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

First-stage intervention | Intermediate outcome | Second-stage intervention
---|---|---
NTX + Lenient Definition of non-response | Week 8 Responders | NTX + TDM
Non-responders | NTX + CBI

NTX + Stringent Definition of non-response | Week 8 Responders | NTX + TDM
Non-Responders | CBI

**Treatment Outset**
- **NTX** → Naltrexone (opioid antagonist)
- **TDM** → Telephone Disease Management
- **CBI** → Combined Behavioral Intervention
- **Lenient Definition** → 5+ heavy drinking days in 1 week
- **Stringent Definition** → 2+ heavy drinking days in 1 week

**Week 24**
- a
- b
- c
- d
- e
- f
- g
- h
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

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**Legend:**
- **NTX**: Naltrexone (opioid antagonist)
- **TDM**: Telephone Disease Management
- **CBI**: Combined Behavioral Intervention

**Definitions:**
- **Lenient Definition**: 5+ heavy drinking days in 1 week
- **Stringent Definition**: 2+ heavy drinking days in 1 week

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**Treatment Outset**

- Week 24

**First-stage intervention**
- NTX
- NTX + TDM

**Intermediate outcome**
- Week 8 Responders
- Non-responders

**Second-stage intervention**
- NTX
- NTX + TDM
- CBI
- NTX + CBI

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**Paths:**
- **a**: NTX
- **b**: NTX + TDM
- **c**: CBI
- **d**: NTX + CBI
- **e**: NTX
- **f**: NTX + TDM
- **g**: CBI
- **h**: NTX + CBI
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?

**Legend:**
- NTX → Naltrexone (opioid antagonist)
- TDM → Telephone Disease Management
- CBI → Combined Behavioral Intervention
- Lenient Definition → 5+ heavy drinking days in 1 week
- Stringent Definition → 2+ heavy drinking days in 1 week
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

PI: Oslin   N=302
ExTENd

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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

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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

TDM → Telephone Disease Management
CBI → Combined Behavioral Intervention
Lenient Definition → 5+ heavy drinking days
Stringent Definition → 2+ heavy drinking days
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

Legend:
- NTX: Non-responders
- NTX+TDM: Week 8 Responders
- NTX+CBI: Non-responders
- CBI: Week 8 Responders

Definitions:
- Lenient Definition of non-response → 5+ heavy drinking days
- Stringent Definition of non-response → 2+ heavy drinking days

TDM → Telephone Disease Management
CBI → Combined Behavioral Intervention

Week 24
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

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*TDM*→ Telephone Disease Management  
*CBI*→ Combined Behavioral Intervention  
**Lenient Definition** → 5+ heavy drinking days  
**Stringent Definition** → 2+ heavy drinking days

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*R*→ Responders  
*NTX*→ Naltrexone  
*NTX+TDM*→ Naltrexone + Telephone Disease Management  
*CBI*→ Combined Behavioral Intervention  
*NTX+CBI*→ Naltrexone + Combined Behavioral Intervention

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

PI: Jones   N=220

Diagram:
- First-stage intervention: rRBT, tRBT
  - Early-compliant: aRBT, tRBT
  - Early-non-compliant: rRBT, tRBT
- Intermediate outcome:
  - Early-compliant: aRBT, tRBT
  - Early-non-compliant: rRBT, tRBT
- Second-stage intervention:
  -分娩: eRBT
- Experimental Conditions:
  - a: rRBT
  - b: rRBT
  - c: rRBT
  - d: tRBT
  - e: tRBT
  - f: tRBT
  - g: tRBT
  - h: eRBT

Abbreviations:
- aRBT: abbreviated RBT
- tRBT: treatment-as-usual RBT
- rRBT: reduced RBT
- eRBT: enhanced RBT
RBT

**Population:**
Pregnant women using opioids or cocaine
RBT

**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.

PI: Jones  N=220

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

**Diagram:**

1. **First-stage intervention**
   - rRBT
   - tRBT

2. **Intermediate outcome**
   - early-compliant
   - early-non-compliant
   - late-compliant
   - late-non-compliant

3. **Second-stage intervention**
   - aRBT
   - rRBT
   - tRBT
   - eRBT

4. **Experimental Conditions**
   - a
   - b
   - c
   - d
   - e
   - f
   - g
   - h
**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
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

Diagram:

- First-stage intervention
- Intermediate outcome
- Second-stage intervention
- Experimental Conditions

- aRBt → abbreviated RBT
- tRBt → treatment-as-usual RBT
- rRBt → reduced RBT
- eRBt → enhanced RBT
RBT

PI: Jones  N=220

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

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
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
**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
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
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/m²
- Motivated to lose weight

- Mobile Application
- Meal Replacement
- Text Messages
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
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

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**Legend:**
- **App**: Mobile Application
- **MR**: Meal Replacement
- **TXT**: Text Messages

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**Diagram Description:**
- The diagram illustrates the flow of the weight loss intervention, starting from treatment outset to month 12.
- The flow includes stages of intervention, response assessment, and the addition of TXT and coaching for non-responders.
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)?
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

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**Diagram:**

- **First-stage intervention:**
  - App
  - App + Coaching

- **Intermediate outcome:**
  - Response
  - Non-Response

- **Second-stage intervention:**
  - Continue
  - Add TXT
  - Add TXT & Coaching
  - Add TXT
  - Add TXT & MR

- **Experimental Conditions:**
  - Subgroups A, B, C, D, E, F

**Legend:**
- App: Mobile Application
- MR: Meal Replacement
- TXT: Text Messages

**Timeline:**
- Treatment Onset
- Assess Non-Response At weeks, 2, 4, and 8
- Week 12
- Month 12
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
MR ➔ Meal Replacement
TXT ➔ Text Messages
Weight Loss
PIs: Spring & Nahum-Shani  N=400

4 Embedded Adaptive Interventions:

AI #2

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

[Diagram of treatment intervention flow]

- App
- App + Coaching
- Add TXT
- Add TXT & Coaching
- Add TXT &MR

Subgroups: A, B, C, D, E, F

- Week 12
- Month 12

Treatment Outset
Assess Non-Response At weeks, 2, 4, and 8

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

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**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
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
SMART Case Studies

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School-based Implementation of CBT

PI: Kilbourne   N=200

**TRAILS**
Transforming Research into Action to Improve the Lives of Students

**ASIC**
Adaptive School-based Implementation of CBT

**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

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[Diagram of the implementation process with phases and conditions]

Three month REP run-in period

Month 0: Start of intervention
Month 3: Intermediate outcome
Month 5: Second-stage intervention
Month 18: Experimental Conditions

Conditions:
- A
- B
- C
- D
- E
- F

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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

REPL → 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
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.
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

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
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?

REPs → 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
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
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
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
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
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
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
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**

**Weight Loss**

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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

App → Mobile Application

MR → Meal Replacement

TXT → Text Messages
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

**ExTENd**

**ASIC**
Comparison of SMARTs

2. **Timing of re-randomization**

At any one of several fixed times
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
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:


Weight Loss is described in:


ASIC is described in: