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

NTX + Lenient Definition of non-response
   Week 8 Responders
      Non-responders

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

Intermediate outcome

Second-stage intervention

NTX
   a
NTX + TDM
   b

CBI
   c
NTX + CBI
   d

NTX
   e
NTX + TDM
   f

CBI
   g
NTX + CBI
   h

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
ExTENd

PI: Oslin  N=302

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

First-stage intervention
NTX + Lenient Definition of non-response
   | Week 8 Responders
   | Non-responders
   | NTX + Stringent Definition of non-response
   | Week 8 Responders
   | Non-Responders

Intermediate outcome
NTX
NTX + TDM
CBI
NTX + CBI
NTX
NTX + TDM
CBI
NTX + CBI

Second-stage intervention
   | a
   | b
   | c
   | d
   | e
   | f
   | g
   | h

Treatment Outset
Week 24

NTX → Naltrexone (opioid antagonist)
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Lenient Definition → 5+ heavy drinking days in 1 week
Stringent Definition → 2+ heavy drinking days in 1 week
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
- 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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**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
**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?

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**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

Lenient: 5+ HDDs
Stringent: 2+ HDDs

PI: Oslin  N=302

NTX \rightarrow \text{Naltrexone (opioid antagonist)}
TDM \rightarrow \text{Telephone Disease Management}
CBI \rightarrow \text{Combined Behavioral Intervention}

\text{Lenient Definition} \rightarrow 5+ \text{heavy drinking days in 1 week}
\text{Stringent Definition} \rightarrow 2+ \text{heavy drinking days in 1 week}
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
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

- Lenient Definition of non-response:
  - Week 8 Responders:
    - NTX
    - NTX + TDM
  - Non-responders:
    - CBI
    - NTX + CBI

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

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

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

ExTEND (PI: Oslin): Treatment of Alcohol Dependence

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

PI: Jones   N=220

**Experimental Conditions**

- a
- b
- c
- d
- e
- f
- g
- h

**Abbreviations**

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

PI: Jones   N=220

Population:
Pregnant women using opioids or cocaine
Rationale:

Reinforcement-based Treatment (RBT) is an efficacious intervention, but
- RBT is costly to administer and time-consuming (high burden) on the part of the participant
- About 40% of participants do not respond as well as desired.
**RBT**

**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  \( N=220 \)

**Intervention Options:**
\[ a_{RBT} < r_{RBT} < t_{RBT} < e_{RBT} \]
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?
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
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

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
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

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**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

Dear Diet,
Things just aren’t going to work between us.
It’s not me, it’s you.
You’re tasteless, boring & I can’t stop cheating on you.
Weight Loss

PIs: Spring & Nahum-Shani  N=400

Population:
Obese/overweight adults

First-stage intervention | Intermediate outcome | Second-stage intervention | Experimental Conditions
--- | --- | --- | ---
App | Response | Continue | Subgroups
App + Coaching | Non-Response | Add TXT | A
App + Coaching | Response | Add TXT & Coaching | B
App + Coaching | Non-Response | Continue | C
App + Coaching | Response | Add TXT | D
App + Coaching | Non-Response | Add TXT & MR | E
App + Coaching | Response | Continue | F

App → Mobile Application
MR → Meal Replacement
TXT → Text Messages
Efficacious weight-loss interventions are costly and burdensome

• 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
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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**Legend:**

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

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**Diagram:**

[Diagram showing the flow of interventions based on response status.]
Weight Loss

PIs: Spring & Nahum-Shani  N=400

4 Embedded Adaptive Interventions:

AI #1

Start with App; if response, continue else add TXT
Weight Loss

PIs: Spring & Nahum-Shani  N=400

4 Embedded Adaptive Interventions:

AI #2

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

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

**Diagram:**
- **First-stage intervention**
- **Intermediate outcome**
- **Second-stage intervention**
- **Experimental Conditions**
- **Subgroups**

**Timeline:**
- **Treatment Outset**
- **Assess Non-Response At weeks, 2, 4, and 8**
- **Week 12**
- **Month 12**

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**Subgroups:**
- **A**: Continue
- **B**: Add TXT
- **C**: Add TXT & Coaching
- **D**: Continue
- **E**: Add TXT
- **F**: Add TXT & MR
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
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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

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
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

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

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

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
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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

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

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.

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

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
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:

**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

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

2. Timing of re-randomization

At one fixed point in time only

ExTENd

ASIC

RBT

**Notes:**
- **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 of 12 weeks
- **Facilitation:** Phone calls with an expert in CBT & strategic thinking for a minimum of 12 weeks
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
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:

Autism is described in:

ASIC is described in: