SMART Case Studies

Outline

- **Four SMART case studies**
- Summary comparison of the four SMARTs

SMART Case Studies

ExTENd (PI: Oslin): Treatment of Alcohol Dependence

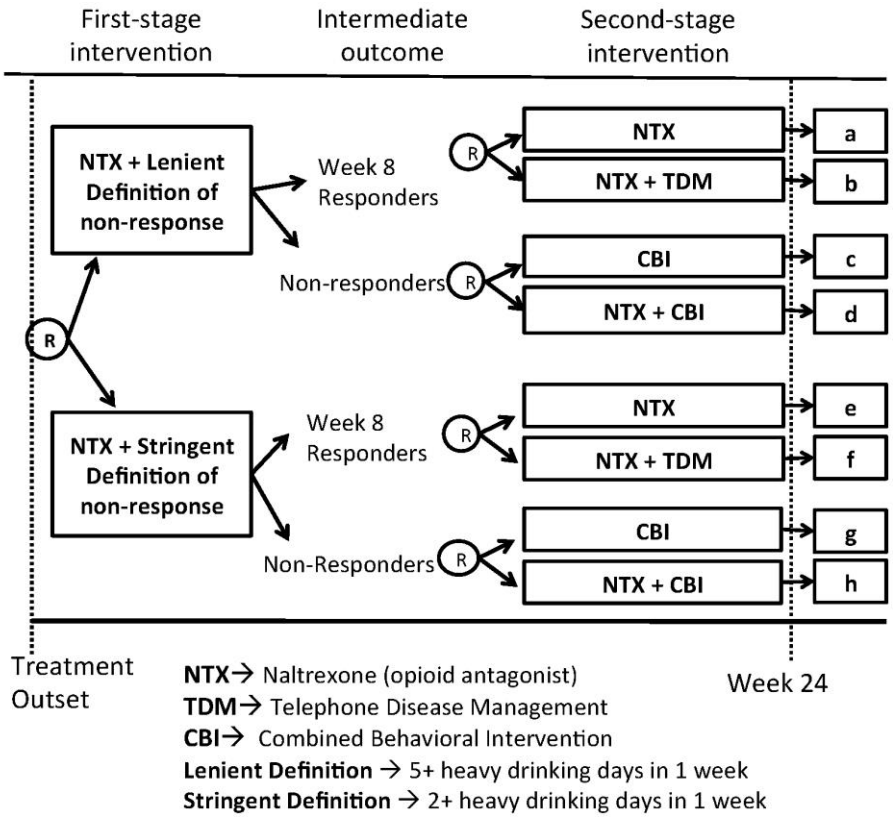
RBT (PI: Jones): Treatment for Pregnant Women who are Drug Dependent

SMART Weight Loss (PIs: Nahum-Shani & Spring): Integrating mHealth in Obesity Treatment

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

ExTENd

PI: Oslin N=302

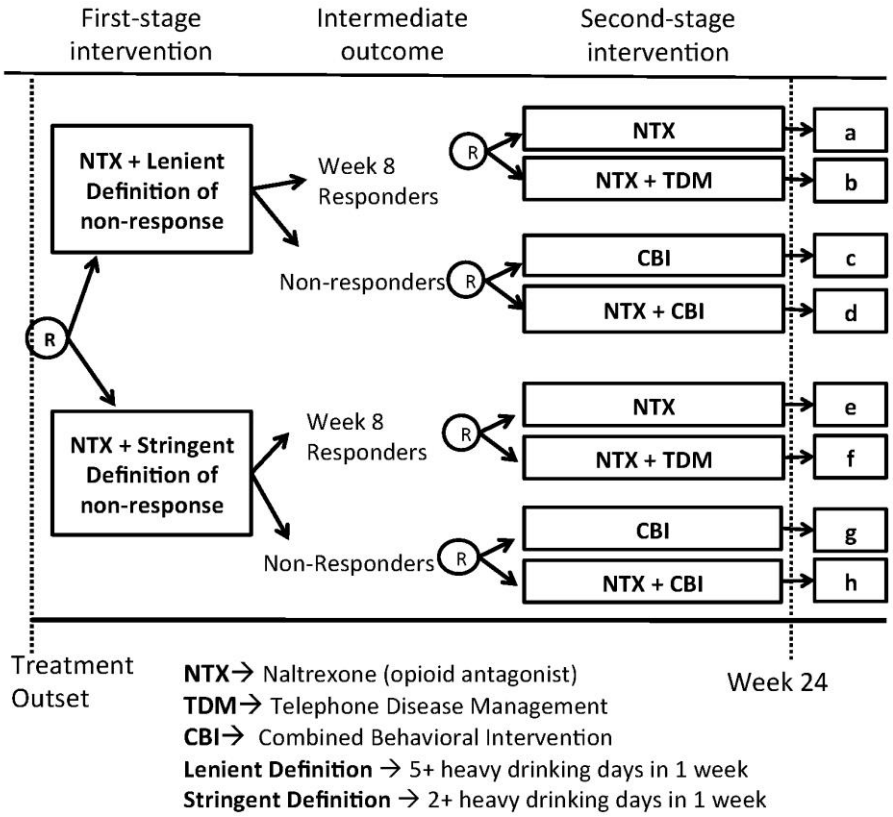


ExTENd

PI: Oslin N=302

Population:

Alcohol-dependent adults completing an intensive outpatient program (IOP)



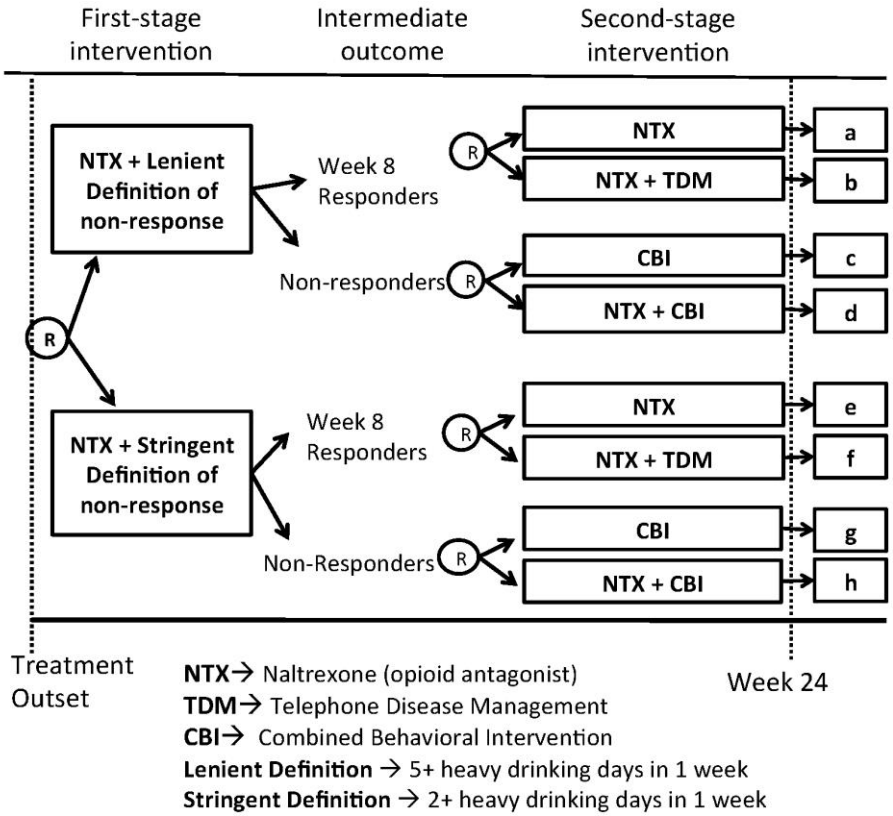
ExTENd

PI: Oslin N=302

Rationale:

Naltrexone (NTX, an opiate antagonist) is efficacious, but

- Around 1/3 of patients relapse while on NTX
- Hence, need to develop rescue tactics for non-responders
- and long-term maintenance tactics for responders
- Relapse because of various barriers: physiological / social / psychological



ExTENd

PI: Oslin N=302

Intervention Options:

First-stage

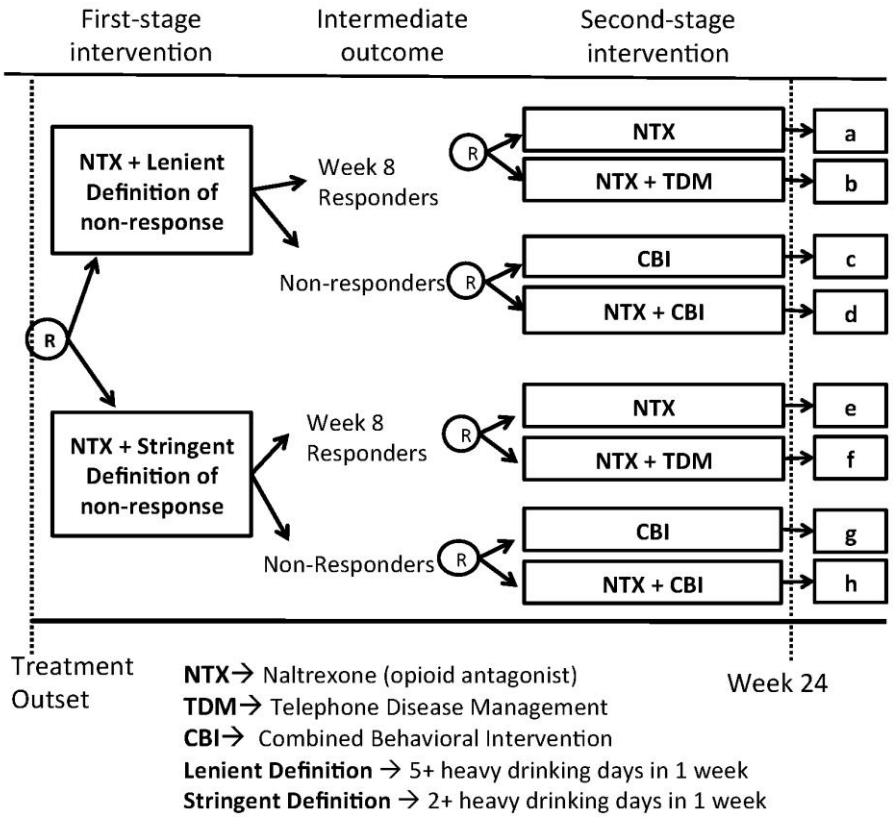
- NTX

Second-stage non-responders

- Add CBI to NTX
- Switch to CBI

Second-stage responders

- Continue NTX
- Add TDM to NTX

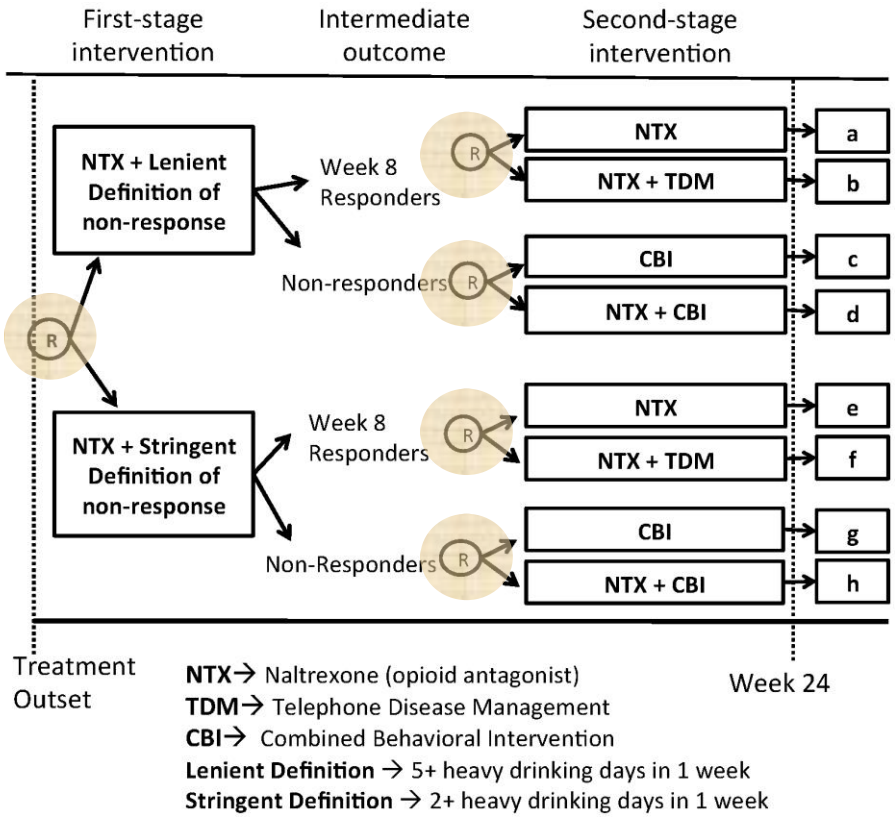


ExTENd

PI: Oslin N=302

Scientific Questions:

- What type of rescue tactic would be useful among non-responders to NTX?
- What type of maintenance tactic would be useful among responders to NTX?
- What extent of drinking behavior best reflects non-response to NTX?



ExTENd

PI: Oslin N=302

Embedded tailoring variable:

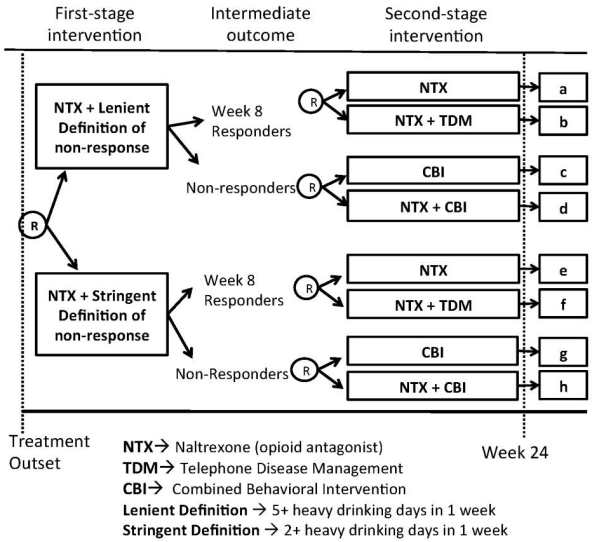
Response/non-response status

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



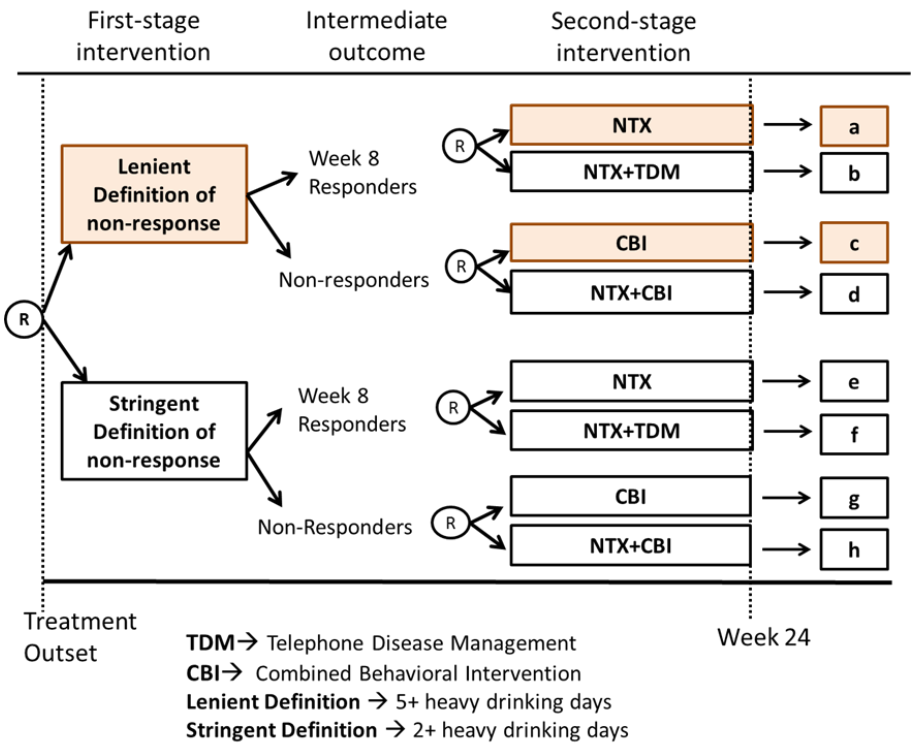
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #1

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



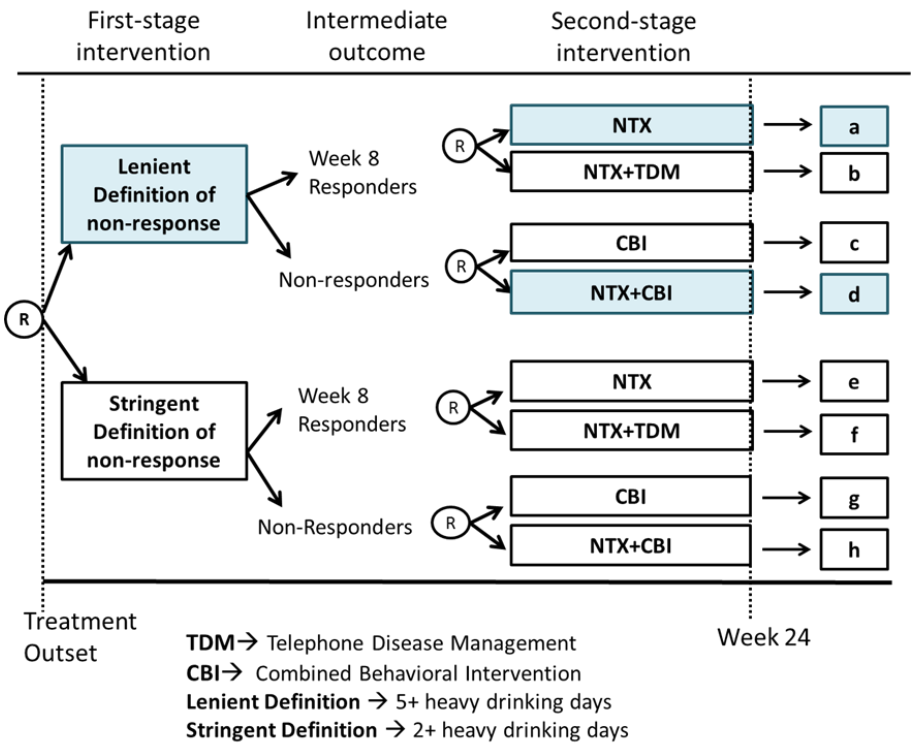
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #2

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



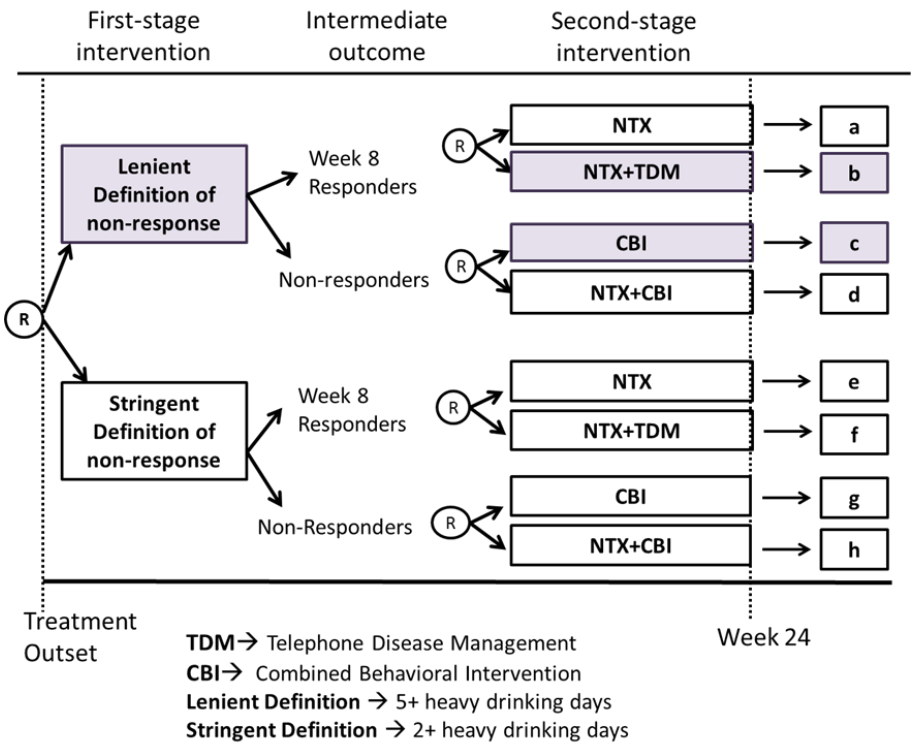
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #3

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



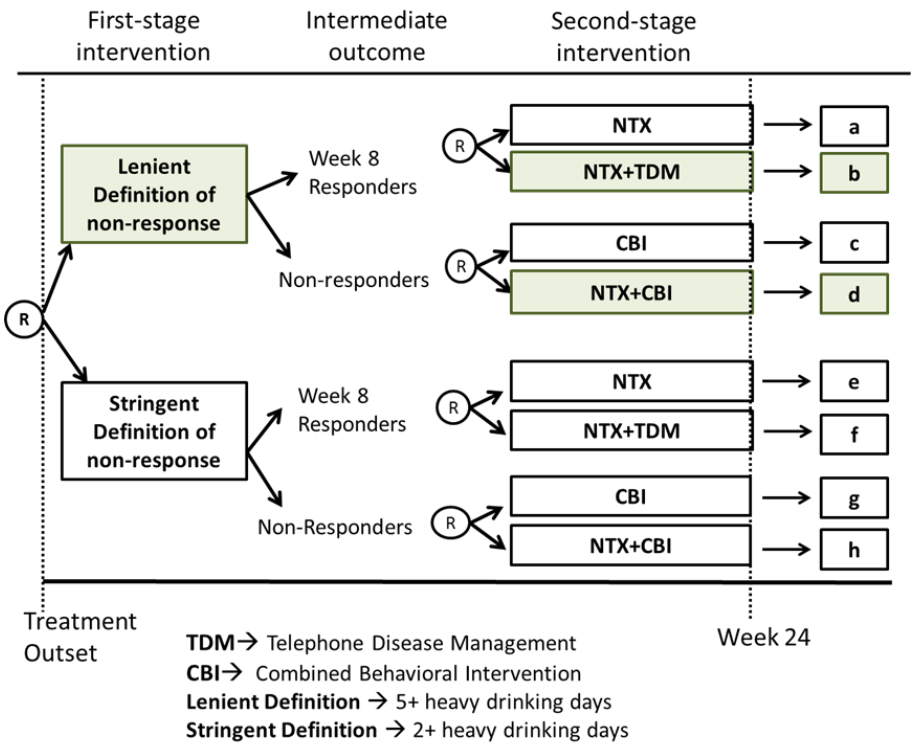
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #4

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



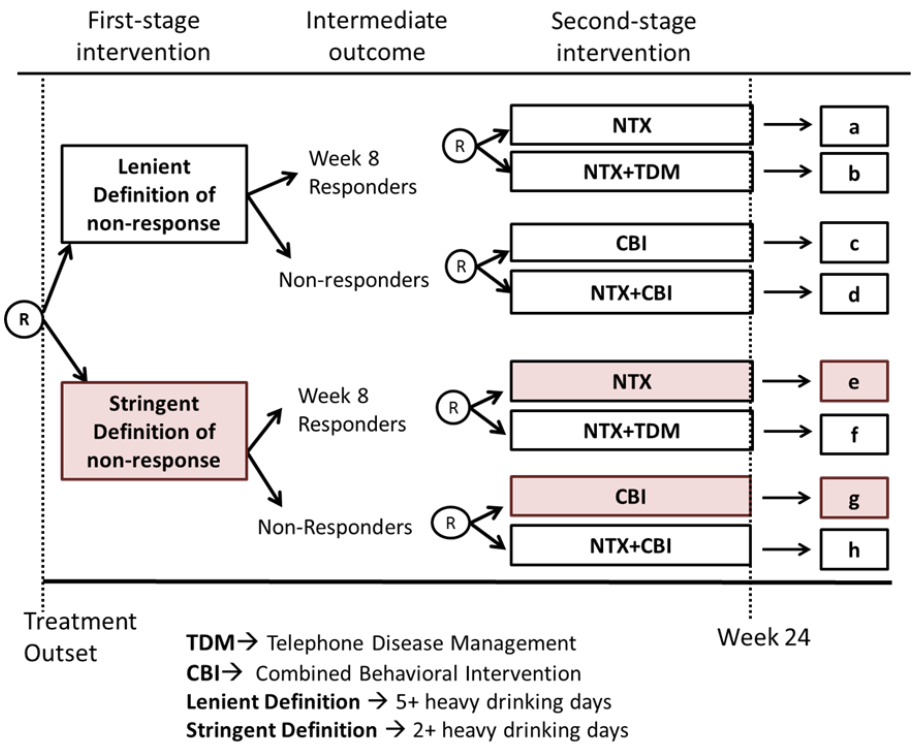
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #5

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



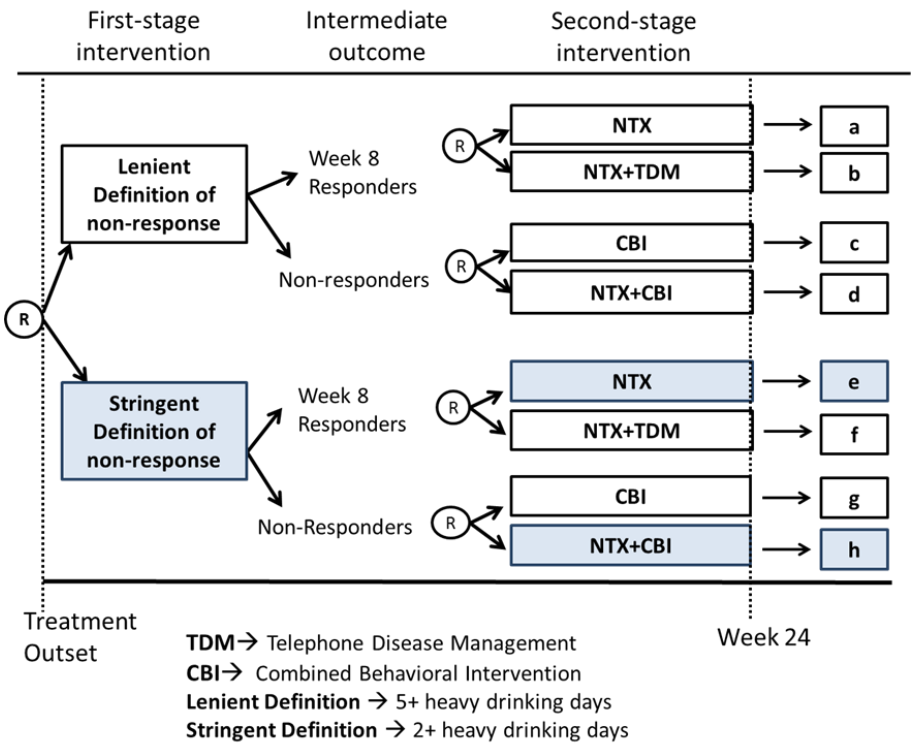
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #6

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



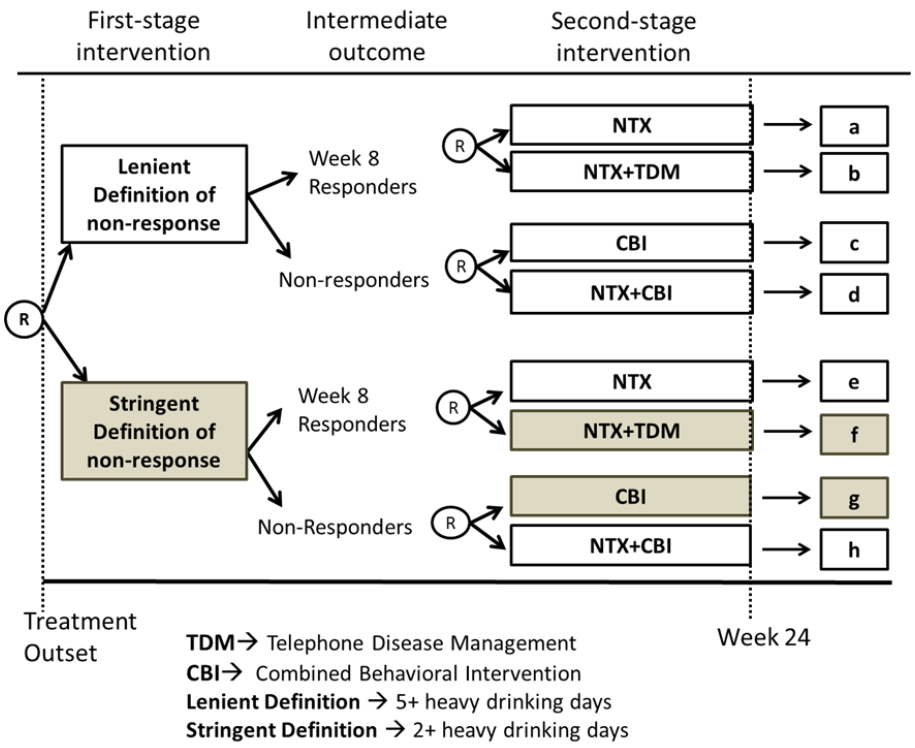
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #7

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



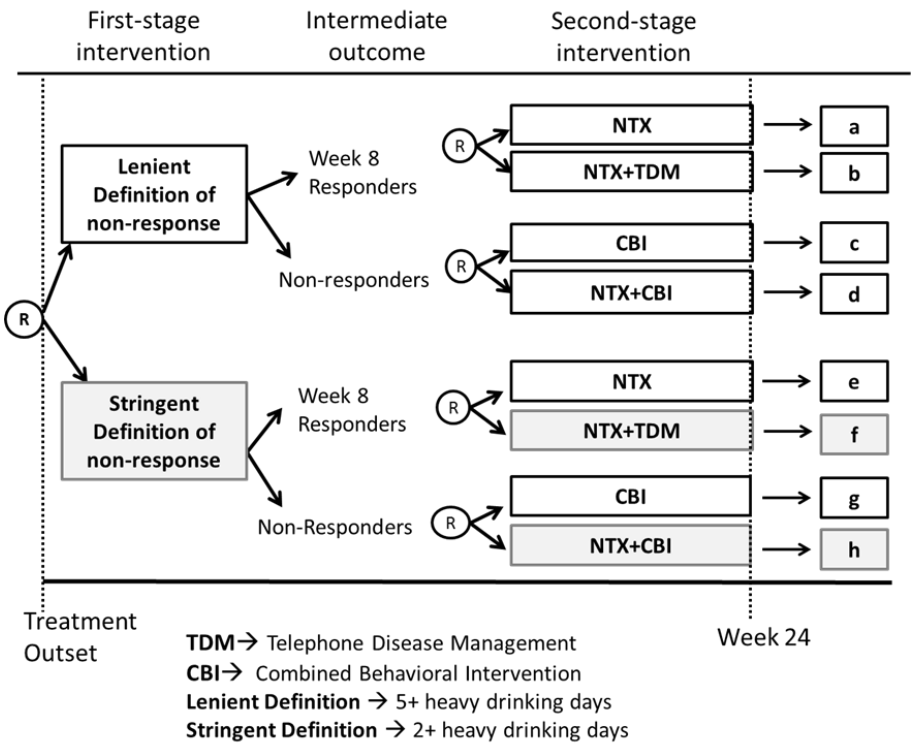
ExTENd

PI: Oslin N=302

8 Embedded Adaptive Interventions:

AI #8

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



ExTENd

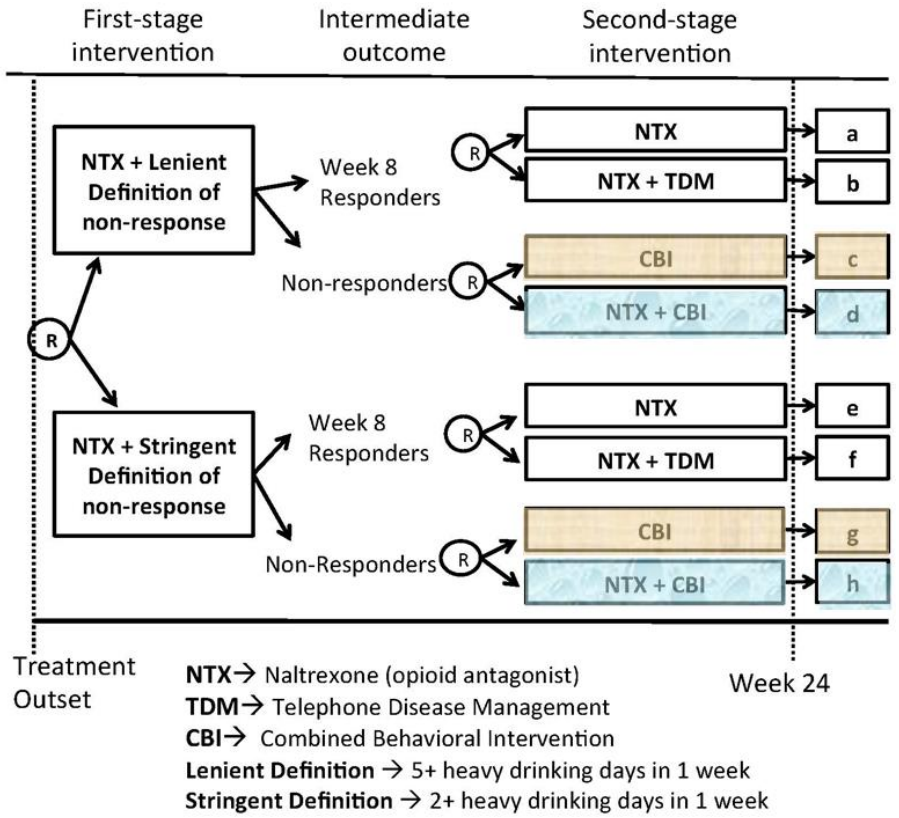
PI: Oslin N=302

Primary Aim:

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

Secondary Aims:

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



SMART Case Studies

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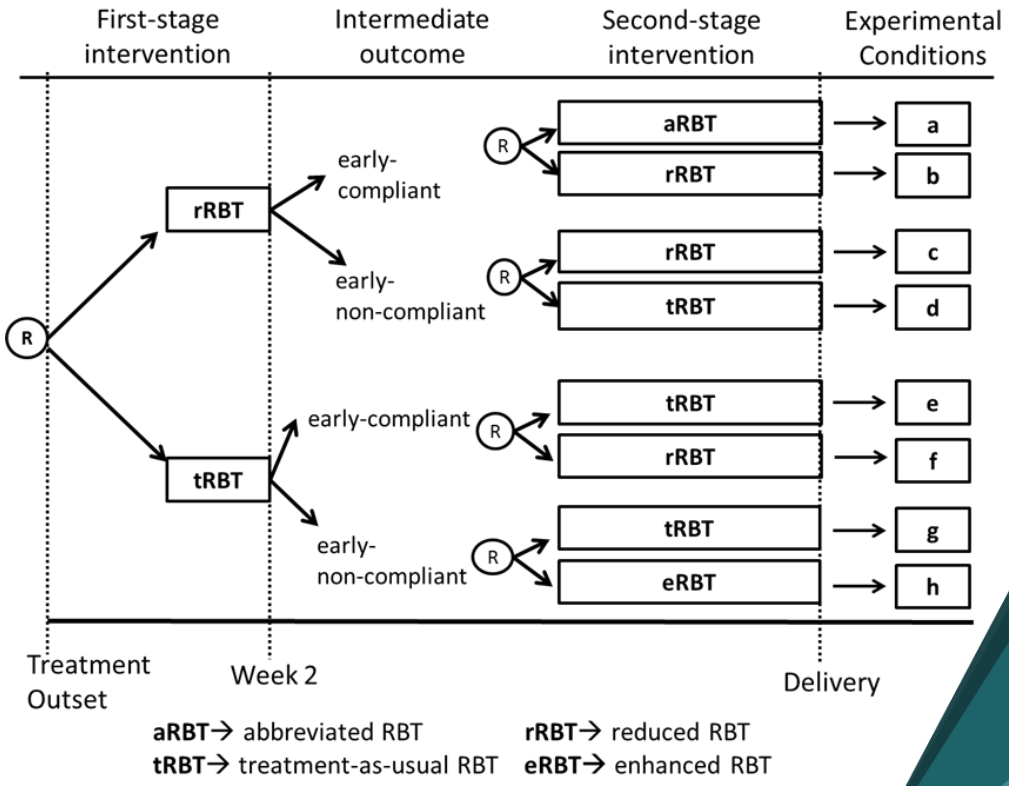
RBT

PI: Jones N=220

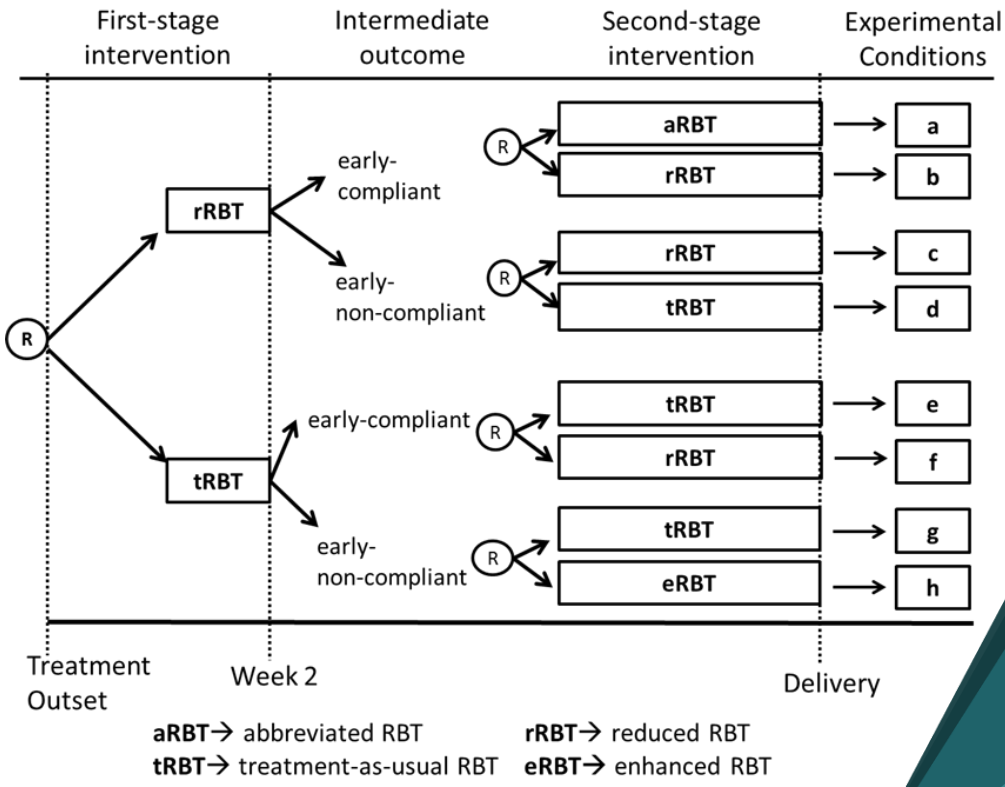


RBT

PI: Jones N=220

Population:

Pregnant women using opioids or cocaine



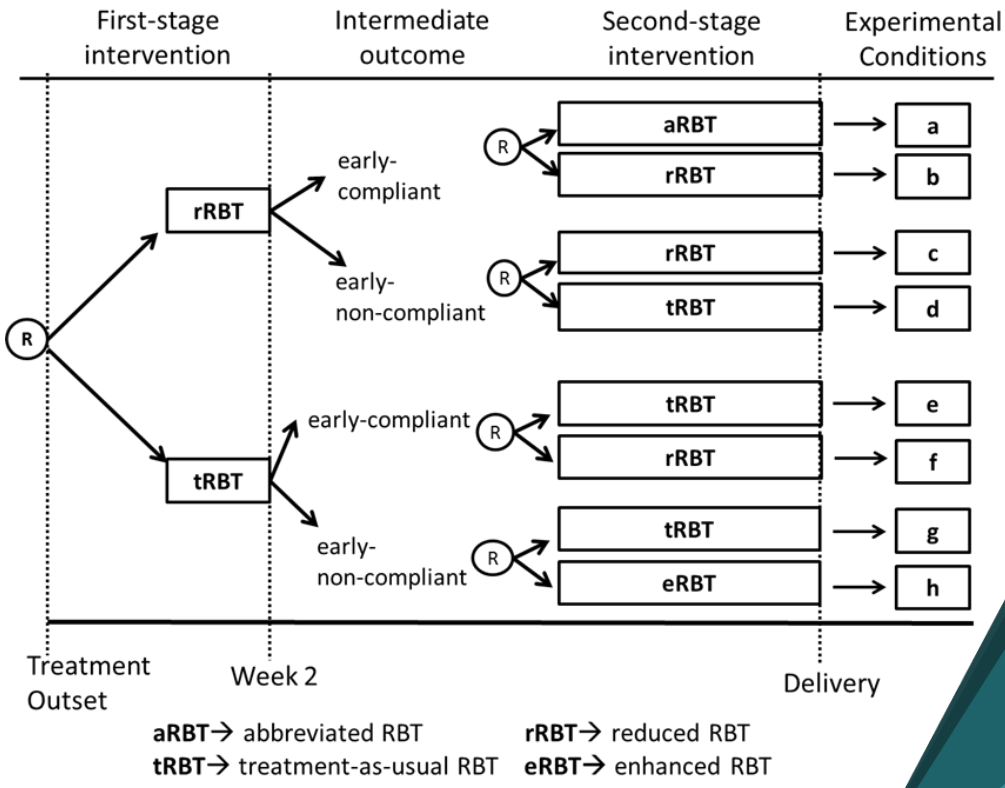
RBT

PI: Jones N=220

Rationale:

Reinforcement-based Treatment (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.

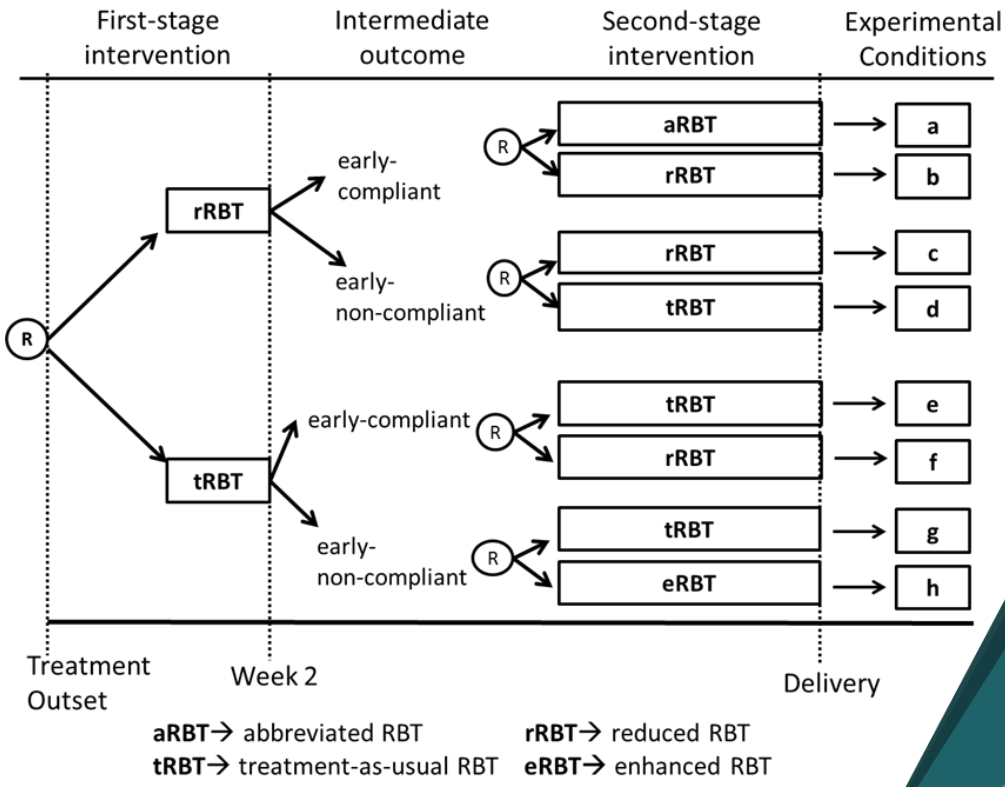


RBT

PI: Jones N=220

Intervention Options:

aRBT < rRBT < tRBT < eRBT



RBT

PI: Jones N=220

Intervention Options:

First-stage

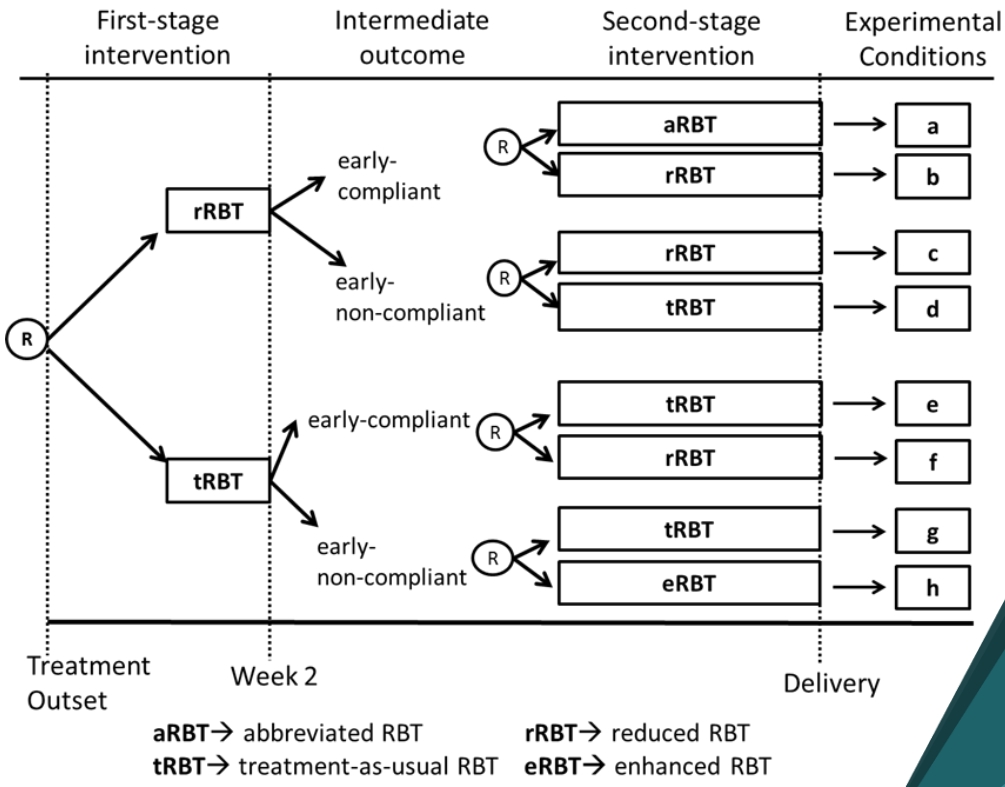
- Treatment as usual (tRBT)
- Reduced RBT (rRBT)

Second-stage non-responders

- Step up
- Continue

Second-stage responders

- Step down
- Continue

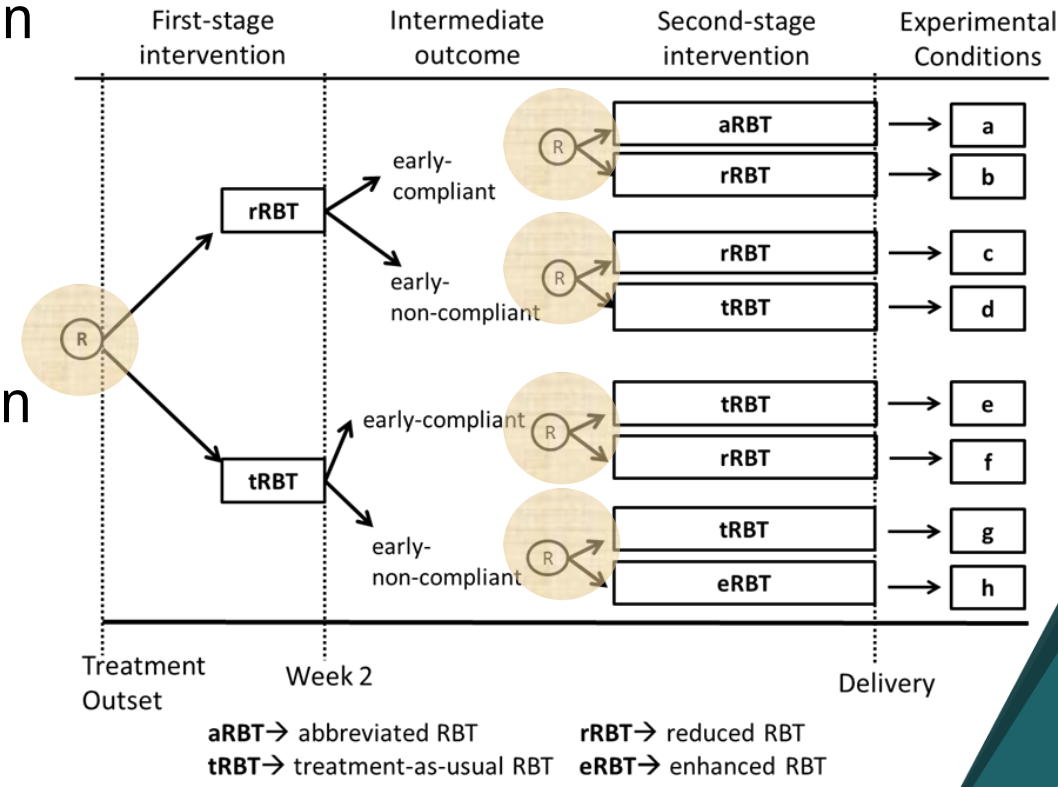


RBT

PI: Jones N=220

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?



RBT

PI: Jones N=220

Embedded tailoring variable:

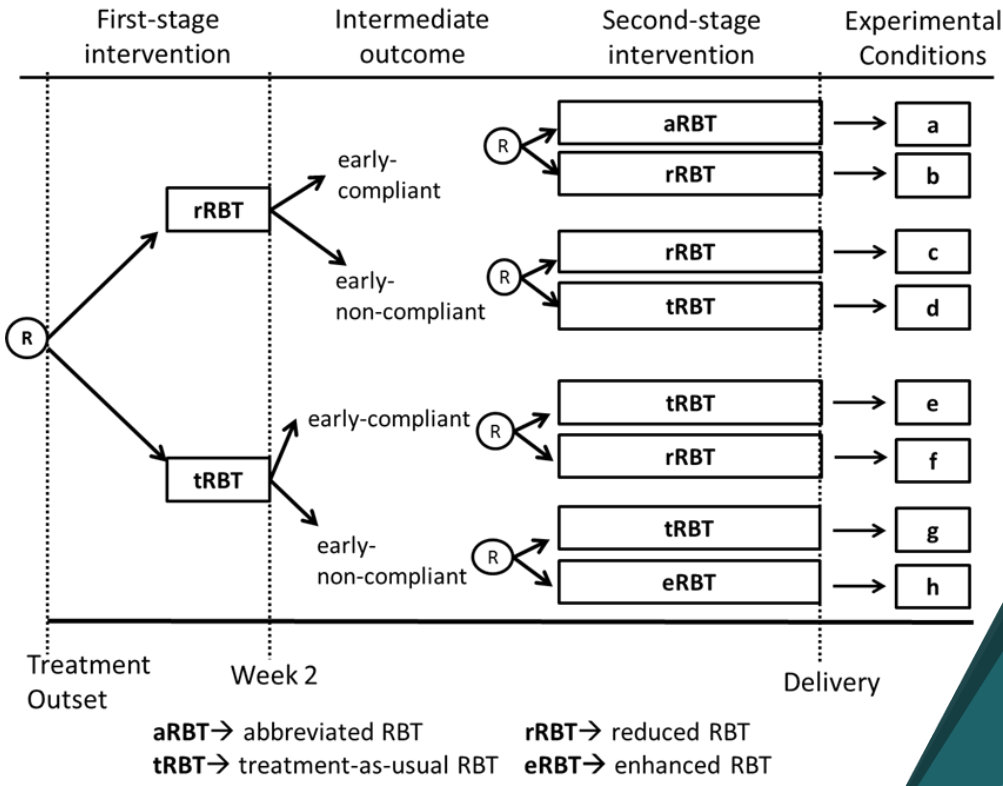
Early compliance status at week 2

Based on:

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

Non-compliant if:

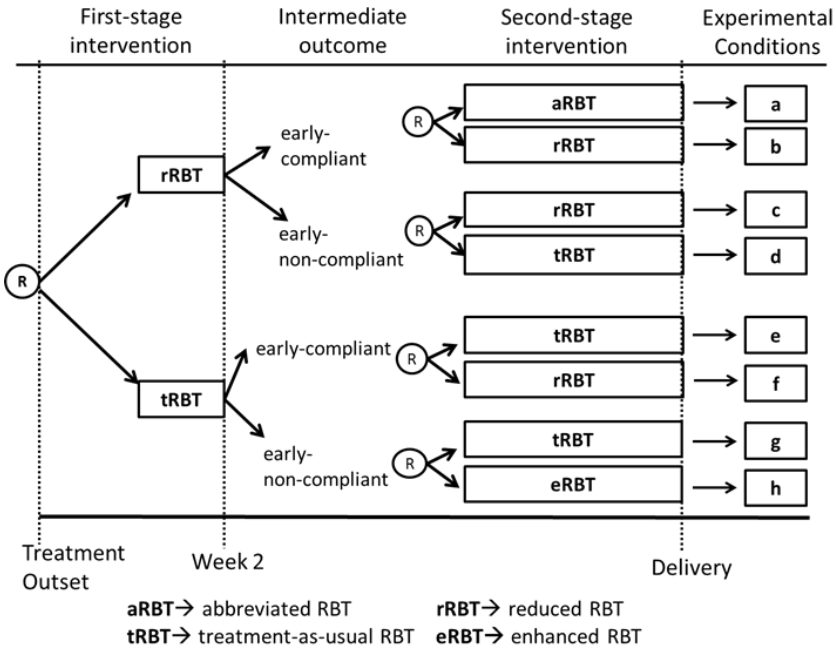
- Missed an intervention day with no excuse OR
- A positive opioid or cocaine urine specimen OR
- Self-reported use of either drug



RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive)



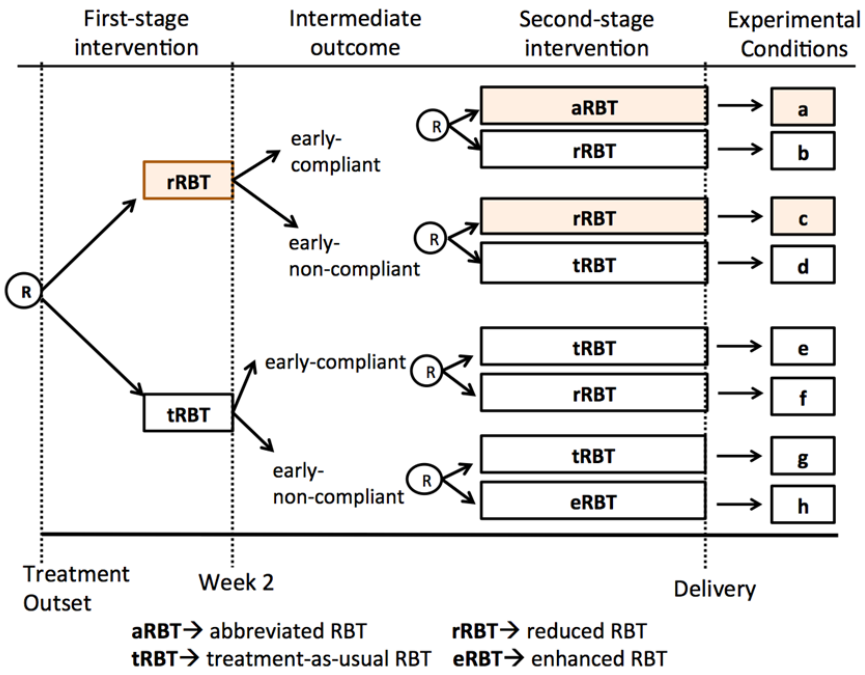
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #1

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



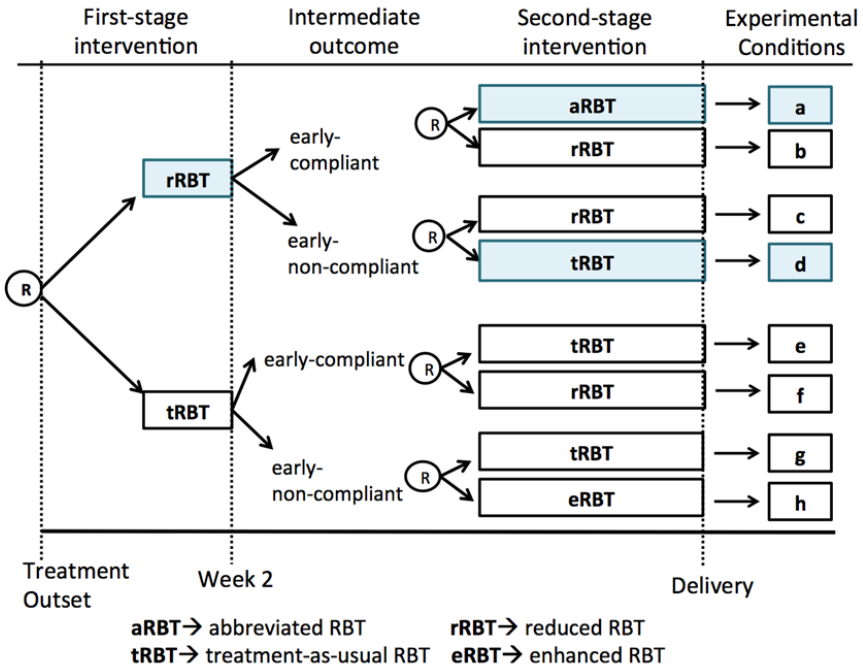
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #2

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



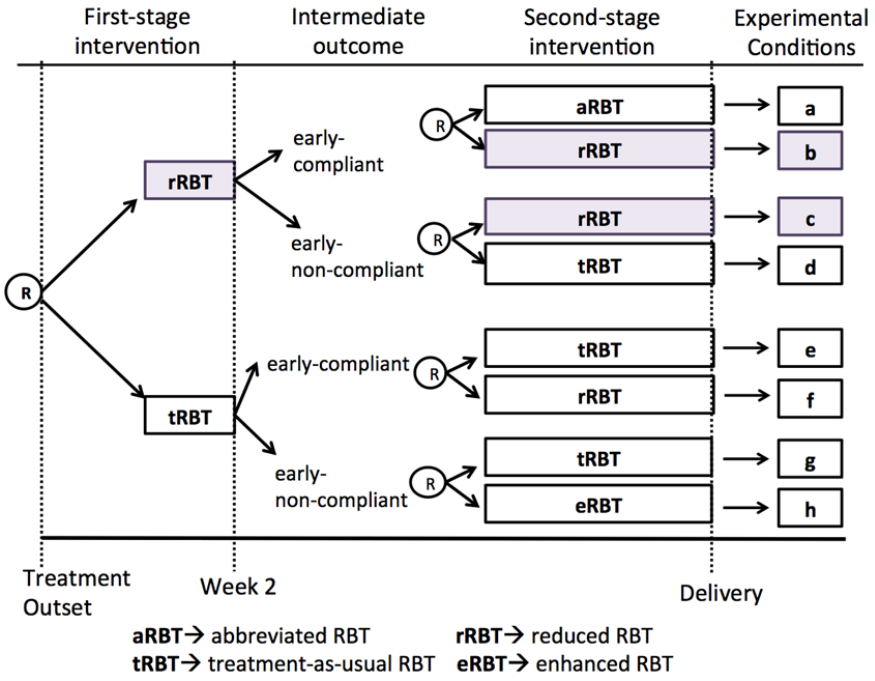
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Non-Adaptive) Intervention #3

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



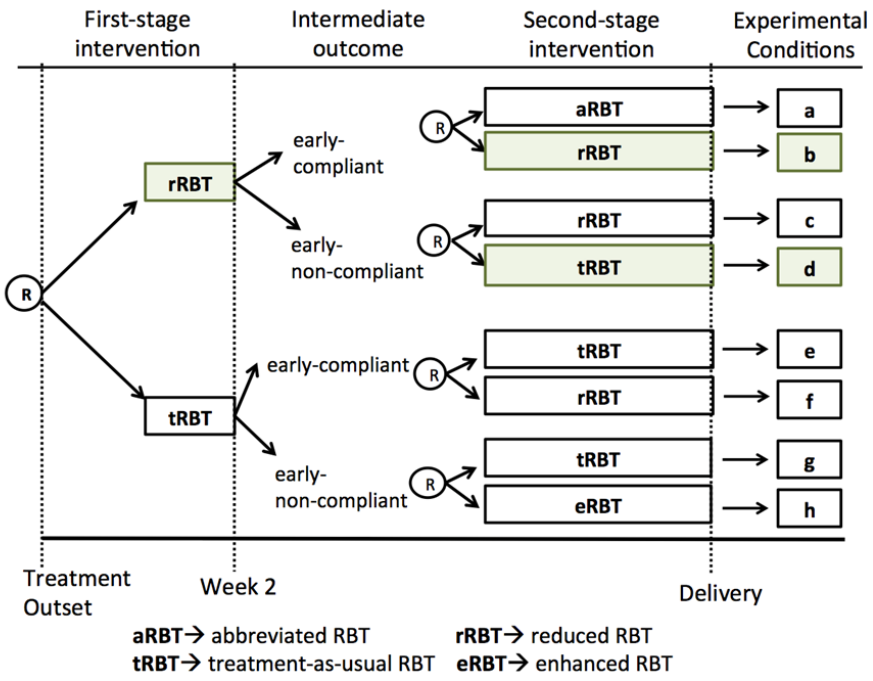
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #4

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



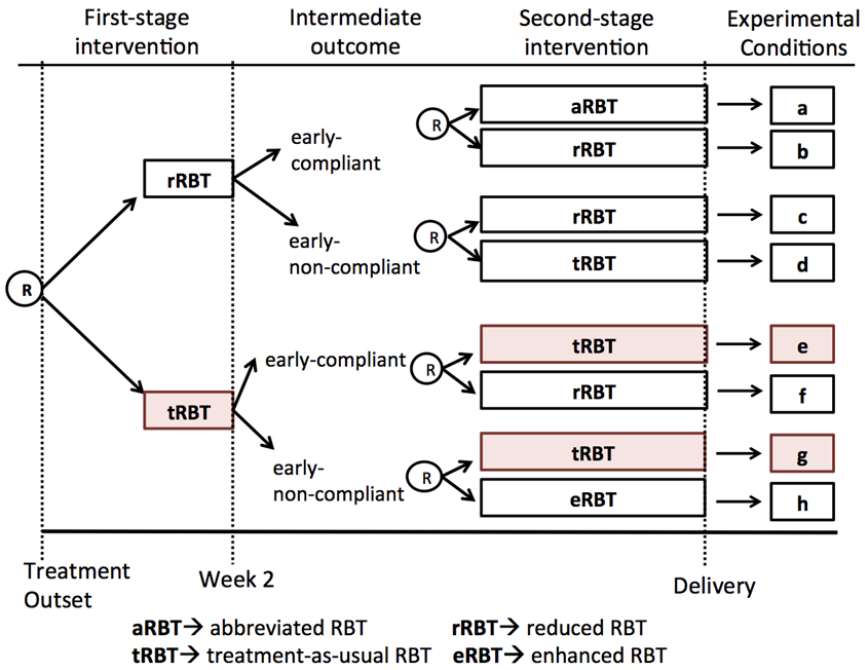
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Non-Adaptive) Intervention #5

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



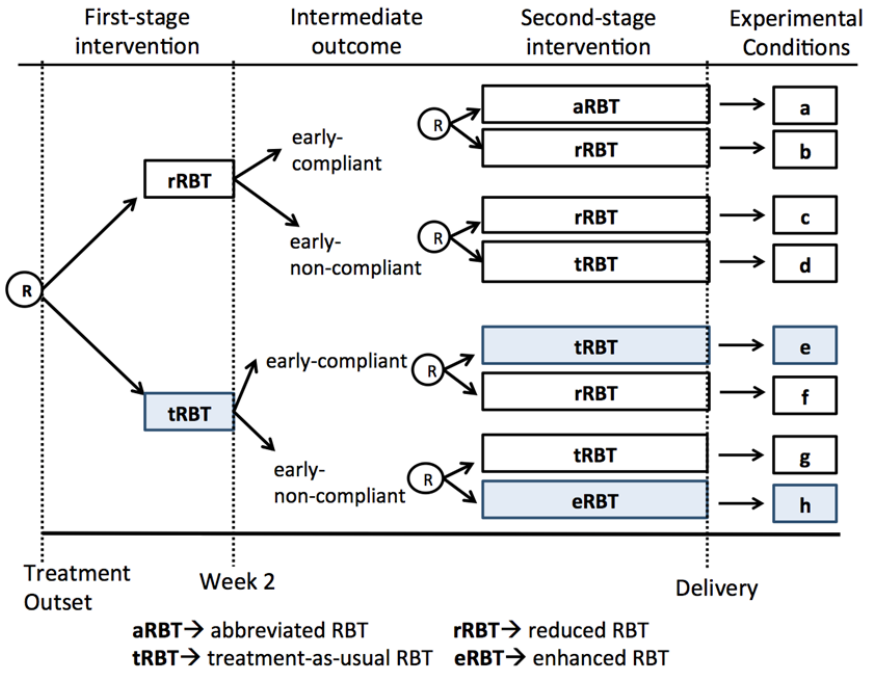
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #6

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



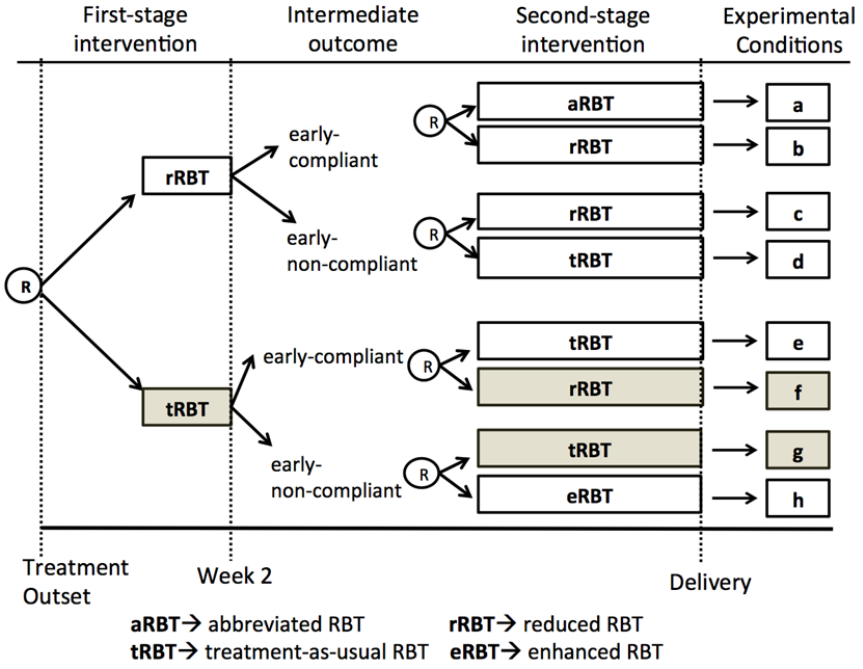
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #7

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



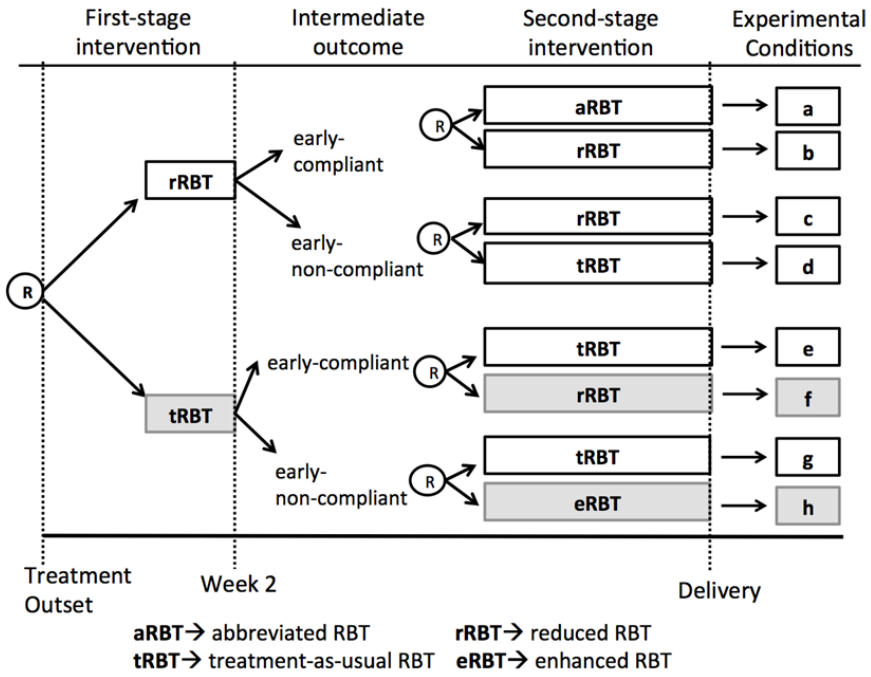
RBT

PI: Jones N=220

8 Embedded Interventions (only 6 of the 8 are adaptive):

(Adaptive) Intervention #8

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



RBT

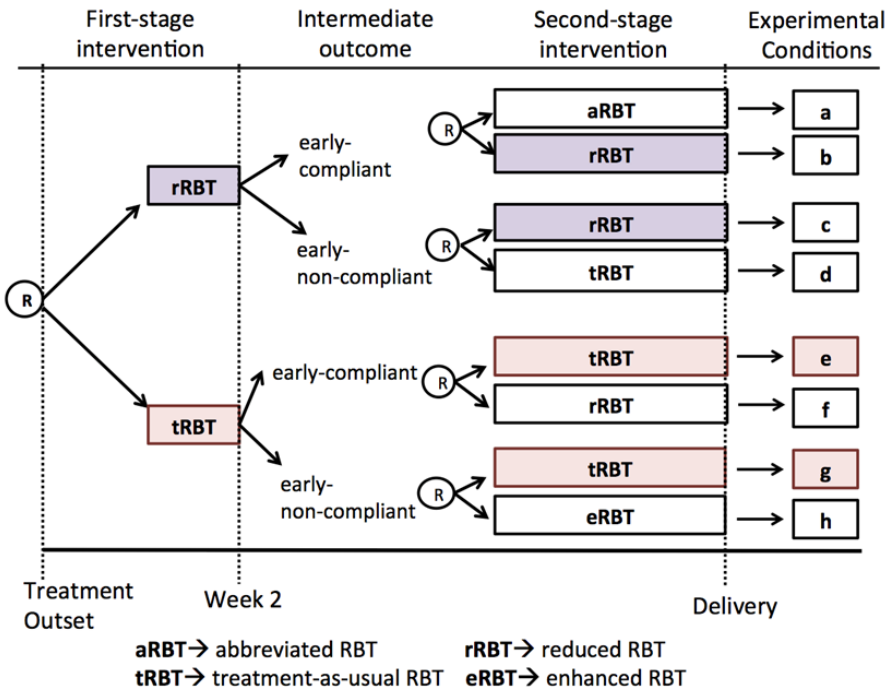
PI: Jones N=220

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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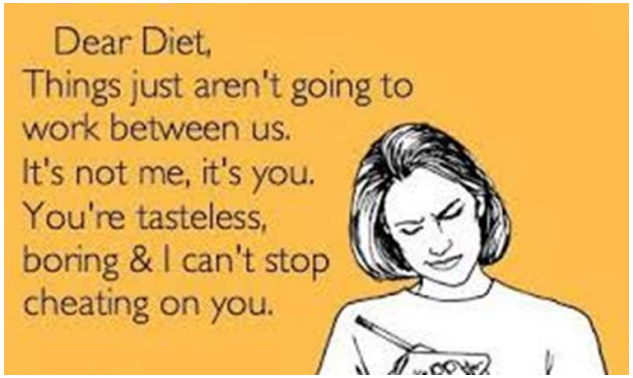
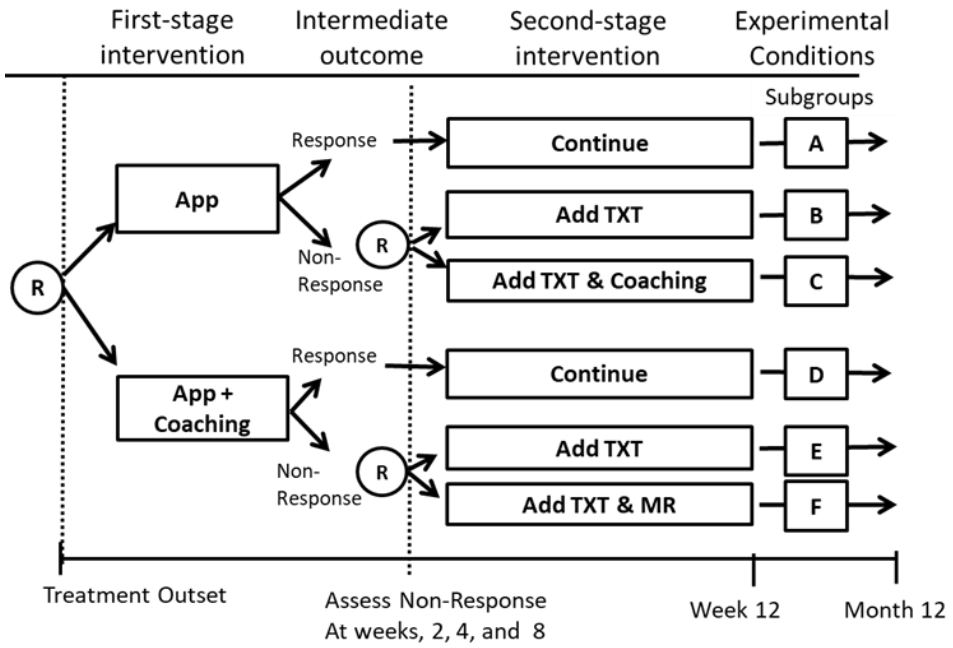
Weight Loss

PIs: Spring & Nahum-Shani N=400





App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

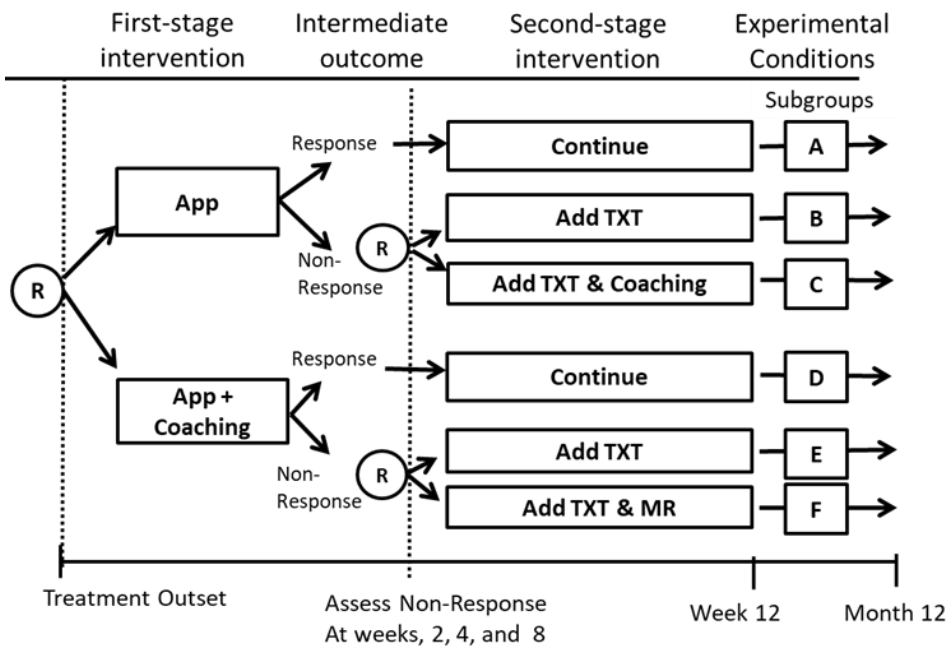
Weight Loss

PIs: Spring & Nahum-Shani N=400

Population:

Obese/overweight adults

- 18-60 years old
- BMI: 27-45 kg/m^2
- Motivated to lose weight



App→ Mobile Application
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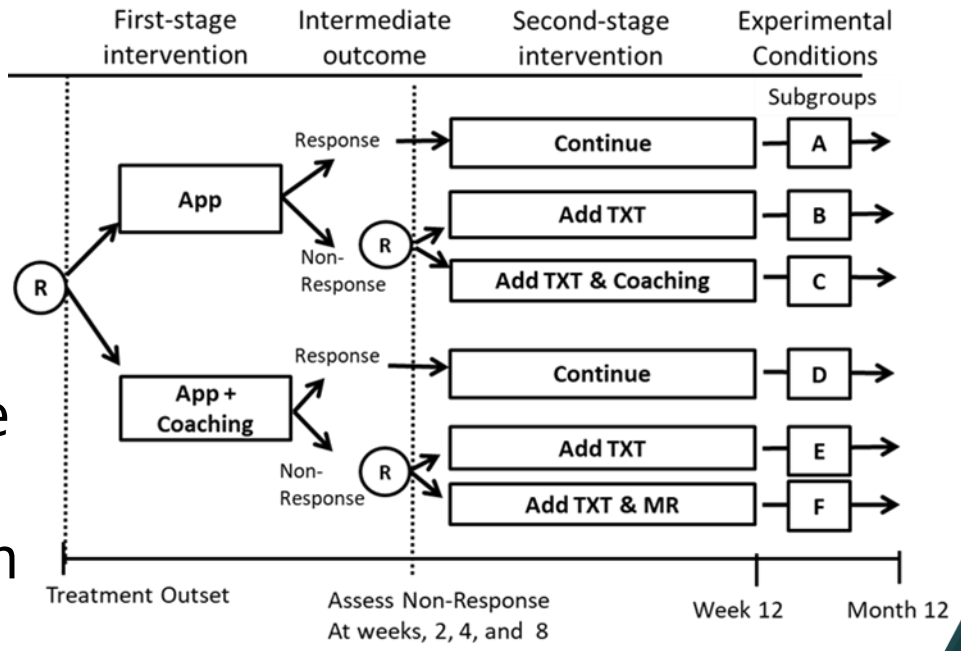
Weight Loss

PIs: Spring & Nahum-Shani N=400

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



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Weight Loss

PIs: Spring & Nahum-Shani N=400

Intervention Options:

First-stage

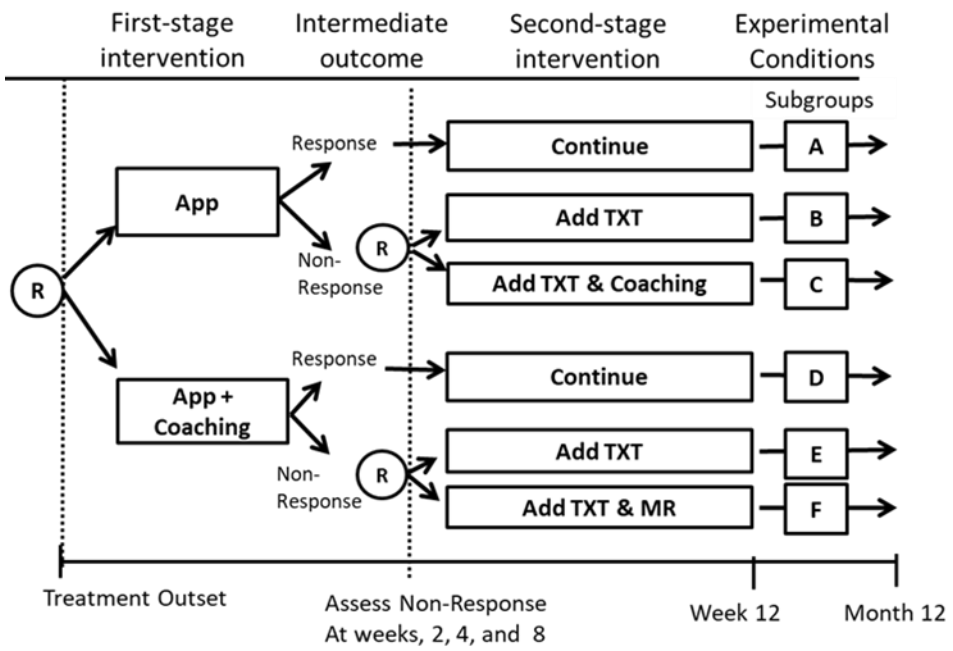
- App
- App + Coaching

Second-stage non-responders

- Add TXT
- Add TXT + Traditional

Second-stage responders

- Continue



App→ Mobile Application
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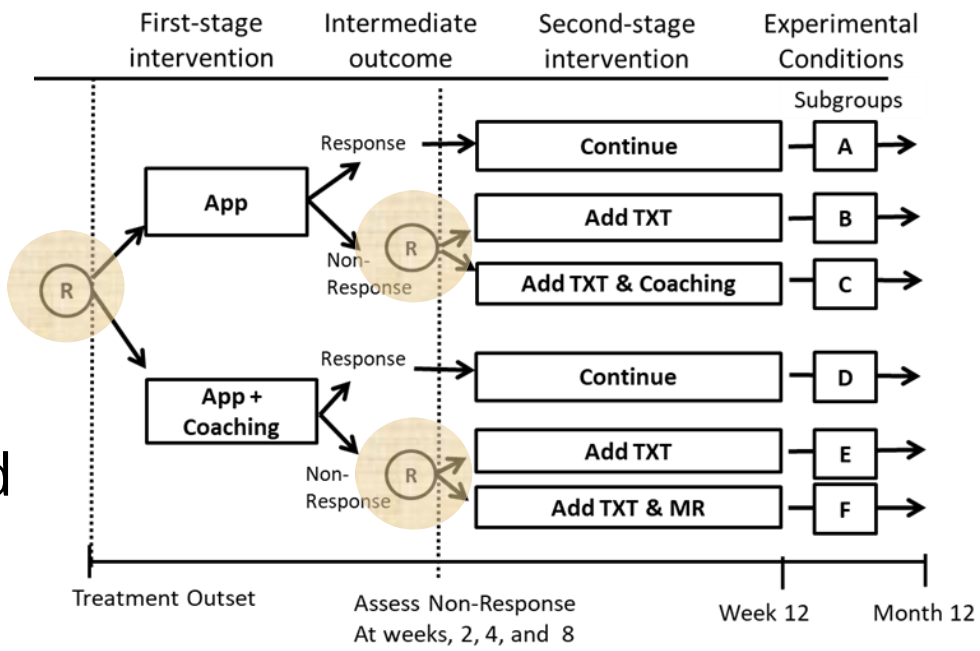
Weight Loss

PIs: Spring & Nahum-Shani N=400

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)?



App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

Weight Loss

PIs: Spring & Nahum-Shani N=400

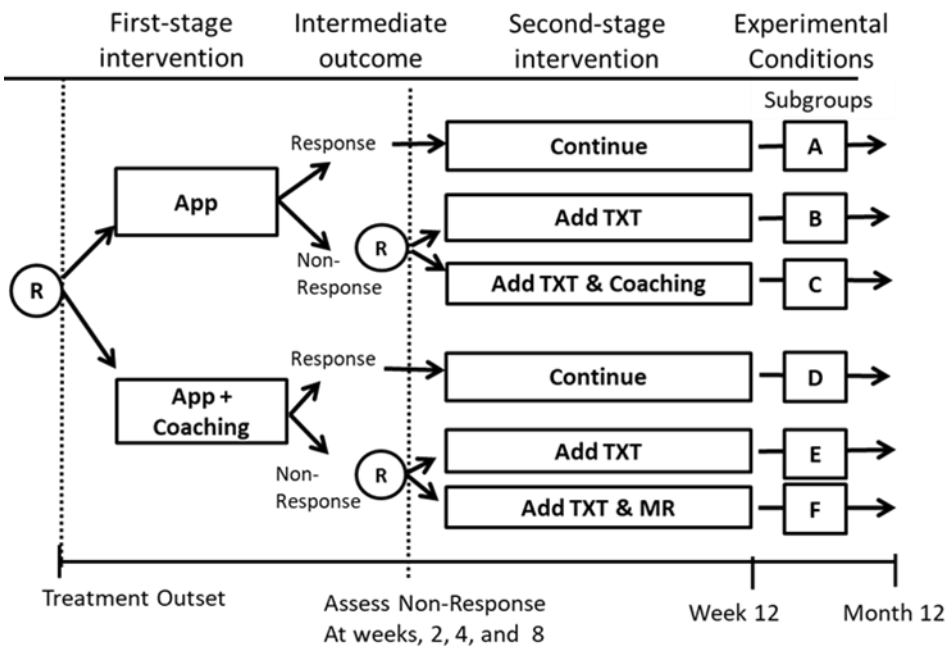
Embedded tailoring variable:

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



App→ Mobile Application
MR→ Meal Replacement
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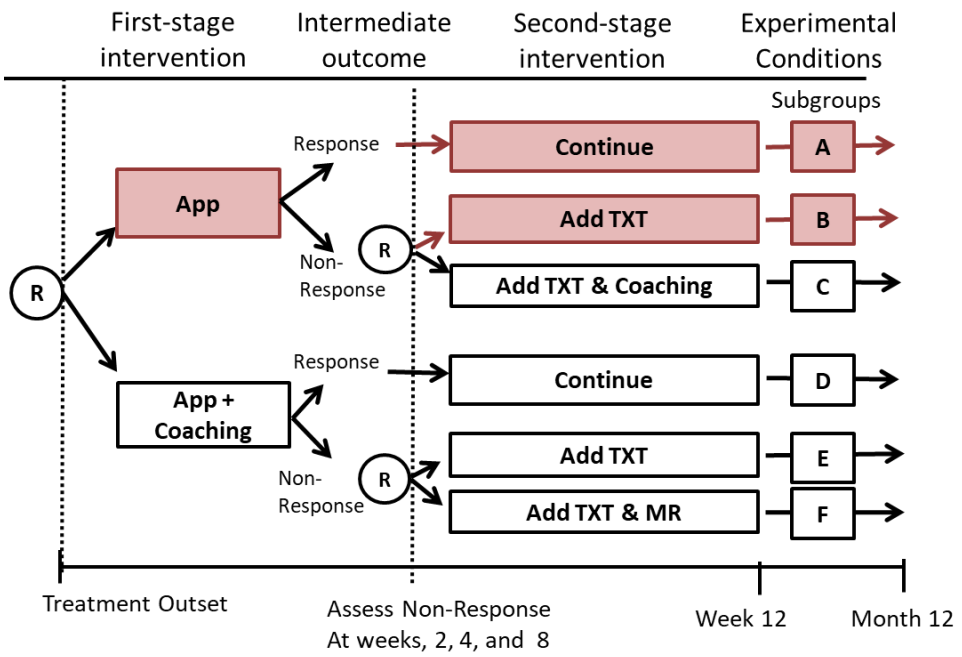
Weight Loss

PIs: Spring & Nahum-Shani N=400

4 Embedded Adaptive Interventions:

AI #1

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



App→ Mobile Application
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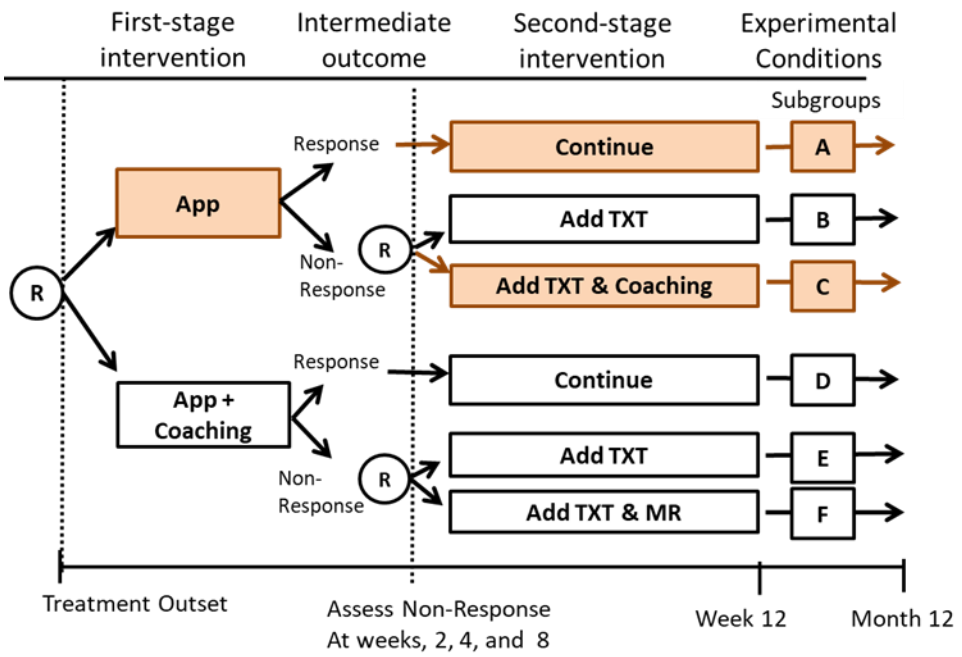
Weight Loss

PIs: Spring & Nahum-Shani N=400

4 Embedded Adaptive Interventions:

AI #2

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



App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

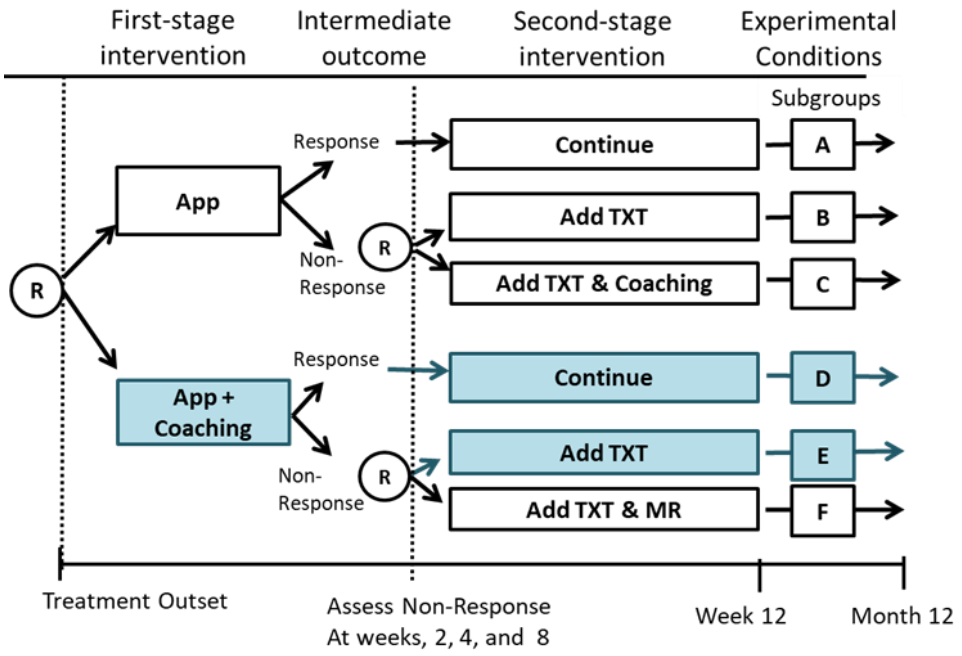
Weight Loss

PIs: Spring & Nahum-Shani N=400

4 Embedded Adaptive Interventions:

AI #3

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



App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

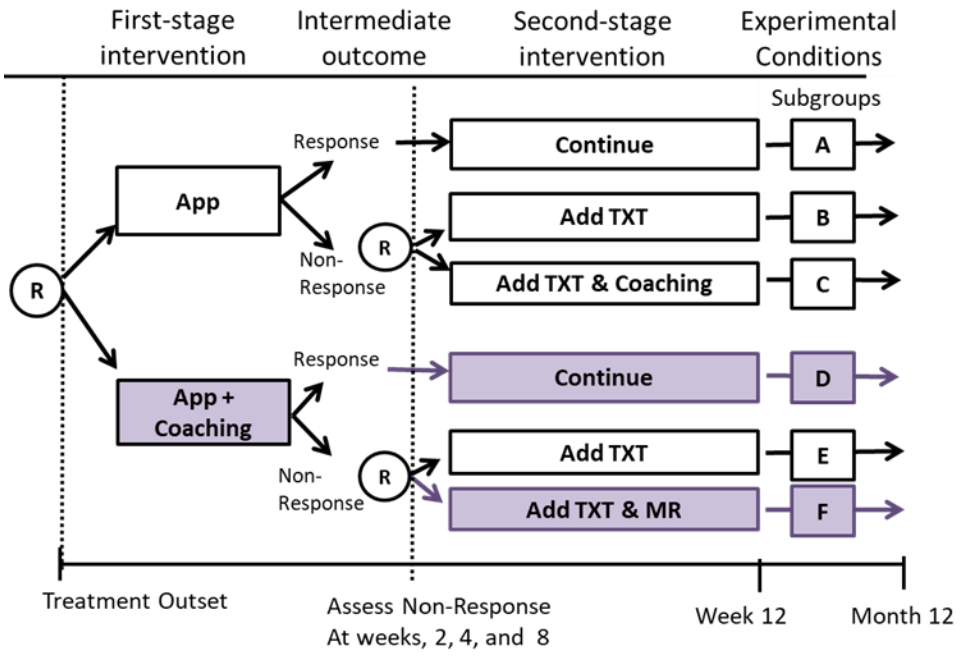
Weight Loss

PIs: Spring & Nahum-Shani N=400

4 Embedded Adaptive Interventions:

AI #4

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



App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

Weight Loss

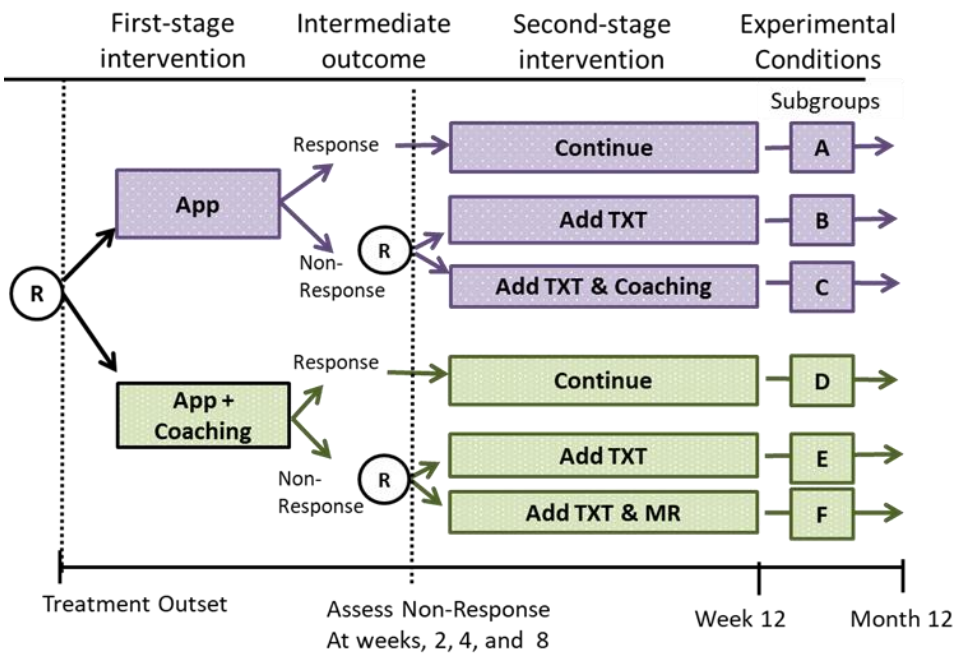
PIs: Spring & Nahum-Shani N=400

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
TXT→ Text Messages

SMART Case Studies

ExTENd (PI: Oslin): Treatment of Alcohol Dependence

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

SMART Weight Loss (PIs: Nahum-Shani & Spring): Integrating mHealth in Obesity Treatment

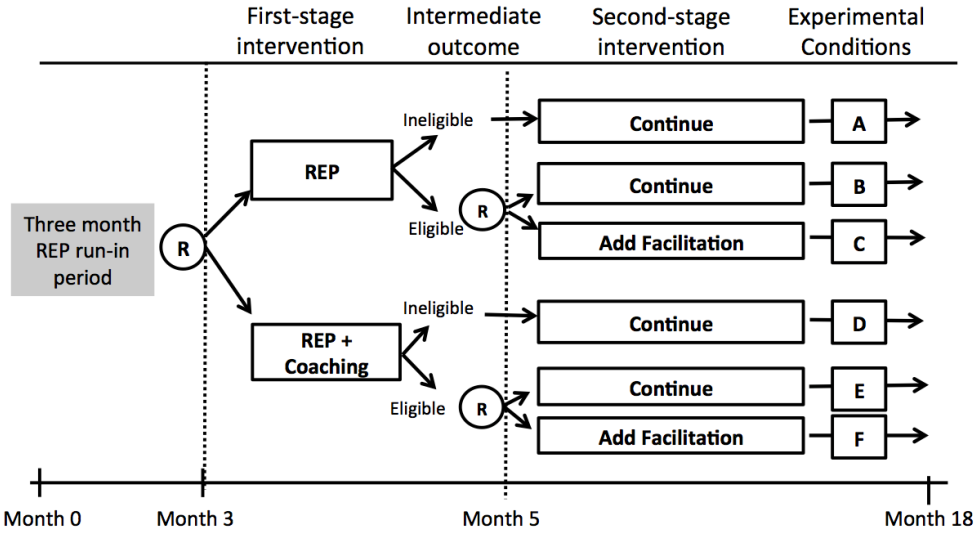
ASIC (PI: Kilbourne): School-based Implementation of Cognitive Behavioral Therapy

School-based Implementation of CBT

PI: Kilbourne N=200

TRAILS

Transforming Research into Action to Improve the Lives of Students



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 of 12 weeks

ASIC

Adaptive School-based Implementation of CBT

d³lab

School-based Implementation of CBT

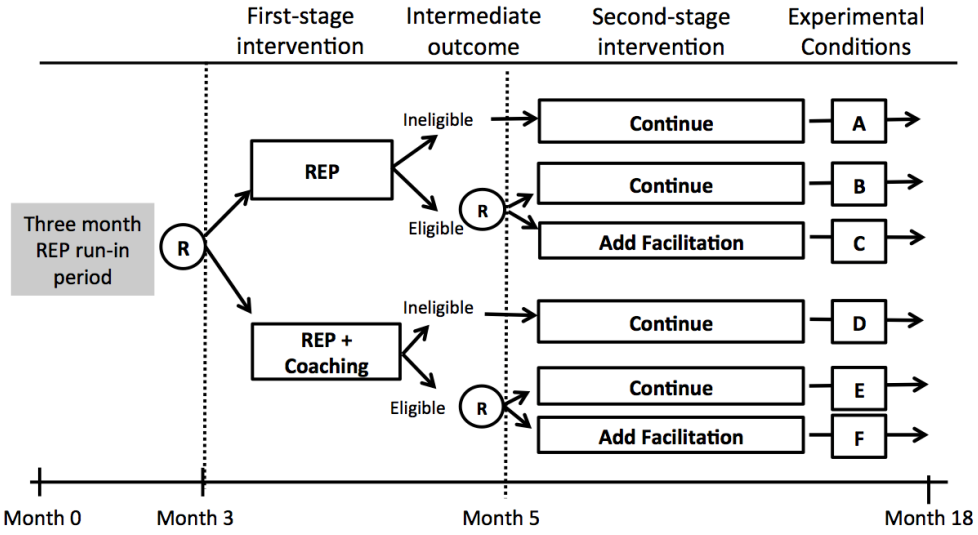
PI: Kilbourne N=200

Population:

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

Recruit 1-3 SPs per school

School-level randomizations



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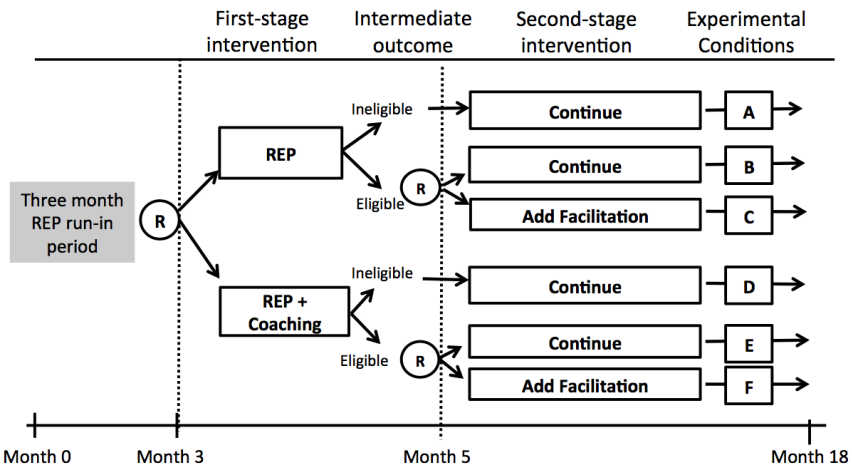
School-based Implementation of CBT

PI: Kilbourne N=200

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.



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School-based Implementation of CBT

PI: Kilbourne N=200

Intervention Options:

First-stage

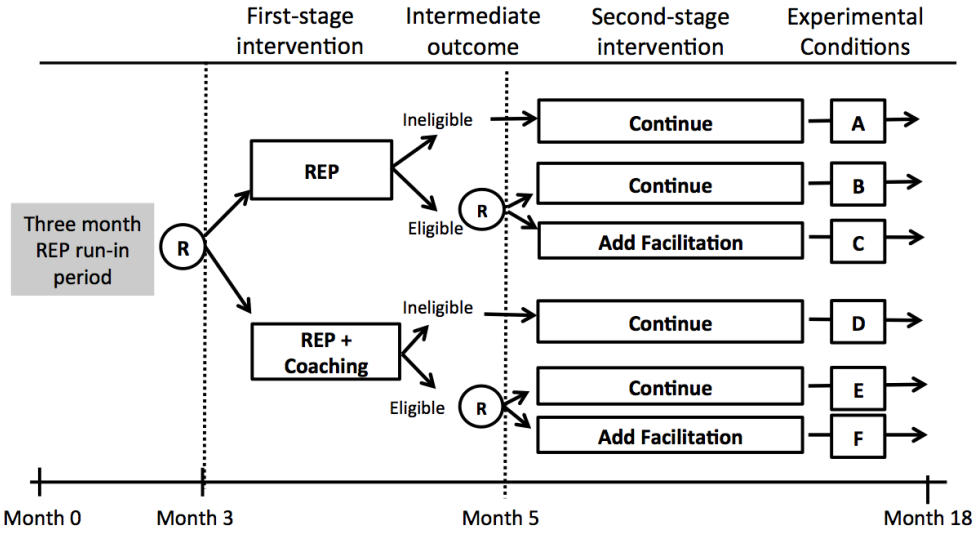
- REP
- REP + Coaching

Second-stage non-responders

- Continue
- Add Facilitation

Second-stage responders

- Continue



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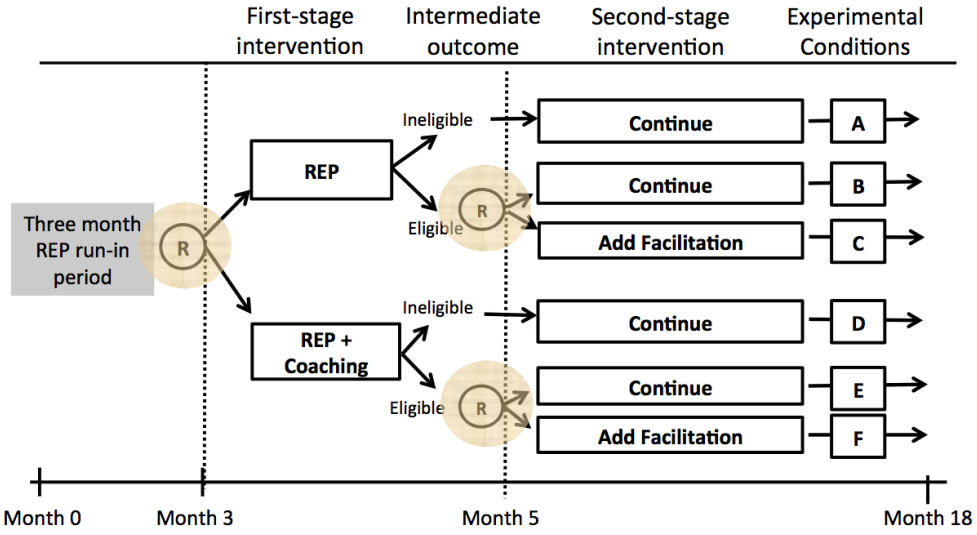
School-based Implementation of CBT

PI: Kilbourne N=200

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?



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School-based Implementation of CBT

PI: Kilbourne N=200

Embedded tailoring variable:

Eligibility for facilitation

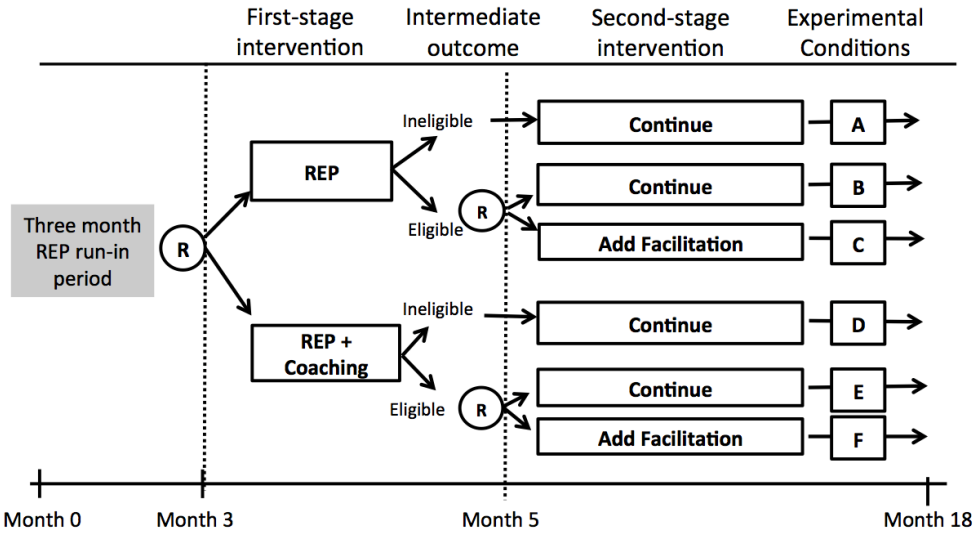
Assessed 8 weeks after first randomization

Based on school-aggregated

- 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



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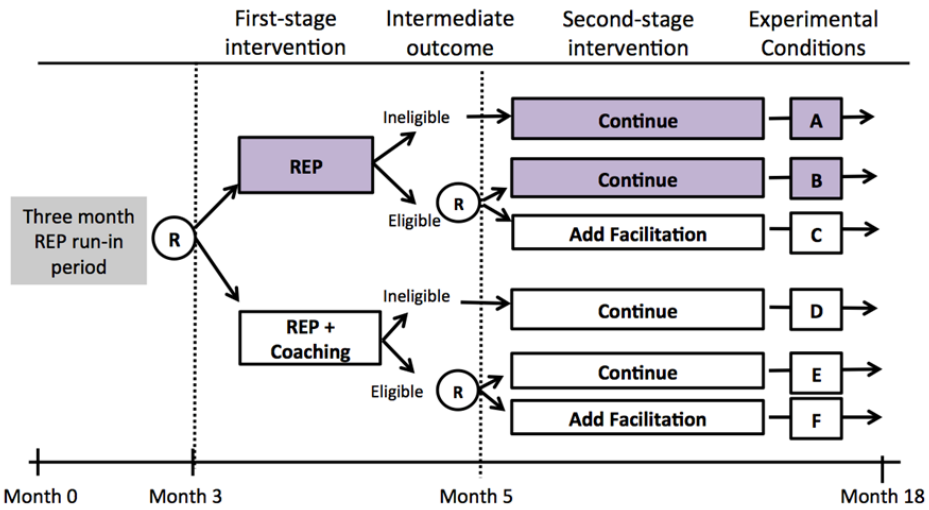
School-based Implementation of CBT

PI: Kilbourne N=200

4 Embedded Interventions (only 2 of the 4 are adaptive):

(Non-Adaptive) Intervention #1

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



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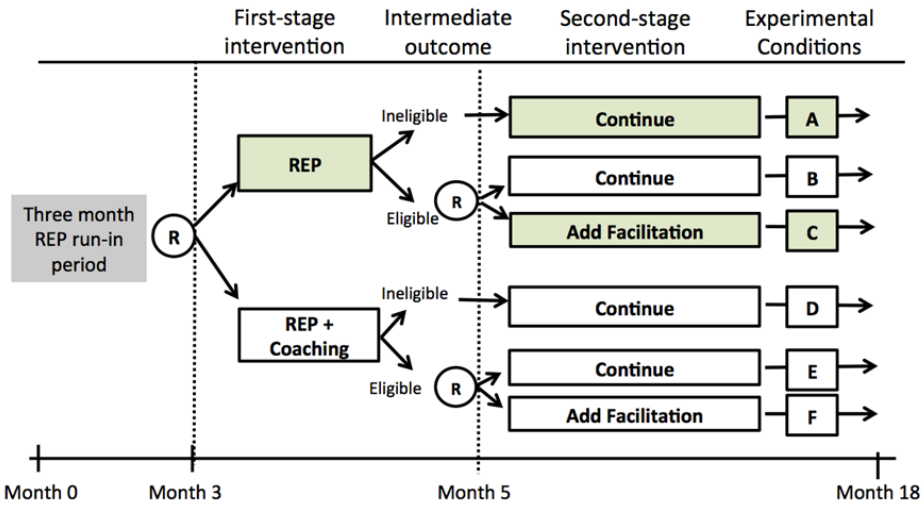
School-based Implementation of CBT

PI: Kilbourne N=200

4 Embedded Interventions (only 2 of the 4 are adaptive):

(Adaptive) Intervention #2

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



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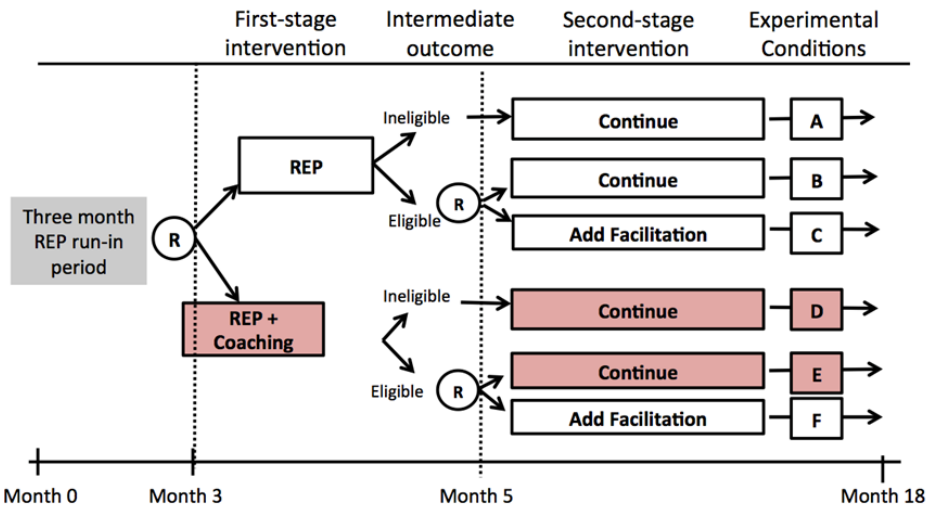
School-based Implementation of CBT

PI: Kilbourne N=200

4 Embedded Interventions (only 2 of the 4 are adaptive):

(Non-Adaptive) Intervention #3

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



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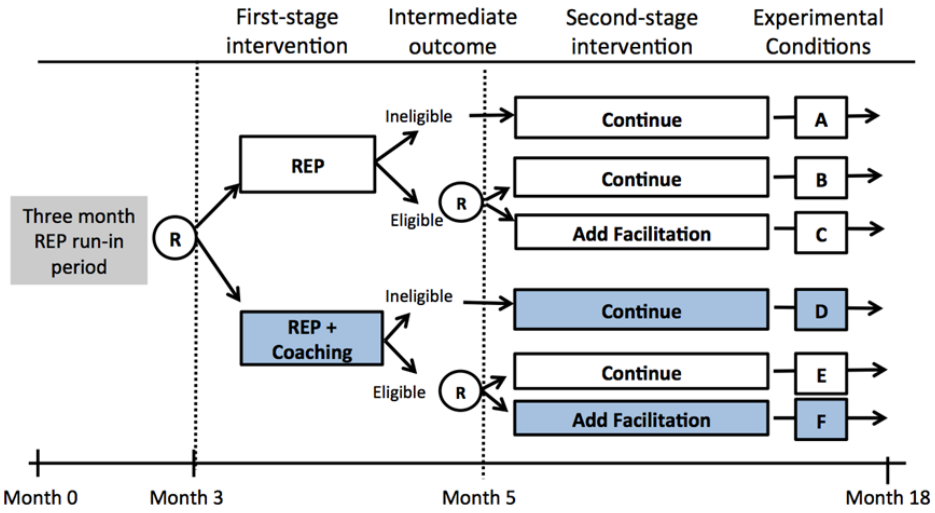
School-based Implementation of CBT

PI: Kilbourne N=200

4 Embedded Interventions (only 2 of the 4 are adaptive):

(Adaptive) Intervention #4

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



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School-based Implementation of CBT

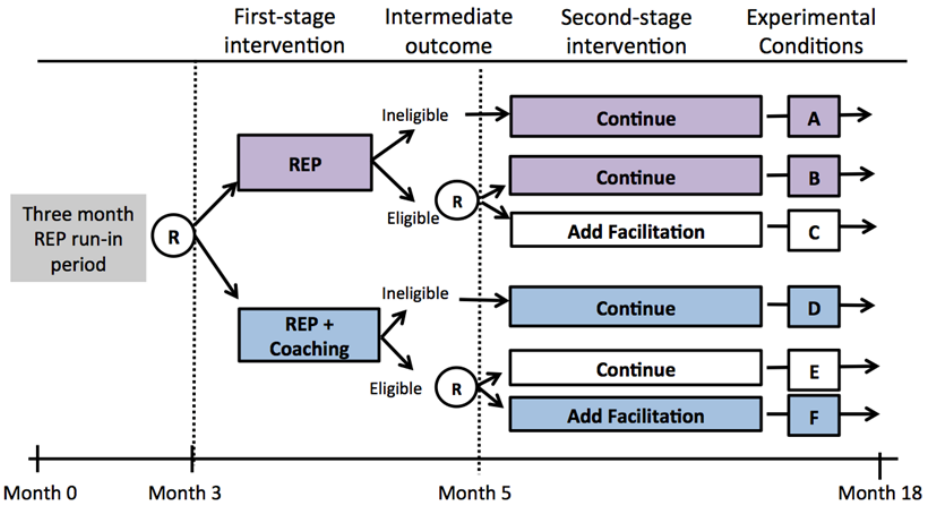
PIs: Kilbourne N=200

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

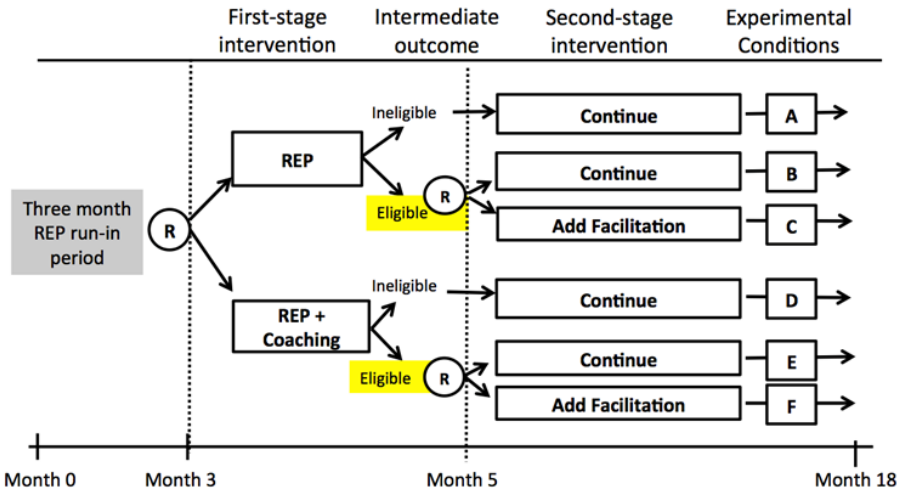
Comparison along 4 dimensions:

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)

Comparison of SMARTs

1. *Which subgroups are randomized multiple times*

All non-responders but only non-responders:



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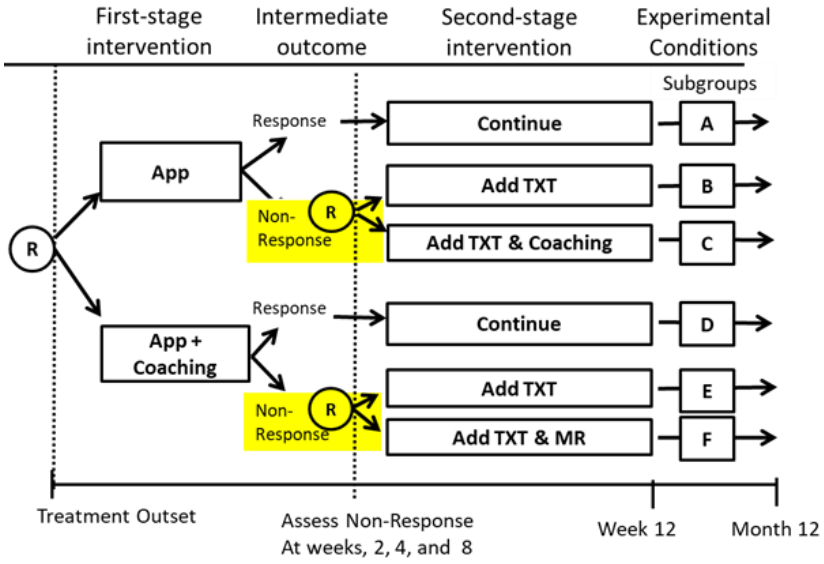
ASIC



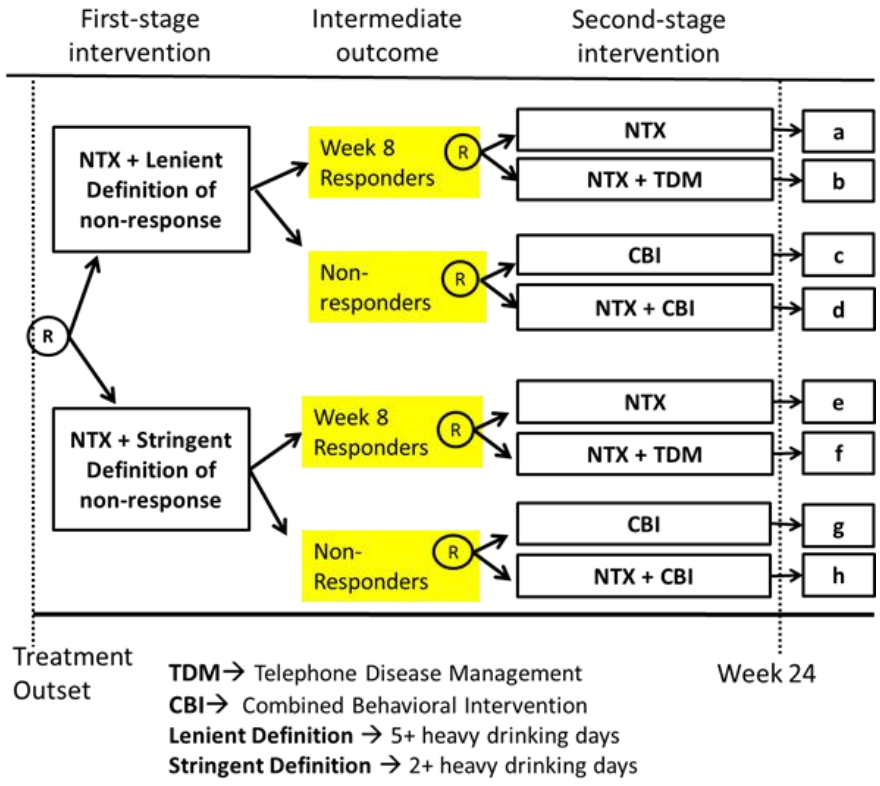
App→ Mobile Application
MR→ Meal Replacement
TXT→ Text Messages

Weight Loss

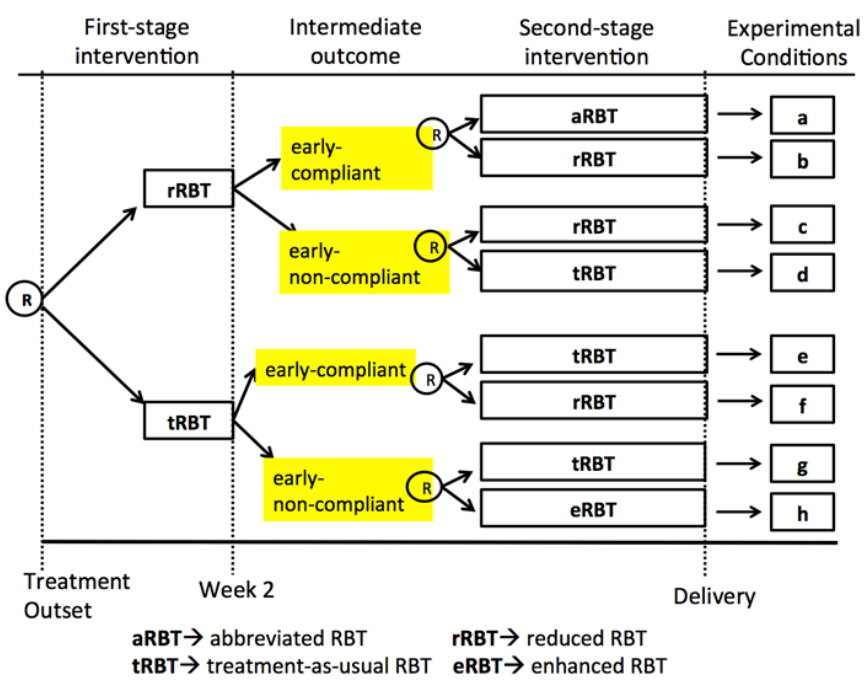
Comparison of SMARTs

1. *Which subgroups are randomized multiple times*

All responders and all non-responders:



ExTENd

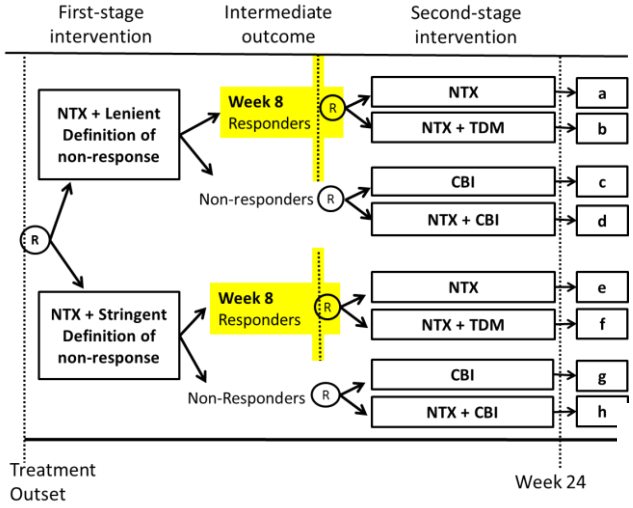


RBT

Comparison of SMARTs

2. *Timing of re-randomization*

At one fixed point in time only



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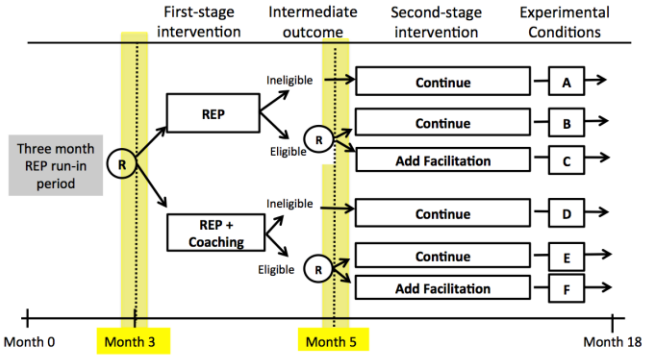

ASIC

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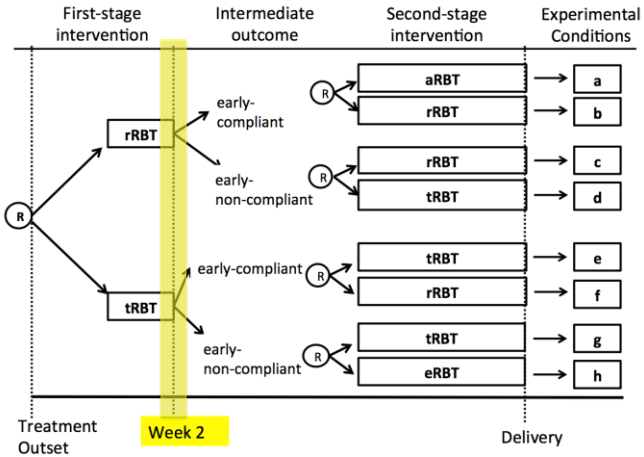


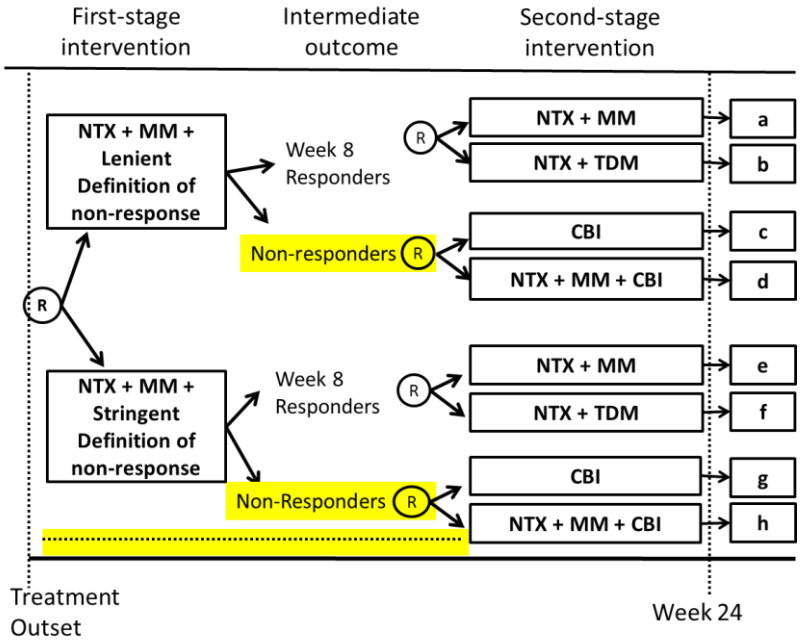
aRBT→ abbreviated RBT **rRBT→** reduced RBT
tRBT→ treatment-as-usual RBT **eRBT→** enhanced RBT

RBT

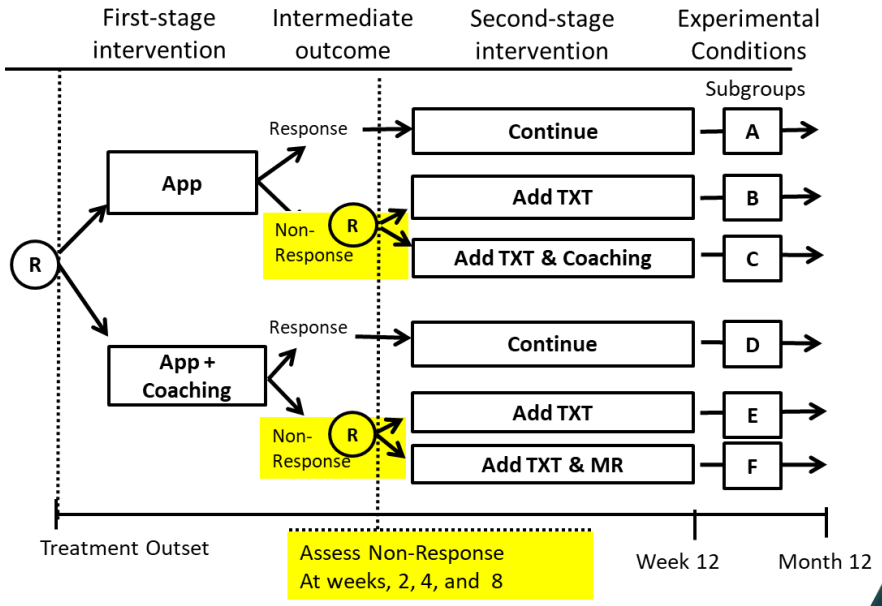
Comparison of SMARTs

2. *Timing of re-randomization*

At any one of several fixed times



ExTENd



Weight Loss

Comparison of SMARTs

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

Comparison of SMARTs

3. *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.