

# Beyond Efficacy—Innovative Designs for Effectiveness

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# 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, **M**ultiple **A**ssignment, **R**andomized **T**rial

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

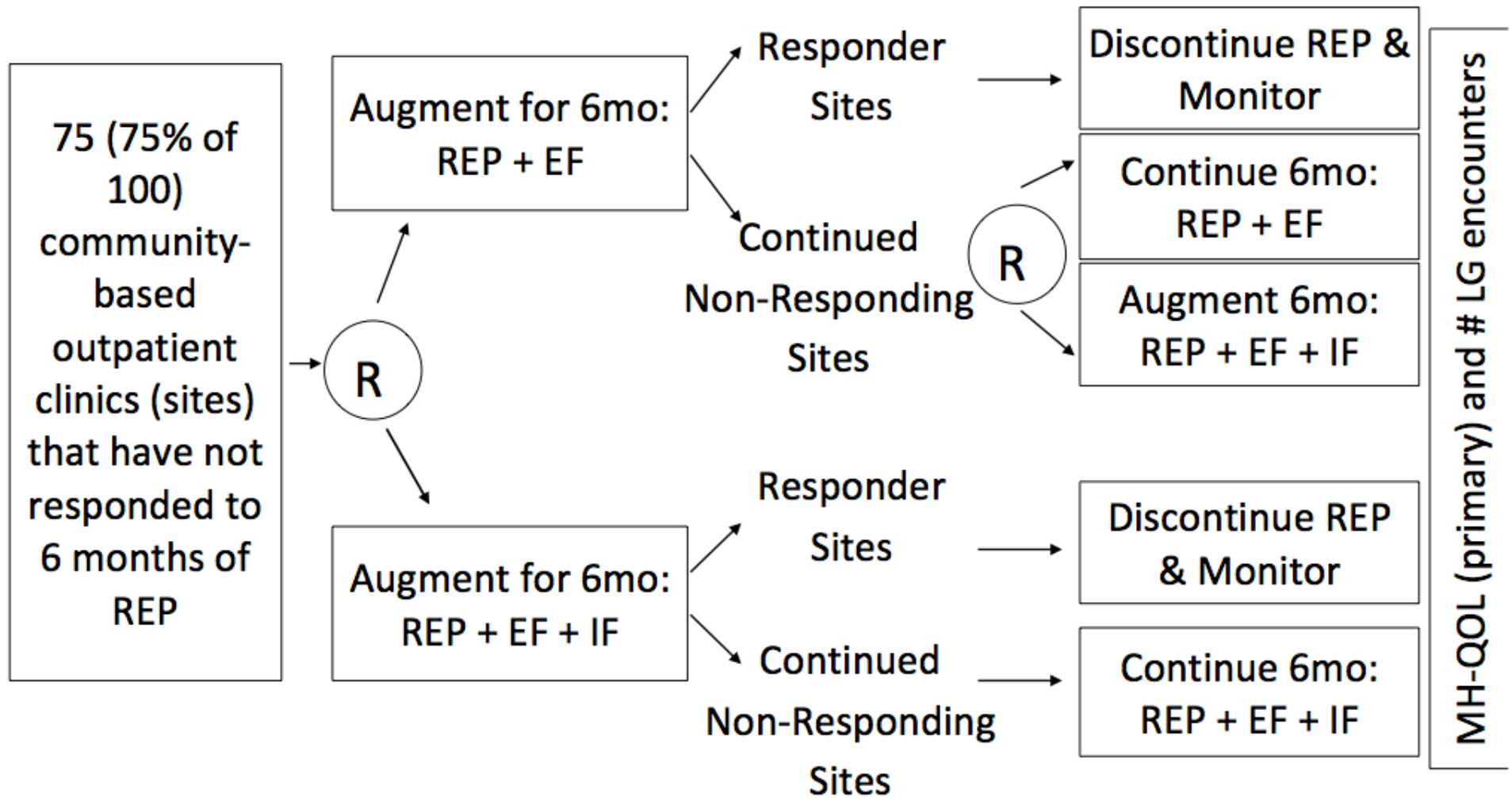
- (1) Which treatment to provide to sites that are insufficient responders to standard REP?
- (2) Which treatment to provide to the sites that continue to show non-response?

# SMART REP

Month 6

12

18-24



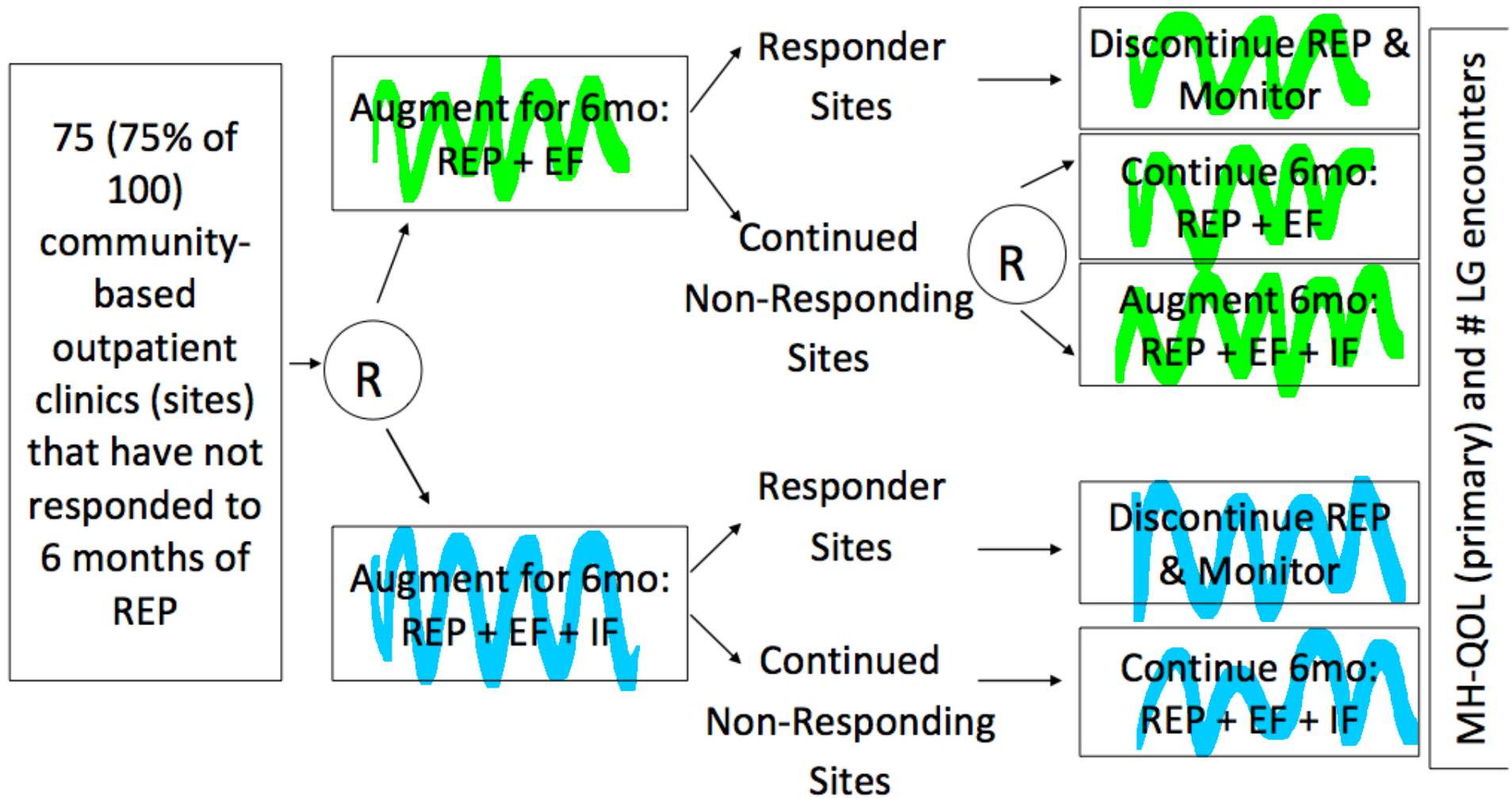
PI Amy Kilbourne

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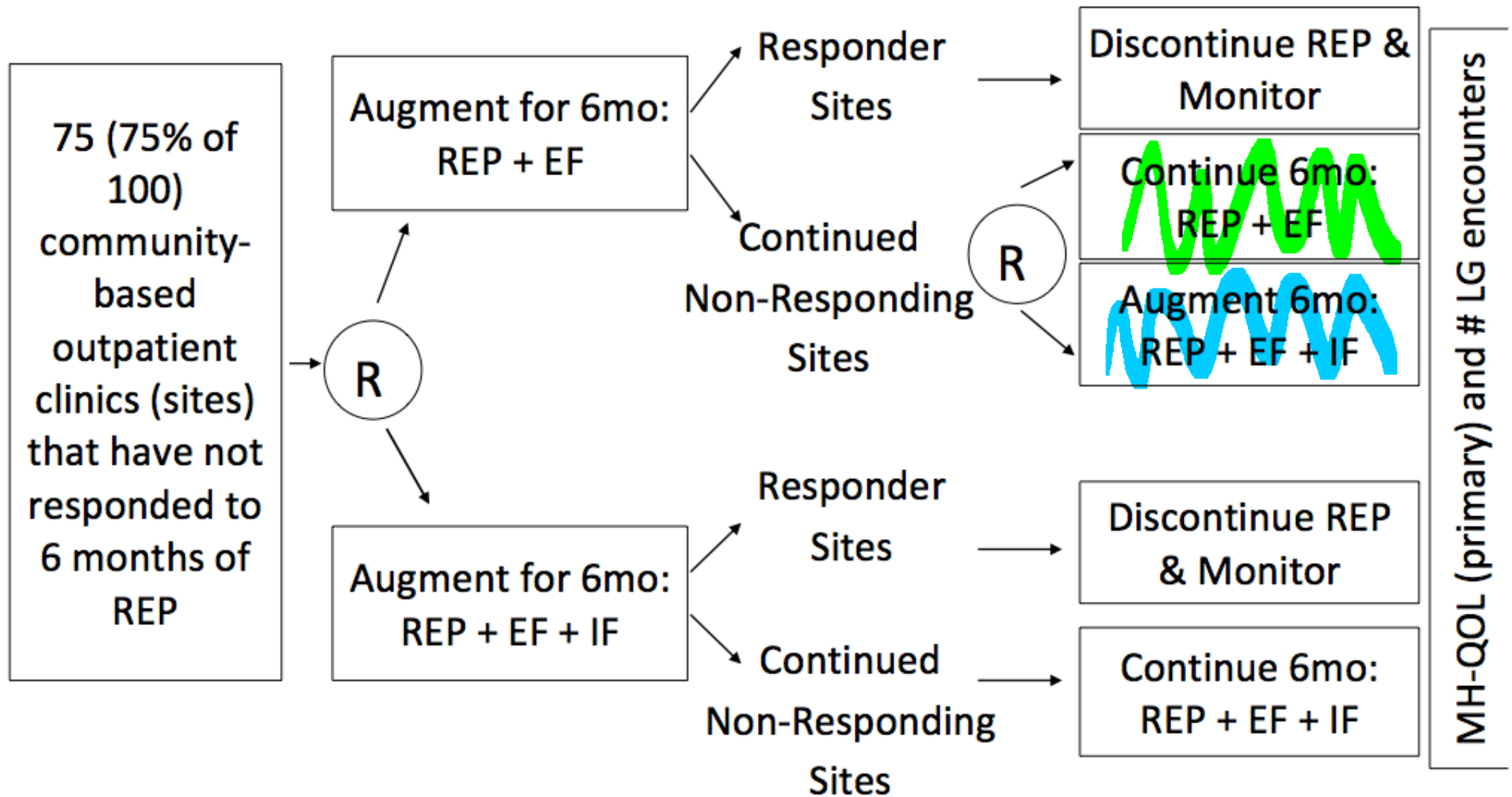


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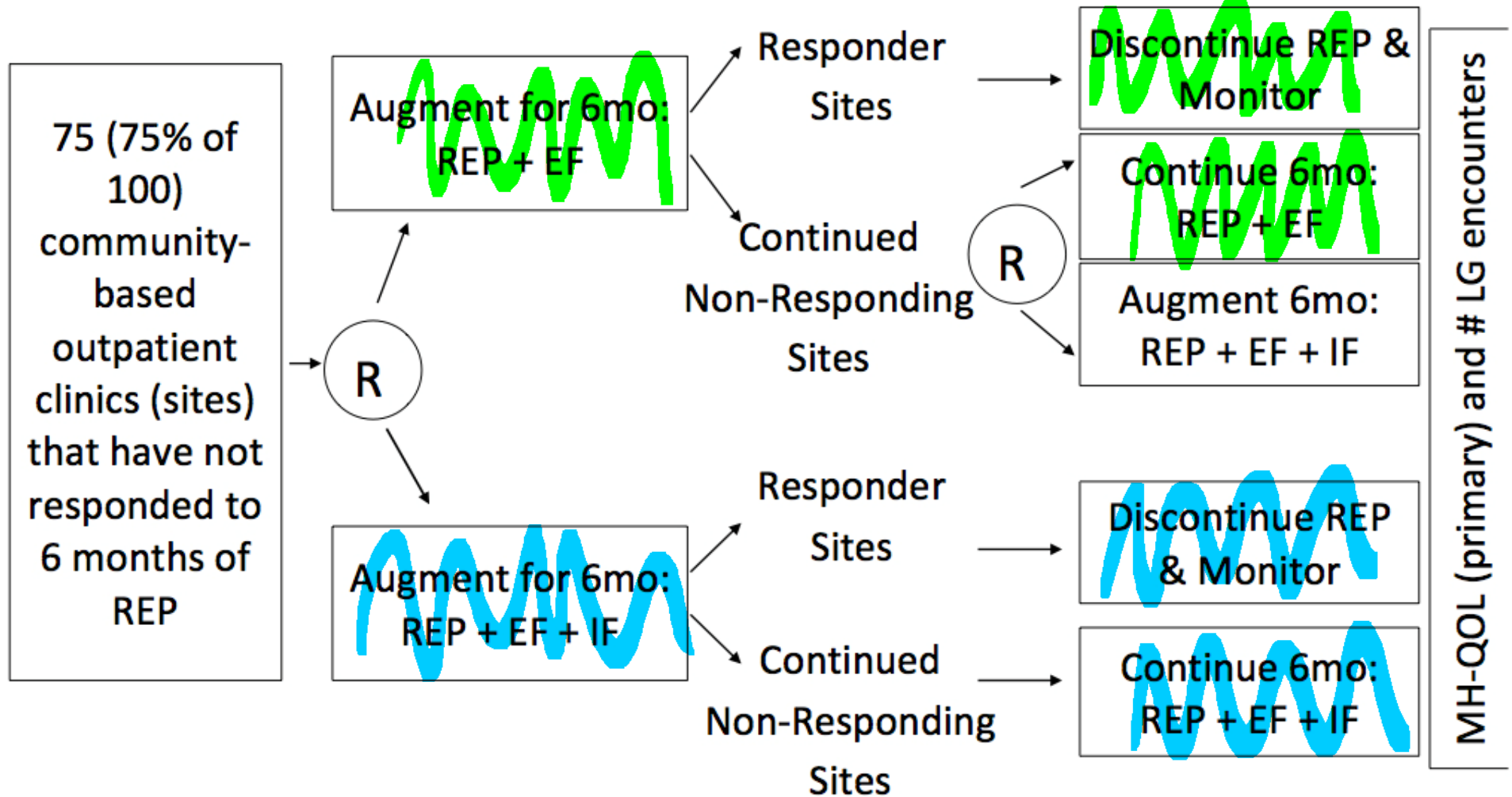
PI Amy Kilbourne

# SMART REP

Month 6

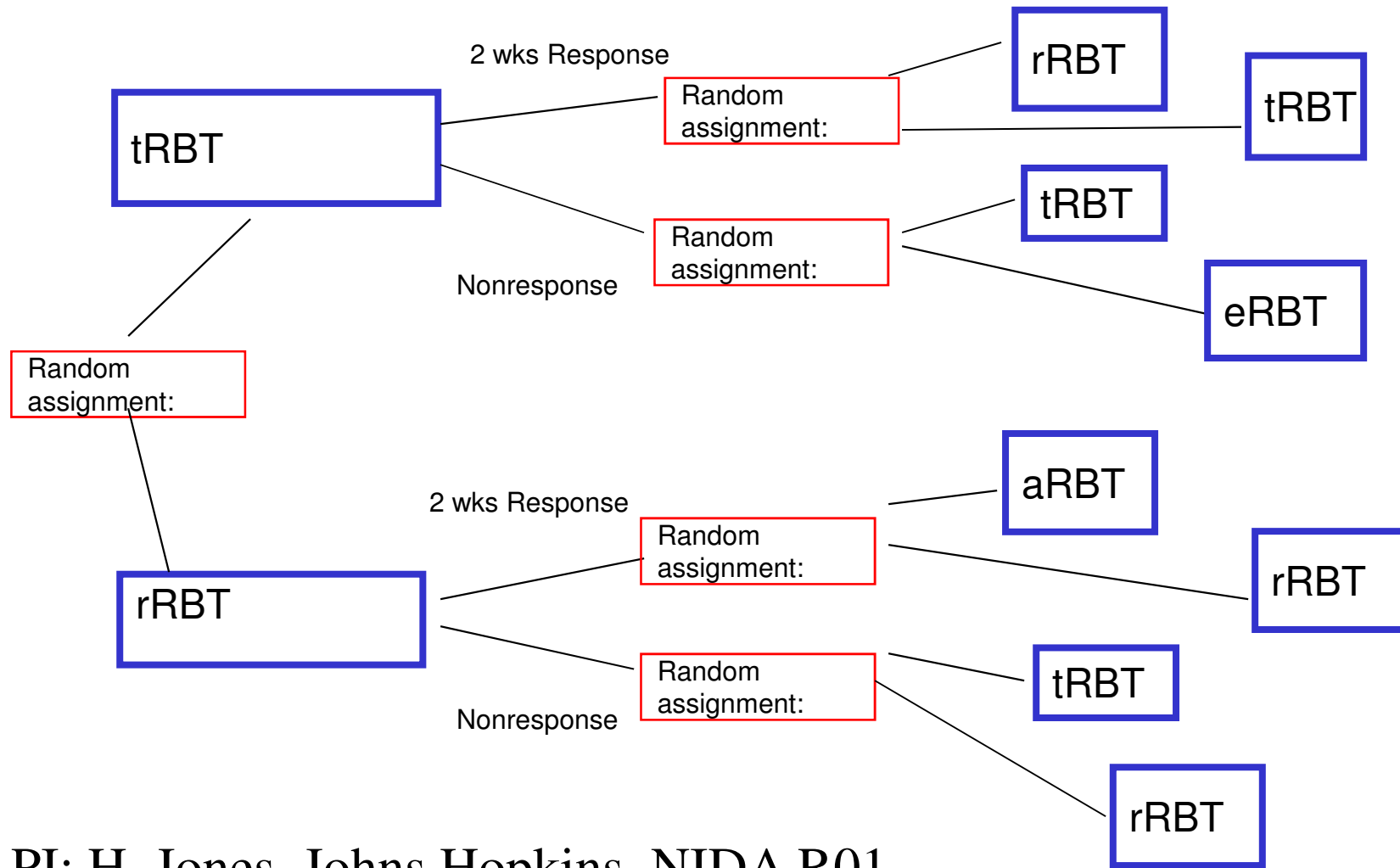
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PI Amy Kilbourne

# 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>

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