Beyond Efficacy—Innovative Designs for Effectiveness

S.A. Murphy

CFAR 10/25/13
Individualized Sequences of Treatment
Why Do We Want Them?

– High heterogeneity in response to any one treatment
  • What works for one person may not work for another
  • What works now for a person may not work later (and relapse is common)
– Lack of adherence or excessive burden is common
Critical Decisions

• Which treatment should be used first, which second?

• What is the best timings of alterations in treatments?

• What information do we use to make these decisions? (how do we individualize the sequence of treatments?)
SMART Studies

Sequential, Multiple Assignment, Randomized Trial

These are multi-stage clinical trials; each participant proceeds through stages of treatment.

Each stage begins with a critical clinical decision; randomization to treatment takes place at each critical decision.

Goal of trial is to inform the construction of an effective sequence of treatments.
Adaptive Implementation
Intervention of
“Replicating Effective Programs”

“Treatments”:
– External Facilitators (EF) and
– Internal Facilitators (IF)
Two Critical Decisions

(1) Which treatment to provide to sites that are insufficient responders to standard REP?

(2) Which treatment to provide to the sites that continue to show non-response?
SMART REP

Month 6

75 (75% of 100) community-based outpatient clinics (sites) that have not responded to 6 months of REP

Augment for 6mo: REP + EF

Responder Sites

Continued Non-Responding Sites

Discontinue REP & Monitor

Continue 6mo: REP + EF

Augment 6mo: REP + EF + IF

Responder Sites

Continued Non-Responding Sites

Discontinue REP & Monitor

Continue 6mo: REP + EF + IF

PI Amy Kilbourne
SMART REP

Month 6

- Augment for 6mo: REP + EF
  - Responder Sites
  - Continued Non-Responding Sites

- Augment for 6mo: REP + EF + IF

12

- Responder Sites
- Continued Non-Responding Sites

18-24

- Discontinue REP & Monitor
- Continue 6mo: REP + EF
- Augment 6mo: REP + EF + IF

MH-QOL (primary) and # LG encounters

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PI Amy Kilbourne
SMART for Drug-Addicted Pregnant Women

PI: H. Jones, Johns Hopkins, NIDA R01
SMARTs are for Developing Individualized Intervention Sequences

• **NIMH Strategic Plan, 2008**: A new generation of clinical trials is needed to gather a wider array of data and examine the kinds of questions that can be used for personalized decision-making in medicine.

• **NIAID Strategic Plan, 2013**: Explore methods of establishing a functional cure that would allow subjects to discontinue antiretroviral treatment for extended periods without viral rebound.

• **NIDA Strategic Plan, 2010**: To develop the knowledge that leads to personalized or customized treatments
Examples of SMARTs
http://methodology.psu.edu/ra/adap-treat-strat/projects


Email with questions: samurphy@umich.edu
SMART REP

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Continue 6mo: REP + EF

Augment 6mo: REP + EF + IF

MH-QOL (primary) and # LG encounters

Month 12

R

Responder Sites

Augment 6mo: REP + EF + IF

R

Continued Non-Responding Sites

Discontinue REP & Monitor

Continue 6mo: REP + EF + IF

PI A. Kilbourne, Univ. Michigan