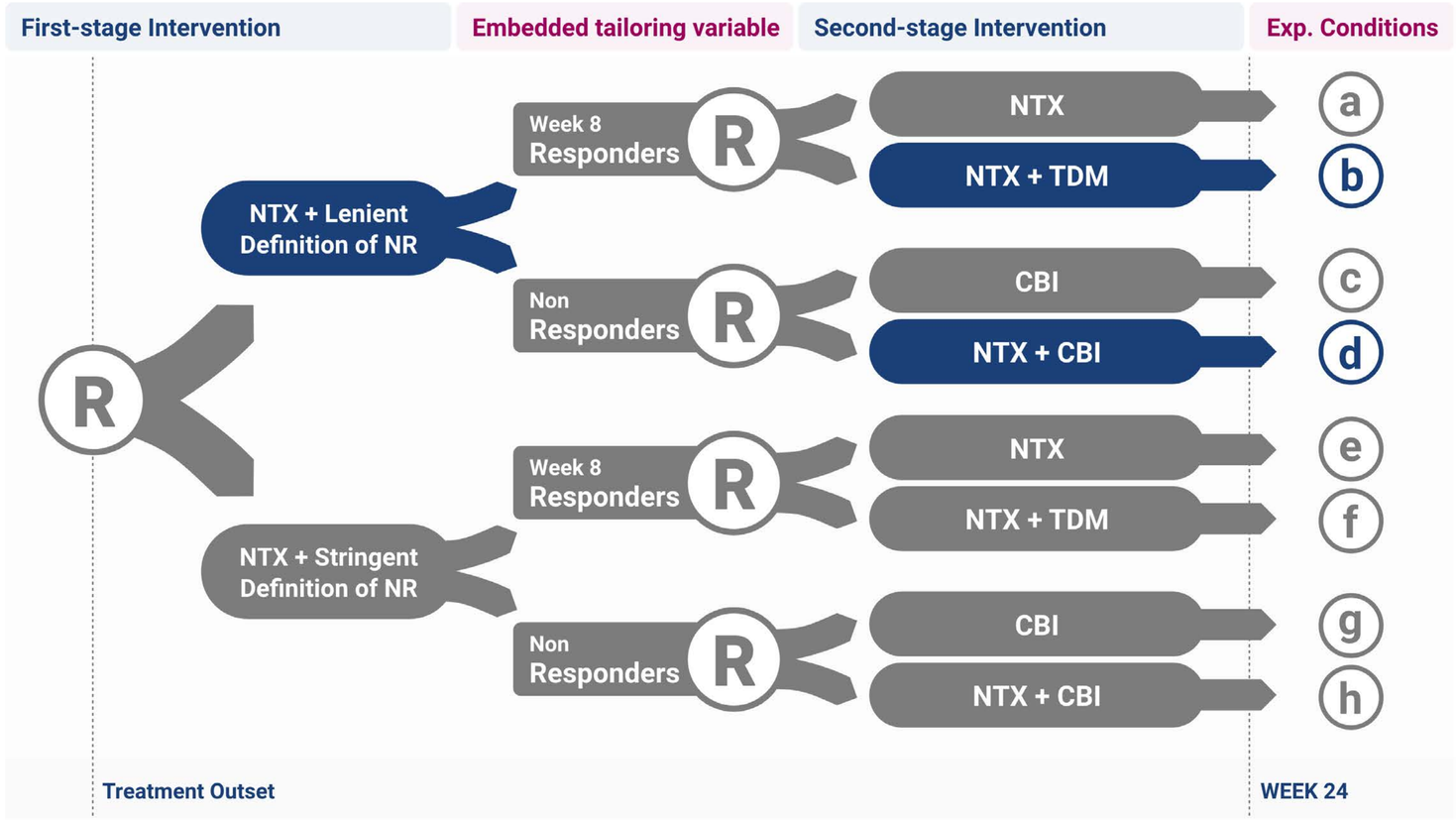
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 4

Start on **NTX**;
if **5+ HDDs prior to week 8**,
augment NTX + CBI;
else at week 8 **offer NTX + TDM**



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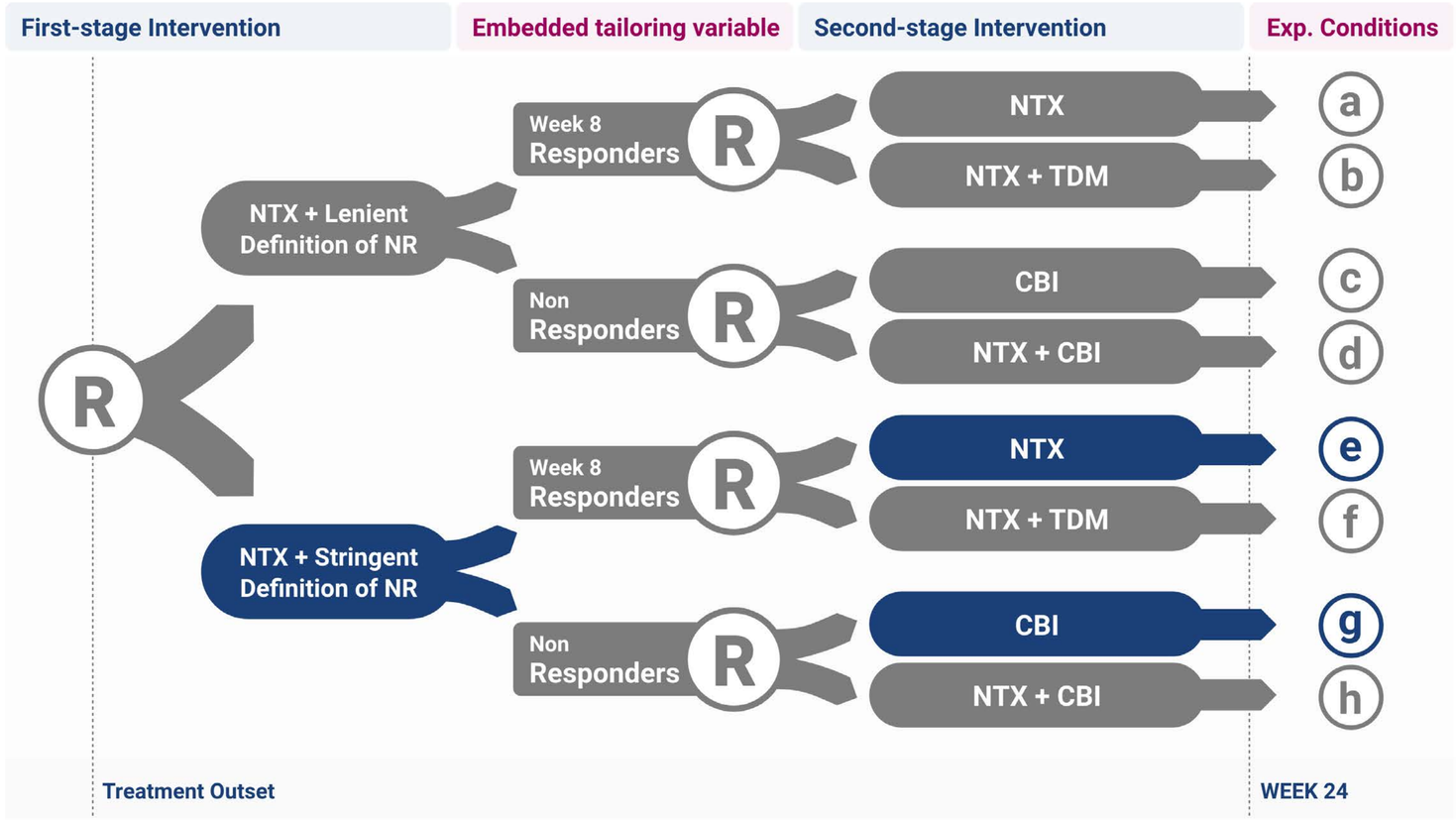
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 5

Start on **NTX**;
if **2+ HDDs prior to week 8**, **switch to CBI**;
else at week 8 **continue NTX**



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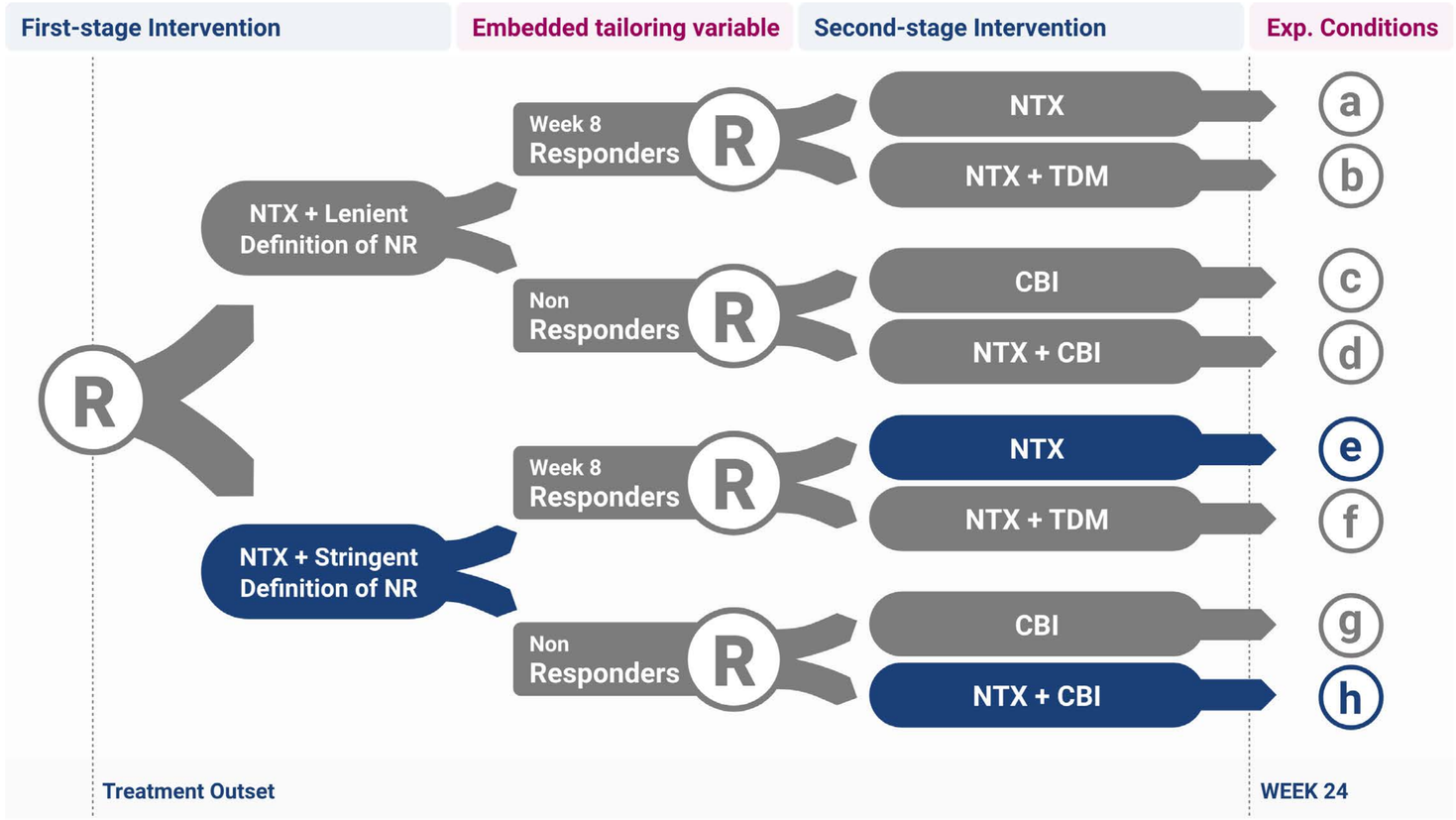
PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 6

Start on **NTX**;
if **2+ HDDs prior to week 8**,
augment NTX + CBI;
else at week 8 **continue NTX**



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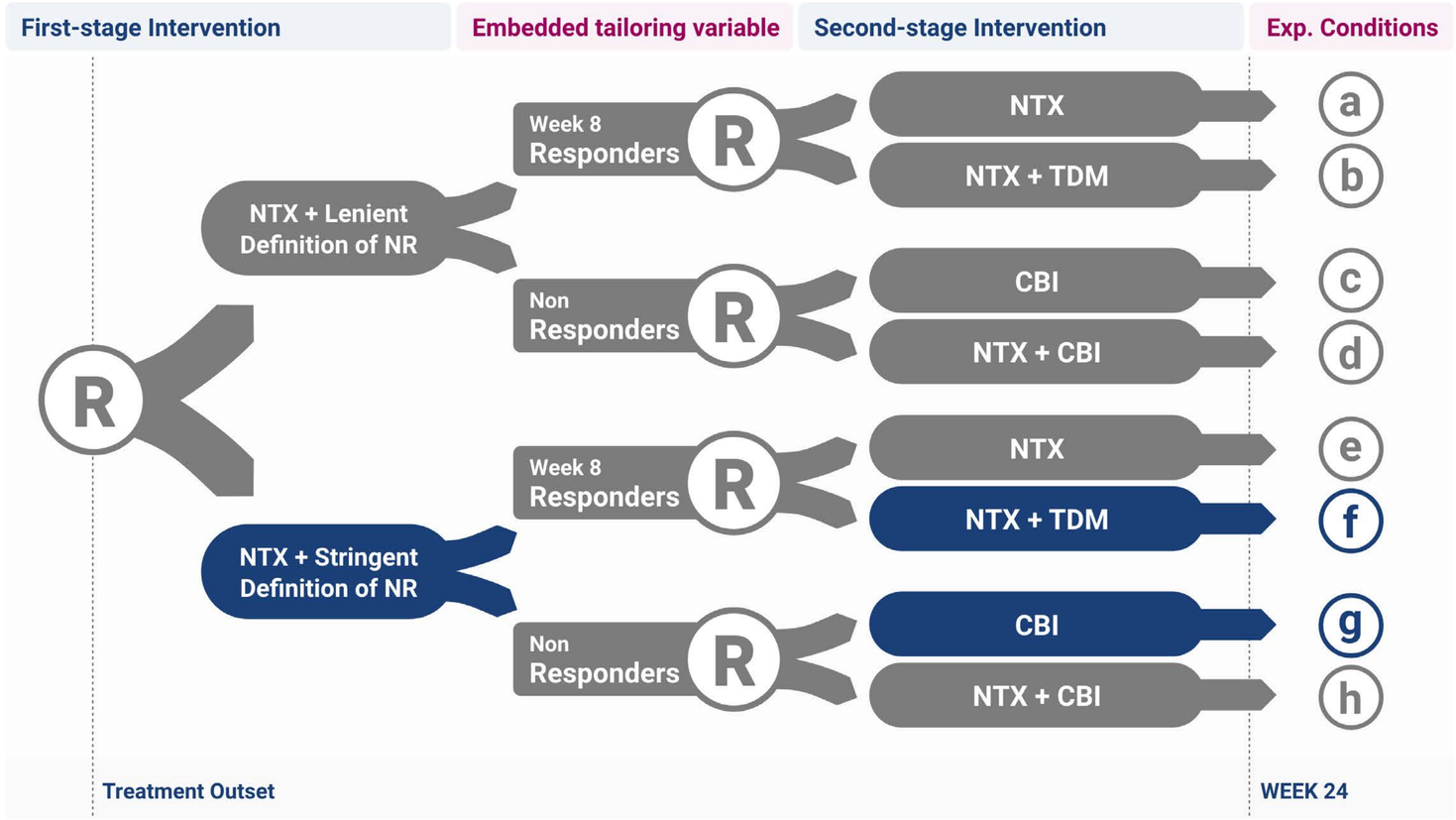
SMART Example ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions

Adaptive Intervention 7

Start on **NTX**;
if **2+ HDDs prior to week 8**, **switch to CBI**;
else at week 8 **offer NTX + TDM**



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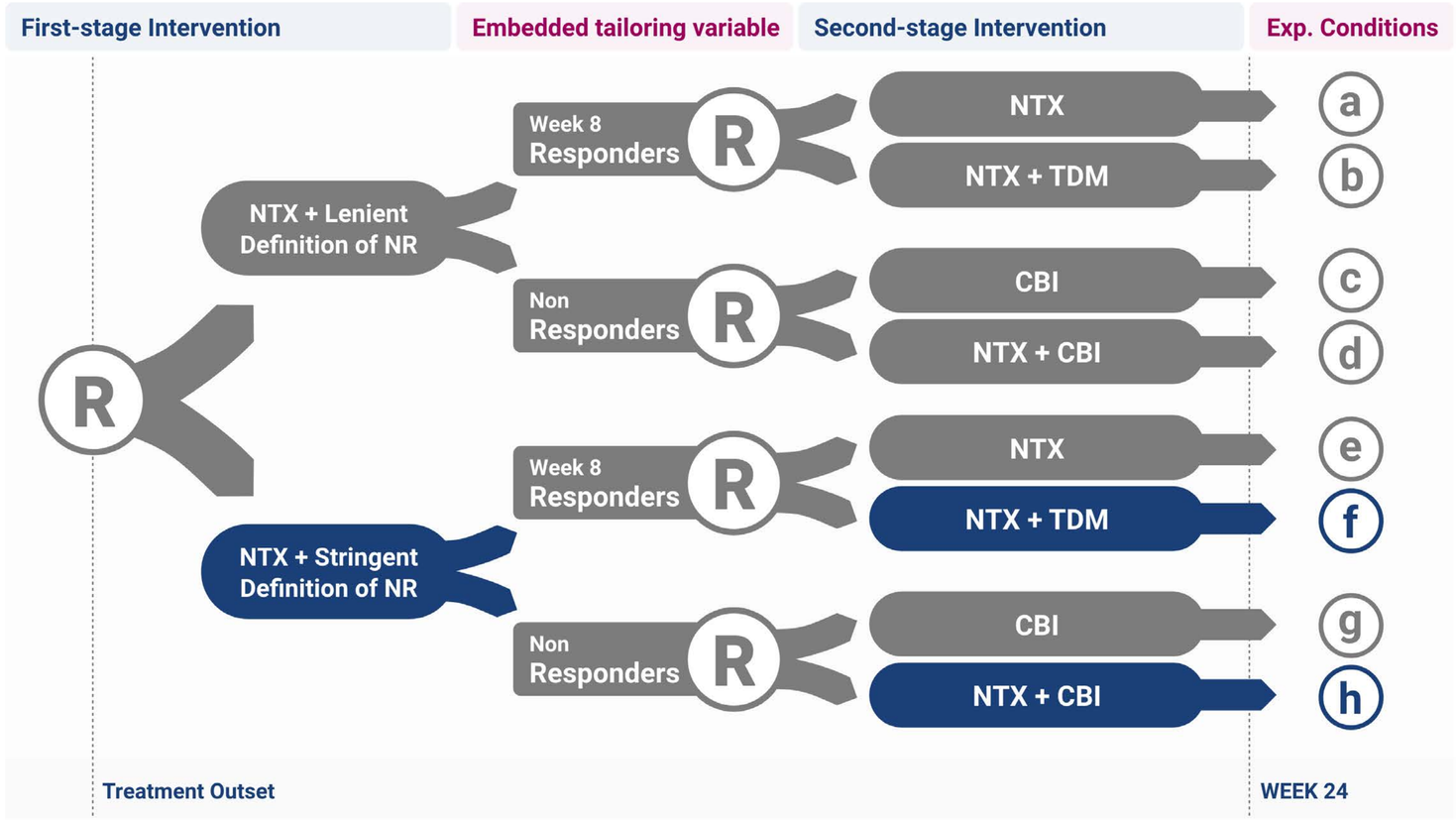
8 Embedded Adaptive Interventions

Adaptive Intervention 8

Start on **NTX**;
if **2+ HDDs prior to week 8**,
augment NTX + CBI;
else at week 8 **offer NTX + TDM**



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SMART Example ExTENd

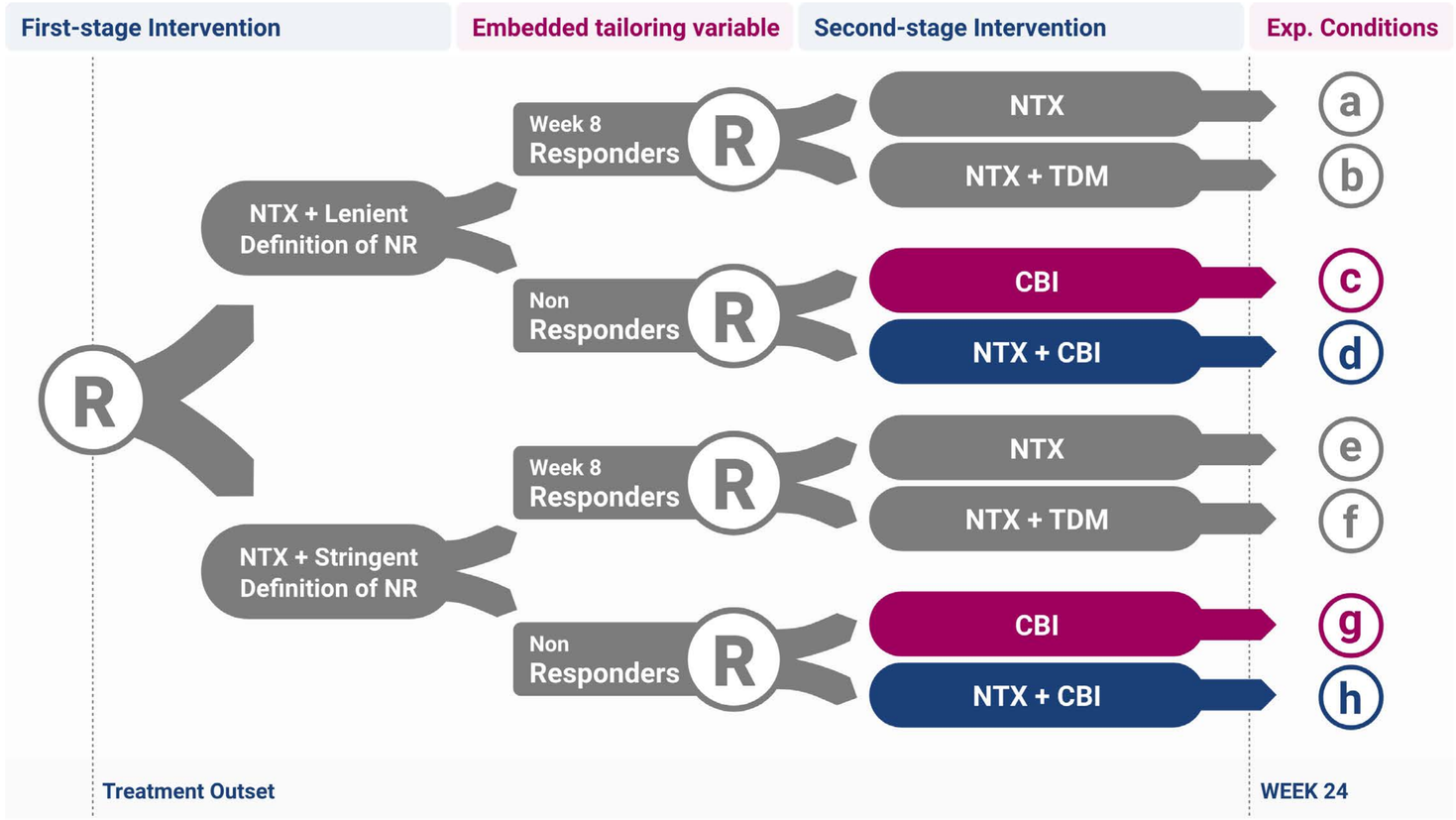
PI: Oslin N=302

Primary Aim

Among non-responders, compare NTX + CBI vs. CBI, in terms of percent days abstinent during the study.

Secondary Aims:

- Compare two criteria for non-response
- Effect of TDM for responders
- Moderators [e.g., distress, severity of dependence, adherence in first stage]



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PI: Kilbourne

RBT

PI: Jones

Population

Pregnant women using opioids or cocaine

Rationale

Reinforcement-**B**ased **T**reatment (**RBT**) is an efficacious intervention, but

- RBT is costly to administer and time-consuming (high burden) for the participant
- About 40% of participants do not respond as well as desired.
- Need to find ways to improve compliance.

Outcomes

Treatment completion through to end of pregnancy · **Drug Use** · **Session Attendance**

RBT

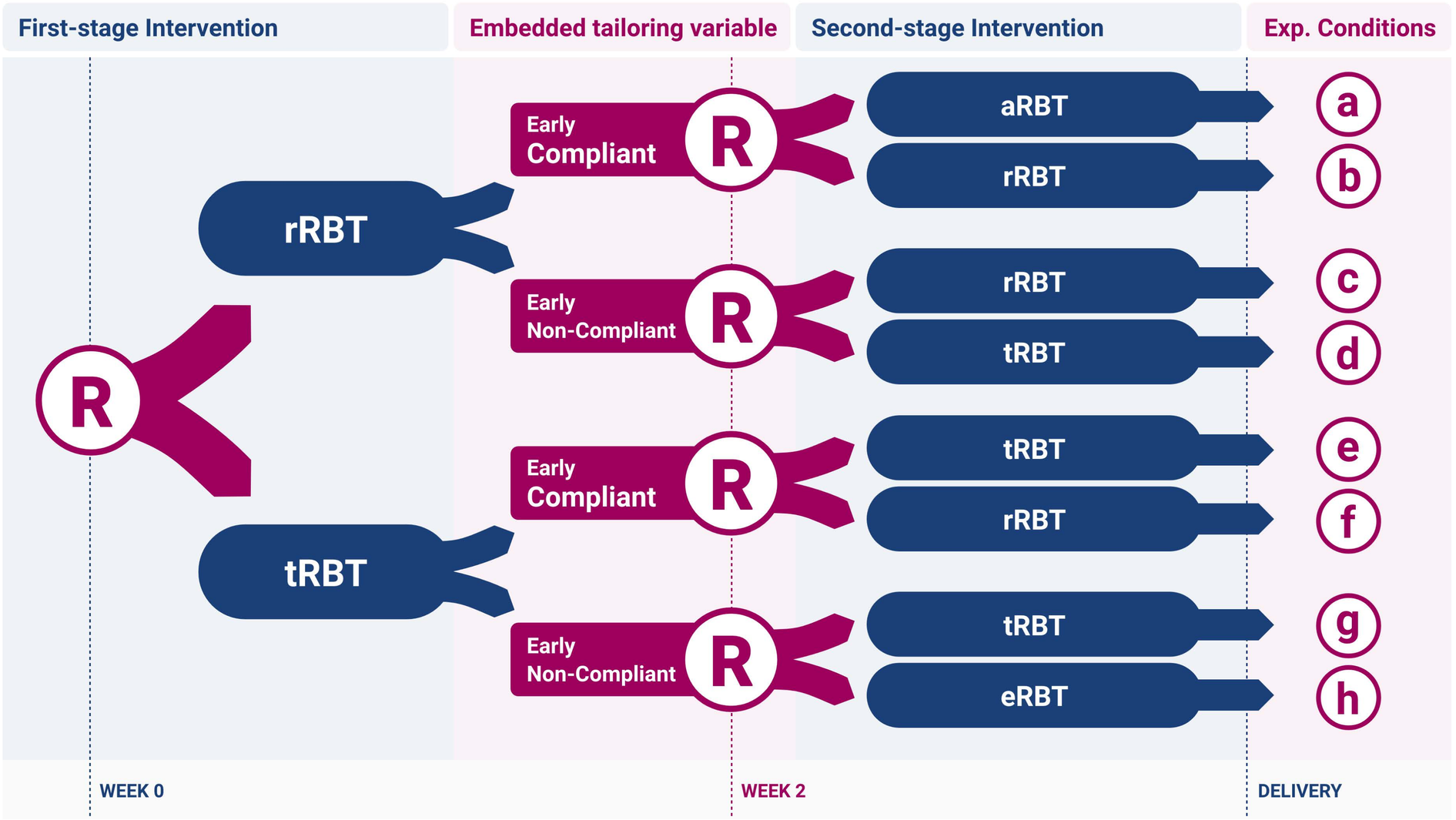
PI: Jones

Scientific Questions

- Can the traditional version of RBT be reduced in intensity and scope?
- Should a woman who does not respond quickly continue the same version or step up to a more intensive, larger-scope version of RBT?
- If a woman responds quickly, can the scope of RBT be reduced?

SMART Example RBT

PI: Jones N=220



aRBT →

Abbreviated RBT

tRBT →

Treatment-as-usual RBT

rRBT →

Reduced RBT

eRBT →

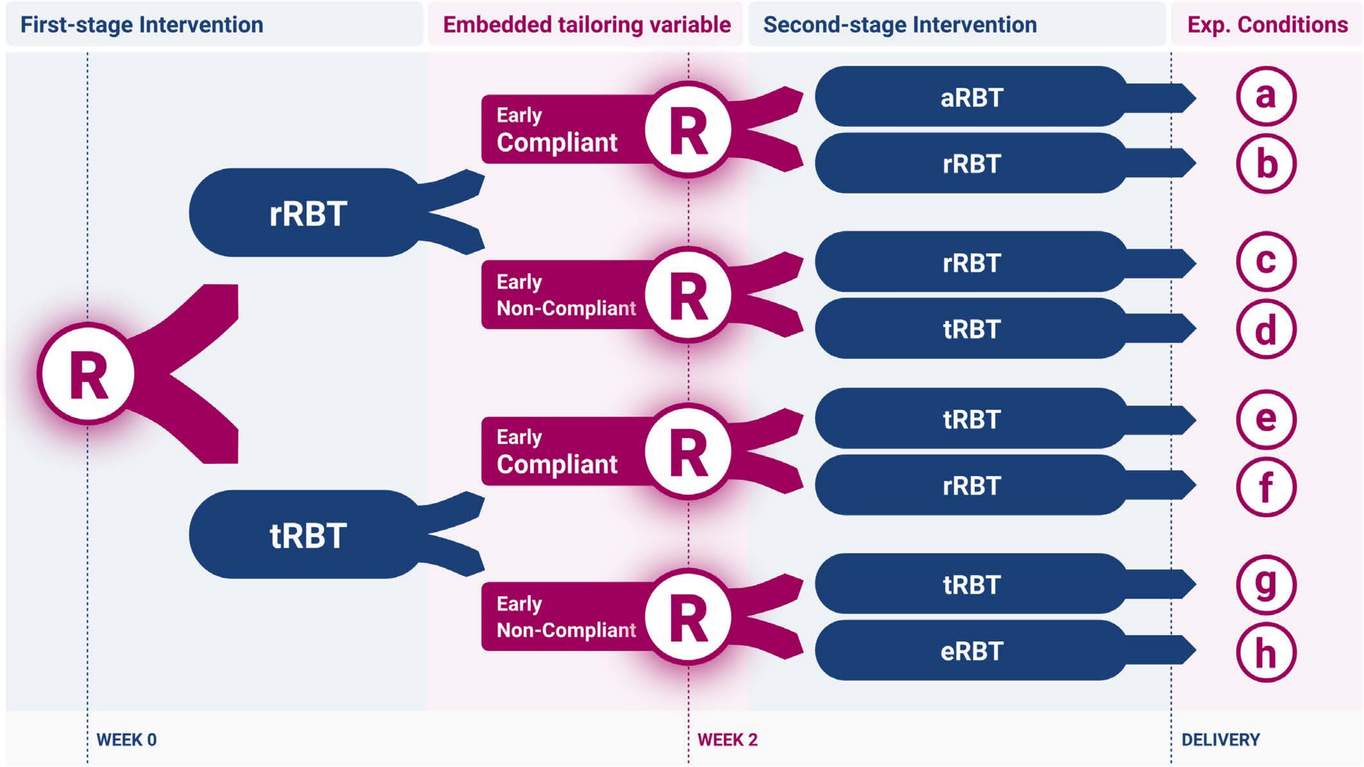
Enhanced RBT

Early non-compliance

A missed unexcused treatment day, a positive opioid or cocaine urine specimen, or self-reported drug use

Scientific Questions:

- Can the traditional version of RBT be reduced in intensity and scope?
- Should a woman who does not respond quickly continue the same version or step up to a more intensive, larger-scope version of RBT?
- If a woman responds quickly, can the scope of RBT be reduced?



SMART Example RBT

PI: Jones N=220

Intervention Options:

First-stage

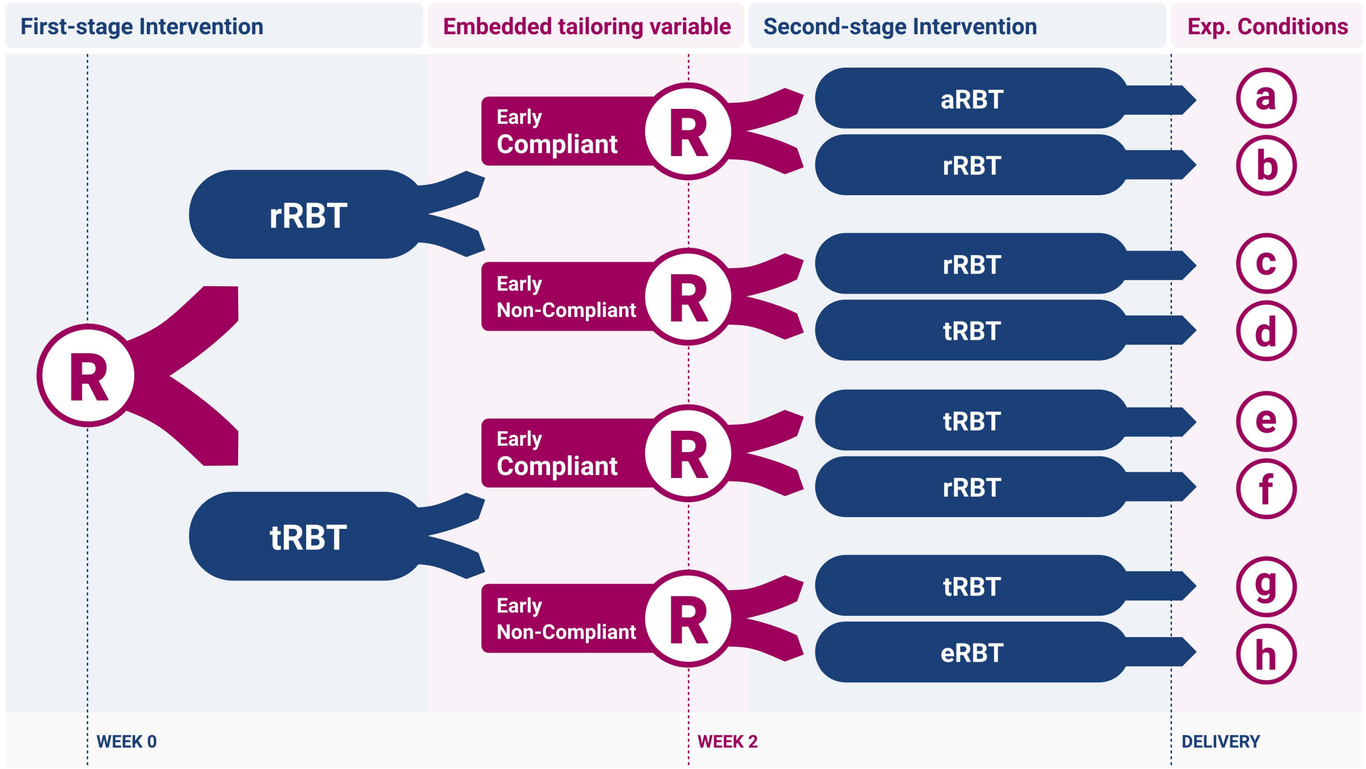
- Treatment-as-usual [tRBT]
- Reduced RBT [rRBT]

Second-stage non-responders

- Step up
- Continue

Second stage responders

- Step down
- Continue



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SMART Example RBT

PI: Jones N=220

Embedded Tailoring Variable:

Early compliance status at week 2

Based on:

- Self-reported drug use
- Urine test results
- Intervention day attendance

Non-response is a combination of non-compliance and non-response.

Non-compliant if:

Missed an intervention day with no excuse

OR A positive opioid or cocaine urine specimen

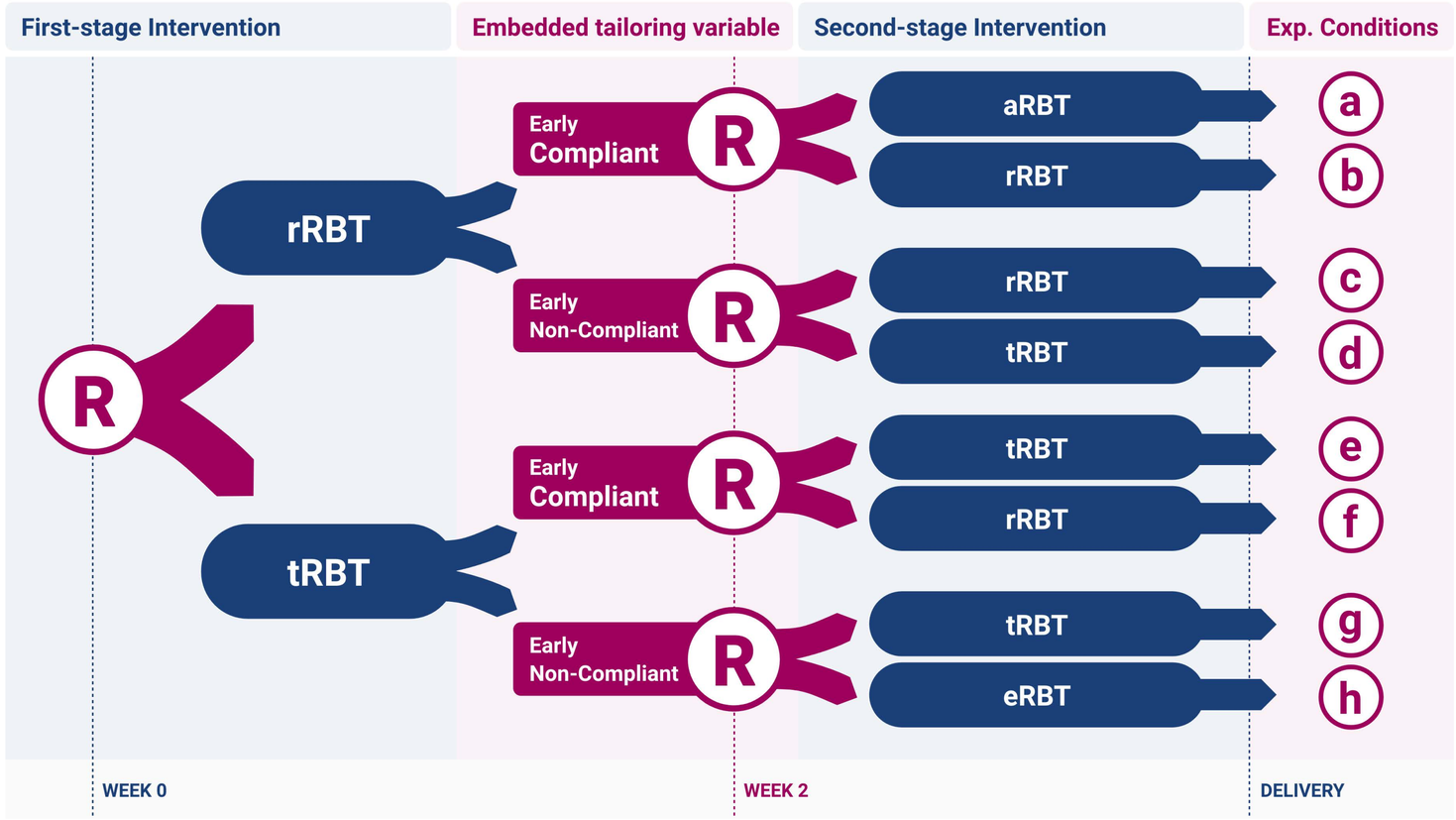
OR Self-reported use of either drug

SMART Example RBT

PI: Jones N=220

8 Embedded Interventions

[only 6 of 8 are adaptive]



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SMART Example RBT

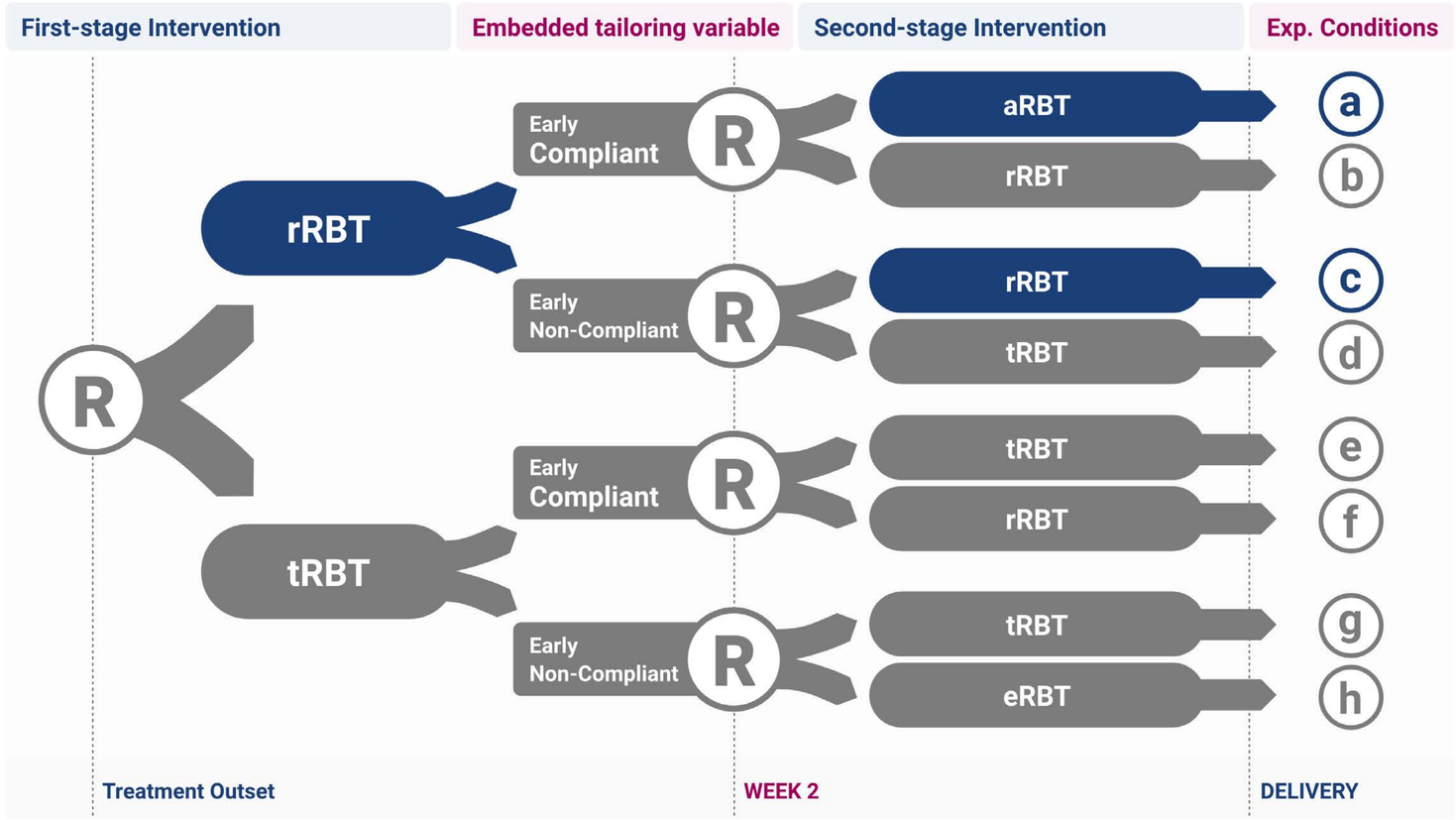
PI: Jones N=220

8 Embedded Interventions

[only 6 of 8 are adaptive]

Adaptive Intervention 1

Start with **rRBT**;
if **early compliant**, **step down to aRBT**;
else **continue rRBT**



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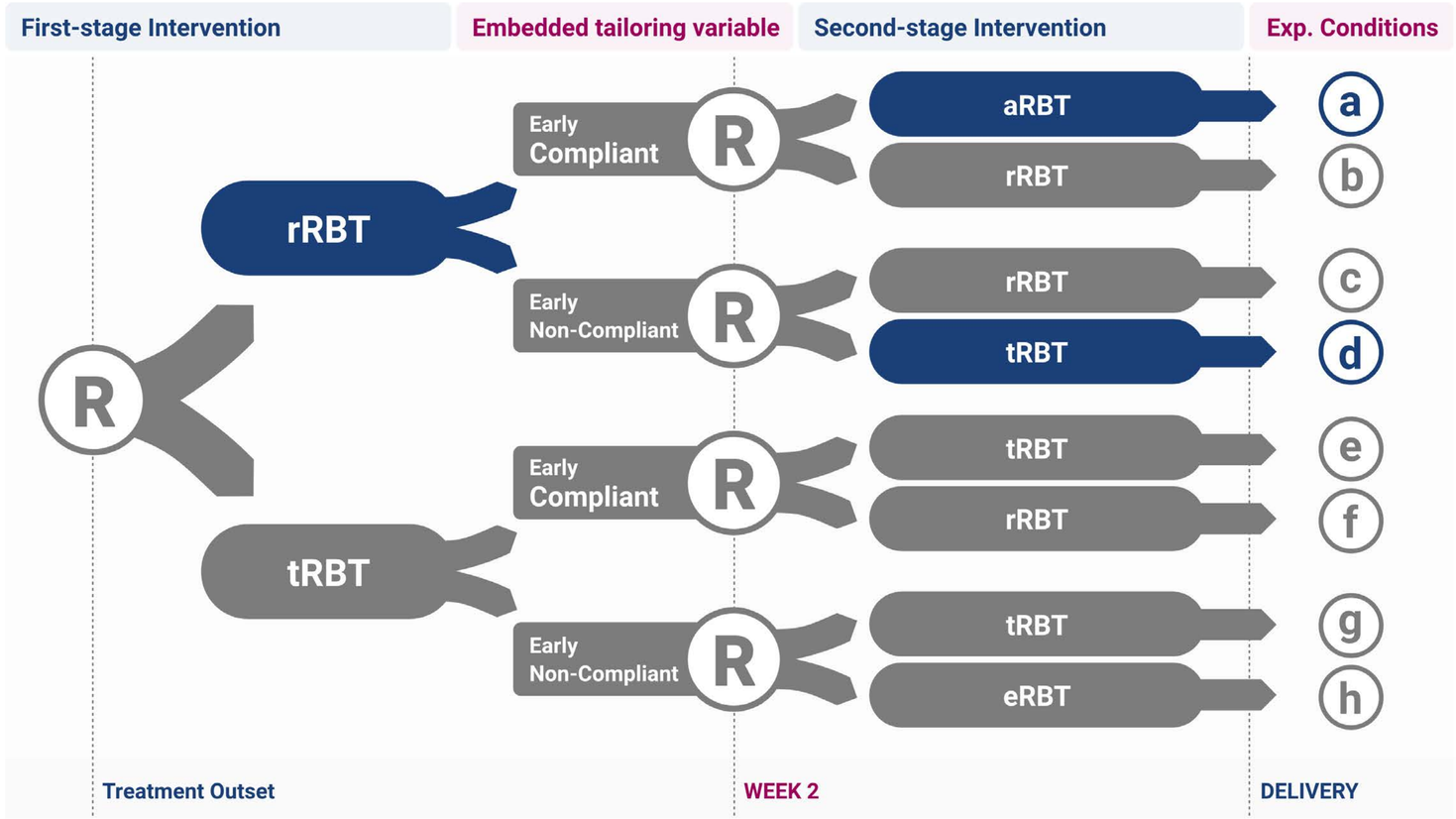
8 Embedded Adaptive Interventions

Adaptive Intervention 2

Start with **rRBT**;
if **early compliant**, **step down to aRBT**;
else **step up to tRBT**



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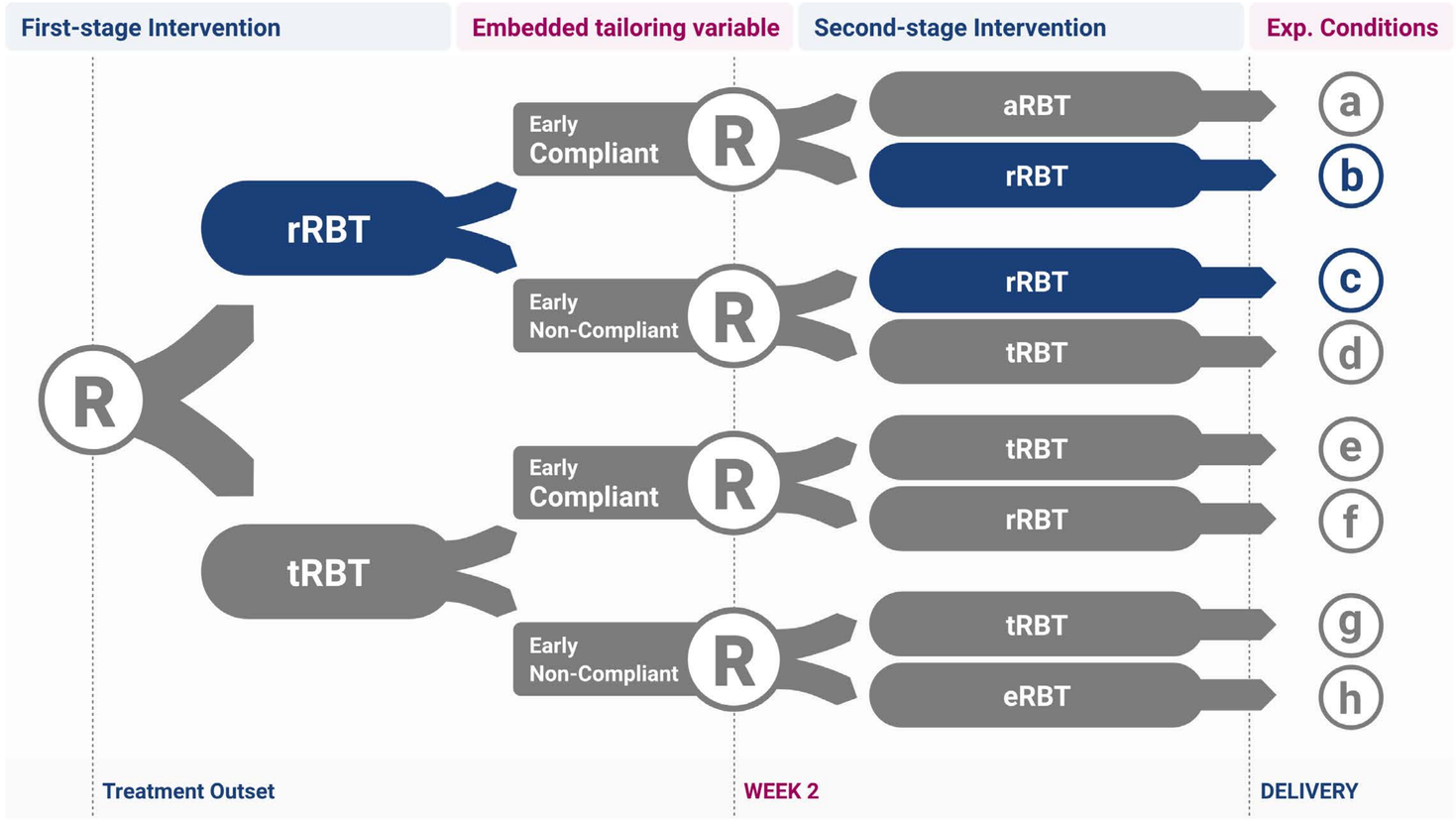
8 Embedded Adaptive Interventions

[Non] Adaptive Intervention 3

Start with **rRBT**;
if **early compliant**, **continue rRBT**;
else **continue rRBT**



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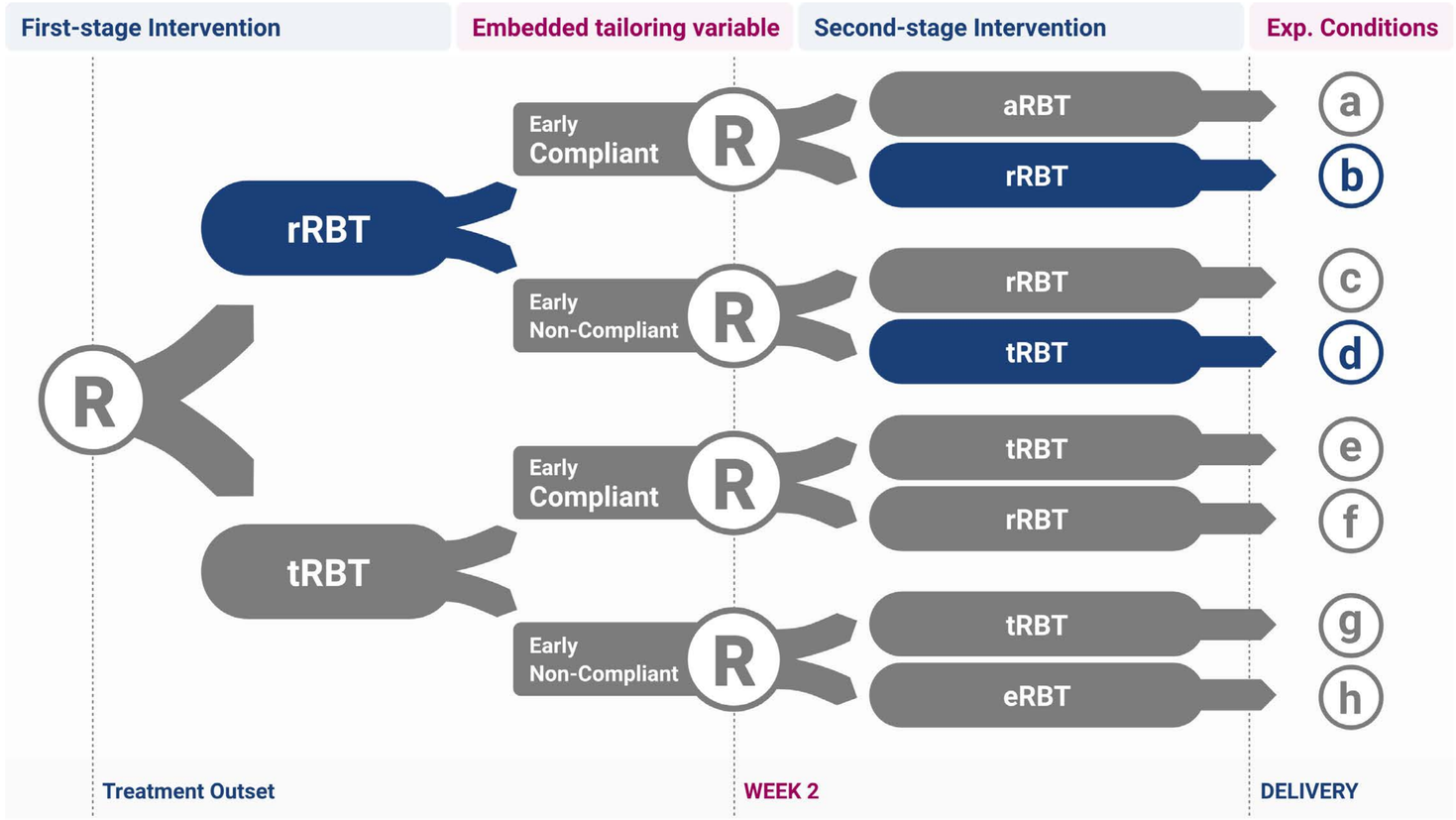
8 Embedded Adaptive Interventions

Adaptive Intervention 4

Start with **rRBT**;
if **early compliant**, **continue rRBT**;
else **step up to tRBT**



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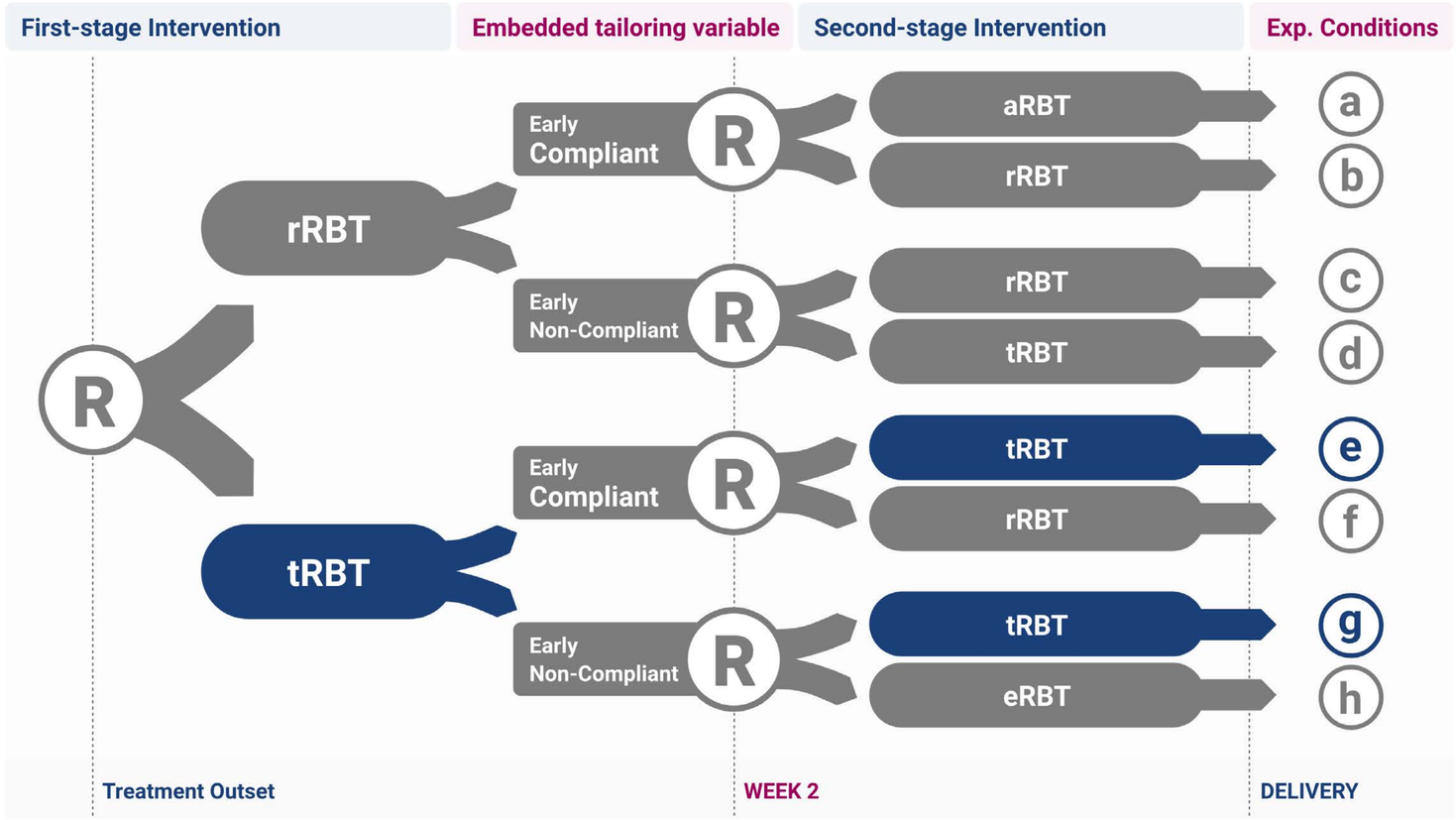
8 Embedded Adaptive Interventions

[Non] Adaptive Intervention 5

Start with **tRBT**;
if **early compliant**, **continue tRBT**;
else **continue tRBT**



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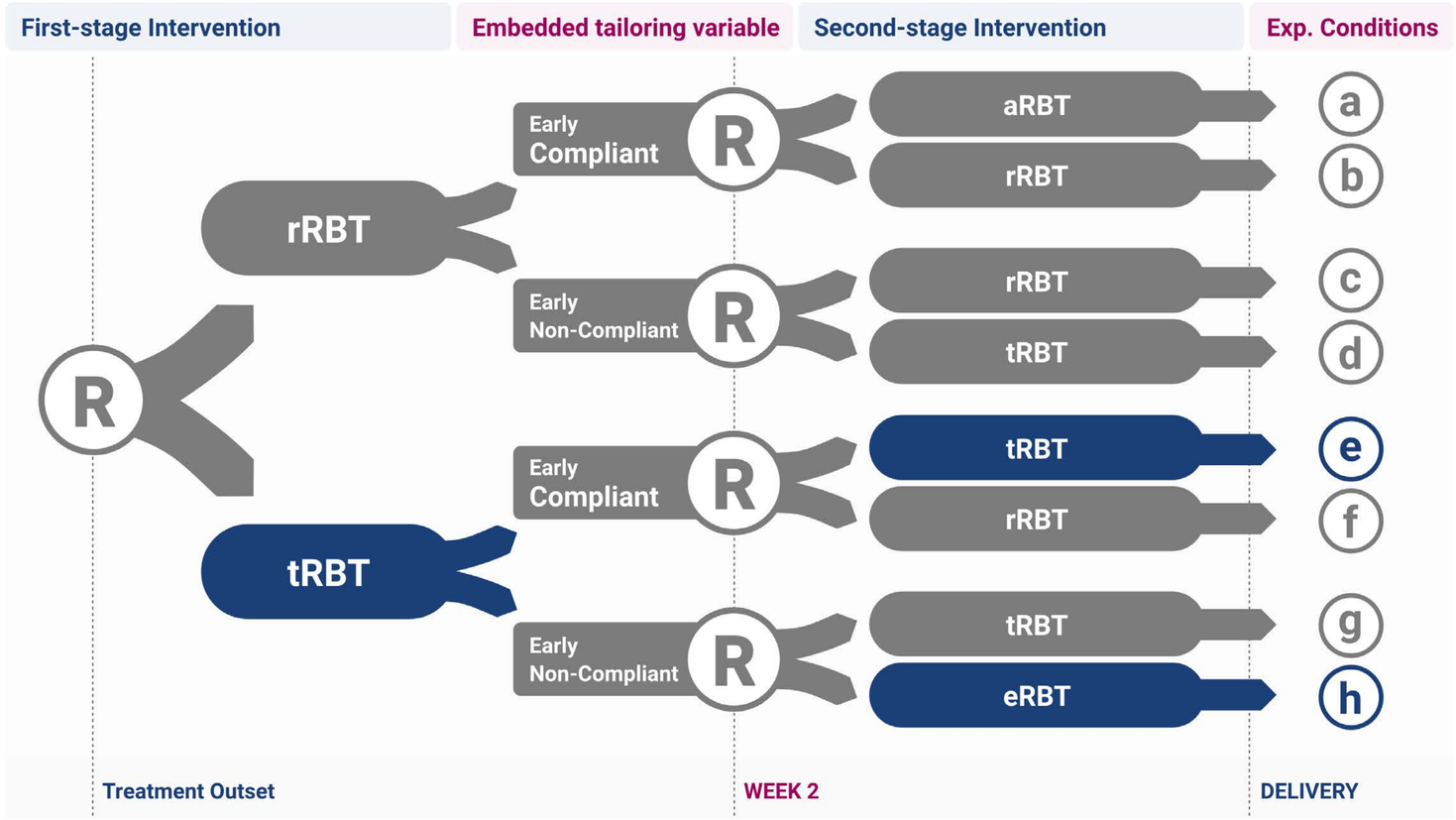
8 Embedded Adaptive Interventions

Adaptive Intervention 6

Start with **tRBT**;

if **early compliant**, **continue tRBT**;

else **step up to eRBT**



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8 Embedded Adaptive Interventions

Adaptive Intervention 7

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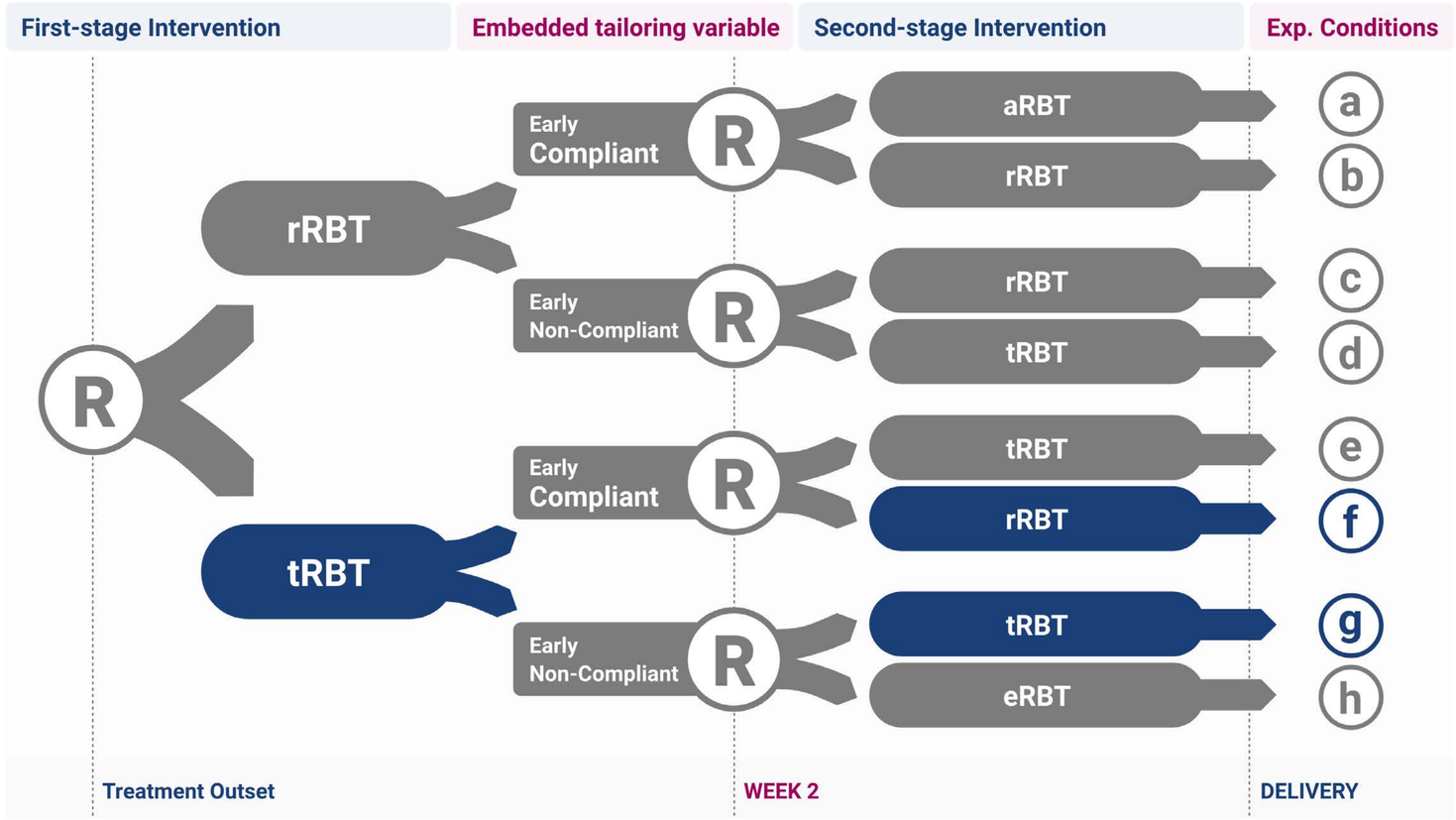
if **early compliant**, **step down to rRBT**;
else **continue tRBT**



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8 Embedded Adaptive Interventions

Adaptive Intervention 8

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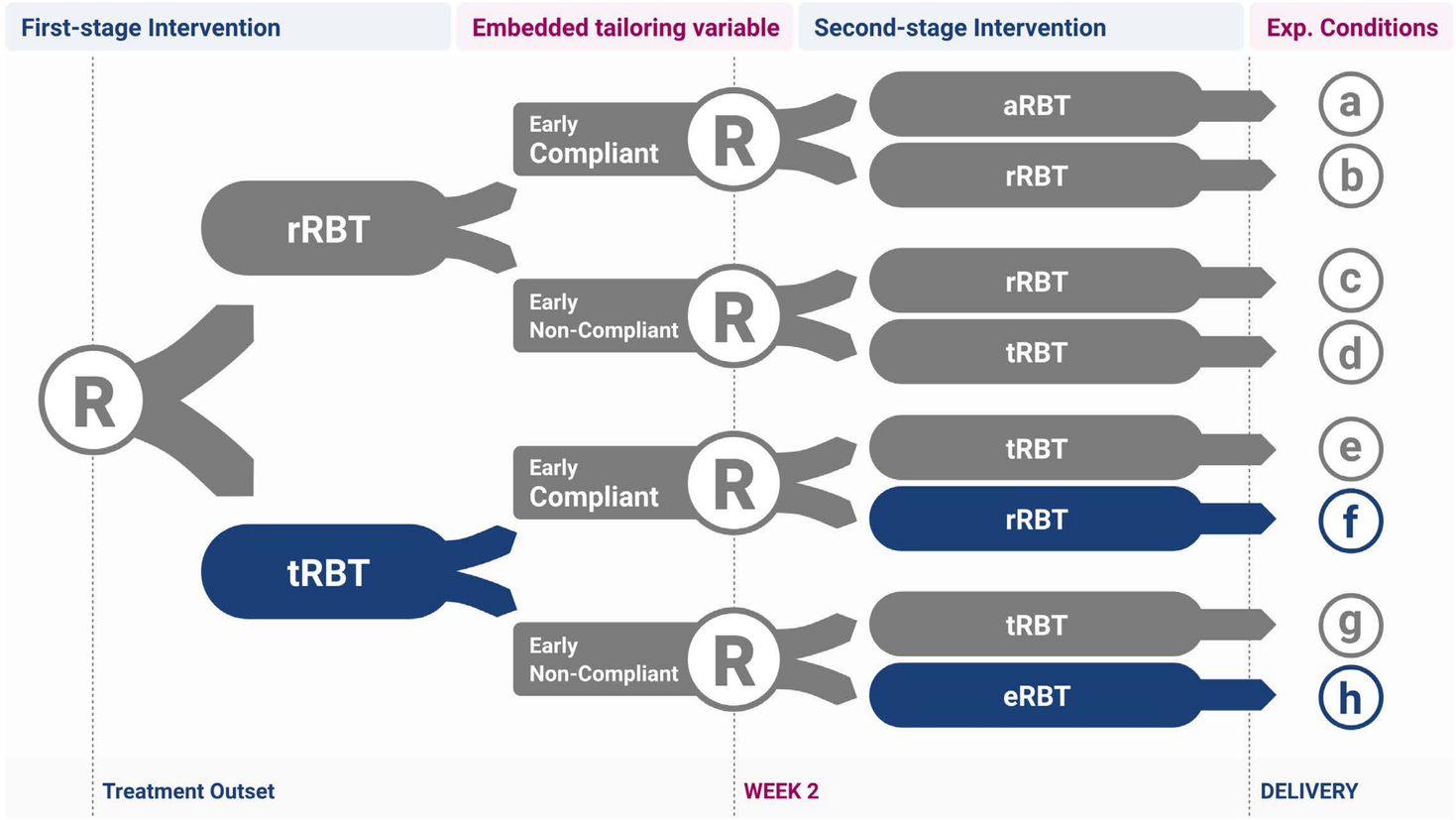
else **step up to eRBT**



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SMART Example RBT

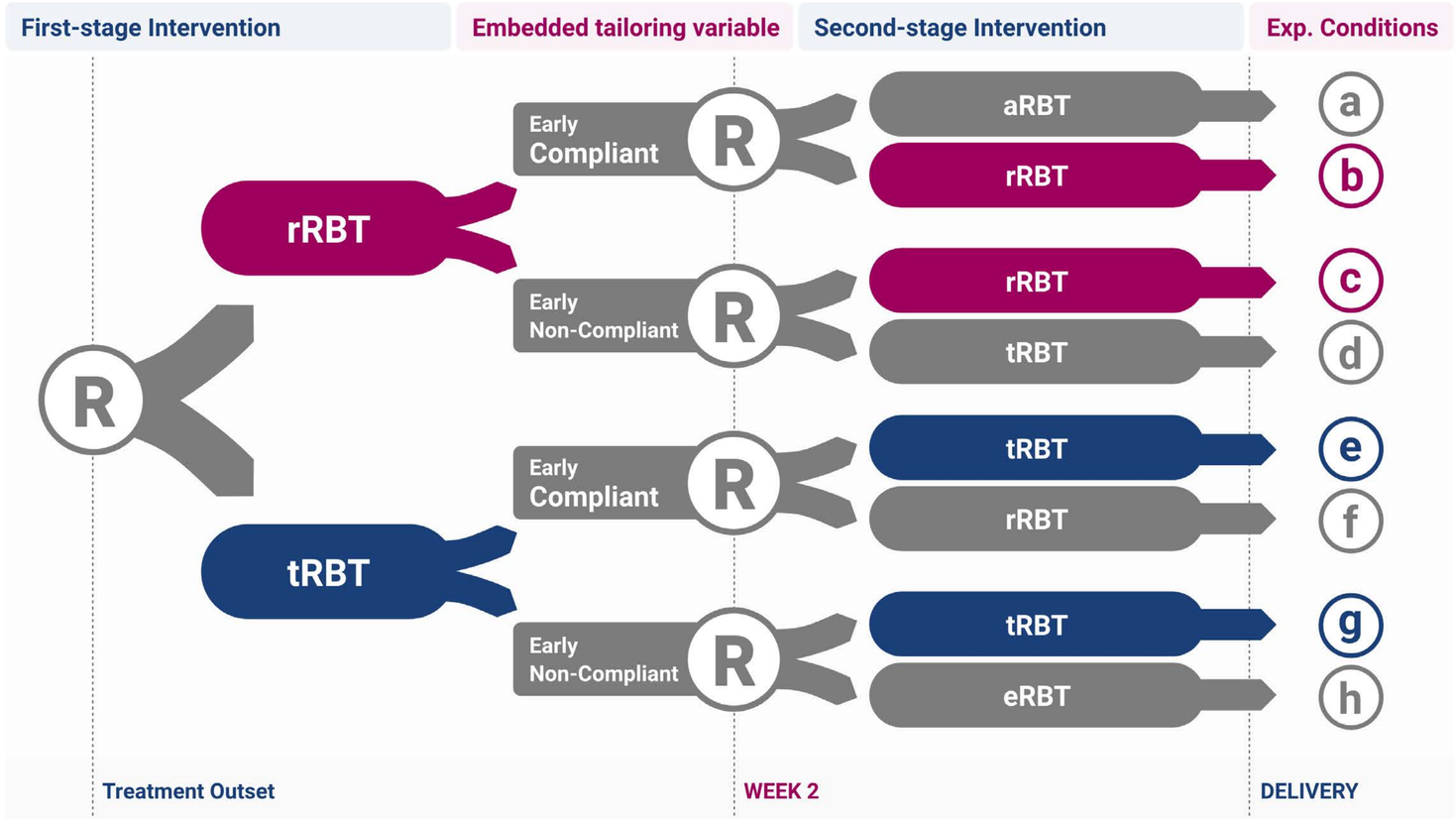
PI: Jones N=220

Primary Aim

Compare always rRBT intervention to always tRBT in terms of program completion (delivery of child while in treatment)

Secondary Aims:

- Investigate moderation by baseline variables
- Investigate whether other variables might be used to tailor treatment



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SMART Weight Loss: Integrating mHealth in Obesity Treatment

PI: Nahum-Shani & Spring

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PI: Kilbourne

Weight Loss

PI: Nahum-Shani & Spring

Population

Obese/overweight adults

Rationale

Efficacious weight-loss interventions are costly and burdensome

- Mobile health (mHealth) tools have shown efficacy, are scalable and inexpensive, but
- High heterogeneity in response to mHealth
- Many people require more than mHealth to succeed
- Need to determine how to best integrate mHealth tools in weight loss promotion

Outcome

Weight change from baseline to six months

Weight Loss

PI: Nahum-Shani & Spring

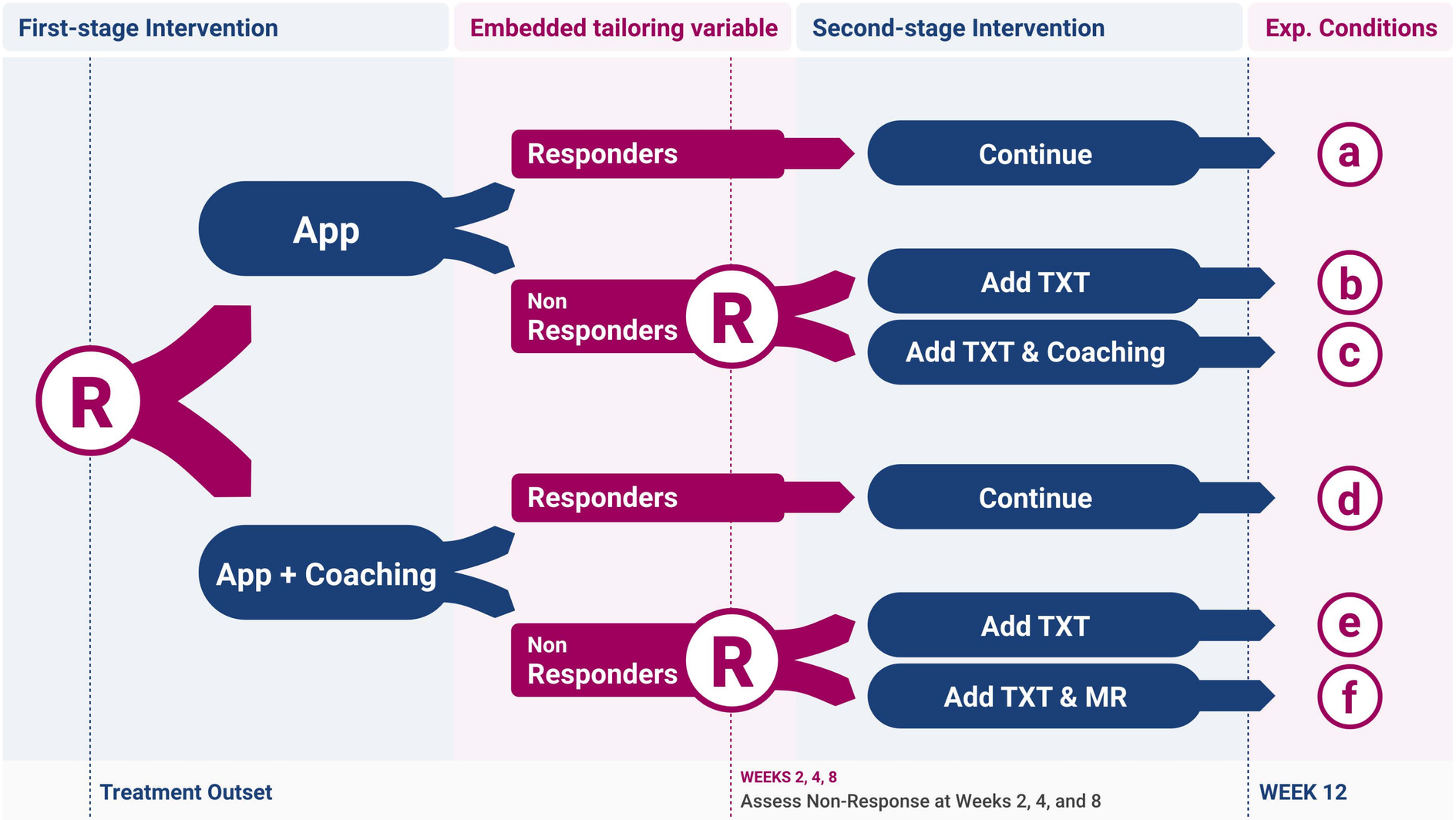
Scientific Questions

- Is App alone non-inferior to App + Coaching initially?

- Is the best augmentation tactic for non-responders to add another mHealth component (TXT) or to add mHealth and a more traditional component (MR or Coaching)?

SMART Example Weight Loss

PI: Nahum-Shani & Spring N=400



App →
Mobile Application

MR →
Meal Replacement

TXT →
Text Messages

SMART Example Weight Loss

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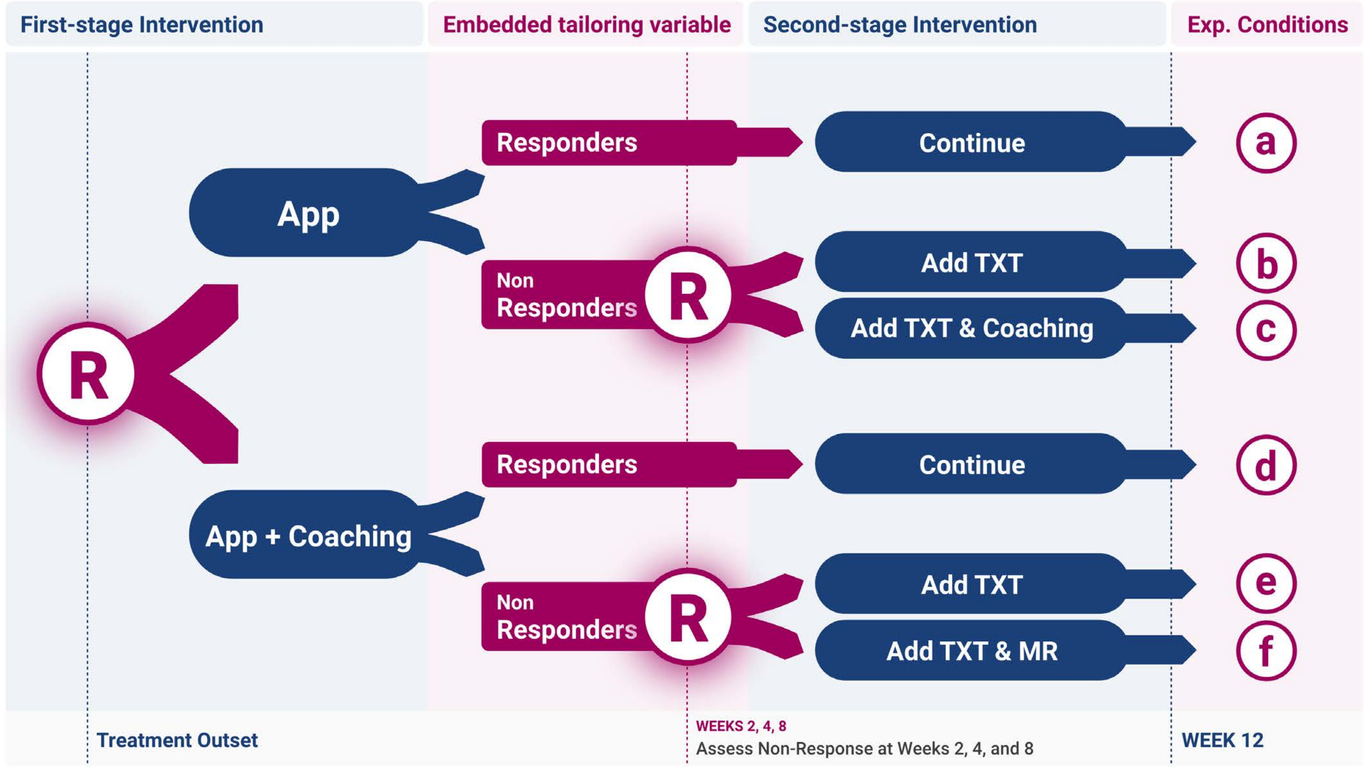

App →
Mobile Application

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TXT →
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SMART Example Weight Loss

PI: Nahum-Shani & Spring N=400

Intervention Options:

First-stage

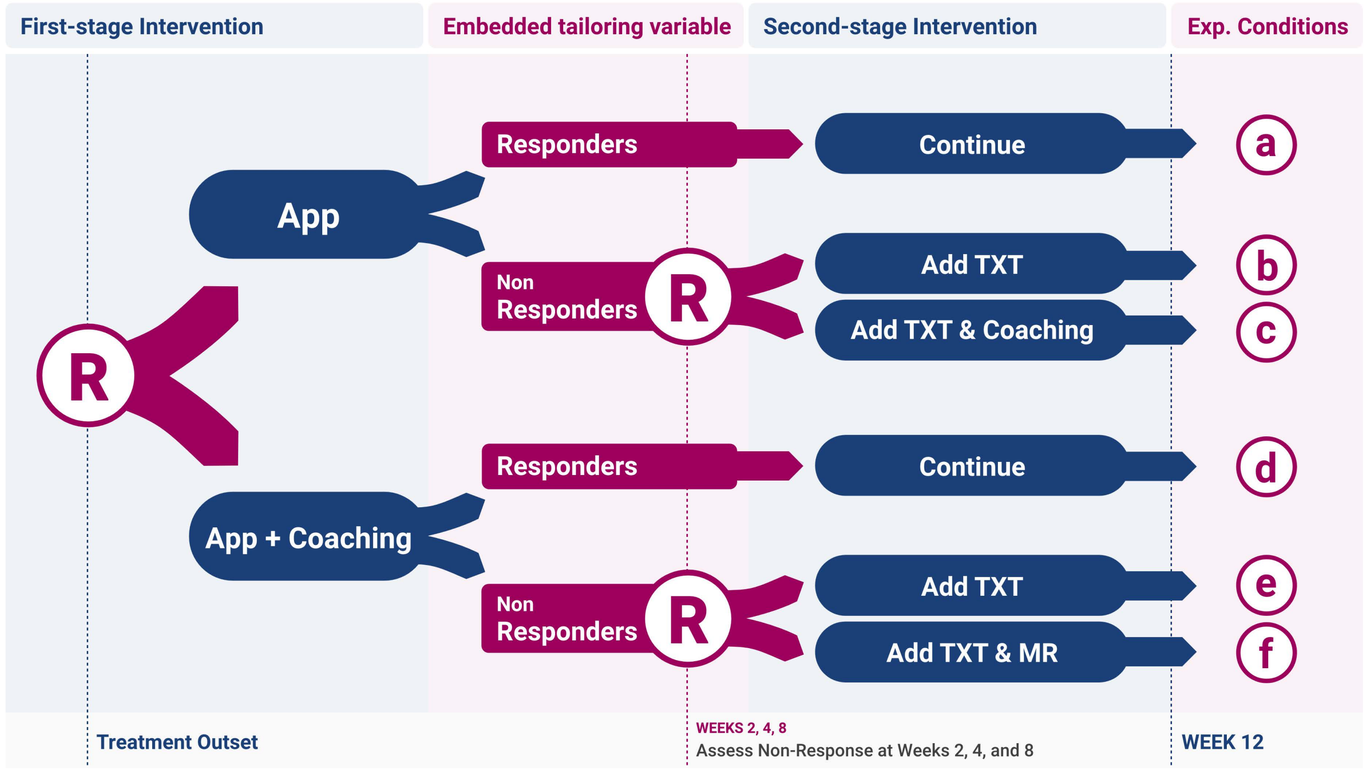
- App
- App + Coaching

Second-stage non-responders

- Add TXT
- Add TXT + Traditional

Second stage responders

- Continue



App → Mobile Application

MR → Meal Replacement

TXT → Text Messages

SMART Example Weight Loss

PI: Nahum-Shani & Spring N=400

Embedded Tailoring Variable:

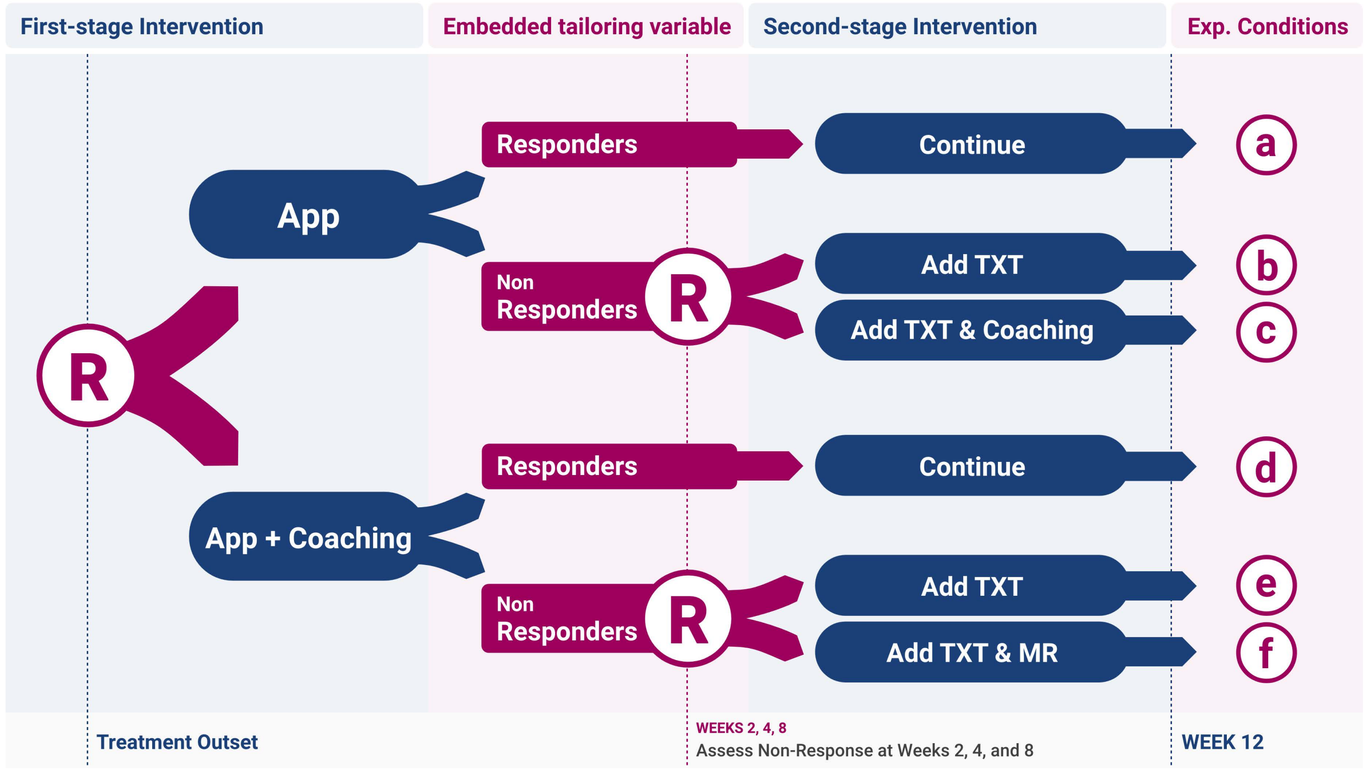
Response/non-response status

Assessed at weeks 2, 4, and 8; based on

Weight loss

Non-response as soon as

Weight loss < 0.5 lbs. on average per week



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Text Messages

SMART Example Weight Loss

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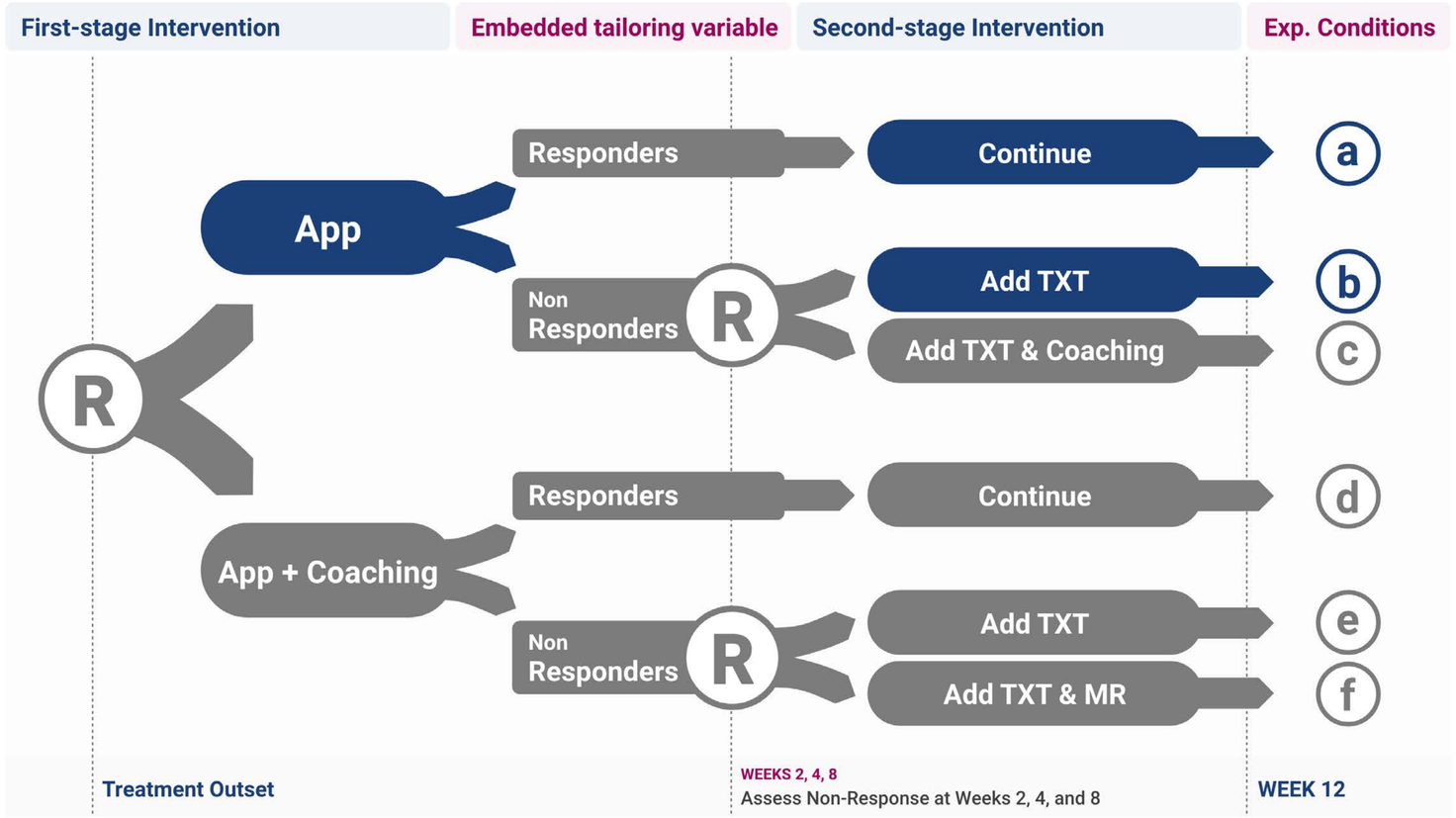
4 Embedded Adaptive Interventions

Adaptive Intervention 1

Start with **App**;
if **response**, **continue**;
else **add TXT**



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Mobile Application

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SMART Example Weight Loss

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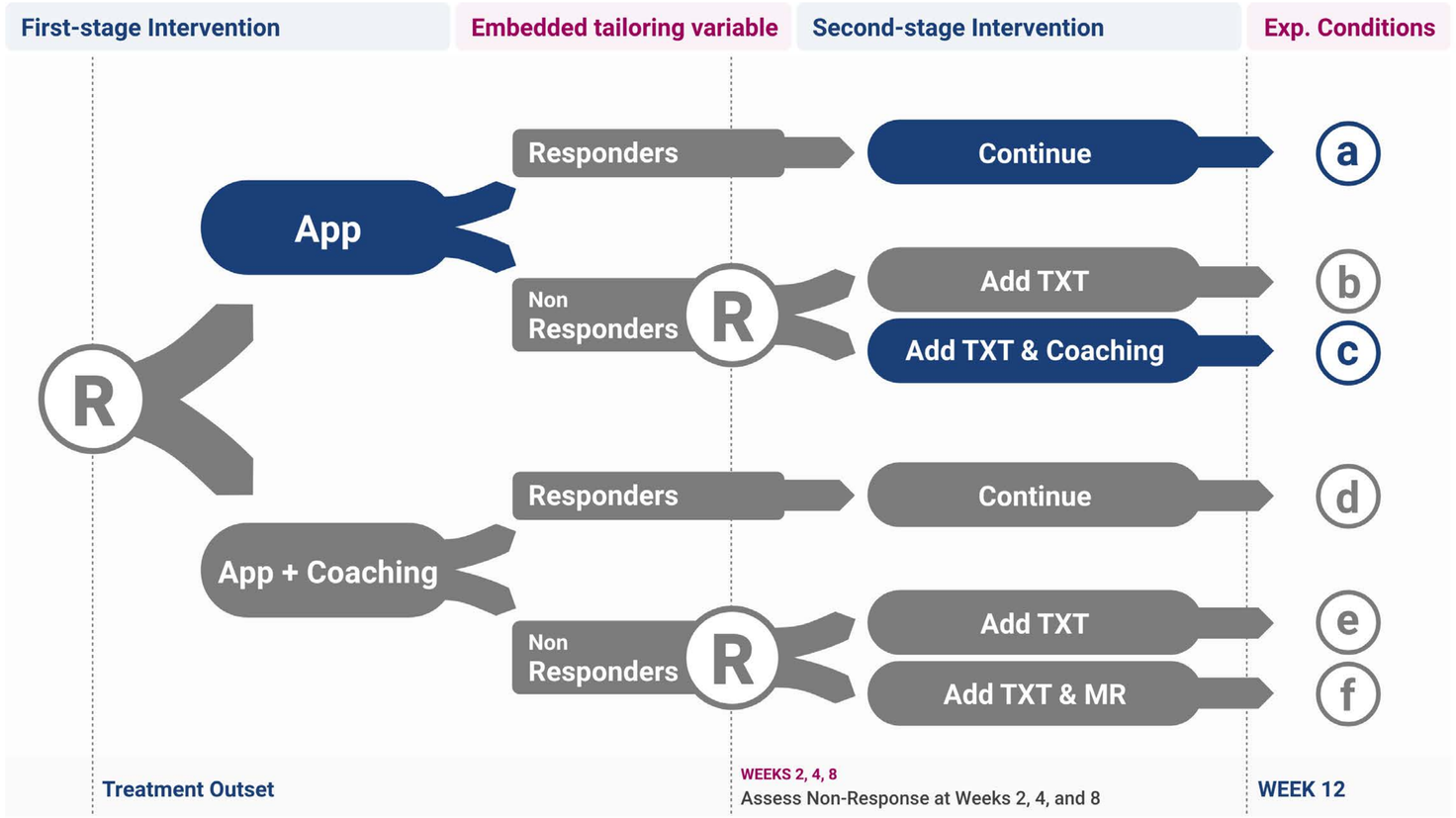
4 Embedded Adaptive Interventions

Adaptive Intervention 2

Start with **App**;
if **response**, **continue**;
else **add TXT + Coaching**



App →
Mobile Application

MR →
Meal Replacement

TXT →
Text Messages

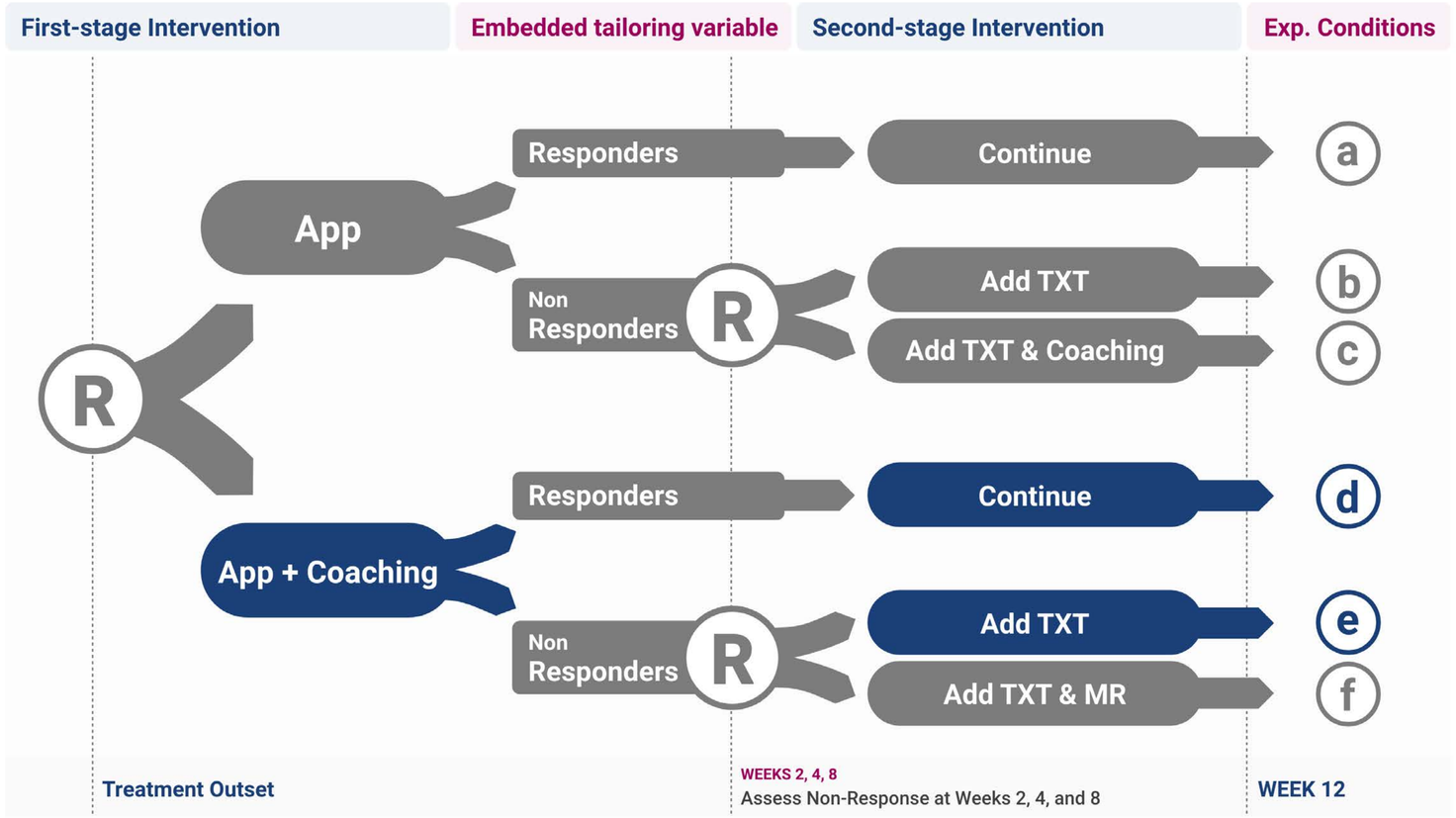
SMART Example Weight Loss

PI: Nahum-Shani & Spring N=400

4 Embedded Adaptive Interventions

Adaptive Intervention 3

Start with **App + Coaching**;
if **response**, **continue**;
else **add TXT**



App →
Mobile Application

MR →
Meal Replacement

TXT →
Text Messages

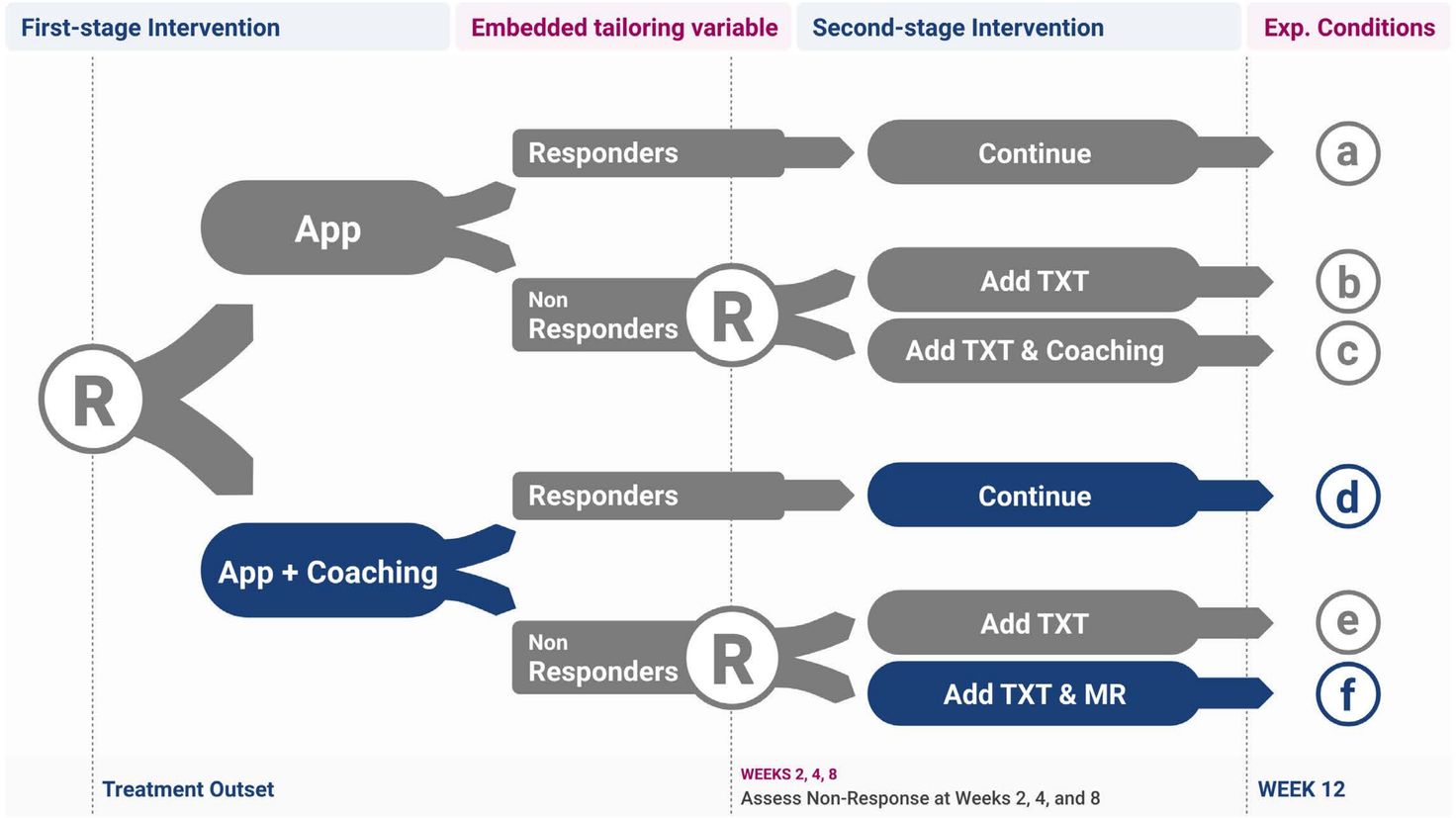
SMART Example Weight Loss

PI: Nahum-Shani & Spring N=400

4 Embedded Adaptive Interventions

Adaptive Intervention 4

Start with **App + Coaching**;
if **response**, **continue**;
else **add TXT + MR**



App →
Mobile Application

MR →
Meal Replacement

TXT →
Text Messages

SMART Example Weight Loss

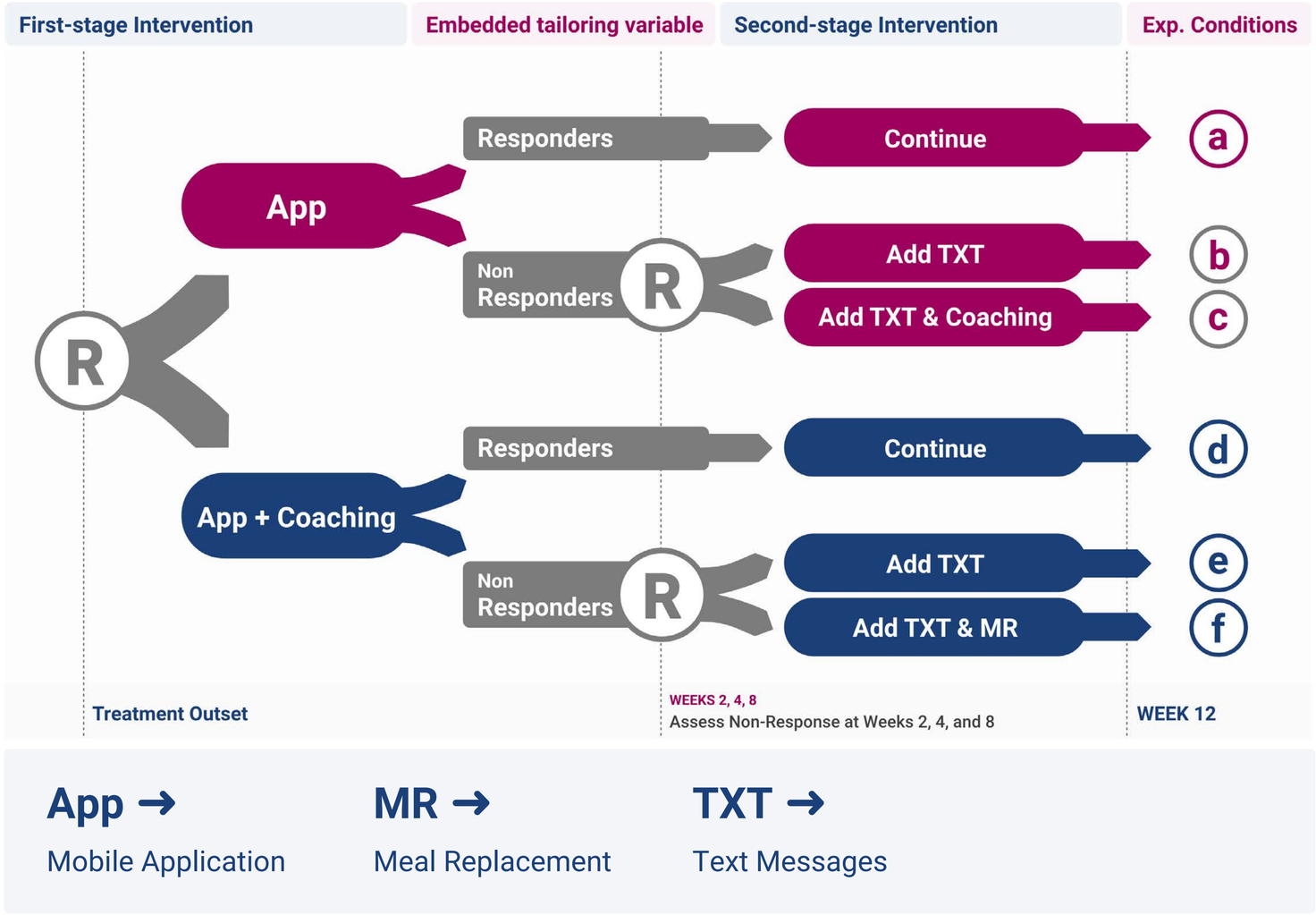
PI: Nahum-Shani & Spring N=400

Primary Aim

Compare App vs. App + Coaching initially, in terms of change in weight loss over 6 months

Secondary Aims:

- Compare augmentation tactics for non-responders
- Compare embedded AIs
- Investigate baseline and time-varying moderators



App → Mobile Application

MR → Meal Replacement

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SMART Case Studies

ExTENd: Treatment of Alcohol Dependence
PI: Oslin

RBT: Treatment for Pregnant Women who are Drug Dependent
PI: Jones

SMART Weight Loss: Integrating mHealth in Obesity Treatment
PI: Nahum-Shani & Spring

ASIC: School-based Implementation of Cognitive Behavioral Therapy
PI: Kilbourne

ASIC

Adaptive School-based Implementation of CBT

TRAILS

Transforming Research into Action to Improve the Lives of Students

ASIC School-Based Implementation of CBT

PI: Kilbourne

Population

School professionals (SPs) (counselors, psychologists, nurses) employed at Michigan high schools

Rationale

- Replicating Effective Programs (REP) is a low-level implementation strategy that will be enough for some (but not most) schools.
- Coaching is effective, but expensive and burdensome, and possibly not needed by all schools.
- Facilitation, which addresses organizational barriers rather than skill-based, may also be needed at some schools
- Need to determine the best way to combine strategies to scale TRAILS out to a wide variety of schools.

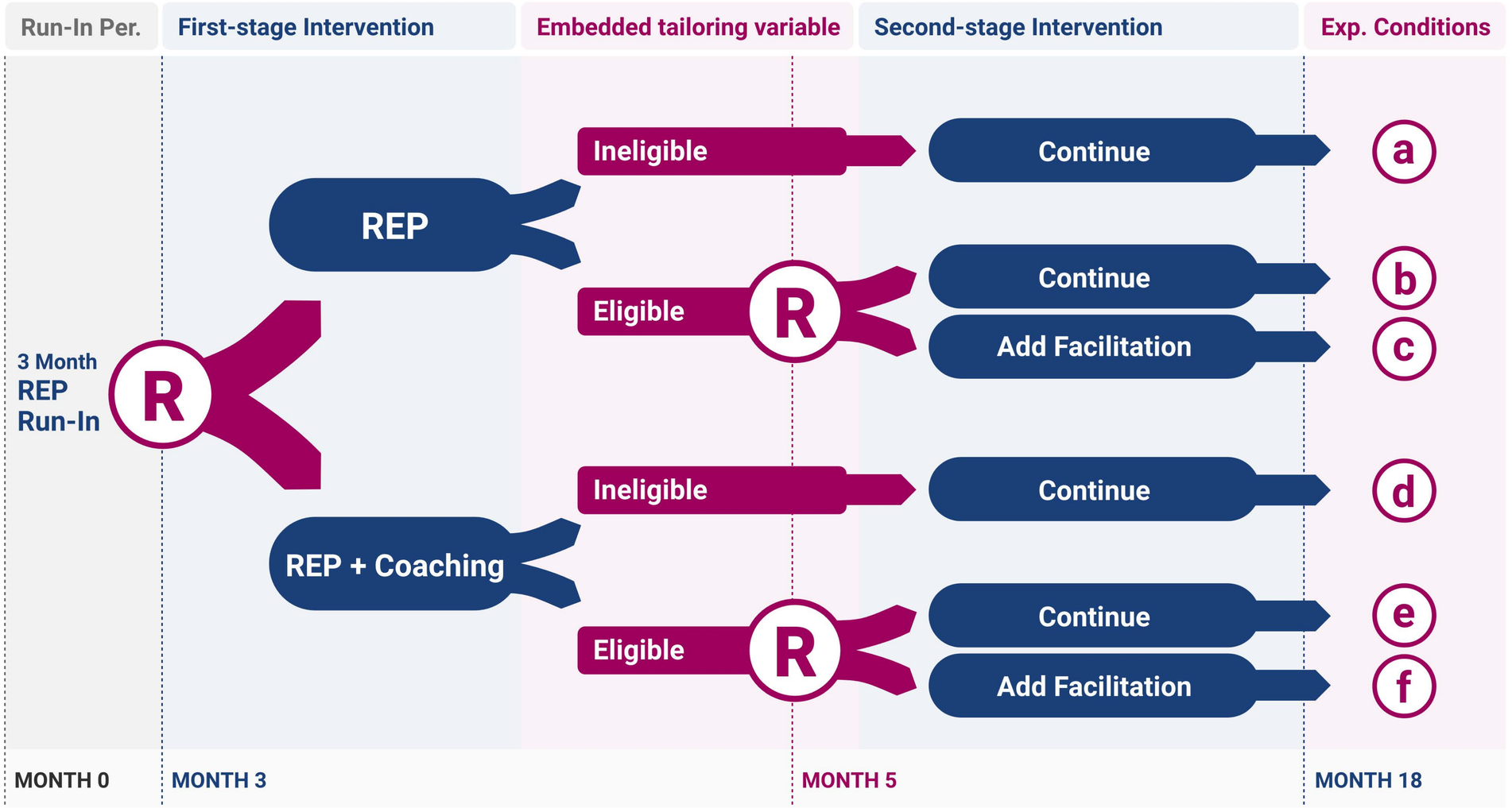
ASIC School-Based Implementation of CBT

Scientific Questions

- Does REP + Coaching outperform REP alone?
- How does adding Facilitation enhance the effectiveness of REP, with or without coaching?
- What moderates the effectiveness of Coaching and Facilitation augmentations to REP?

SMART Example School-Based Implementation of CBT

PI: Kilbourne N=200



REP →

Replicating Effective Programs; low-level implementation strategy that provides manualization of intervention (e.g., CBT), didactic training, & technical assistance

Coaching →

In-person coaching during CBT groups at the school for a minimum 12 weeks

Facilitation →

Phone calls with an expert in CBT & strategic thinking for a minimum 12 weeks.

SMART Example **School-Based Implementation of CBT**

PI: Kilbourne N=200

Scientific Questions:

- Does REP + Coaching outperform REP alone?
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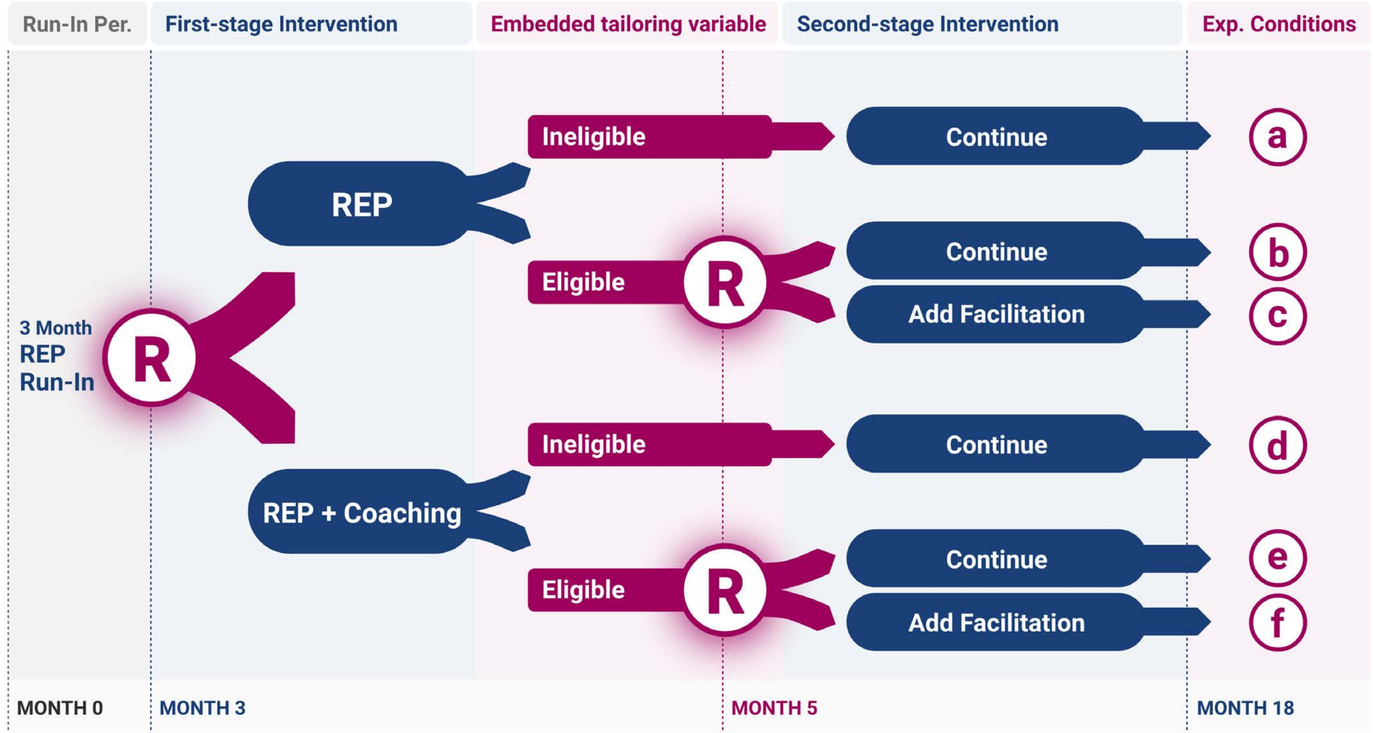

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SMART Example **School-Based Implementation of CBT**

PI: Kilbourne N=200

Intervention Options:

First-stage

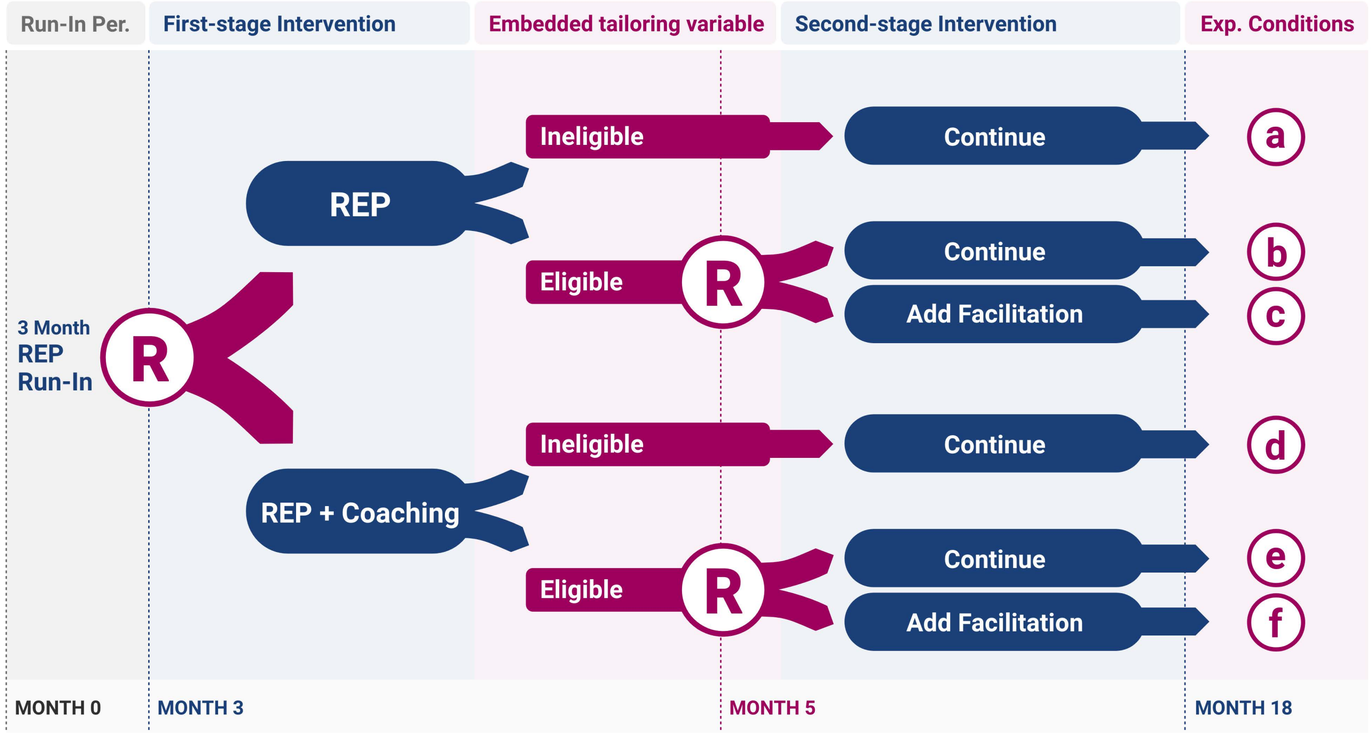
- REP
- REP + Coaching

Second-stage non-responders

- Continue
- Add Facilitation

Second stage responders

- Continue



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SMART Example **School-Based Implementation of CBT**

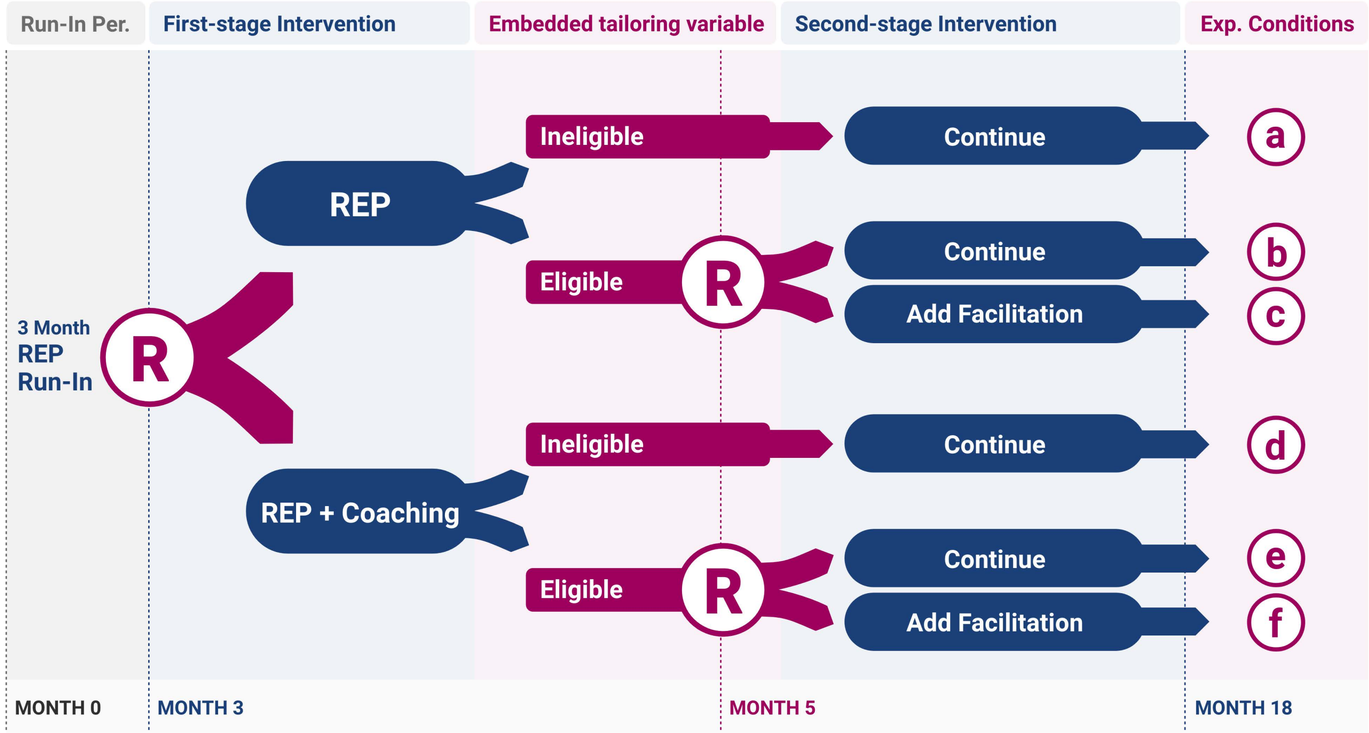
PI: Kilbourne N=200

Embedded Tailoring Variable:

Response/non-response status

Assessed 8 weeks after first randomization; based on

- **Self-reported CBT delivery**
- **Self-reported barriers to CBT**



Schools are eligible if

1+ SP does *not* deliver 3+ CBT components to 10+ students

OR Mean # of barriers to CBT reported is >2

SMART Example School-Based Implementation of CBT

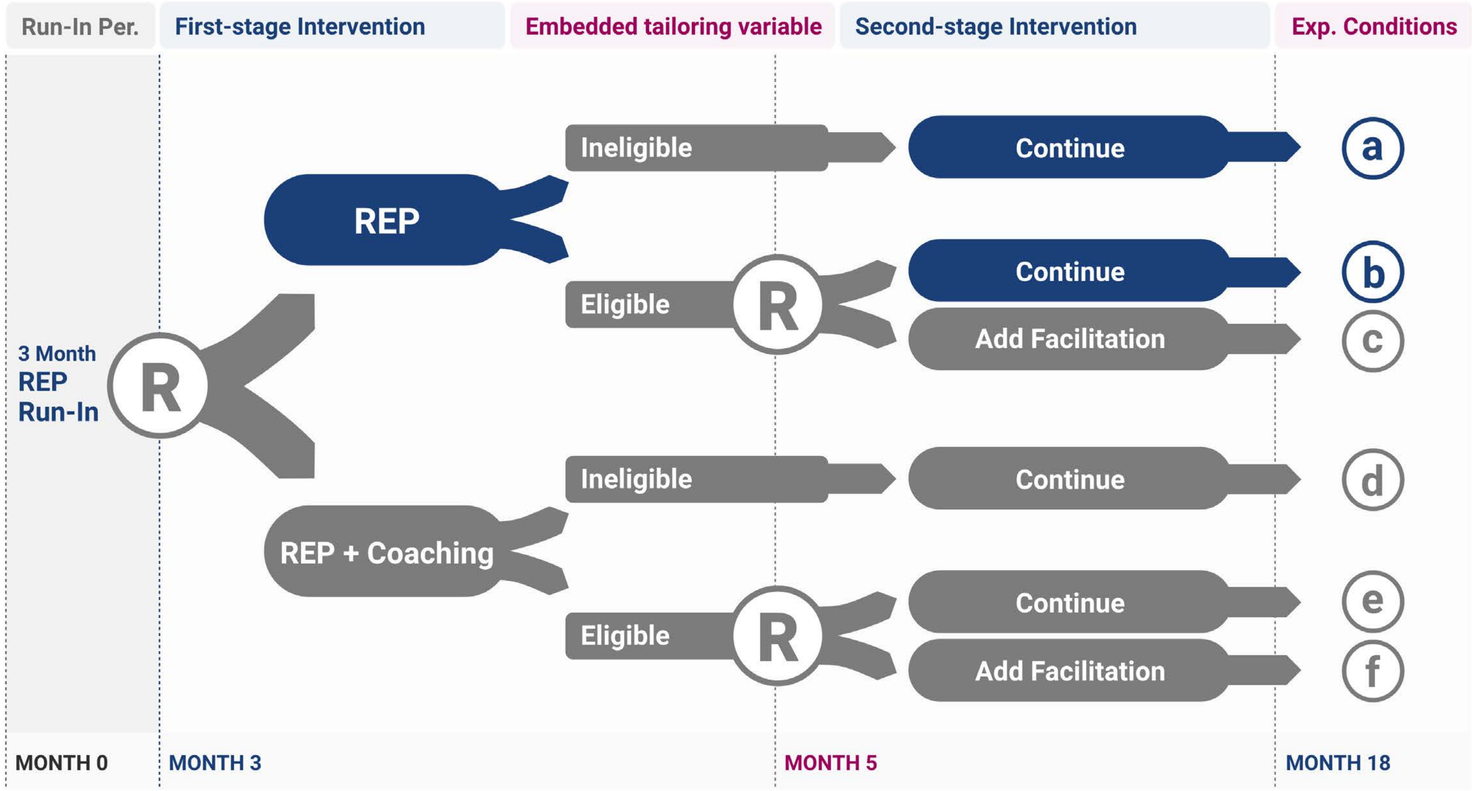
PI: Kilbourne N=200

4 Embedded Interventions

[only 2 of 4 are adaptive]

[Non] Adaptive Intervention 1

Start with **REP**;
if **ineligible**, **continue REP**;
else **continue REP**



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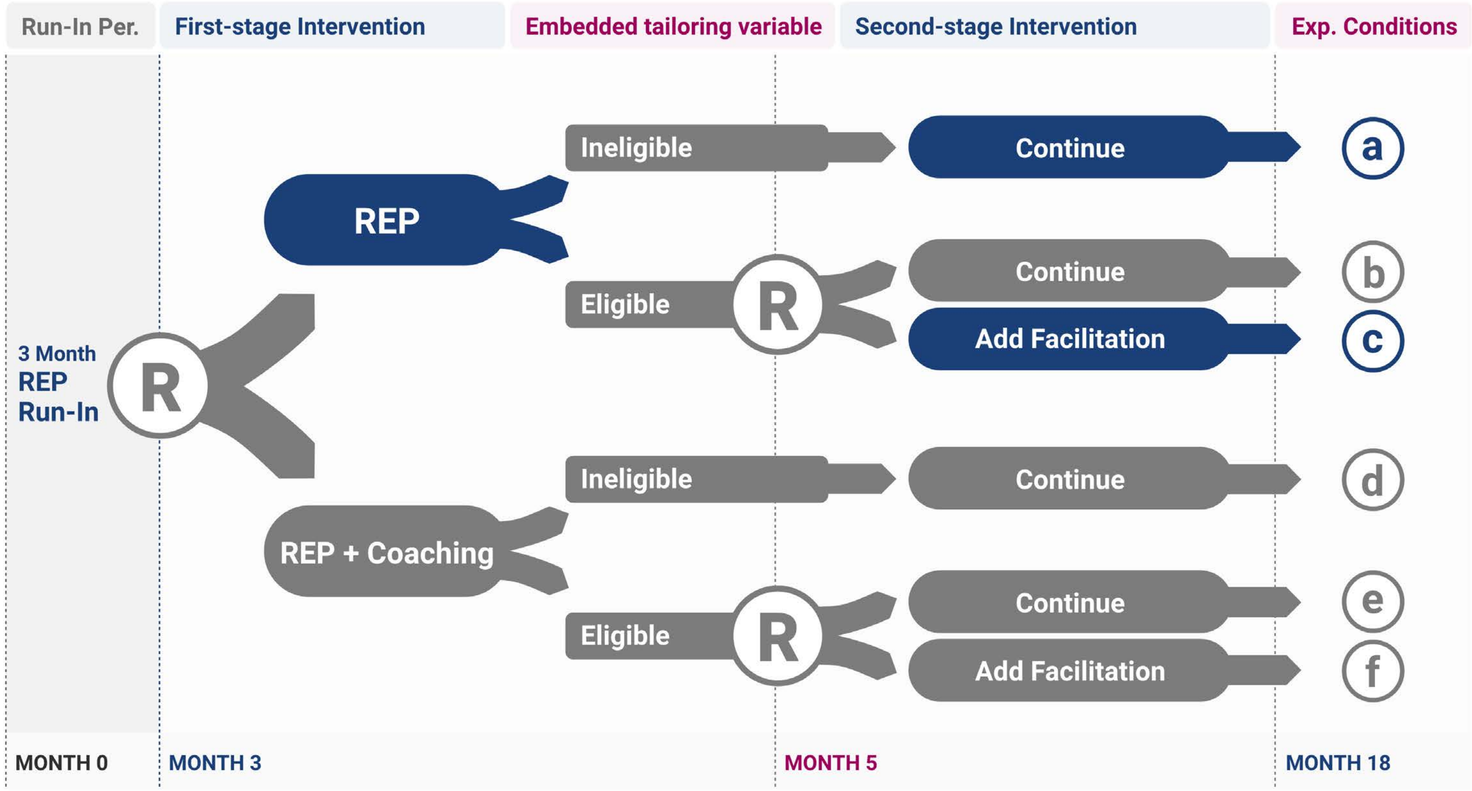
SMART Example **School-Based Implementation of CBT**

PI: Kilbourne N=200

4 Embedded Adaptive Interventions

Adaptive Intervention 2

Start with **REP**;
if **ineligible**, **continue REP**;
else **add Facilitation**



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Coaching →

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Facilitation →

Phone calls with an expert in CBT & strategic thinking for a minimum 12 weeks.

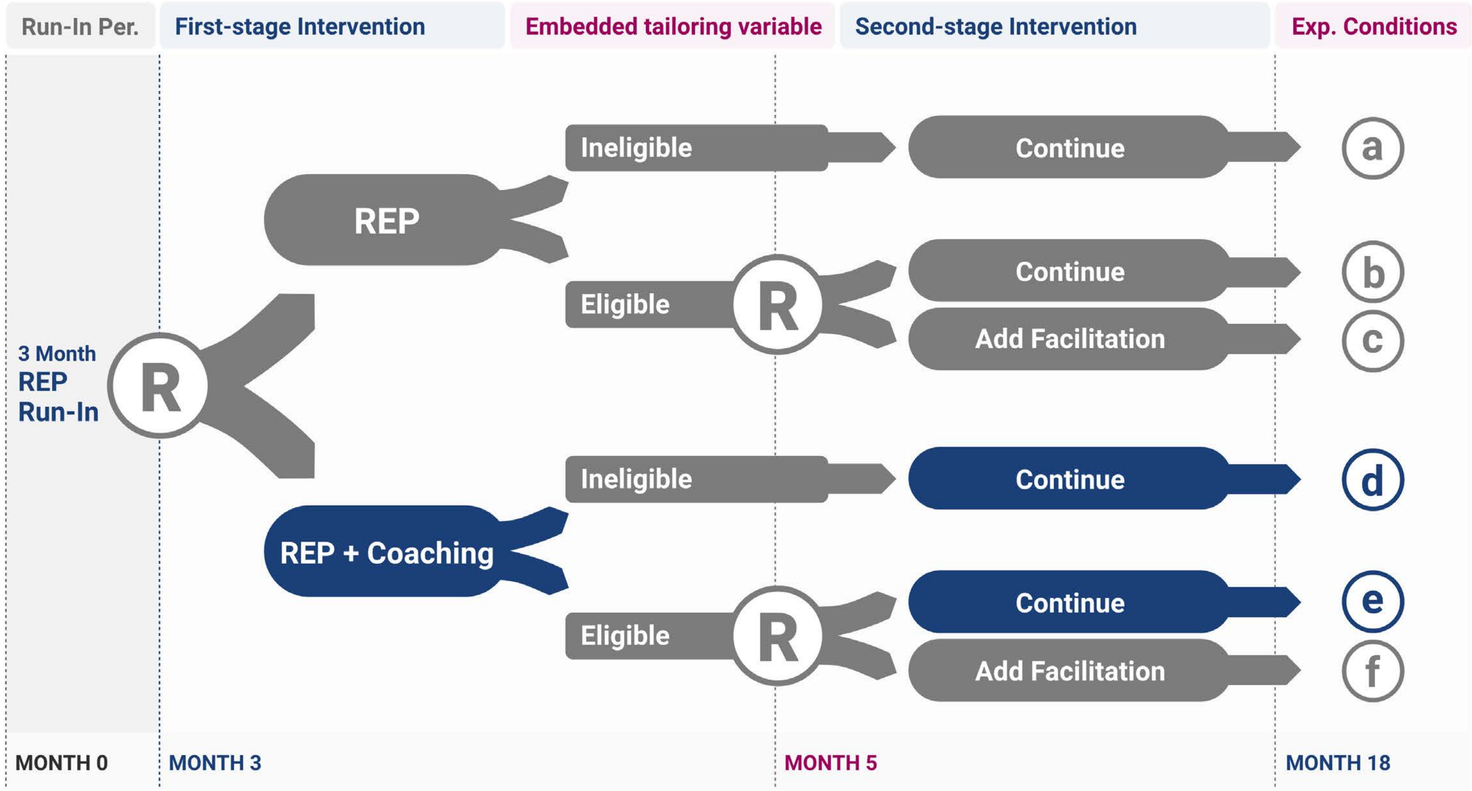
SMART Example **School-Based Implementation of CBT**

PI: Kilbourne N=200

4 Embedded Adaptive Interventions

[Non] Adaptive Intervention 3

Start with **REP + Coaching**;
if **ineligible**, **continue REP + Coaching**;
else **continue REP + Coaching**



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Coaching →

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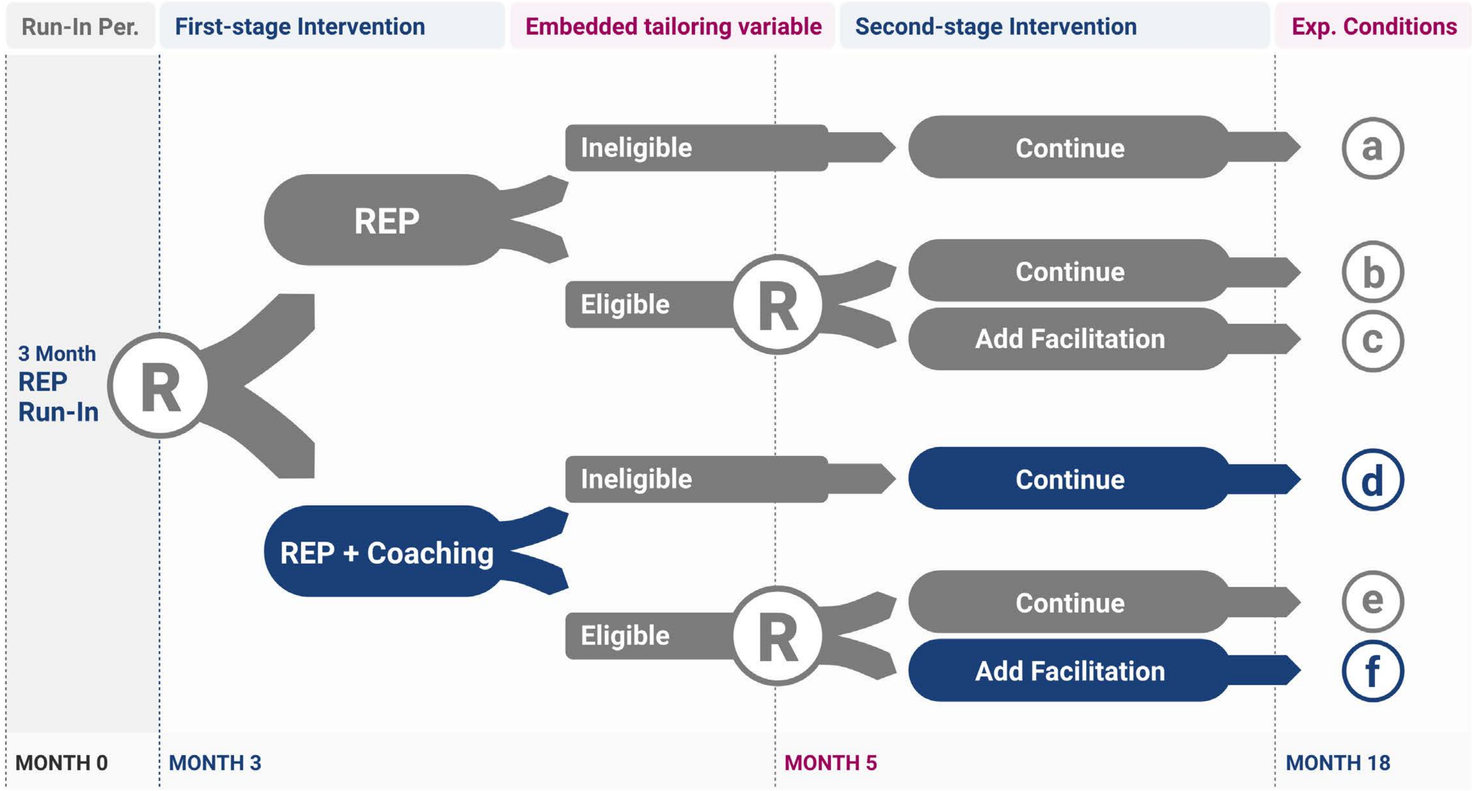
SMART Example **School-Based Implementation of CBT**

PI: Kilbourne N=200

4 Embedded Adaptive Interventions

Adaptive Intervention 4

Start with **REP + Coaching**;
if **ineligible**, **continue REP + Coaching**;
else **add Facilitation**



REP →

Replicating Effective Programs; low-level implementation strategy that provides manualization of intervention (e.g., CBT), didactic training, & technical assistance

Coaching →

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Facilitation →

Phone calls with an expert in CBT & strategic thinking for a minimum 12 weeks.

SMART Example **School-Based Implementation of CBT**

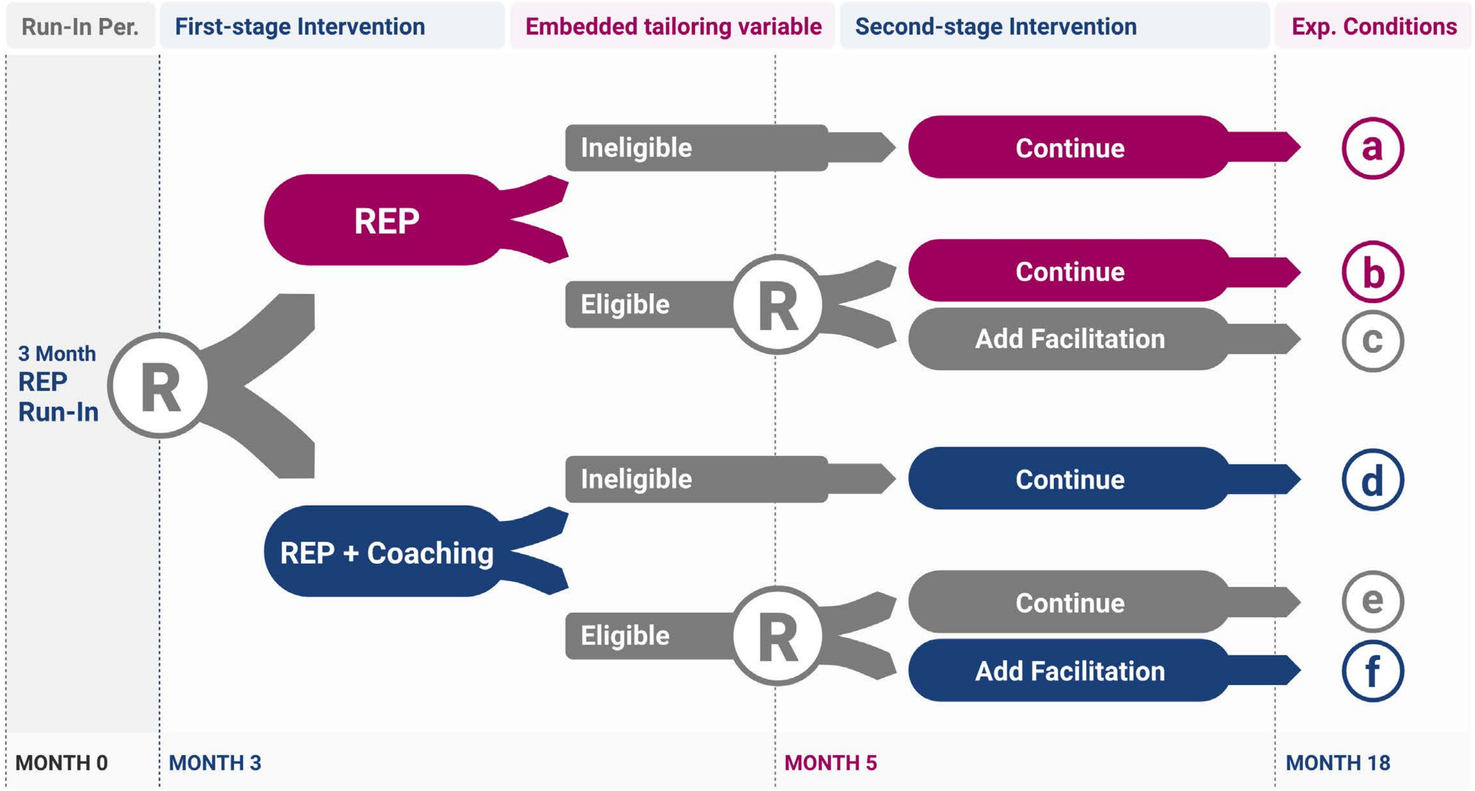
PI: Kilbourne N=200

Primary Aim

Compare always-REP intervention to REP + Coaching + Facilitation AI in terms of number of CBT sessions delivered by SPs over 18 months.

Secondary Aims:

- Investigate baseline and time-varying moderators of Coaching and Facilitation
- Cost-effectiveness of different interventions
- Investigate mechanisms of Coaching and Facilitation



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Outline

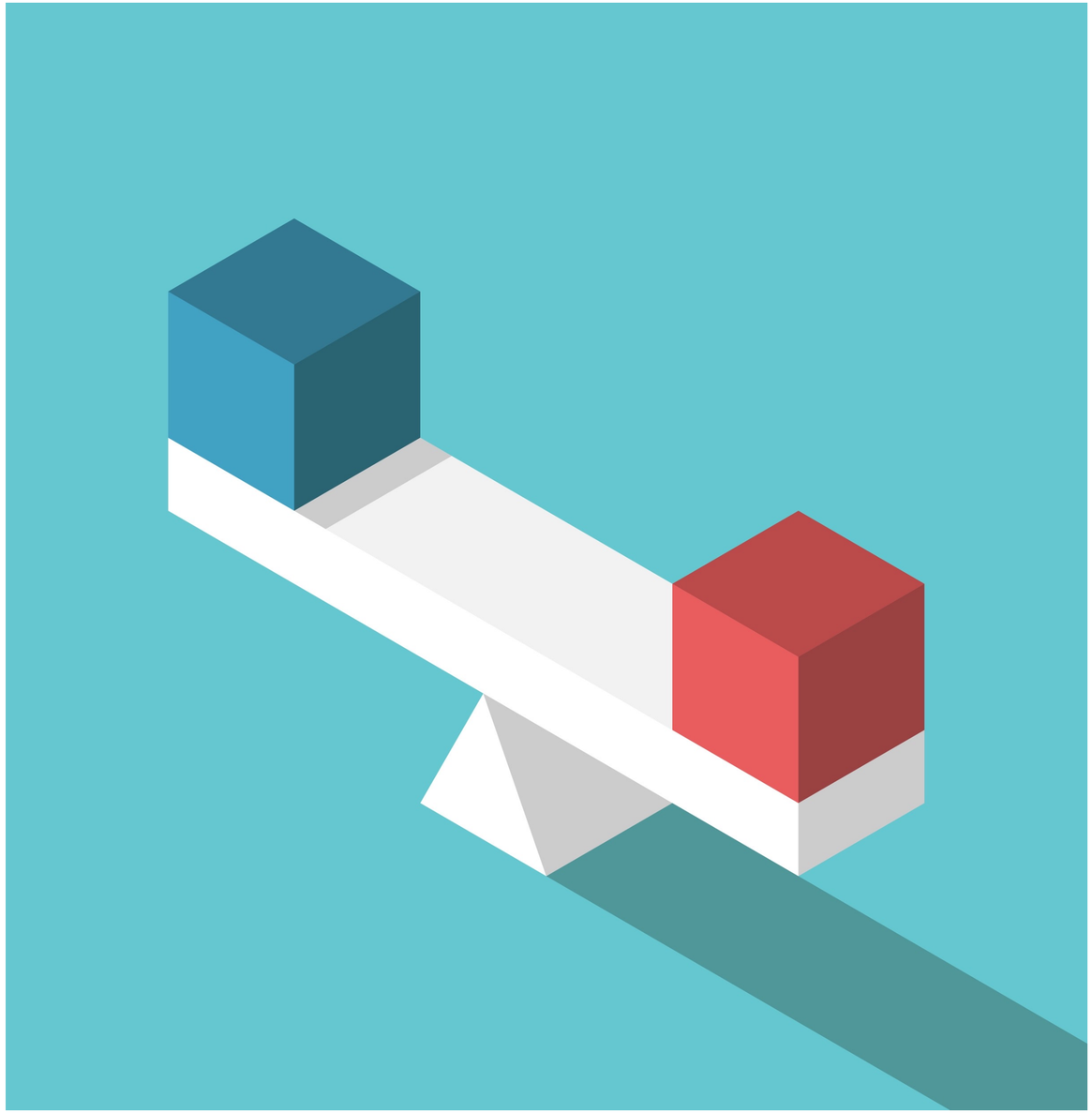
Four SMART case studies

Summary comparison of the four SMARTs

Comparison of SMARTs

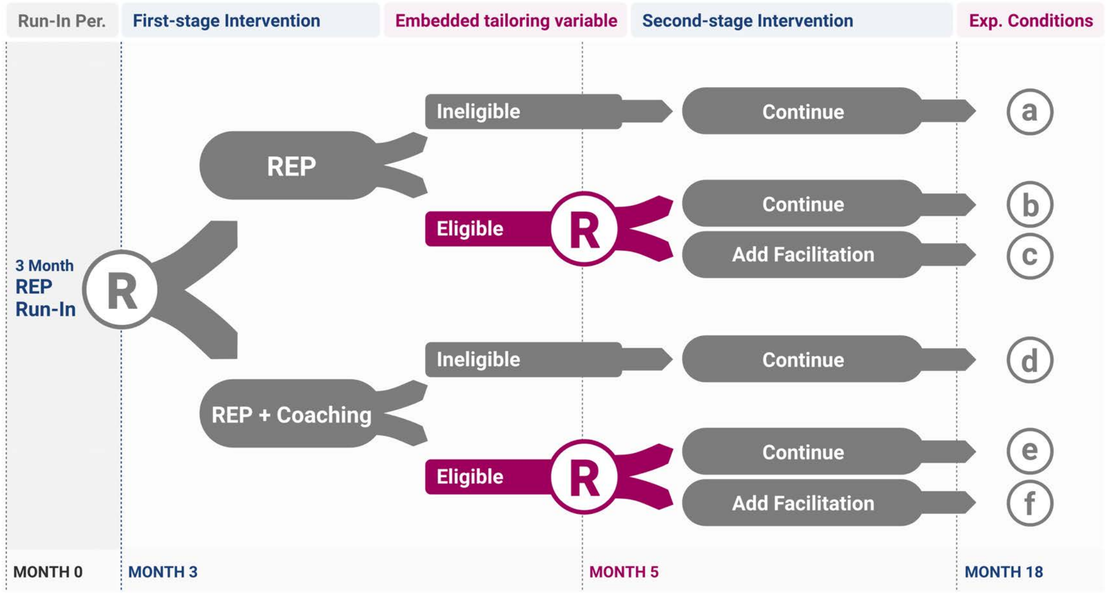
Comparison along 4 dimensions:

1. Which subgroups are randomized multiple times
2. Timing of re-randomization
3. Types of scientific questions
4. Types of primary aims [implications for study sizing]

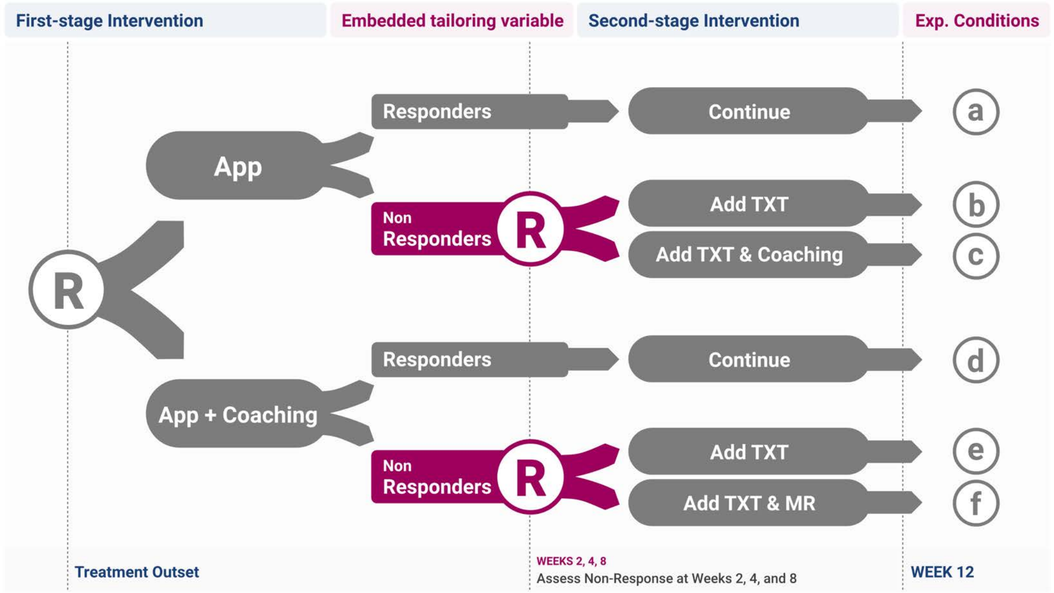


1. Which subgroups are randomized multiple times?

All non-responders but only non-responders.



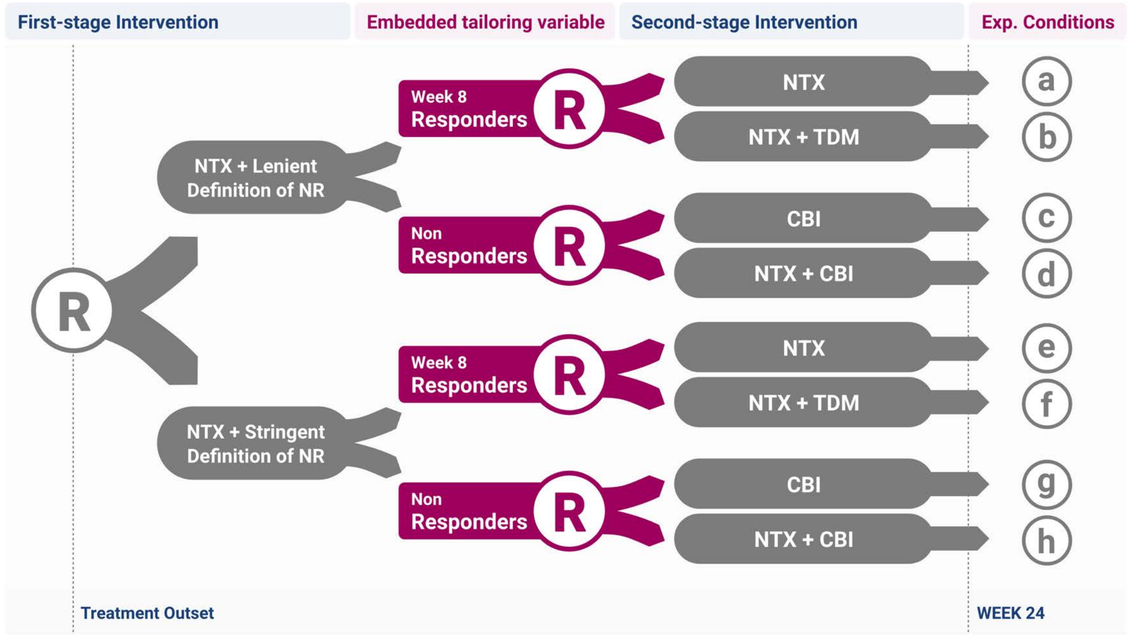
ASIC



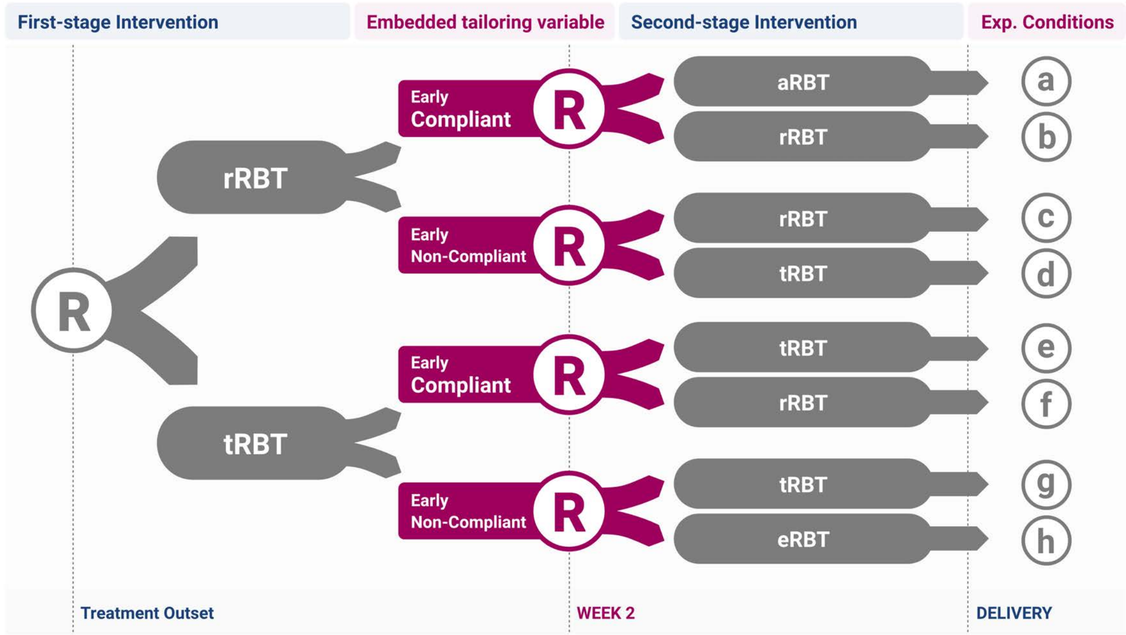
Weight Loss

1. Which subgroups are randomized multiple times?

All responders and all non-responders.



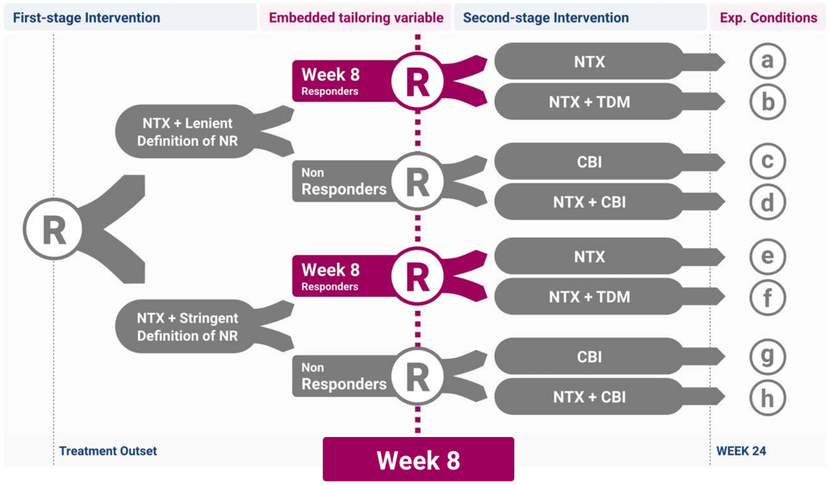
ExTENd



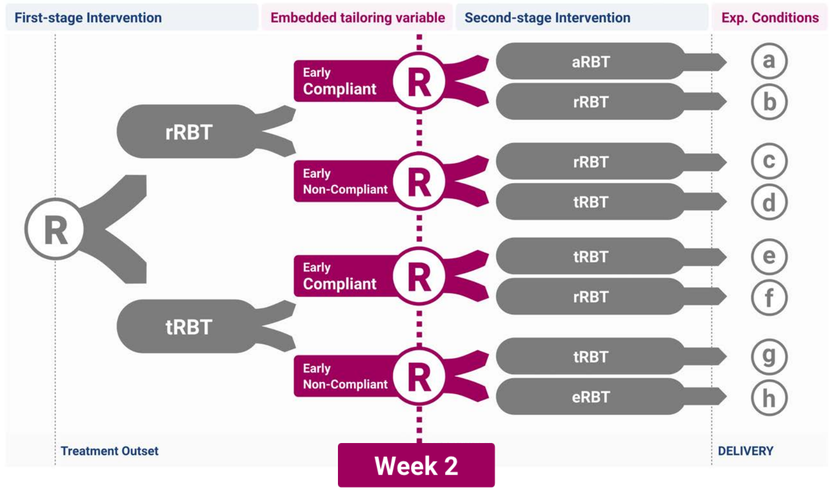
RBT

2. Timing of re-randomization

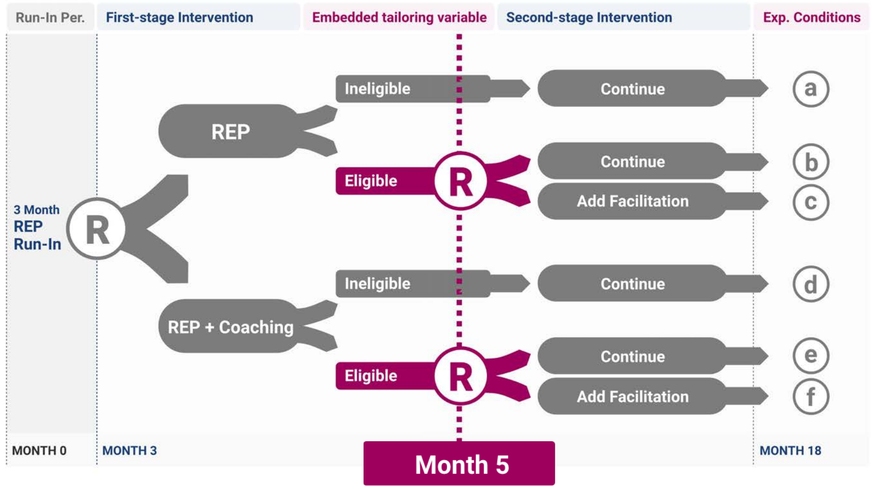
At one fixed point in time only.



ExTENd



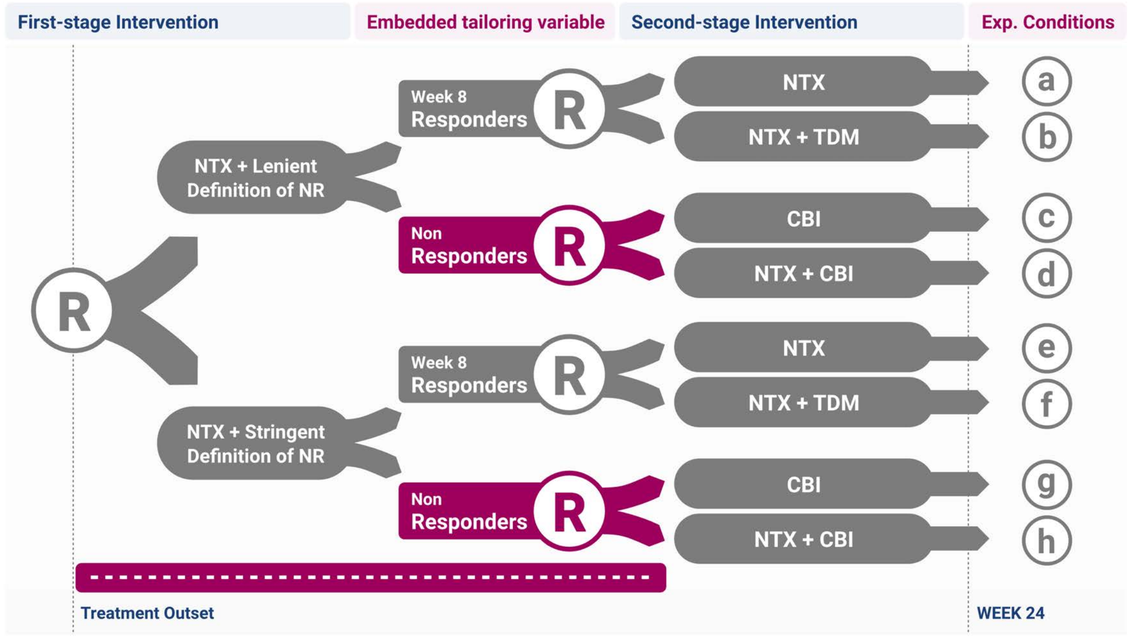
RBT



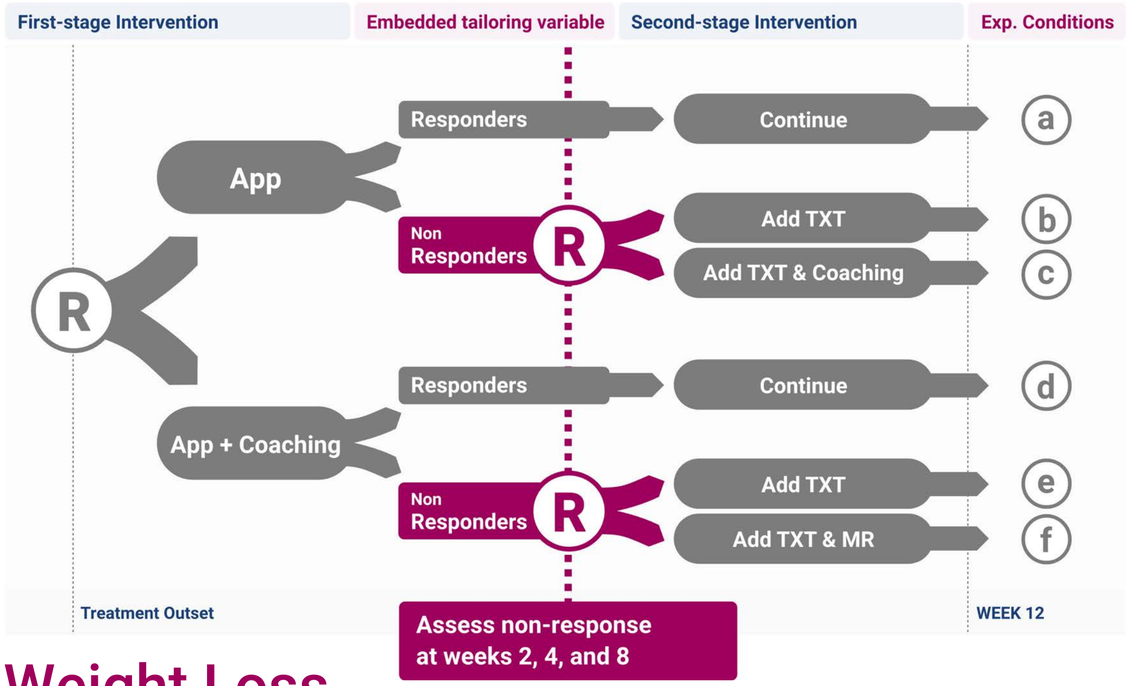
ASIC

2. Timing of re-randomization

At any one of several fixed times.



ExTENd



Weight Loss

3. Types of Scientific Questions

Which treatment first and which second?

Weight Loss

How to define non-response and which treatment to provide next?

ExTENd

More intensive vs. less intensive treatment?

ASIC RBT

4. Types of Primary Aims

Main effect of first-stage treatment

Weight Loss

Main effect of second-stage treatment

ExTENd [among non-responders to NTX

Comparison of two embedded interventions

ASIC RBT

Primary References

ExTENd is described in:

H. Lei, I. Nahum-Shani, K. Lynch, D. Oslin and S.A. Murphy. (2012). A SMART Design for Building Individualized Treatment Sequences, *The Annual Review of Clinical Psychology,* Vol. 8: 21-48

Weight Loss is described in:

Pfammatter, A. F., Nahum-Shani, I., DeZelar, M., Scanlan, L., McFadden, H. G., Siddique, J., ... & Spring, B. (2019). SMART: Study protocol for a sequential multiple assignment randomized controlled trial to optimize weight loss management. *Contemporary clinical trials*, *82*, 36-45.

ASIC is described in:

Kilbourne, A. M., Smith, S. N., Choi, S. Y., Koschmann, E., Liebrecht, C., Rusch, A., ... & Almirall, D. (2018). Adaptive School-based Implementation of CBT (ASIC): clustered-SMART for building an optimized adaptive implementation intervention to improve uptake of mental health interventions in schools. *Implementation Science*, *13*(1), 119.

Smith, S. N., Almirall, D., Choi, S. Y., Koschmann, E., Rusch, A., Bilek, E., ... & Kilbourne, A. M. (2022). Primary aim results of a clustered SMART for developing a school-level, adaptive implementation strategy to support CBT delivery at high schools in Michigan. *Implementation Science*, *17*(1), 1-19.

Q&A

🕐 10 min