Study Designs for D&I Science

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Mentored Training for Dissemination and Implementation Research in Cancer
Goals

• Survey fundamental concepts of study design
• Link characteristics of D&I science to study design decisions
• Describe situations where non-experimental designs are preferred over traditional RCT-type designs for important D&I research questions
The epistemological problem of D&I Science
Translation research framework

A social-ecological framework for D&I research

Inspired by Glass & McAtee, 2006, SSM
## D&I science characteristics & implications for study design

<table>
<thead>
<tr>
<th>Point #</th>
<th>Characteristic</th>
<th>Implication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systems Perspective</td>
<td>Context is critical</td>
<td>Research should focus on and describe context</td>
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<tr>
<td></td>
<td>Multilevel complexity</td>
<td>Most problems, and interventions are multilevel and complex</td>
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<tr>
<td></td>
<td>Focus on systems characteristics</td>
<td>More emphasis needed on interrelationships among system elements and systems rules</td>
</tr>
<tr>
<td>Robust, Practical Goals</td>
<td>Representatives and reach</td>
<td>Focus on reaching broader segments of population and those most in need</td>
</tr>
<tr>
<td></td>
<td>Generalizability</td>
<td>Study generalization (or lack of such) across settings, subgroups, staff, and conditions</td>
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<tr>
<td></td>
<td>Pragmatic and practical</td>
<td>Producing answers to specific questions relevant to stakeholders</td>
</tr>
<tr>
<td></td>
<td>Scalability and sustainability</td>
<td>From outset, greater focus on scale-up potential and likelihood of sustainability</td>
</tr>
<tr>
<td>Research Methods to Enhance Relevance</td>
<td>Rigorous</td>
<td>Identify and address plausible threats to validity in context of question. Greater focus on replication</td>
</tr>
<tr>
<td></td>
<td>Rapid</td>
<td>Approaches that produce faster answers</td>
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<td></td>
<td>Adaptive</td>
<td>Best solutions usually evolve over time, as a result of informed hypotheses and mini-tests with feedback</td>
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<tr>
<td></td>
<td>Integration of methods; triangulation</td>
<td>For greater understanding, integrated Quantitative and Qualitative methods are often required</td>
</tr>
<tr>
<td></td>
<td>Relevance</td>
<td>Relevance to stakeholders should be top priority</td>
</tr>
<tr>
<td>Flexibility</td>
<td>Multiplicity</td>
<td>Encourage and support diverse approaches with the above characteristics (all models are wrong)</td>
</tr>
<tr>
<td></td>
<td>Respect for diverse approaches; humility</td>
<td>Different perspectives, goals, methods and approaches are needed. Continuing the same existing approaches will produce the same unsatisfactory results</td>
</tr>
</tbody>
</table>

Selecting study designs – function of three criteria

• What question are you asking?
• What type of evidence do you need?
• What constraints do you have on how you will design the study and collect the data?
  • Ethical
  • Political
  • Budget
  • Time
Study design rises out of epistemology

- Epistemology – How we know what we know?
- Fundamental study design characteristics that allow us to connect observations to inference
  - Reliability – consistency and accuracy of measurement
  - Internal validity - the extent to which a causal conclusion based on a study is warranted
  - External validity - to what populations, settings, treatment variables, and measurement variables can an effect be generalized
## Threats to internal validity

<table>
<thead>
<tr>
<th>Threats</th>
<th>Study Design Feature to minimize threat/improve internal validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambiguous temporality</td>
<td>Can you demonstrate that the exposure occurred before the outcome? Minimized when you manipulate the exposure or can assess multiple observations over time</td>
</tr>
<tr>
<td>Selection</td>
<td>Are the participants systematically different from the target population, comparison group or those who dropped-out of the study? Use randomization and retention strategies to minimize.</td>
</tr>
<tr>
<td>History</td>
<td>Events outside of the study effect outcomes (e.g. policy changes, natural disaster). Select participants from the same general location, ensure testing schedules are similar across groups.</td>
</tr>
<tr>
<td>Maturation</td>
<td>Subjects change between measurements. Select groups at ~ the same stage of maturation (e.g. age, time since adoption, experience with organization, etc).</td>
</tr>
<tr>
<td>Regression to the mean</td>
<td>Participants selected based on extreme scores. Randomize a large # of extreme scorers if criteria is necessary, select participants based on multiple measures</td>
</tr>
<tr>
<td>Attrition</td>
<td>Use strategies to reduce differential and high dropout rates &amp; statistical methods to minimize attrition bias. Underscores the need to build strong partnerships.</td>
</tr>
<tr>
<td>Testing</td>
<td>How can testing cause participants to be more sensitive to interventions. Use unobtrusive testing, similar instruments for all individual or groups.</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>Avoid switching instruments during the study, repeat measures over time.</td>
</tr>
<tr>
<td>Threats</td>
<td>Responses</td>
</tr>
<tr>
<td>---------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Units</td>
<td>Groups of subjects respond differently to the intervention effect. Document or estimate the representativeness of participants examine effect across vulnerable sub-groups.</td>
</tr>
<tr>
<td>Treatment variations</td>
<td>Level of implementation or dose or timing of intervention produces variations in treatment effect</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Consult with stakeholders prior to study design to anticipate generalizability over outcomes, measure multiple outcomes</td>
</tr>
<tr>
<td>Settings (effect modification)</td>
<td>Setting influences intervention effect/effect found in one setting can’t be generalized to other settings. Conduct studies in single large sites (e.g. university, hospitals) with multiple sub-settings</td>
</tr>
<tr>
<td>Context (mediation)</td>
<td>Aspects of the setting (e.g. leadership, collaboration, etc) influence the intervention effect. Identify &amp; study mediators over multiple contexts</td>
</tr>
</tbody>
</table>
McGrath’s 3-horned dilemma

# IOM: Match the evidence to the questions

<table>
<thead>
<tr>
<th>Why do we care?</th>
<th>What should we do?</th>
<th>How do we implement?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health burden</td>
<td>Medical or behavioral interventions reduce the health burden</td>
<td>Methods to scale-up use of interventions in target settings</td>
</tr>
<tr>
<td>Strength of the risk factors relationship with disease</td>
<td>Mediating mechanisms of intervention</td>
<td>Strategies to improve fidelity to core components of intervention</td>
</tr>
<tr>
<td>Inequities in cancer mortality</td>
<td>Readiness of settings to implement</td>
<td>Processes of implementation that are feasible for settings</td>
</tr>
</tbody>
</table>

From Rebecca Lobb & IOM Report
Traditional and non-traditional study designs
Study design categories for D&I research

- Experimental and quasi-experimental
- Non-experimental and observational
- Qualitative
- Computational modeling
What is a ‘study design?’

- Study designs are recipes that describe how observations are systematically structured to allow for valid inference.
- Study design ‘ingredients’ include the following:
  - Observation unit of analysis
  - Levels of:
    - Selection/Randomization
    - Intervention
    - Measurement
  - Time (cross-sectional, retrospective, prospective)
  - Use of control/comparison group
  - Types of data and analyses (only loosely coupled with study design)
Experimental/Quasi-experimental designs

- Randomized controlled trial (RCT)
- Controlled clinical trial (CCT)
- Controlled before-and-after study (CBA)
- Practical Clinical Trial (PCT)
- Staggered enrollment trial (SET)

\[
\begin{array}{ccc}
   I_x: & 0 & x & 0 \\
   C: & 0 & x & 0 & x & 0
\end{array}
\]

- Regression-discontinuity design
- Stepped-wedge design
- Interrupted time series (ITS)
  - \( I_x \) must be introduced at clearly defined point in time
  - Need at least 3 data points before and after \( I_x \)
- Adaptive designs
When might you choose quasi-experimental designs?

- When random assignment is not possible
  - ethics
  - expense
  - infeasible because participants won’t accept randomization
- When external validity is very important and:
  - intervention takes many forms and levels of quality
  - diversity of the population requires multiple adaptations
  - intervention is part of a complex, multi-level approach requiring adaptations
- When control group contamination is likely
- When there are issues with the unit of analysis
  - multiple units of analysis
  - large unit where there is difficulty achieving adequate numbers

From Lobb, 2014
Non-experimental & computational modeling designs

• Non-experimental
  ▪ Cross-sectional studies
  ▪ Case-control studies
  ▪ Longitudinal cohorts
  ▪ Geographic mapping

• Computational modeling & systems science
  ▪ System dynamics
  ▪ Network analysis and modeling
  ▪ Agent-based modeling
When might you choose computational modeling designs?

• When important empirical data are missing or are hard to get

• When the interest is in identifying and exploring behavioral dynamics and system feedback

• When there are issues with the unit of analysis

From Lobb, 2014
When might you choose computational modeling designs?

- When important empirical data are missing are hard to get
- When the interest is in exploring and understanding system dynamics
  - Feedback loops
  - Unintended consequences of interventions
  - The rich effects on behavior of characteristics of physical and social contexts (e.g., social networks)
- When it is difficult or impossible to do traditional empirical designs
Complex systems

- Made up of a large number of *heterogeneous* elements;
- That *interact* with each other;
- Producing an *emergent effect* that is different from the effects of the individual elements;
- And this effect *persists* over time and *adapts* to changing circumstances.

http://www.necsi.edu/visual/systems.html
Three common methods

- **System dynamics**
  - Models and computer simulations used to understand endogenous sources of complex system behavior

- **Network analysis**
  - The study of relationships and flows among social actors, including people and organizations

- **Agent-based modeling**
  - Use of computer simulations to examine how elements of a system behave as a function of their interactions with each other and their environment
1 + 16 reasons to do complex systems modeling

- Prediction
- 16 other reasons
  - Explain
  - Guide data collection
  - Illuminate core dynamics
  - Suggest dynamical analogies
  - Discover new questions
  - Promote scientific habit of mind
  - Bound outcomes to plausible ranges
  - Illuminate core uncertainties
  - Offer crisis options in near-real time
  - Demonstrate tradeoffs
  - Challenge robustness of prevailing theory
  - Expose prevailing wisdom as incompatible with available data
  - Train practitioners
  - Discipline the policy dialogue
  - Educate the public
  - Reveal the simple to be complex, and vice versa

From Epstein, J. M., 2008, JASS, Why Model?
Computational modeling to forecast future effects of TC policies

Briefs

Smoking Prevalence in 2010: Why the Healthy People Goal Is Unattainable

David Mendez, PhD, and Kenneth E. Warner, PhD

From Mendez & Warner, 2000, AJPH

FIGURE 1—Combinations of initiation and cessation rates that would produce a 13% adult smoking prevalence in the year 2010.
SimSmoke – Using systems modeling to examine counterfactuals

<table>
<thead>
<tr>
<th>Policy Implementation</th>
<th>Year</th>
<th>1989</th>
<th>2000</th>
<th>2010</th>
<th>2010 Lower Bound*</th>
<th>2010 Upper Bound*</th>
<th>2050 Lower Bound*</th>
<th>2050 Upper Bound*</th>
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<tbody>
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<tr>
<td>Smoking prevalence</td>
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<tr>
<td>Counterfactual: all policies at 1989 level</td>
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<td></td>
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<td></td>
<td></td>
<td>24.9%</td>
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<td>All policies implemented</td>
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<td>10.3%</td>
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<tr>
<td>Percent reduction in smoking prevalence from policy change*</td>
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<td></td>
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<tr>
<td>All policies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>-27.4%</td>
<td>-45.9%</td>
<td>-27.8%</td>
<td>-66.4%</td>
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<tr>
<td>Price only</td>
<td></td>
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<td>-18.4%</td>
<td>-27.1%</td>
<td>-21.2%</td>
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<tr>
<td>Smoke-free air only</td>
<td></td>
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<td></td>
<td>-4.7%</td>
<td>-7.6%</td>
<td>-3.9%</td>
<td>-11.3%</td>
</tr>
<tr>
<td>Mass media campaign only</td>
<td></td>
<td>0.0%</td>
<td></td>
<td></td>
<td>-3.5%</td>
<td>-1.8%</td>
<td>-5.3%</td>
<td>-4.5%</td>
</tr>
<tr>
<td>Marketing restrictions only</td>
<td></td>
<td></td>
<td>-5.3%</td>
<td></td>
<td>-7.7%</td>
<td>-3.9%</td>
<td>-11.4%</td>
<td>-9.8%</td>
</tr>
<tr>
<td>Health warnings only</td>
<td></td>
<td></td>
<td></td>
<td>-0.6%</td>
<td>-4.4%</td>
<td>-2.2%</td>
<td>-6.5%</td>
<td>-6.5%</td>
</tr>
<tr>
<td>Cessation treatment only</td>
<td></td>
<td></td>
<td></td>
<td>-1.8%</td>
<td>-5.5%</td>
<td>-1.3%</td>
<td>-24.8%</td>
<td>-9.5%</td>
</tr>
<tr>
<td>Youth access restrictions only</td>
<td></td>
<td>0.0%</td>
<td></td>
<td></td>
<td>-0.2%</td>
<td>0.0%</td>
<td>-0.1%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*Represents the percent change in prevalence due to a particular policy or all policies relative to the counterfactual with all policies maintained at their 1989 level.

doi:10.1371/journal.pmed.1001336
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001336
Using network analysis to explain patterns of dissemination of evidence-based guidelines

Figure A1. Contact, collaboration, and dissemination networks in Indiana. Nodes sized by betweenness centrality. Betweenness centrality for the lead agency (darker node) was .127 for contact, .207 for collaboration, and .423 for dissemination.

Odds ratios for final model (M3) for all states

<table>
<thead>
<tr>
<th></th>
<th>Indiana OR (95% CI)</th>
<th>Texas OR (95% CI)</th>
<th>Wyoming OR (95% CI)</th>
<th>DC OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edges</td>
<td>0.01 (0.00-0.02)</td>
<td>0.23 (0.09-0.63)</td>
<td>0.07 (0.04-0.15)</td>
<td>0.00 (0.00-0.00)</td>
</tr>
<tr>
<td>Degree (GWDegree)</td>
<td>0.06 (0.03-0.11)</td>
<td>0.05 (0.02-0.19)</td>
<td>0.02 (0.01-0.03)</td>
<td>0.12 (0.04-0.35)</td>
</tr>
<tr>
<td>TC Experience</td>
<td>1.08 (1.03-1.13)</td>
<td>0.95 (0.88-1.02)</td>
<td>1.08 (1.02-1.15)</td>
<td>1.24 (1.12-1.37)</td>
</tr>
<tr>
<td>Geographic Reach (Homophily)</td>
<td>1.72 (1.44-2.04)</td>
<td>5.33 (3.84-7.42)</td>
<td>0.62 (0.50-0.77)</td>
<td>3.95 (3.00-5.20)</td>
</tr>
<tr>
<td>Agency Distance</td>
<td>1.00 (0.98-1.02)</td>
<td>0.92 (0.91-0.92)</td>
<td>0.99 (0.98-0.99)</td>
<td>0.99 (0.98-1.01)</td>
</tr>
<tr>
<td>Network Contact</td>
<td>2.38 (2.28-2.48)</td>
<td>1.64 (1.43-1.88)</td>
<td>1.64 (1.57-1.71)</td>
<td>1.46 (1.34-1.59)</td>
</tr>
<tr>
<td>Network Collaboration</td>
<td>1.78 (1.70-1.86)</td>
<td>2.99 (2.67-3.35)</td>
<td>1.76 (1.68-1.84)</td>
<td>7.29 (6.55-8.12)</td>
</tr>
</tbody>
</table>

Agent-based modeling to explore effects of multiple TC policies

» Computational agent-based modeling study

» Goal: examine how implementation of different types of tobacco retailer density reduction policies may affect tobacco purchasing and consumption

> Initial funding from NCI

> Research team from Washington University, Brookings Institution, University of North Carolina, Stanford
Early policy effects evidence from computational model
Implementation research for the control of infectious diseases of poverty

Strengthening the evidence base for the access and delivery of new and improved tools, strategies and interventions
Box 3.2. Research studies for creating an access plan

The following list of 13 research studies provide information and analysis needed for creating an access plan for a health technology. Although designed for health technologies, the list can be adapted to studies that would help develop an access plan for "soft" technologies and health interventions.

**Architecture**

1. Problem analysis
   This research study examines the public health need for a product (including epidemiological data) and assesses the scientific and market problems in developing an effective product. This includes an assessment of access barriers and an evaluation of whether a product has commercial market potential, and if so, in which markets and under what conditions.

2. Target product profile
   This study describes the technical characteristics of the product under development. These characteristics include health impact, indications and usage, target population, mechanism, route of administration, dosage schedule, efficacy, safety, clinical pharmacology, price, product presentation, and storage.

3. Partnership analysis
   This study evaluates different potential partners and their roles. It also examines the structural and organizational challenges to coordinating partners. Managing the architecture often requires aligning the different interests and values of key stakeholders.

4. Political analysis
   This study conducts stakeholder analysis and designs political strategies to manage partners and to create expert consensus and set the policy agenda in international technical agencies.

**Adoption:**

5. Product acceptability study
   The information gathered in this study is particularly important in designing products that meet the needs and desires of the target population (including both end-users and providers).

6. Communications and branding study
   This study is important for designing messages and brands targeted to end-users and providers.

**Health systems:**

13. Health system analysis
   This study identifies health system functions that are needed to assure that effective access is produced for specific health technologies. The diagnostic process in the book *Getting Health Reform Right* provides one method for assessing health system barriers and designing interventions to assure access.

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For more information…

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