SMART Case Studies

Module 3

*Getting SMART:* Experimental Design and Analysis Methods for Developing Adaptive Interventions
These are primarily hypothesis generating or strategy developing trials. These trials are not confirmatory in the sense of confirming that one dynamic regime is best.

Outline

• **ADHD** (PI: Pelham): Treatment of ADHD
• **RBT** (PI: Jones): Treatment for Pregnant Women who are Drug Dependence
• **ExTENd** (PI: Oslin): Treatment of Alcohol Dependence
• **REP** (PI: Kilbourne): Implementation Intervention
• Summary Comparison of the five SMAR1s
SMART Case Studies

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- **REP** (PI: Kilbourne): Implementation Intervention
- Summary Comparison of the five SMAR1s
Population: Children with autism spectrum disorders who are nonverbal (not using spoken language) by age 5 despite involvement in traditional intervention programs. N=90 was the planned sample size; but this N was not achieved due to recruitment difficulties. The final study had only N=61.

Primary Aim: To compare change in outcome measures of communication and language across three time periods (times 0, 3 months and 6 months) between strategies starting with JASP+EMT vs the strategy starting with JASP+EMT+SGD.

Primary outcome: Total spontaneous communicative utterances

JASP (Joint Attention Symbolic Play Engagement and Regulation) focuses on early social-communication skills, including coordinated joint attention gestures known to be associated with the development of later spoken language of children with autism. Includes the creation of contextually relevant and meaningful learning opportunities during interactions with adult partners (therapists, parents) who are responsive to child interests and actions, who model and expand play and gesture use and maintain joint engagement.

EMT (Enhanced Milieu Teaching) is a naturalistic early language intervention that uses 7 core strategies to teach language in social interaction: following the child’s lead in conversation and play, responding to communicative initiations from the child with target language, expanding child utterances by adding words to increase complexity while
maintaining the child’s meaning, arranging the environment to support and elicit communication from the child, and systematic use of prompts (model, time delays, and prompts).

SGD (speech generating device): SGDs display symbols that produce voice output communication when selected. The child can use the SGD to communicate.

JASP+EMT: 2 sessions per week, each 1 hour length.

JASP+EMT+SGD: 2 sessions per week, each 1 hour length.

Intensified JASP+EMT+SGD: This intervention was identical in content to JASP+EMT+SGD but occurred for a total of 3 hours per week for an additional 12 weeks.

Intensified JASP+EMT: This intervention was identical in content to JASP+EMT but occurred for a total of 3 hours per week for another 12 weeks.
Autism Study (Kasari) $N=61$

**Population:**
Children with ASD who are non-verbal by age 5, despite receiving traditional intensive behavioral language interventions.

![Diagram showing the study design and outcomes](image_url)

- **First-stage intervention**
- **Intermediate outcome**
- **Second-stage intervention**
- **Subgroups**

**Legend:**
- JASP—Joint Attention and joint Engagement
- EMT—Enhanced Milleu Teaching
- SGD—Speech Generating Device (e.g., an iPad or DynaVox)
Rationale:

These children experience poor outcomes, yet represent 25-30% of children with ASD.

Crucial to plan for a “rescue” if the first treatment fails.

SGDs (e.g., iPads) are costly + no rigorous research, despite all the rave!

Can SGDs improve outcomes in the context of promising behavioral language interventions?

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**Diagram Legend:**

- JASP → Joint Attention and joint Engagement
- EMT → Enhanced Milleu Teaching
- SGD → Speech Generating Device (e.g., an iPad or DynaVox)
Autism Study (Kasari) $N=61$

**Treatments:**

JASP+EMT: promising naturalistic behavioral intervention  
SGD: Speech generating device
Autism Study (Kasari) \(N=61\)

Critical questions:

In the context of JASP+EMT, do we provide SGD's to all children with ASD from the start?

Among slow responders to JASP+EMT alone, should we intensify JASP+EMT or augment with SGD?

JASP→ Joint Attention and Engagement
EMT→ Enhanced Milieu Teaching
SGD→ Speech Generating Device (e.g., an iPad or DynaVox)
The above measures are collected via videotapes of the child and therapist sessions.
Improvement was calculated as the difference in the average assessment between the first two intervention sessions and the last two intervention sessions during the first stage of the intervention; or in terms the difference between the assessment at the screening visit and the month-three visit.

Preliminary studies indicated that these interventions should show changes within a 3 month period; this time frame is consistent with recommendations by the National Research Council.
Autism Study (Kasari) $N=61$

Three embedded AIs:

1. Start with JASP+EMT; continue for early responders; augment with SGD for slow responders
Three embedded AIs:

(2) Start with JASP+EMT; continue for early responders; intensify JASP+EMT for slow responders
Three embedded AIs:

(3) Start with JASP+EMT+SGD; continue for early responders; intensify JASP+EMT+SGD for slow responders
Primary Analyses involve:
Outcomes such as Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4) (given at 0, 6, 9 months): This test for receptive vocabulary development and is appropriate for children aged 2.6 years and older, and Verbal Motor Production Assessment for Children (VMPAC) (given at 0, 6, 9 months). The VMPAC is designed to examine oral and speech-motor control in children. The items are arranged from basic to complex and assess three main areas: Global motor control, focal oromotor control and sequencing.

Secondary Analyses involve:
The baseline variables included severity of repetitive compulsive behaviors, degree of apraxia, and developmental variables (based on cognitive and language test results). In particular, the research team hypothesized that children with greater severity of apraxia would do better on beginning with JAE + AAC than beginning with JAE + EMT because the communication device would better provide a means to communicate.
SMART Case Studies

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- **ExTENd** (PI: Oslin): Treatment of Alcohol Dependence
- **REP** (PI: Kilbourne): Implementation Intervention
- Summary Comparison of the five SMARTs
MED is Ritalin.
BMOD is behavioral modification, itself a multi-component behavioral intervention.

The interventions include differing doses of MED methylphenidate (a psychostimulant drug) and differing intensities of behavioral modification BMOD (consisting of a school-based component with the teacher, a Saturday treatment component involving social skills development, and a parent-training component targeted at helping parents to identify problematic behaviors with the relevant child-functioning domains).

Intensified MED: The higher-dose option for methylphenidate includes late-afternoon doses, if needed.

Intensified BMOD: The higher-intensity option for the behavioral modification includes more intensive training in social skills in the school-based component and, if needed, both additional individual parent training sessions that target specific behavior management issues and practice sessions with children.

- Average performance on the teacher rated Individualized Target Behavior Evaluations – ITB-- is less than 75% AND
- Rating by teachers as impaired (i.e., greater than 3) on the (Impairment Rating Scale) IRS in at least one domain.

N=153

Primary outcome is measure of child behavior at 8 months, end of school year.

Sized for the primary comparison of initial treatments (MED vs. BMOD). That is, sized for the
main effect of initial treatment.
ADHD (Pelham) N=153

Population:
Children with ADHD, ages 6-12
For example, a task force of the American Psychological Association recommends psychosocial first (Brown et al. 2007), whereas the guidelines of the American Academy of Child and Adolescent Psychiatry (2007) recommend using medication first.
The interventions include differing doses of MED methylphenidate (a psychostimulant drug) and differing intensities of behavioral modification BMOD (consisting of a school-based component with the teacher, a Saturday treatment component involving social skills development, and a parent-training component targeted at helping parents to identify problematic behaviors with the relevant child-functioning domains).

Intensified MED: The higher-dose option for methylphenidate includes late-afternoon doses, if needed.

Intensified BMOD: The higher-intensity option for the behavioral modification includes more intensive training in social skills in the school-based component and, if needed, both additional individual parent training sessions that target specific behavior management issues and practice sessions with children.
ADHD (Pelham) N=153

Critical questions:

Which treatment to provide first: BMOD vs MED?

Which rescue tactic to provide non-responders: intensify initial treatment vs augment with the other?
The Impairment Rating Scale (IRS) (Fabiano et al. 2006) and an individualized list of target behaviors (ITB) (e.g., Pelham et al. 1992). The IRS provides a comprehensive index of a child’s impairment in various domains such as peer relationships, classroom behavior, family functioning, and academic achievement. The ITB was used to assess improvement on child-specific behavior goals.

Investigators felt that 8 weeks was needed in order to obtain a reasonable assessment of children’s response to treatment and to give clinicians time to implement the school-based.
You can also conceptualize the second-stage treatments in these embedded adaptive interventions as tactics rather than treatments.
ADHD (Pelham) N=153

4 embedded adaptive interventions:

(2) Start with BMOD; continue for responders; augment for non-responders
ADHD (Pelham) N=153

4 embedded adaptive interventions:

(3) Start with MED; continue for responders; intensify for non-responders
ADHD (Pelham) N=153

4 embedded adaptive interventions:

(4) Start with BMOD; continue for responders; intensify for non-responders
ADHD (Pelham) N=153

Primary Aim:
Starting with MED vs starting with BMOD
In terms of change in teacher ratings of child behavior across 8 months

Secondary Aims
Baseline moderators of the effect of initial treatment/secondary treatment/AIs.
SMART Case Studies

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- Summary Comparison of the five SMARTs
N=300 drug-abusing pregnant women

Outcomes included treatment completion through to the end of pregnancy (primary), repeated weekly and bi-weekly assessments of drug-use and session attendance.

Early non-compliance: a missed unexcused treatment day, a positive opioid or cocaine urine specimen, or self-reported drug use.

Sized to detect a difference between rRBT throughput and tRBT throughout.
The women must have first completed an eight-day residential detoxification stay.

Inner-city Baltimore.
Reinforcement-Based Treatment (RBT) is a relatively new and innovative behavioral treatment strategy that may assist in improving maternal and neonatal outcomes. RBT’s theoretical underpinnings include both operant conditioning principles (behavior is a reaction based on past consequences of actions), and social learning theory (behavior is shaped by understanding of the relationship between the behavior and receiving a reward or punishment, and the value placed on that reward or punishment).
tRBT: 3 days/week for 2-3 hours/day.
eRBT also include individual therapy 6 time per week
rRBT- 2 days per week
aRBT 1 day per week
RBT (Jones) \(N=300\)

Critical Questions:

- Can the traditional version of RBT be reduced in intensity and scope;
- Whether a woman who does not respond quickly should continue on the same version of RBT or be moved to a more-intensive, larger-scope version;
- Can the intensity and scope of RBT be reduced if a woman responds quickly.
The non-compliance criterion is in fact a combination of non-compliance and non-response.
8 Embedded AIs:

1) Start with rRB; reduce for compliant; continue for non-compliant (least costly/burdensome)
8 Embedded AIs:

2) Start with rRB; reduce for compliant; intensify for non-compliant
**8 Embedded AIs:**

3) Always rRBT (not adaptive)
8 Embedded AIs:

4) Start with rRB; continue for compliant; intensify for non-compliant
8 Embedded AIs:

5) Always tRBT (non-adaptive)
8 Embedded AIs:

6) Start with tRB; continue for compliant; intensify for non-compliant. (most costly/burdensome)
8 Embedded AIs:

7) Start with tRB; reduce for compliant; continue for non-compliant.
8 Embedded AIs:
8) Start with tRB; reduce for compliant; intensify for non-compliant.
RBT (Jones) \(N=300\)

**Primary Aim:**
Compare always tRBT vs. always rRBT
In terms of program completion (delivery of child while in treatment).

**Secondary Aim:**
Baseline moderators
  e.g., baseline amount of illegal activity (e.g., prostitution).
SMART Case Studies

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- Summary Comparison of the five SMARTs
Alcohol dependent subjects begin on Naltrexone, an opioid receptor antagonist (that blocks the euphoric effects of drinking) then in ensuing two months are monitored for heavy drinking

N=302

Study was sized to detect the contrast between two alternatives for non-responders: CBI vs CBI + Naltrexone

Primary outcome (drinking behavior from the TLFB)
TDM: Telephone Disease Management: phone-based basic, minimal clinical support for the use of effective pharmacotherapy and reduction in drinking.

MM is a face-to-face, basic, minimal clinical support for the use of effective pharmacotherapy and reduction in drinking (Pettinati et al. 2004, 2005).

CBI: multicomponent intervention that includes components targeting adherence and motivation for change + family/community involvement when possible. It is a multicomponent intervention that includes components targeting adherence to pharmacotherapy and enhancement of participant motivation for change. This intervention includes family involvement when possible and emphasizes the utilization of the participant’s social/community context to reinforce abstinence (Longabaugh et al. 2005, Miller et al. 2003). TDM includes the same content as MM, but it is delivered via telephone.

Heavy drinking days (≥5 drinks/day for males; ≥4 for females)
ExTENd (Oslin) $N=302$

**Population:**
Alcohol Dependent Adults, completing an Intensive Outpatient Program (IOP)

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**Diagram Description:**
- **First-stage intervention:**
  - NTX + Lenient Definition of non-response
- **Week 8:**
  - Responders
  - Non-responders
  - NTX + Stringent Definition of non-response
- **Week 24:**
  - NTX
  - NTX + TDM
  - CBI
  - NTX + CBI

**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
ExTENd (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 to for responders
- Because of various barriers: Physiological/social/psychological

![Diagram showing the treatment outcomes and interventions for ExTENd (Oslin) study.](image)
NTX= NTX+MM (minimal in-person medical management support).

Primary outcome (drinking behavior from the TLFB)

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Heavy drinking days (≥5 drinks/day for males; ≥4 for females)
ExTENd (Oslin) $N=302$

Critical 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?
This criterion was supported by preliminary data generated from a prior NTX study conducted.

This study gave alcohol dependent subjects for 100mg/day or placebo with a less structured form of medical monitoring called BRENDA for 32 weeks. Results indicated that subjects who had taken the NTX (not placebo) and had 2 to 5 days of heavy drinking in the first 60 days were not likely to reduce their drinking if they just continued NTX and medical management.
ExTENd (Oslin) N=302

8 embedded AIs:
1) Start on NTX; if 5+ HDDs prior to week 8, switch to CBI; else at week 8 continue NTX
ExTENd (Oslin) \( N=302 \)

8 embedded AIs:

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

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Lenient Definition of non-response

Stringent Definition of non-response

Week 8 Responders

Non-responders

Treatment Outset

TDWT = telephone distress management
CBI = Combined Behavioral Intervention
Lenient Definition \( \rightarrow 5+ \) heavy drinking days
Stringent Definition \( \rightarrow 2+ \) heavy drinking days

Week 24
ExTENd (Osln) N=302

8 embedded AIs:
3) Start on NTX; if 5+ HDDs prior to week 8, switch to CBI; else at week 8 offer NTX+TDM

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Treatment Outset  | Week 24

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

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

Note:
- HDD = heavy drinking days
- NTX = naltrexone
- CBI = Combined Behavioral Intervention
- Lenient Definition: 5+ heavy drinking days
- Stringent Definition: 2+ heavy drinking days

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8 embedded AIs:
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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**ExTENd (Osln) N=302**

**Lenient Definitions of non-response**
- Non-responders
- Week 8 Responders

**Stringent Definition of non-response**
- Non-Responders
- Week 8 Responders

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<td>Lenient Definition</td>
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LMIC: Telephone Case Management
CBI: Combined Behavioral Intervention
Lenient Definition: ≥ 5+ heavy drinking days
Stringent Definition: ≥ 2+ heavy drinking days

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8 embedded AIs:
5) Start on NTX; if 2+ HDDs prior to week 8, switch to CBI; else at week 8 continue NTX
8 embedded AIs:
6) Start on NTX; if 2+ HDDs prior to week 8, augment NTX+CBI; else at week 8 continue NTX
ExTENd (Osln) $N=302$

8 embedded AIs:

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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TDHMI = Telephone lifestyle management
CBI = Combined Behavioral Intervention
Lenient Definition = 5+ heavy drinking days
Stringent Definition = 2+ heavy drinking days
ExTENd (Oslin) N=302

8 embedded AIs:

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

- Lenient Definition of non-response
- Stringent Definition of non-response

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Treatment Outset: Telephone Intake Management
CBI → Combined Behavioral Intervention
Lenient Definition → 5+ heavy drinking days
Stringent Definition → 2+ heavy drinking days

Week 24
ExTENd (Osln) \(N=302\)

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

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

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**Diagram Description:****
- **First-stage intervention:**
  - NTX + Laxient Definition of non-response
  - NTX + Stringent Definition of non-response

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

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

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

**Week 24**
SMART Case Studies

- **ADHD** (PI: Pelham): Treatment of ADHD
- **RBT** (PI: Jones): Treatment for Pregnant Women who are Drug Dependence
- **ExTENd** (PI: Oslin): Treatment of Alcohol Dependence
- **REP** (PI: Kilbourne): Implementation Intervention
- Summary Comparison of the five SMARTs
REP (Kilbourne) $N=60$ (sites); 1200 (patients)

- REP: Replicating Effective Programs (core components)
- EF: External Facilitator (external to the site)
- IF: Internal Facilitator (internal at the site)

Diagram showing the flow of interventions over time:
- Month 1
  - REP
  - Non-responding Sites
- Month 2
  - REP+EF
  - Non-responding Sites
- Month 3
  - REP+IF
  - Non-responding Sites

Subgroups:
- A: Discontinue
- B: Continue REP+EF
- C: Augment: REP+EF+IF
- D: Discontinue
- E: Continue: REP+EF+IF

[Outcomes through Month 24]
Total sites in first-phase: k=80. (Expect k=60 to not-respond at month 6.)
Total sites in second-phase: k=60
Patients per site: n=20
Total patients: N=1200
As described by Professor Amy Kilbourne, PhD, Univ of Michigan:
LG is an evidence-based psychosocial treatment based on the collaborative care model that has been shown in six randomized controlled trials across mental health and primary care settings to improve medical and psychiatric outcomes in patients with mood disorders (including bipolar disorder or depression). LG was also cited as an EBP in a recent meta-analysis and systematic review of collaborative care models. LG is based on social cognitive theory and delivered in four two-hour weekly group sessions and at least six tailored care management contacts that encourage active discussions focused on individuals’ personal goals that are aligned with healthy behavior change and symptom management strategies.
Recall LG involves four two-hour weekly group sessions and at least six tailored care management contacts

REP: Disseminate LG package, identify patients for LG, train site providers in LG, monitor LG and provide feedback via monthly report sheets.

REP+EF: External Facilitators (EFs) are part of the study team and reside outside the clinic and provide technical expertise to providers in adapting EBPs to address organizational and financial barriers. The EF’s core functions through the technical assistance calls include dissemination of additional information and materials on LG implementation based on site-specific needs. The EFs will initially contact the LG provider and set measurable objectives in implementing LG (e.g., number of patients completing at least one group session), and review progress based on these measures via monthly calls for six months.

Monthly calls will last one hour and primarily include discussion of barriers to LG implementation.

REP+EF/IF: In contrast to EFs, Internal Facilitators (IFs) reside within each site and have an internal working knowledge of the site. In contrast to the site LG provider (“champion”) IFs act as third parties and are responsible for enhancing the uptake of LG, notably by incorporating input to support the adoption of the EBP from frontline providers and aligning the EBP with organizational priorities via a direct reporting line with leadership. Using their knowledge of the local site’s culture and needs, the IFs will identify the site’s priorities, align the goals of implementing LG with these priorities, and identify other provider champions to assist in implementing LG. About $5500 in costs.
Critical Questions:
- Among sites not-responsive to REP at month 6, should we augment REP with EF vs EF+IF?
- Among sites not-responsive to REP+EF at month 12, should we augment with IF or continue?
Recall LG involves four two-hour weekly group sessions and at least six tailored care management contacts.

May appears to be a low bar; however, based on prior data 75% sites do not meet this criteria! And those that do not meet at month 6, are highly likely not to meet it 6 months later.
3 embedded adaptive implementation interventions:

(1) Begin with REP;
   if responsive at 6mo, continue REP for 12mo;
   else if non-responsive at 6mo provide REP+EF for 6mo;
   if response at 12mo, discontinue;
   else, continue REP+EF
3 embedded adaptive implementation interventions:

(2) Begin with REP;
   if responsive at 6mo, continue REP for 12mo;
   else if non-responsive at 6mo provide REP+EF for 6mo;
   if response at 12mo, discontinue;
   else, augment with REP+EF+IF
3 embedded adaptive implementation interventions:

(2) Begin with REP;
   if responsive at 6mo, continue REP for 12mo;
   else if non-responsive at 6mo provide REP+EF+IF for 6mo;
   if response at 12mo, discontinue;
   else, continue REP+EF+IF

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REP (Kilbourne) N=60 (sites)

First-phase intervention
                          Second-phase intervention
                          Third-phase intervention

REP

Responding sites
Non-responding sites

REP+EF

Responding sites
Non-responding sites

REP+EF+IF

Responding sites
Non-responding sites

Discontinue
Continue
Augment REP+EF+IF
Discontinue
Continue: REP+EF+IF

At the outset
Month 6
Month 12

REP ⇒ Replicating Effective Programs (core components)
EF ⇒ External Facilitator (external to the site)
IF ⇒ Internal Facilitator (internal at the site)

Subgroups
A
B
C
D
E

Month 18
(Outcomes through Month 24)
Primary aims:
Compare sites receiving REP+EF vs REP+EF+IF, in terms of patient-level MH-QOL (primary), functioning, #LG encounters (secondary).

Secondary Aim:
- REP+EF vs REP+EF+IF among 12 mo non-responding sites.
- Cost-effectiveness comparison of 3 AIs

MH-QOL—mental health quality of life
### SMART Case Studies

- **ADHD** (PI: Pelham): Treatment of ADHD
- **RBT** (PI: Jones): Treatment for Pregnant Women who are Drug Dependence
- **ExTENd** (PI: Oslin): Treatment of Alcohol Dependence
- **REP** (PI: Kilbourne): Implementation Intervention

| Summary Comparison of the five SMARTs |
Quick Comparison of 5 SMARTs

• Comparison along 4 dimensions:
  1. Which sub-groups are randomized multiple times?
  2. When does the re-randomization occur?
  3. Types of the critical questions
  4. Primary aims (=> study sizing)
The larger the number of categories of people re-randomized, the larger the number of embedded adaptive treatment strategies.
Quick Comparison of 5 SMARTs

(1) Which sub-groups are randomized multiple times?
   - All non-responders, but only non-responders:
Quick Comparison of 5 SMARTs

(1) Which sub-groups are randomized multiple times?
- All responders and all non-responders
Quick Comparison of 5 SMARTs

(2) When is the second randomization?
- At one fixed point in time only
Quick Comparison of 5 SMARTs

(2) When is the second randomization?
   – At any one of several fixed times
Quick Comparison of 5 SMARTs

(3) What kinds of critical questions?

- Which treatment first and which second?
  - Autism
  - ADHD
  - RBT

- Which treatment second and which third?
  - REP

- How to define non-response and which treatment to provide next?
  - ExTENd
Quick Comparison of 5 SMARTs

(4) What are primary Aims?

- Main effect of stage 1 treatment
  - Autism
  - ADHD
  - REP

- Main effect of stage 2 treatment
  - ExTENd (among non-responders to NTX)

- Comparison of two embedded (non-adaptive) interventions
  - RBT
Primary Reference

- ExTENd, ADHD and RBT are described in

- REP is described in:

- Autism is described in:
Practicum

- Major goal: draft an initial SMART
- 60min total: 30min individually or in groups; 30min feedback.
  1. List 2 to 4 critical scientific questions that you need to answer to develop a high-quality AI in your field.
  2. Sketch a SMART design to address these scientific questions
  3. Sketch (2-3 sentences) rationale for your SMART