The Stepped Wedge Cluster Randomized Trial Design: Opportunities for Implementation Research and Practical Challenges of Its Application

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Grand Rounds: A Shared Forum of the NIH HCS Collaboratory and PCORnet
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Disclosures

• Grants
  – PCORI
  – NIH, NHLBI
  – AHA

• RWI
  – Novartis
  – J&J, Janssen
  – St. Jude

• First and foremost, I am a CLINICIAN.
Overview

1. DECIDE-LVAD Trial Case Study
2. Stepped Wedge Design
3. Applying Stepped Wedge
Part 1: 
DEcIDE-LVAD trial case study

A Multicenter Trial of a Shared Decision Support Intervention for Patients and their Caregivers Offered Destination Therapy for End-Stage Heart Failure

Principal Investigator
Larry A. Allen, MD, MS

Organization
University of Colorado Denver

Funding Announcement
Communication and Dissemination Research

Project Budget
$2,052,964

Project Period
3 Years

Year Awarded
2014
DECIIDE-LVAD Trial

**Objective:** Understand the **effectiveness and implementation** of a shared decision support intervention for advanced heart failure patients considering DT LVAD.

1. Decision Aids (video and pamphlet)
2. Decision Support Coaching
Evaluation Framework

• **Reach:**
  – % eligible patients and caregivers

• **Effectiveness**
  – Increased knowledge
  – Value-treatment concordance

• **Adoption**
  – Taken up by key personnel

• **Implementation**
  – Consistently used

• **Maintenance**
  – Continued use after trial completion
Evaluation Framework

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Evaluation Procedures

• **Reach & Effectiveness:**
  Assess decision quality among patients and caregivers
  – Patients and caregivers
  – Surveys:
    • Baseline
    • 1 month
    • 6 months

• **Adoption, Implementation & Maintenance**
  Evaluate education and consent procedures at sites
  – Clinicians and staff at each site
  – Qualitative interviews:
    • Baseline
    • Post-intervention implementation
    • Post-study completion
  – Checklist of education materials/procedures for each patient

**Phases**

- **Control:** current education and consent process
- **Intervention:** new shared decision support (including decision aids)
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DECIDE-LVAD Trial

Key Considerations:

1. Desire to evaluate implementation in multiple real-world settings
2. Specific small population (DT LVAD 15-40 per site/year)
3. Max 5-6 sites due to budget constraints ($2M)
4. Randomization needed to assess effectiveness
5. Intervention involves both patients and clinicians/program
Threat of Diffusion (Contamination)

- Classic patient-level randomization
Site-Level Approach

- **Cluster randomization**
  - Groups or sites randomized to intervention or control
  - **Advantages**
    - Limits diffusion across individuals
    - Logical for interventions that apply to staff / programs
  - **Disadvantages**
    - Requires slightly higher number of participants for power
    - Must account for homogeneity among groups
    - Challenges when only small number of clusters are targeted
Study Design Options for DECIDE-LVAD Trial

- **Classic patient-level randomization**
  - Intervention is patient AND program-based; not at individual-level
  - Diffusion among participants at each site is probable

- **Cluster randomization**
  - Concerns about statistical power with only 6 total sites
    - 3 sites intervention, 3 sites control
  - Homogeneity of intervention participants and control participants

- **Stepped wedge cluster randomization** . . .
Part 2: Stepped Wedge Design

(a) Parallel cluster study

(b) Parallel cluster study with a baseline period

(c) Stepped wedge study

(d) Stepped wedge study including transition period
Stepped-Wedge Design

- A cross-over design where the different clusters switch at different time points
  - Clusters cross over in one direction only
    - typically from control to intervention
  - Clusters are randomized to an order in which they rollout the intervention

"waiting list design"
Stepped Wedge Design Ideal When...

- **Diffusion** of intervention to control participants is likely
- **Implementation** is a focus
  - Iterative adjustment possible at each phase
  - All clusters go through implementation (not half)
- **Staggered** rollout provides *logistical*, practical, or financial advantages
- **All sites** wish to receive the intervention
- **Gain in statistical power** is desired
  - Both *within* and *between* cluster differences
- Time trends are *not* expected OR study length is relatively short
Stepped Wedge Design

• However…
  – May extend the length of the study
  – Analysis is complex
  • Bulk of control happens early and bulk of intervention happens late, so need to control for temporal trends
Gambia Hepatitis Intervention Study

• Considered first use of “experimentally staged introduction” when an innovation could not be delivered to all groups concurrently

• Study started in 1986

• Investigate effectiveness of a vaccine for hepatitis B in preventing liver cancer and other chronic liver diseases
  – Vaccine rolled out in national infant vaccination program
  – A phased and random implementation of vaccine was used
  – Geographically defined areas of the country were randomized
  – Steps of 10-12 week intervals over 4 years

Systematic Review: 25 studies (pre 2011)

• Studies primarily in healthcare
  – also in education, criminal justice, social policy, and technology
• Terminology: 12 studies used term “stepped wedge”
  – Others: delayed intervention, delayed treatment, waiting list, phased implementation, phased enrollment, staggered implementation, crossover
• Half of studies published 1987-2006; other half between 2007-2009; indicating recent rise in use. (Multiple PCORI studies using).
• Motivation for stepped wedge design use included:
  – Methodological  – Logistical
  – Resource limitations  – Ethical
  – Social acceptability  – Political acceptability
• Characteristics of design varied considerably across studies
  – Number of steps – 2 to 36 steps
  – Period between steps – 12 days to 1.5 years

Part 3: Applying Stepped Wedge

A decision aid for Left Ventricular Assist Device (LVAD) for Destination Therapy
A device for patients with advanced heart failure

Exploring Options

You are being considered for an LVAD. This booklet is designed to help you understand what an LVAD is and to help you, your family, and your doctor think about what is best for you. Your values and goals are the most important factors in making a decision.

What are your current feelings about being considered for an LVAD?

Think about:
- how you want to live the rest of your life
- your hopes and fears
- your biggest questions
### Figure 5. Stepped wedge randomization scheme.

<table>
<thead>
<tr>
<th>Site</th>
<th>Pre 4 months</th>
<th>Phase 1 4 months</th>
<th>Phase 2 4 months</th>
<th>Phase 3 4 months</th>
<th>Phase 4 4 months</th>
<th>Post 4 months</th>
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<tbody>
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<td>1 Random Site</td>
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- **Control Period**
- **Roll-Out**
- **Intervention Period**
Data collection same during control and intervention periods:

- **Effectiveness**: patients and caregivers surveyed
- **Implementation**: clinicians and programs assessed

- **Funding Starts**: (12.1.14)
- **All-Site Kickoff Meeting**: (3.20.15)
- **Patient/Caregiver Data Collection Starts – Control Period**: (5.31.15)
- **Site Baseline Interviews (1-mo pre-intervention)**
- **Intervention Begins**
- **Site Post-Implementation Interviews (3-9 months post-intervention)**
- **Patient/Caregiver Data Collection Ends**: (7.1.17)
- **Site Post-Study Interviews**
- **Funding Ends**: (11.30.17)
Advantages

• 168 dyads
• Semi-randomized (CU first)
• Every site from control to intervention (6 sites, not 3)
• Study personnel tasks better spread out
  – Start up and data capture at beginning
  – Intervention later and in stages
• Core intervention constant, learned implementation
Disadvantages / Challenges

• Confounding Factors:
  – Validity could be challenged by temporal trends
    • LVAD technology changing
    • Shared decision making becoming more accepted

• Diffusion:
  – Sites may start using intervention principles during the control phase
Disadvantages / Challenges

• Enrollment Consistency:
  – Must have consistent enrollment across time intervals – even
    number of participants in control and intervention phases
    • Could consider triggering steps on number of enrollees or
      events rather than time

• Practical:
  – All sites start and end at the same time
    • no staggered start dates as can happen with patient or cluster
      randomization
  – Must have committed sites
    • Contracts and IRB executed promptly
    • Agreement to implement intervention at designated time
Thank You

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