Transforming Implementation & Improvement Into Science: A skills building series

February 28, 2018
Engage with CIIS

Guide & Innovate
• Provide guidance, support & innovation to design projects that rigorously evaluate the effectiveness of efforts to implement change

Accelerate & Promote Sustainability
• Identify strategies that accelerate the adoption & promote sustainability of effective healthcare interventions

Educate
• Provide implementation & improvement sciences education to faculty, trainees, students
Overview: Implementation & Improvement Sciences

Implementation Science
Focuses on optimal strategies to promote evidence uptake in real-world settings

Addresses
Did stakeholders perform the desired endeavor?
Why or why not?
How well?

Aims
Translate research into practice
Systematically implement evidence-based practices

Improvement Science
Focuses on rigorously measuring outcomes associated with efforts to improve care delivery

Addresses
Did the new endeavor measurably improve desired outcomes?

Aims
Improve the quality of healthcare
## Identifying High-Quality Projects

<table>
<thead>
<tr>
<th>Main NIH Criteria</th>
<th>Issues Applying NIH Criteria to Implementation &amp; Improvement (IIS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Overall impact</td>
<td>• Broad, non-specific to IIS</td>
</tr>
<tr>
<td>• Significance</td>
<td>• Criteria could be operationalized to better describe high-quality IIS</td>
</tr>
<tr>
<td>• Innovation</td>
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<tr>
<td>• Approach</td>
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<tr>
<td>• Investigator team</td>
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<td>• Research environment</td>
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<tr>
<td>Proctor’s 10 Key Ingredients</td>
<td>NIH Criteria</td>
</tr>
<tr>
<td>-----------------------------------------------------</td>
<td>------------------------------------------------</td>
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<tr>
<td>1. Quality/care gap</td>
<td>Impact; Significance</td>
</tr>
<tr>
<td>2. Evidence-based treatment</td>
<td>Significance; Innovation</td>
</tr>
<tr>
<td>3. Conceptual model, theoretical justification</td>
<td>Approach; Innovation</td>
</tr>
<tr>
<td>4. Stakeholder priorities, engagement in change</td>
<td>Impact; Approach; Research Environment</td>
</tr>
<tr>
<td>5. Setting’s readiness to adopt new services</td>
<td>Impact; Approach; Environment</td>
</tr>
<tr>
<td>6. Implementation strategy/process</td>
<td>Impact; Significance; Innovation</td>
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<tr>
<td>7. Team experience with the setting, treatment,</td>
<td>Approach; Investigator Team</td>
</tr>
<tr>
<td>processes</td>
<td></td>
</tr>
<tr>
<td><strong>8. Feasibility of proposed research design</strong></td>
<td><strong>Approach; Investigator Team</strong></td>
</tr>
<tr>
<td>9. Measurement &amp; analysis section</td>
<td>Approach; Investigator Team</td>
</tr>
<tr>
<td>10. Policy/funding environment; support for</td>
<td>Impact; Significance</td>
</tr>
<tr>
<td>sustaining change</td>
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<table>
<thead>
<tr>
<th>Tentative Date</th>
<th>Session Title</th>
<th>Proposal Areas Addressed</th>
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<tr>
<td>10/25/2017</td>
<td>Identifying Your Implementation &amp; Improvement Sciences Research Question</td>
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<td>Implementation Strategies Versus Study Interventions</td>
<td>Implementation Strategy</td>
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<td><strong>Designing an Implementation &amp; Improvement Sciences Study</strong></td>
<td>Study Design, Measurement, Analytic Methods</td>
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<td>Stakeholder Engagement, Feasibility, Team, Policy Environment</td>
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Series Goal

Proctor’s 10 Key Ingredients

CIIS Educational Series

High-Quality Implementation & Improvement Sciences

Significant Contributions to Improve Care, Advance Fields
Designing an Implementation & Improvement Sciences Study

Allan Walkey, MD
Co-Director, CIIS
• Identify key considerations for selecting the best study design for implementation & improvement sciences (IIS) questions

• Discuss the strengths & weaknesses of different study designs
What Do You Mean, Design?

- Qualitative vs. Quantitative Methods?
  - No, these are analytic approaches
  - Can be applied to almost any design
  - Not a topic for today

- Efficacy vs. effectiveness vs. implementation vs. hybrid?
  - A little...We’ll discuss

We mostly mean:

How will you set up the project to gain knowledge?
What Can IIS Designs Address?

Any or multiple aspects of implementation, including:

- **Factors** affecting implementation
- **Process** of the implementation
  - Studying the strategies, not the interventions
- **Outcomes** of the implementation
  - e.g. comparative effectiveness of different strategies
- **End-Products** of the implementation
  - Effectiveness
You want to do something good

Traditional purviews of Implementation Science:
- Adoption
- Fidelity
- Sustainability...

Assessments
- Qualitative
- Quantitative

Are people doing what you want?

Implementation + Improvement

Are outcomes improving?

Traditional purview of Effectiveness +/- Improvement Studies
**Hybrid Studies**

- Evaluate both effectiveness & implementation strategies
  - Do not assume real world effectiveness of efficacious interventions
  - Can use most of the designs we will discuss

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
<th>Type 3</th>
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</table>
| • Testing effectiveness  
  • Also gather some data to inform future implementation | • Effectiveness & implementation strategies are tested simultaneously, with equal weight | • Testing implementation strategies  
  • Also gather some measures of effectiveness |

Hybrid Type 1: Primarily Testing Effectiveness

- Examine **patient function/symptoms as primary outcomes** in response to the intervention while also examining some implementation outcomes (often feasibility and acceptability of the implementation strategy).

- Implementation outcomes typically measured through qualitative or mixed methods.

- Recommended use when **there is some efficacy data available but effectiveness (real world) of intervention not fully demonstrated**
  - Some quality work can fall here: Evidence-informed, but not strongly evidence-based interventions.
  - *It may or may not help, and if it does, we’re not sure how to get people to do it*
Hybrid Type 2:
Equally Testing Implementation & Effectiveness

- Equal focus on testing effectiveness of clinical intervention (clinical data at patient-, clinic-, population-level) & implementation strategy (process data at provider-, clinic-, site-level)

- Implementation outcomes typically measured through qualitative or mixed methods (survey, interviews, EMR)

- Recommended use when **there is robust clinical intervention data available & the implementation research is preliminary**
  - *It probably works, but may not in my patients because they’re different than those in trials, & I’m not sure how to get people to do it*
Hybrid Type 3: Primarily Testing Implementation

• Focus is testing implementation strategy while gathering information on the intervention’s impact on patient outcomes

• Focus of implementation strategies tends to go beyond feasibility & acceptability to adoption, penetration, fidelity

• Implementation outcomes measured through qualitative or mix methods (survey interviews, EMR, fidelity checks)
  • Patient outcomes examined quantitatively, but far less focus

• Recommended use when robust clinical intervention data available but effects suspected to be “vulnerable” to implementation
  • What is the best way to get people to do this thing with strong evidence?
  • Will the way that we implement affect improvement in patient outcomes?
When Should We Evaluate Change?

- Observe during study, report on observations.
- Observe during the study, report on observations.
- Observe at the end, report on what happened.
- Observe during study, and make changes during the study based on observations.
Process Evaluation

• What influences the conduct & quality of implementation?
  • Prior to, during, after the study?

• Results do not change the study processes, but describe them

• May be used more in Hybrid Type 1
  • What happened?
  • How might it inform future implementation?
Formative Evaluation

• Measures take during the study influence later processes in the study

• What’s happening? Is it what we want or expected? Can we perturb the strategy to get what we want?
  • Plan Do Study Act is one formative evaluation strategy

• More in Hybrid Type 2 or Type 3
Summative Evaluation

- What happened at the end of the study?
- What were the measure of success or failure?
Study Design Examples

- Case Series
- Case Report
- Uncontrolled Pre-Post
- Controlled Pre-Post (Diff-in-Diff)
- Interrupted Time Series
- Regression Discontinuity
- Randomized Stepped Wedge
- Cluster Randomized
- Patient-Level, Randomized, Controlled
Causal Inference Theory 101

• There was an intervention
  • For our purposes today, an implementation strategy

• We measured some outcomes of interest
  • Could be qual- or quant-itative measures
  • Depends on your question

• Did the intervention change the process and/or outcome?
  • We want to know: Did the intervention WORK?
• Work is ONLY done when a force that is applied to an object moves that object

\[ W = \text{Force} \times \text{Distance} \]
Did our force (strategy) move the outcome?

- We can identify individuals to whom we gave an intervention.
- We can measure individuals’ outcomes.
- We cannot measure that would have happened if we did not give the intervention to the individual.
  - The counter-factual, or potential outcomes.
- We can only measure pseudo-counterfactuals between individuals, some who got the intervention and some who didn’t.
The Fundamental Challenge

Implementing something is hard

• How do we know if our strategy worked?

We need to know...

• What would have happened if we did not implement something?
• Who are the “counterfactuals” to our intervention/implementation strategy?
The study design you choose is the method you use to build your counterfactuals.

Who is like my intervention group, but did not get the intervention?

Are these people similar to the ones who I’ll end up using this on?

Good counterfactuals → Internally valid design

Risk-benefits in study sample = Risk-benefits in target population → External validity
Level of Causal Inference (Internal Validity)

Case report
Case series
(Quasi-experimental)
Controlled pre-post
Interrupted time series
Regression discontinuity

Uncontrolled pre-post

Level of External Validity, Resources, Ease, Ethics

Cluster randomization
Step wedge RCT

Individual RCT without contamination
Case Studies

• No counterfactuals
  • So not used for estimating causal effects
  • But valuable!

• Pre-intervention case study
  • Evaluate readiness to change
  • Facilitators/barriers
  • Plan theoretical models, develop strategies

• Similar for post-intervention
  • What went wrong or right?
Uncontrolled Pre-Post

• Probably the most common study design

**PRO:**
• Simple
• Measure/do/measure (OXO)
• Can adjust for measured confounders

**CON:**
• Anything that has changed over time breaks the counterfactual
• Unmeasured confounding by time

• Commonly “confounding by secular trends”
Quasi-Experimental Designs

• Intervene in a way that offers a minimally confounded control group
  • Create a better counterfactual

• The econometrics designs
  • Difference-in-Difference
  • Interrupted Time Series
  • Regression Discontinuity Design
Controlled Pre-Post/Difference-in-Difference

Intervention Group

Intervention

Control Group

Nothing
Interrupted Time Series (ITS)

- For interventions implemented at a specific time
- An improvement over simple pre-post design because it takes into account confounding by secular trends

\[
\text{Outcome} = \text{exposure} + \text{other variables} + \text{time}
\]

- CON: Need ~6M pre-post, sharp cut-off in intervention (no continuous Plan Do Study Act)
A multifaceted intervention to improve sepsis management in general hospital wards with evaluation using segmented regression of interrupted time series.

Simple Pre-Post Analysis

<table>
<thead>
<tr>
<th>% Recieving antibiotics in 4 hours</th>
<th>% with lactate measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>Post</td>
</tr>
</tbody>
</table>

p<0.05

Interrupted Time Series Analysis

No difference!

Regression Discontinuity Design (RDD)

- For interventions planned to be implemented at a **threshold** of a continuous value

- Like ITS, but you choose a value to implement on that may have clinical meaning
  - E.g., only do intervention for highest risk

- Noise in intervention assignment at implementation threshold $\rightarrow$ randomization
  - People assigned just above and below the threshold are counterfactuals

- **CONs:**
  - Need threshold
  - Correct functional form
  - No manipulation of score
  - Requires large N (4x RCT)
A Randomized Controlled Trial

Predicted Mortality

Observed Mortality

Randomization

Control

Intervention

Effect Estimate

Predicted Mortality

Observed Mortality
A Regression Discontinuity Design

Intervention Threshold

Observed Mortality

No Intervention

Effect Estimate

Predicted Mortality

Counterfactual

Intervention
RDD As Continuous Evaluation of Implementation & Improvement

- Did Implementation Occur?
  - Why, why not?

- Did Improvement Occur?
  - Why, why not?
Theoretical Model for Evaluating Readmission
Reduction with RDD – 3 at same time

1. Follow-up call, follow-up appointment
2. Pharmacy & specialty consult at discharge
3. Super utilizer team

BMC Score: Increasing Risk for Readmission

Readmit Rate
Stepped Wedge Cluster RCT

- Start intervention sequentially at randomly chosen sites
- A controlled pre-post, but at many sites, at different times

**PRO:**
- Every site gets the intervention, eventually!
- Limit contamination of individual RCT
- Cluster randomization waived consent

**CON:**
- Need many sites
- Power calculations are difficult (site & time correlations)
- Blinding
- Secular trends can confound
Conventional Parallel Cluster Study (with Variations) & the Stepped Wedge Study

(a) Parallel cluster study
(b) Parallel cluster study with a baseline period
(c) Stepped wedge study
(d) Stepped wedge study including transition period

Cluster exposed to intervention  Cluster unexposed to intervention (control)  Cluster in transition period

<table>
<thead>
<tr>
<th></th>
<th>Intra-cluster correlation 0.01</th>
<th>Intra-cluster correlation 0.1</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Simple parallel cluster RCT</td>
<td>Stepped wedge trial</td>
</tr>
<tr>
<td>Number of clusters</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Cluster size</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Total sample size</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Number of steps</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Number of clusters per step</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Power*</td>
<td>0.97</td>
<td>0.88</td>
</tr>
</tbody>
</table>

*Power*

Parallel Cluster Randomization

**PRO:**
- Similar to stepped wedge
- No contamination, waived consent
- Avoid confounding by secular time trend

**CON:**
- Similar to stepped wedge
- Not all sites get the intervention in the end
Individual Patient RCT

**PRO:**
- Most efficient statistically
- Blinding

**CON:**
- Contamination for most implementation & improvement initiative across individual patients
- Infrastructure for consent & individual data collection
- Ethics of randomizing individuals to strategies meant to improve evidence-based interventions
Factorial Designs

Test multiple different intervention components simultaneously

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<tbody>
<tr>
<td>1</td>
<td>Pictograph</td>
<td>100 Incremental</td>
<td>Benefits first</td>
<td>Present</td>
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<tr>
<td>2</td>
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<td>Risks first</td>
<td>Absent</td>
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<tr>
<td>3</td>
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<td>Benefits first</td>
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<td>Risks first</td>
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<td>Pictograph</td>
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<td>Benefits first</td>
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<tr>
<td>6</td>
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<td>Risks first</td>
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<td>7</td>
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<td>8</td>
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<td>9</td>
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<td>14</td>
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<td>16</td>
<td>Prose only</td>
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What’s the Worst Study Design?

• INCONCLUSIVE

• How to avoid:
  • Clearly defined intervention, strategy, outcomes
  • Methods match goals
  • Adequate sample size for realistic effect estimate
  • Mixed methods
Putting It All Together

Can I Assign the Exposure?

Yes → Can I Randomize Exposure?

Yes → Experimental Study
   - Randomized Controlled Trial
   - Cluster Randomized Trial
   - Stepped-Wedge Design
   - Adaptive Design
   - Hybrid Design

No → Quasi-Experimental Study
   - Controlled Before-and-After Study
   - Interrupted Time Series Design
   - Regression-Discontinuity Design

No → Observational Study
   - Cohort Study Design
   - Cross Sectional Design
   - Case-Control Design

Experimental Study

Level of Randomization

- Individual
  - RCT
  - Stepped-Wedge Design
- Organizational/System
  - Cluster RCT
  - Stepped-Wedge Design
- Multiple
  - Split-Plot Design

Considerations
- Hybrid Design
- Adaptive Design

Quasi-Experimental Study

<table>
<thead>
<tr>
<th>Group by Appropriate Control Site</th>
<th>Group by Specific Qualifying Characteristics</th>
<th>Group by Time</th>
</tr>
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<tr>
<td>Controlled Before-and-After Study Design</td>
<td>Regression-Discontinuity Design</td>
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Randomization Plan

<table>
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<th>Randomized by Intervention</th>
<th>Randomized by Time</th>
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<tr>
<td>RCT</td>
<td>Stepped-Wedge Design</td>
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<tr>
<td>Cluster RCT</td>
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## An Intervention to Prevent Bad Outcomes in Your Favorite Disease

<table>
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<tr>
<th></th>
<th>Efficacy</th>
<th>Effectiveness</th>
<th>Implementation</th>
</tr>
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<tbody>
<tr>
<td><strong>Hypothesis</strong></td>
<td>RCT, randomize at patient level, quantitative methods</td>
<td>RCT or quasi-experimental at patient level, quantitative methods</td>
<td>RCT, quasi-experimental, observational, at provider or organizational level, mixed methods</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Clinical outcomes, primary stressed</td>
<td>Small number of clinical outcomes, risk-harm balance</td>
<td>Emphasize implementation outcomes – adoption, penetration, coverage, fidelity, etc.</td>
</tr>
<tr>
<td><strong>Intervention clinicians</strong></td>
<td>Make it consistent at all costs</td>
<td>Work within typical conditions of clinic</td>
<td>Local conditions</td>
</tr>
<tr>
<td><strong>Intervention fidelity</strong></td>
<td>Lots of support, not part of usual care</td>
<td>Research support, but separate from regular clinic activities</td>
<td>Research support for training only</td>
</tr>
</tbody>
</table>
Study designs abound, but not all are equal
• Need to understand strengths/weaknesses of each design

Study designs need to match YOUR questions
• Efficacy, effectiveness, implementation, Hybrid

Can perform qualitative or quantitative within any design
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Tell Us About Your Projects

• What is your research question?

• Which of the study designs we discussed work for your research?

• Where do you get stuck? What is a puzzle here that is hard to sort out and solve?
2018 CIIS Pilot Grant Funding

Intent to Submit Form 3/18/18

Receive CIIS Feedback

Study Proposal Application 6/15/18
Contact CIIS
Website: http://sites.bu.edu/ciis/
Email: ciisinfo@bu.edu