



Sequential Multiple Assignment Randomized Trials (SMART) & Adaptive Designs for Implementation Studies

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Disclosures

- The views expressed are those of the presenter and do not necessarily represent the views of the Department of Veterans Affairs
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Objectives

- SMART and adaptive designs
- Application to implementation studies
- Testing different implementation strategies

Sequential Multiple Assignment Trial (SMART) Designs

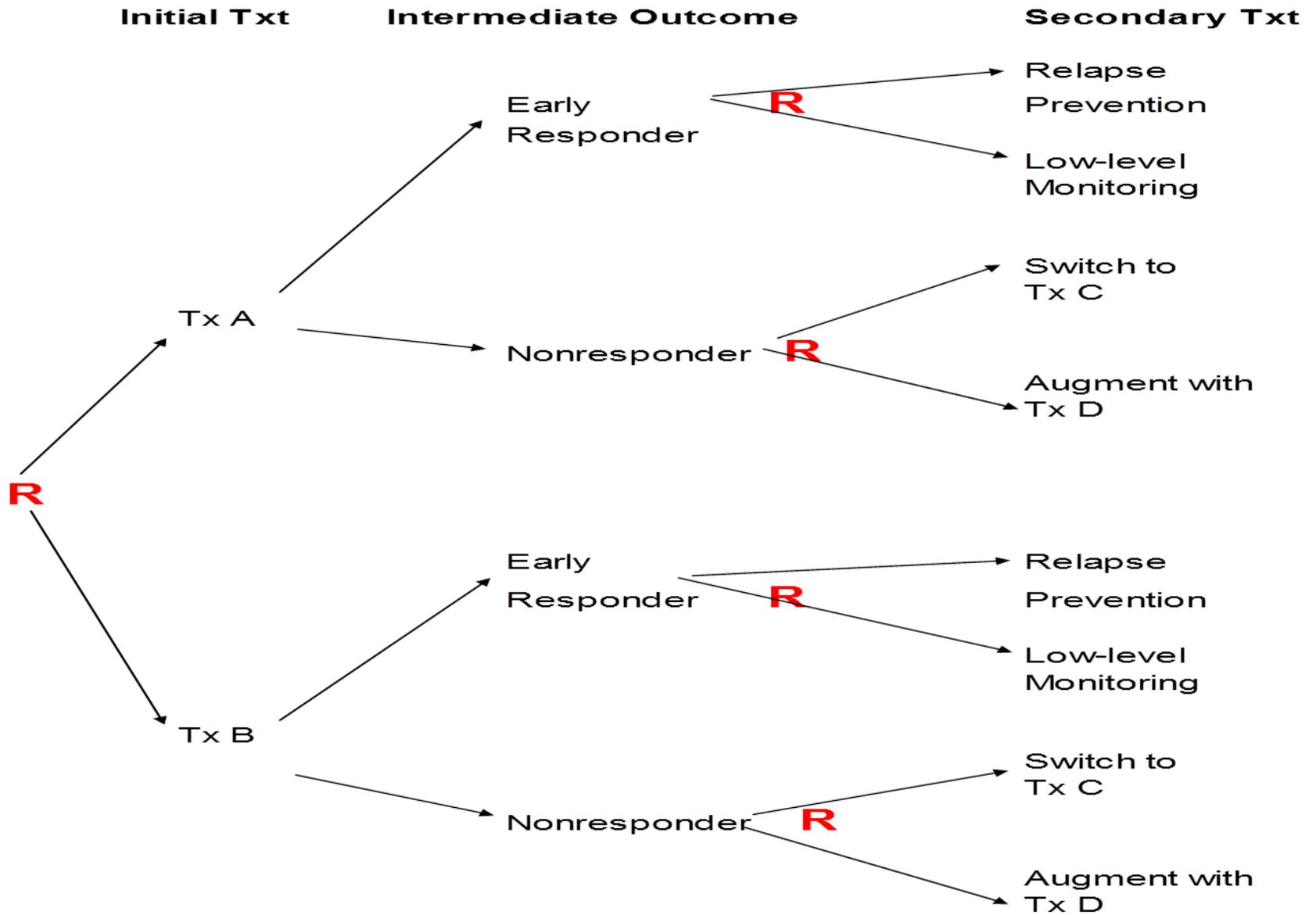
- Multi-stage trials; same subjects throughout
- Each stage corresponds to a critical decision point
 - Pre-specified measure of responsiveness
- Treatment options at randomization restricted depending on history of responsiveness
- Subjects randomized to set of treatment options

The goal of a SMART is to inform development of adaptive intervention strategies

SMART Designs: Critical Decisions

- Usually 2-3 critical decisions to address, e.g.,
 - Sequencing decisions: Which treatment to try first? Which treatment to try if sign of nonresponse?
Which treatment to try if subject doing well?
 - Timing decisions: How soon do we declare nonresponse? How soon do we declare response?
- Which decisions are most controversial or need investigation?
- Which decisions are likely to have the biggest impact on the outcome?

Sequential Multiple Assignment Randomization



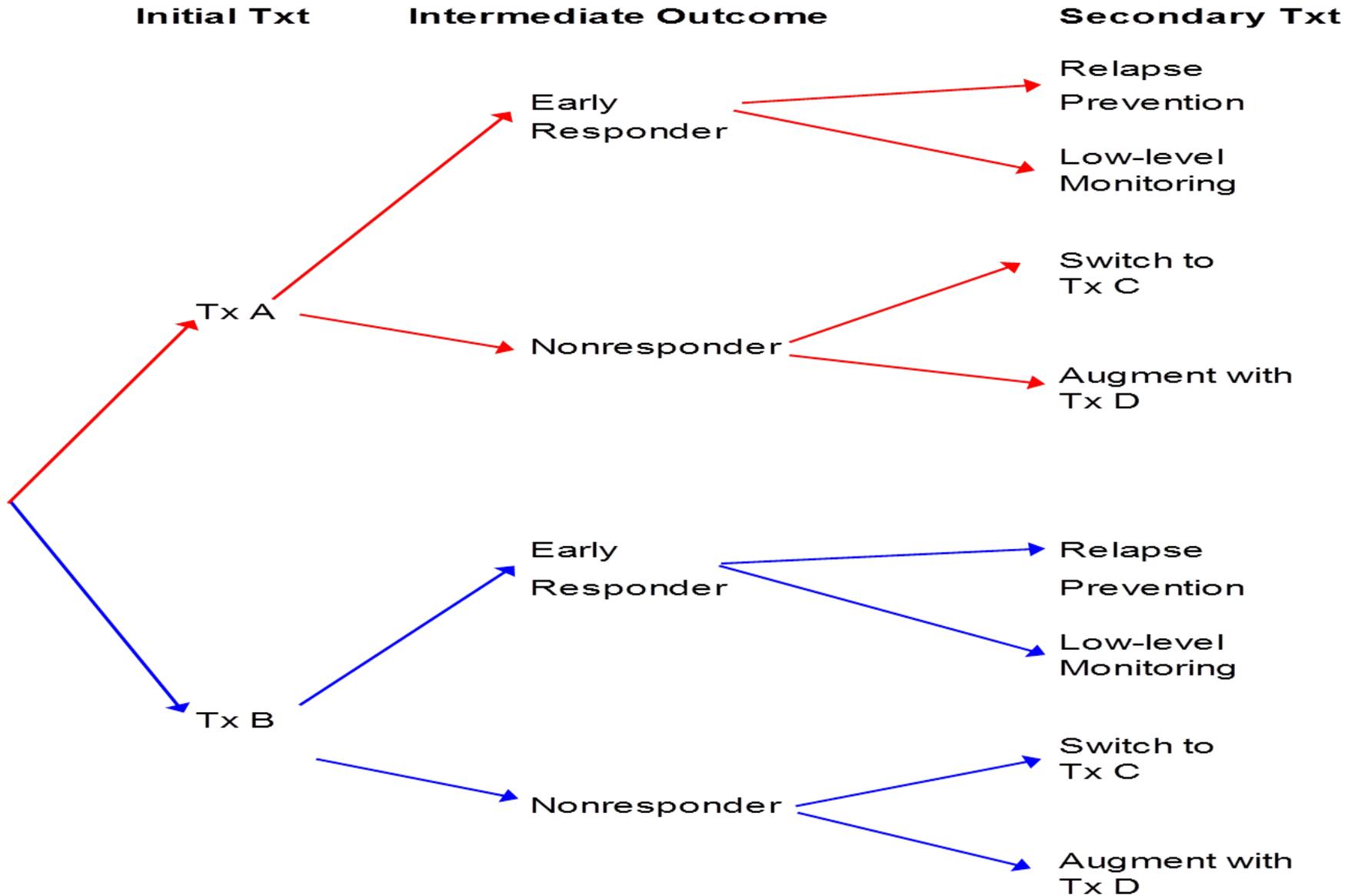
SMART and the KISS principle

- *Power for simple important primary hypothesis*
- At each stage (critical decision point), restrict class of interventions based on ethical, feasibility or strong scientific considerations
- For implementation strategies define response based on an outcome under provider control
- Collect intermediate outcomes that might be useful in ascertaining for whom each intervention works best (inform adaptive intervention)

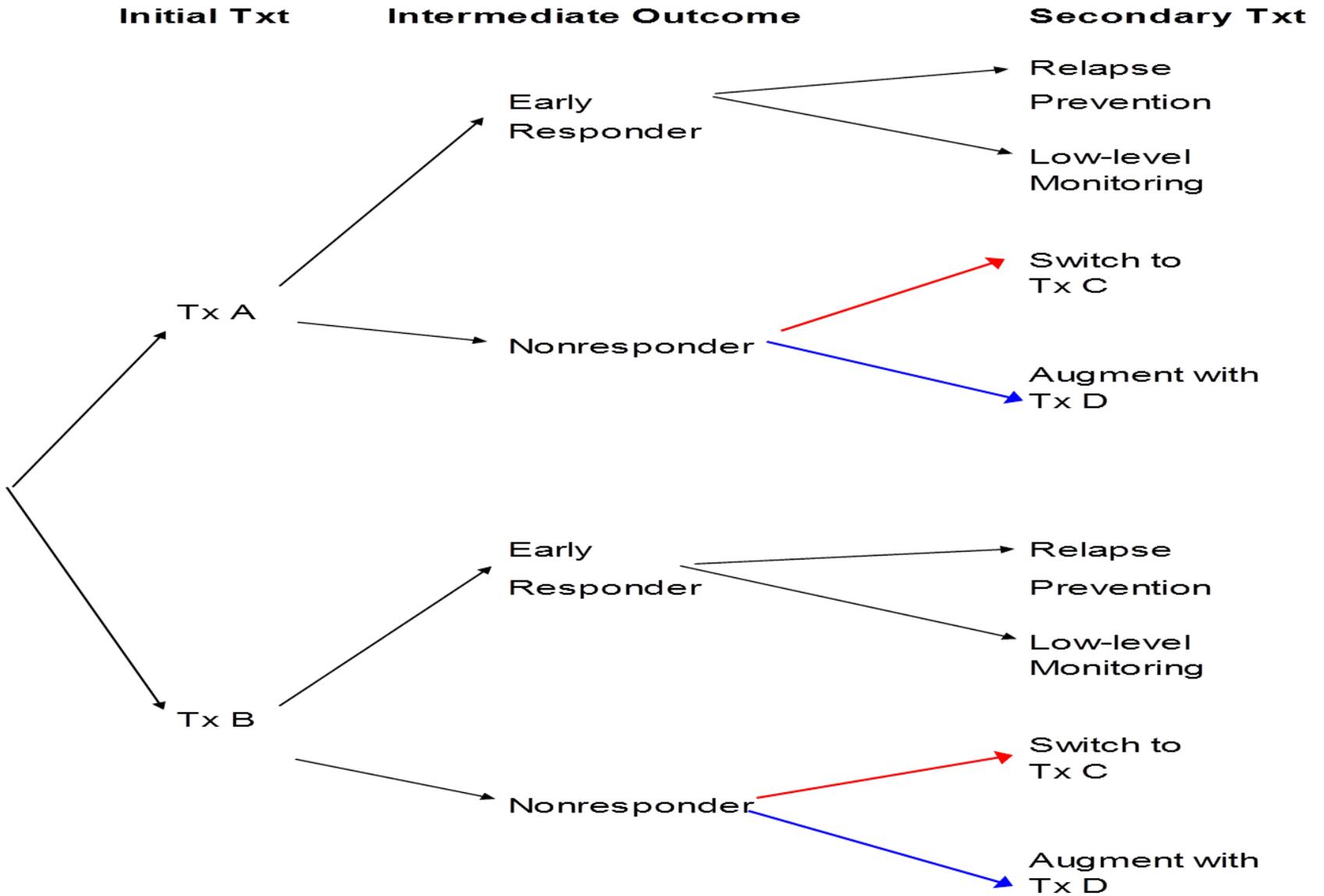
SMART and Primary Hypotheses

- EXAMPLE 1: (*sample size is highly constrained*):
Hypothesize that initial treatment A results in better outcome than the initial treatment B
- EXAMPLE 2: (*sample size is less constrained*):
Hypothesize that switch to treatment C results in better outcomes than an augment with treatment D

EXAMPLE 1



EXAMPLE 2



Adaptive Interventions

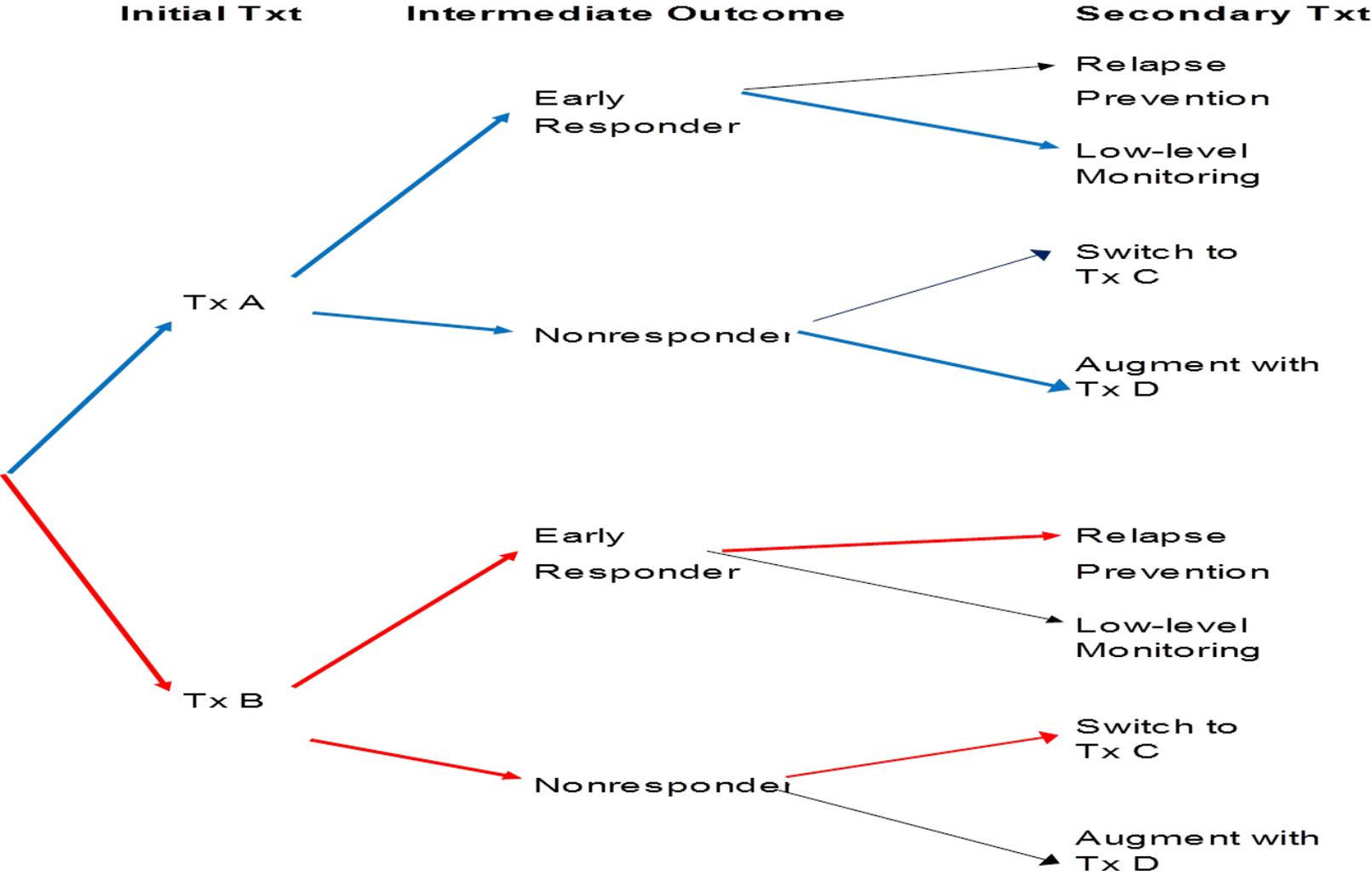
Sequence of individually tailored decision rules that specify whether, how, and when to alter the intensity, type, dosage, or delivery of treatment at critical decision points in the medical care process.

Adaptive Interventions operationalize sequential decision making with the aim of improving clinical practice
aka: dynamic treatment regimes, adaptive treatment strategies, treatment algorithms, structured treatment interruptions, ...

Example 3: Embedded Adaptive Intervention in a SMART Study

- Hypothesize that embedded adaptive treatment strategy 1 (in blue) results in improved outcomes compared to embedded adaptive treatment strategy 2 (in red)

EXAMPLE 3



Why SMART Designs → Adaptive Interventions for Implementation Research?

- Heterogeneity of practices/providers
- Not all barriers/facilitators observable
- Deliver implementation strategies where needed
- React to non-responsiveness/limited uptake
- Reduce implementation burden; use only what is necessary (“Chevy vs. Cadillac”)
- Sift through available implementation strategies
 - ⇒ More site-specific attention over time
 - ⇒ Improving sustainability

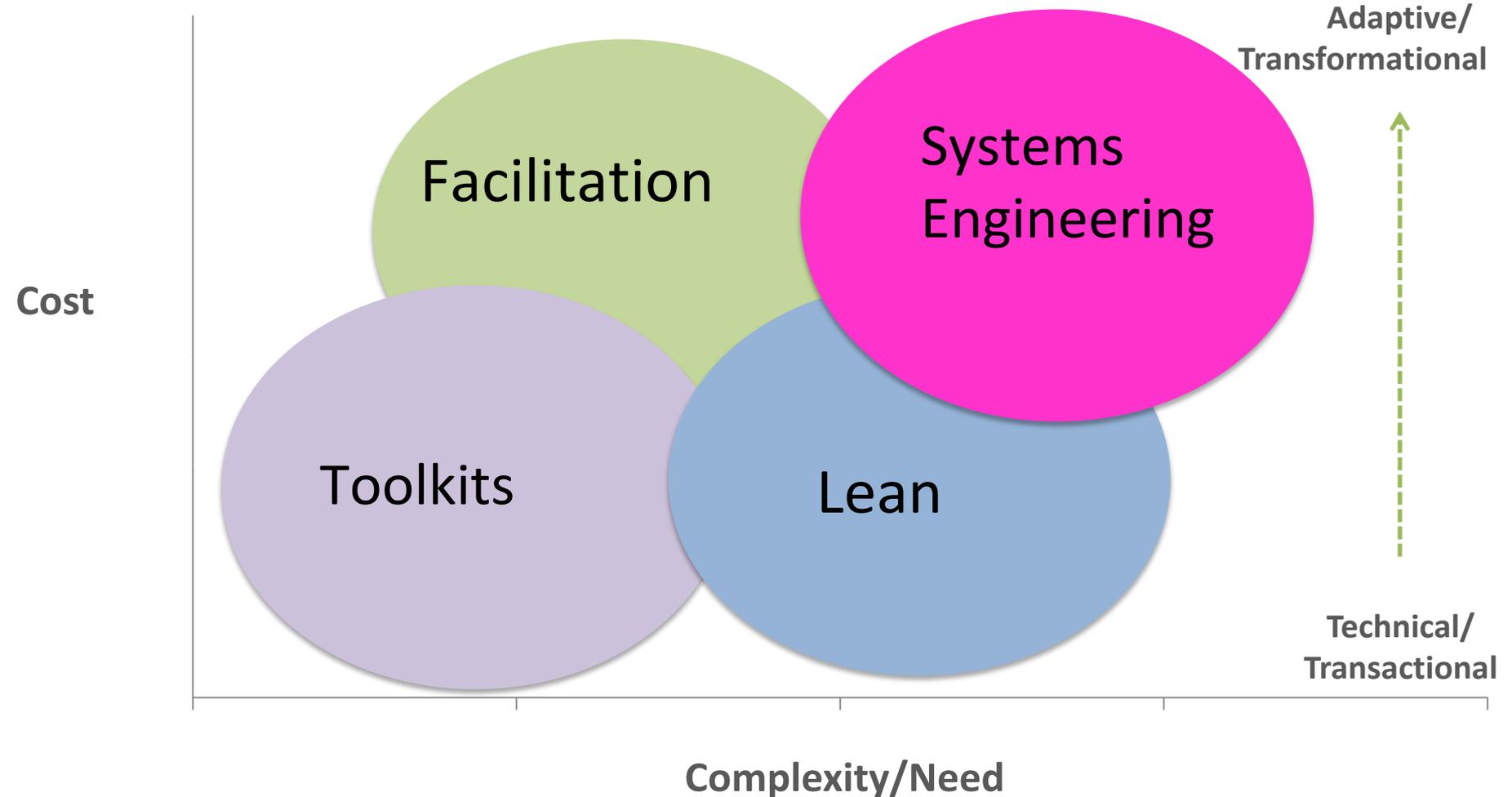
Implementation Strategies

Highly-specified, systematic processes used to help promote use of treatments/practices, often at the clinic or provider level, into usual care settings

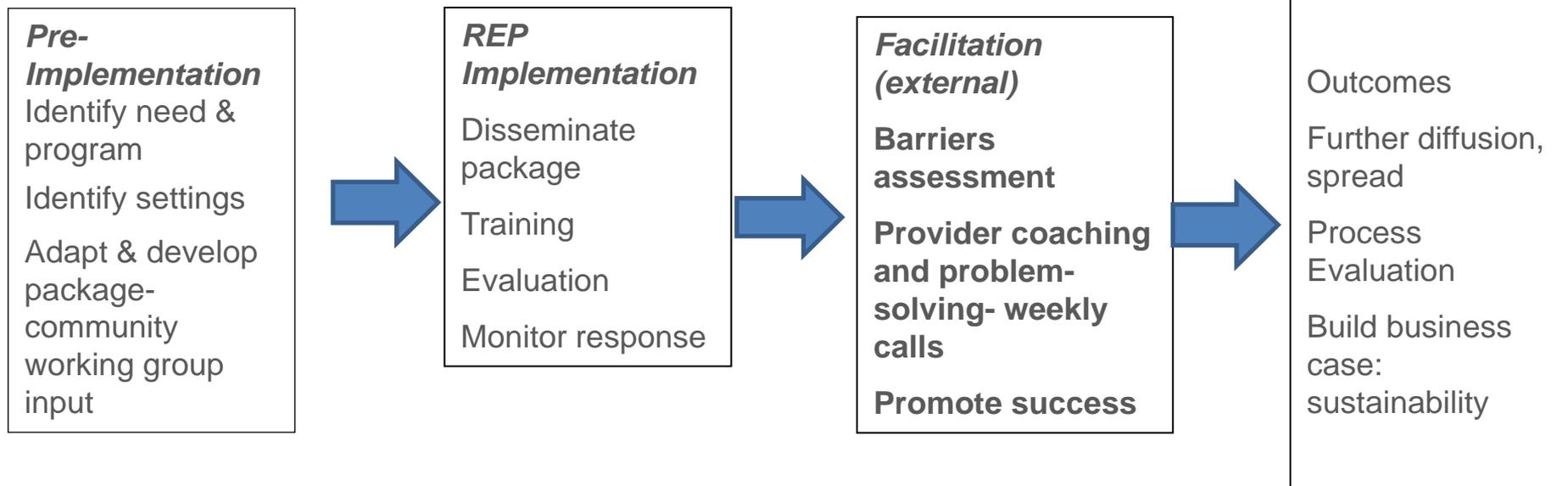
Examples:

- Evidence-based Quality Improvement (EBQI)
- Blended Facilitation: Promoting Action on Research Implementation in Health Services (PARiHS)
- Getting to Outcomes (GTO)
- Enhanced Replicating Effective Programs (REP)

Implementation Strategies: Current Landscape



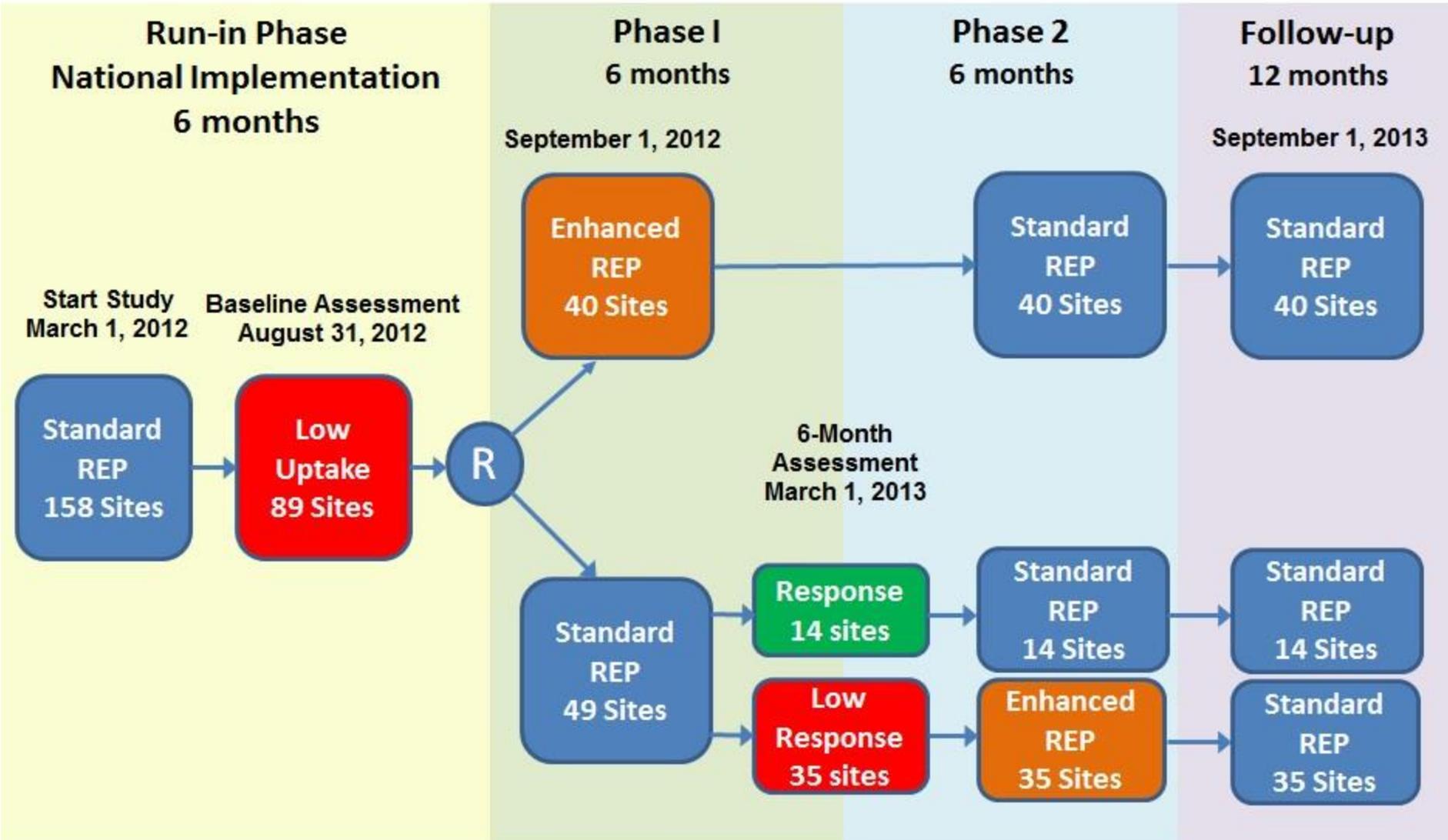
Example: Enhanced REP Implementation Strategy



Enhanced REP National Adaptive Implementation Strategy (Re-Engage)

- Determine, among VA sites not initially responding to a standard implementation strategy (REP), the effect of adding Facilitation (Enhanced REP) immediately versus delayed on Re-Engage program uptake, patient use
- Two-arm cluster randomized trial taking advantage of a natural experiment of national program rollout
 - REP initially used to implement program in 158 sites
 - 89 non-responding sites randomized to receive added External Facilitation or continue standard REP

Re-Engage Study Design



Re-Engage Program

1. Local Recovery Coordinators received list of Veterans with SMI who dropped out of care with last known patient contact information
2. Attempt to contact Veteran to assess status
3. For successful contacts – assess clinical needs and schedule VA appointment if Veteran desires to return to care
4. Document efforts in a web-based registry*

* Non-response: sites with < 80% of patients with updated clinical status documented within 6 months of list receipt

Implementation Strategies

Standard REP

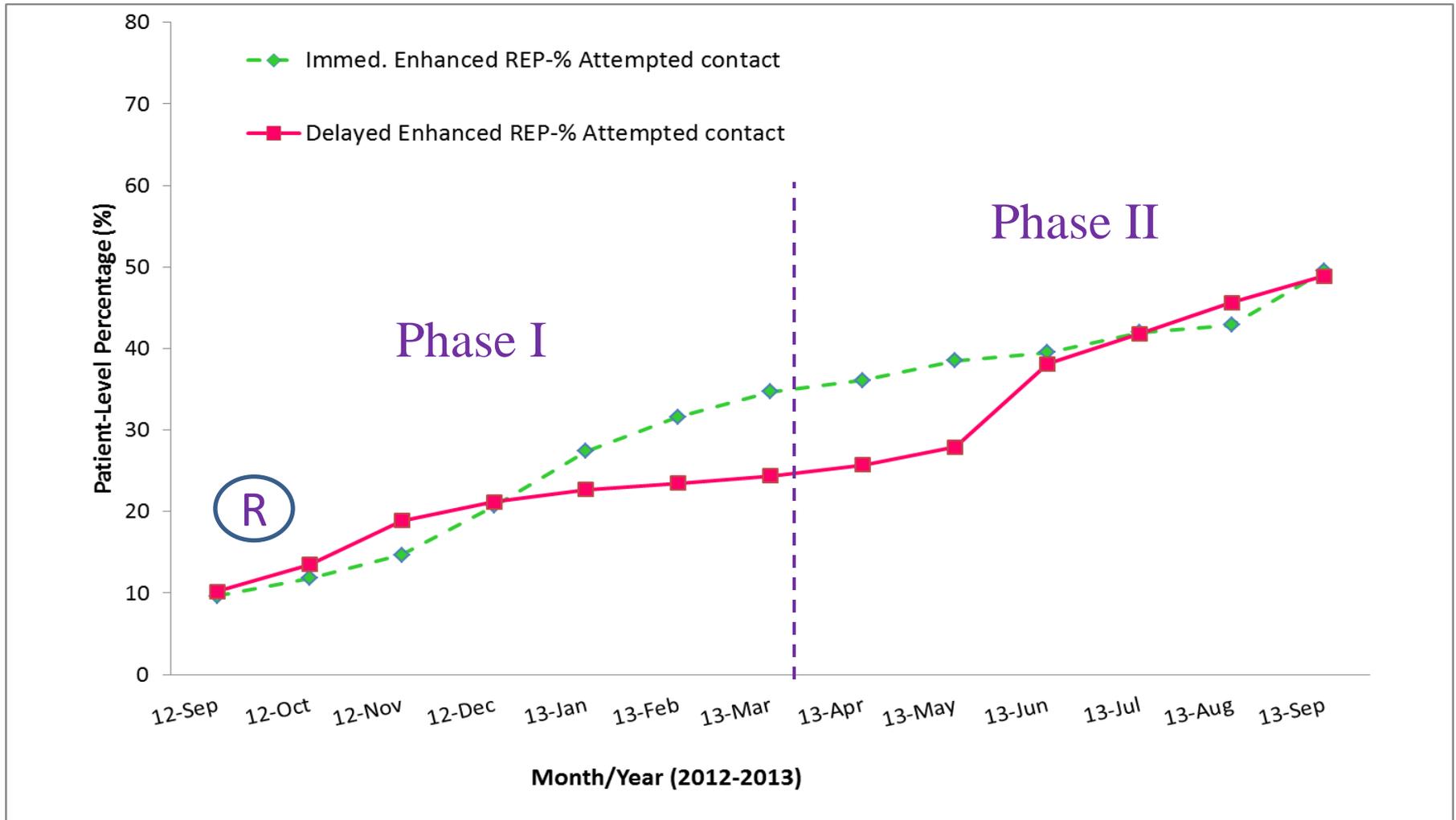
- Package (toolkit, guide)
- Training (calls, website)
- Brief technical assistance
- Uptake monitoring reports

Enhanced REP*

- Package (toolkit, guide)
- Training (calls, website)
- Brief technical assistance
- Uptake monitoring reports
- ❖ Needs Assessment
- ❖ Garner local support
- ❖ Identify problems/barriers
- ❖ Problem-solve/action plan
- ❖ Feedback/link to resources

* External facilitation by 3 doctoral-level mental health implementation consultants

12 Month Uptake Results



Is External Facilitation Enough?

(Building an adaptive implementation strategy- SMART)

- Added External Facilitation in Enhanced REP not consistent across all sites (Kilbourne, 2014)
- Little impact on patient-level use
- External Facilitation relatively low-cost (One “dose” of 6-month Facilitation =7.3 hours per site)
- Some sites might need additional internal agent to address local barriers to treatment adoption (Kirchner, 2014)

SMART Trial: Adaptive Implementation of Effective Programs Trial (ADEPT)

Primary Aim: Among sites not initially responding to REP to implement collaborative care program, sites receiving External and Internal Facilitator (REP+EF/IF) vs External Facilitator alone (REP+EF):

1. Improved 12-month patient outcomes (QOL, sx)
2. Improved uptake (# collaborative care visits)

Secondary Aims:

- Effect of continuing REP+EF versus adding IF
- Effect of continuing with REP+ EF/IF for longer time period

ADEPT Design

- 60 community clinics (1200 patients) from Michigan and Colorado
- Sequential Multiple Assignment Randomized Trial (SMART) design
- Non-response, within 6 months:
 - <50% patients enrolled by provider in collaborative care program AND
 - Enrolled patients completing <75% collaborative care sessions

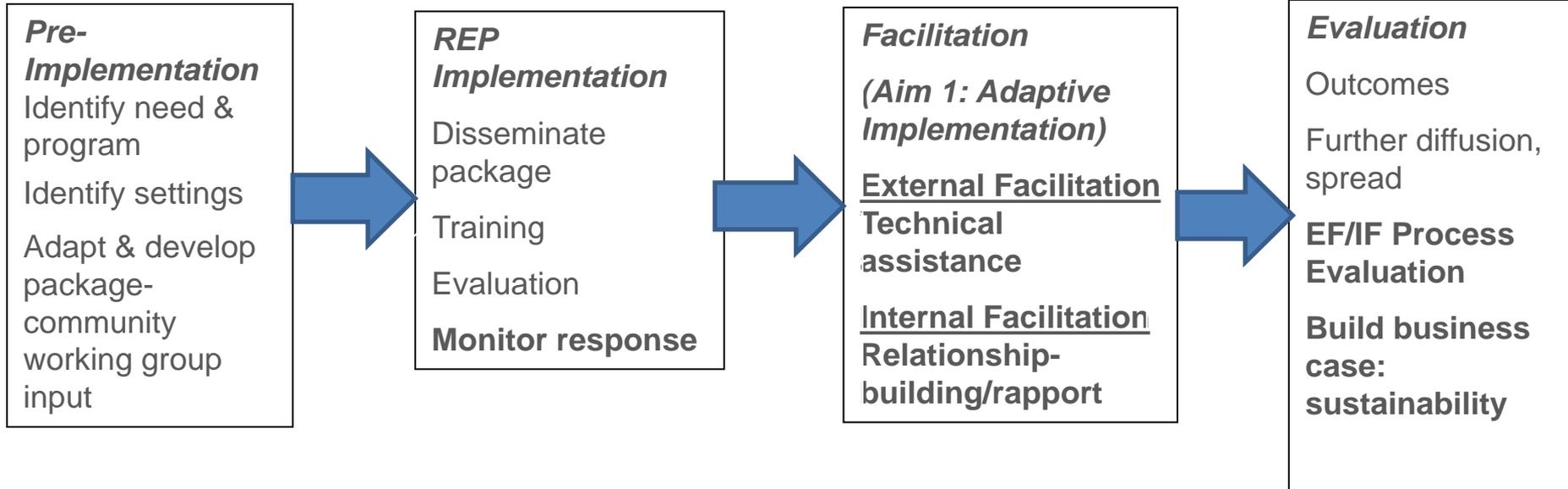
Reference: <http://www.implementationscience.com/content/9/1/132>

ADEPT: Implementation Strategies

- External Facilitator (EF): coaching in technical aspects of clinical treatment or intervention
- Internal Facilitator (IF): on-site clinical manager
 - Direct reporting line to leadership
 - Some protected time
 - Address unobservable organizational barriers
 - Develop sustainability plan with leadership

Enhanced REP

Adding Facilitation based on PARiHS Framework



External facilitator (EF): off-site, research team, technical assistance

Internal facilitator (IF): on-site provider with direct reporting line to leadership, protected time to build relationships, address unobservable organizational barriers, develop sustainability plan

Kilbourne AM et al. 2013; Goodrich et al. 2012

ADEPT Design

Study Start

Run-In Phase

All sites offered REP to implement EBP;
Patients start EBP by **Month 3**

Month 6 Assessment

Phase 2

Follow Up

Month 18 and 24 Assessments

REP
k=80 sites

Non-Responders
(<10 out of 20 enrolled patients receiving EBP or <75% sessions completed)
k=60 sites

R

Add External Facilitation
REP+EF
k=30 sites
N=600 patients

Responders

Non-responders

R

Continue follow-up assessments

Continue REP+EF

Add IF (REP+EF/IF)

Continue follow-up assessments (A)

Continue REP+EF (B)

Continue REP+EF/IF (C)

Add Internal & External Facilitation
REP+EF/IF
k=30 sites
N=600 patients

Responders

Non-responders

Continue follow-up assessments

Continue REP+EF/IF

Continue follow-up assessments (D)

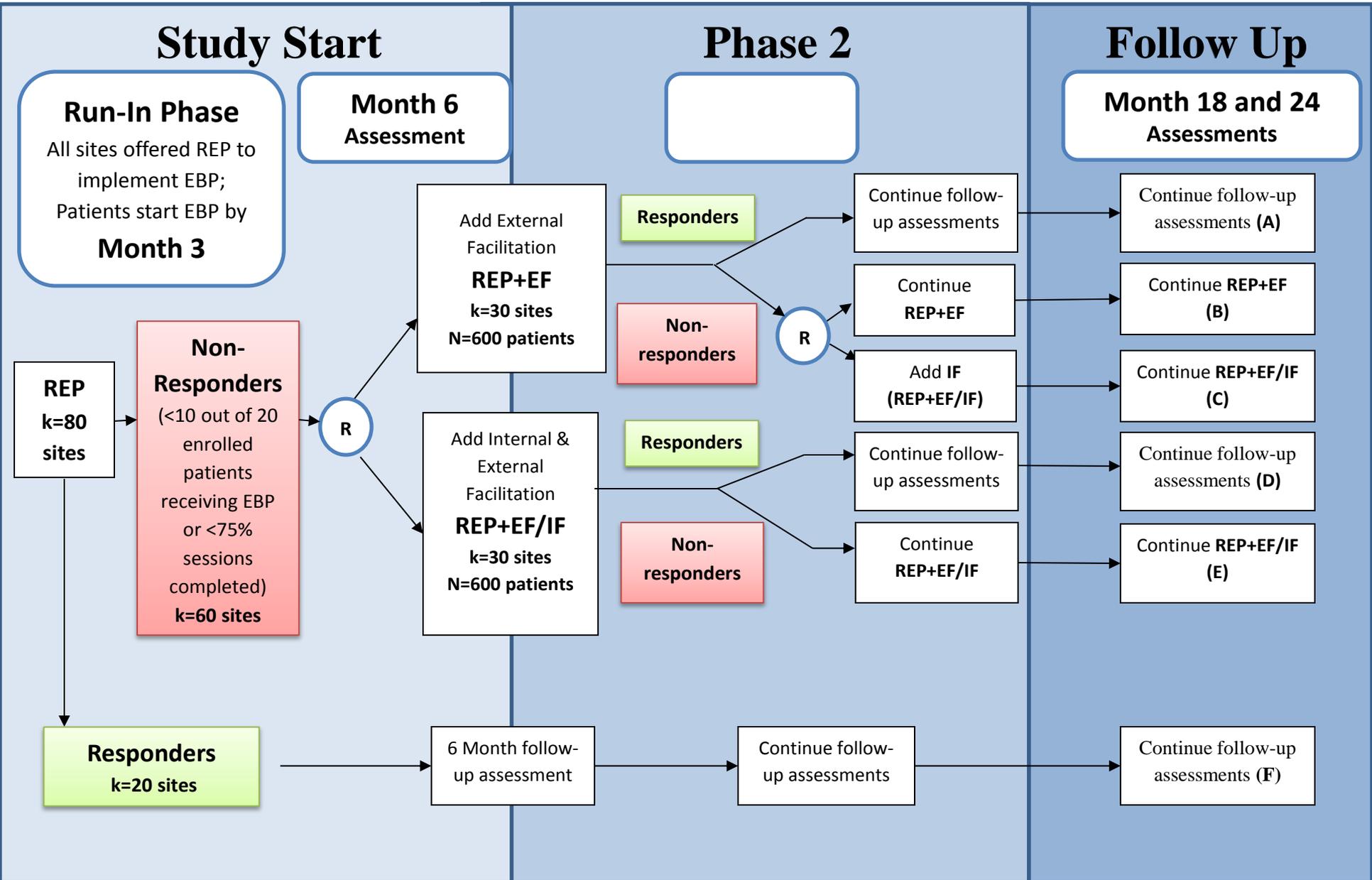
Continue REP+EF/IF (E)

Responders
k=20 sites

6 Month follow-up assessment

Continue follow-up assessments

Continue follow-up assessments (F)



Challenge/Opportunities

- Multiple sites needed (randomization unit)
- Valid and feasible non-response, outcome measures
- Delayed effects: timing of response measure
- Catching a moving train- building SMART/adaptive trials into national roll-outs
- Beyond toolkits: transformational and intrinsic motivators towards EBP uptake, sustainability

Questions?

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