NIH Collaboratory *Rethinking Clinical Trials®*

Health Care Systems Research Collaboratory

Living Textbook Grand Rounds Series

Preparing for the Unknown: Conducting Pragmatic Research in Real-World Contexts

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Designing With Implementation in Mind

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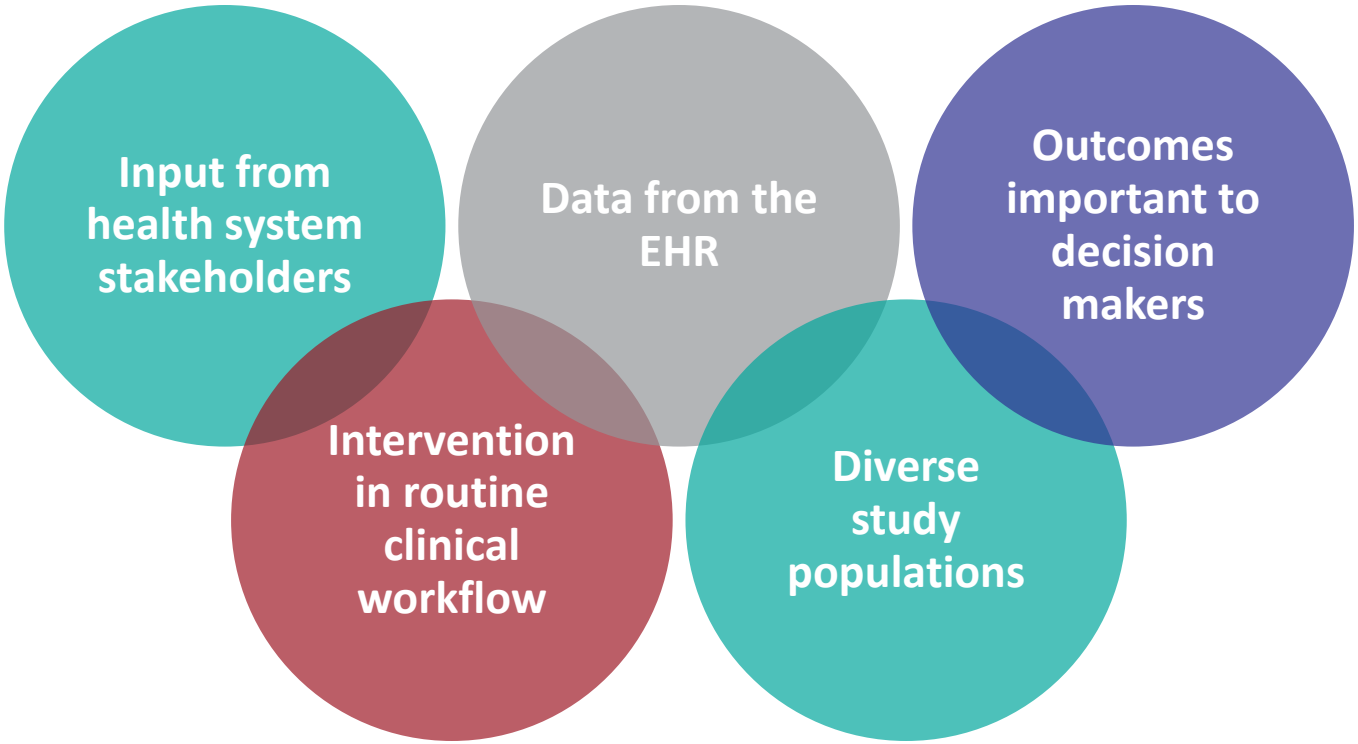
In the Living Textbook

What Is a PCT?

Large, efficient study conducted in the real world that provides evidence for adoption of an intervention into clinical practice



Important Things to Know

- Pragmatic trials can simultaneously address effectiveness and implementation aims
- Healthcare systems vary in how they change practice based on evidence from a clinical trial
- Methods that integrate pragmatic trials and implementation science frameworks are in development

Hybrid Trials

- In contrast to efficacy and effectiveness trials, “hybrid trials” are designed both to establish efficacy and to change practice
- Three types of hybrid trials
  - Test the effects of the intervention on outcomes while observing and gathering information about aspects of and level of implementation
  - Test both clinical and implementation intervention strategies
  - Test the implementation strategy while observing and gathering information about the effects of the intervention on outcomes

If You Build It, Will They Will Come?

Translated to ePCTs:

If you build it together…
the health system should be more likely to implement than if it still looks like a "researcher-delivered" intervention.

Considerations to Design the Trial for Implementation and Sustainability

- Consider how the intervention fits within the workflow of the healthcare setting
  - Who will deliver the intervention?
  - How difficult is it to prepare healthcare system staff to implement?
- Think about how the intervention might be delivered differently across similar kinds of healthcare settings like hospitals, emergency departments, or nursing homes
- Consider the value proposition of the intervention for the healthcare system's leadership

Keep Implementation Pragmatic

- Translating an efficacy trial into an effectiveness trial
  - Implementation by healthcare system staff, not research staff
  - New staff workflow and responsibility acknowledged
  - Triage or case selection by healthcare system staff using existing structures with some modification

Document the Implementation

- Critical to determine whether and how much variation there is in healthcare system staff adherence to intervention fidelity
  - Understand if variation is due to intrinsic factors about the organization or extrinsic factors (environmental or policy changes)?
- Must be able to compare and contrast differences in implementation across participating intervention sites
- Understanding variation in implementation is key to understanding intervention effect

Pragmatic Documentation of Implementation

- New codes, algorithms, or sections of the EMR may be needed to document intervention activities
- Feeding performance data back to healthcare units may stimulate intervention implementation adherence

Implementation Case Studies

- Active Bathing to Eliminate (ABATE) Infection
- Pragmatic Trial of Video Education in Nursing Homes (PROVEN)

NIH Collaboratory Case Study: ABATE Infection

- Cluster randomized trial of 53 hospitals comparing routine bathing to decolonization with universal chlorhexidine and targeted nasal mupirocin in non–critical-care units
- Intervention did not reduce MRSA or VRE cultures or all-cause bloodstream infections
- In post hoc analysis, high-risk subgroup of patients with medical devices had significant benefit
  - 32% reduction in all-cause bacteremia
  - 37% reduction in MRSA or VRE clinical cultures

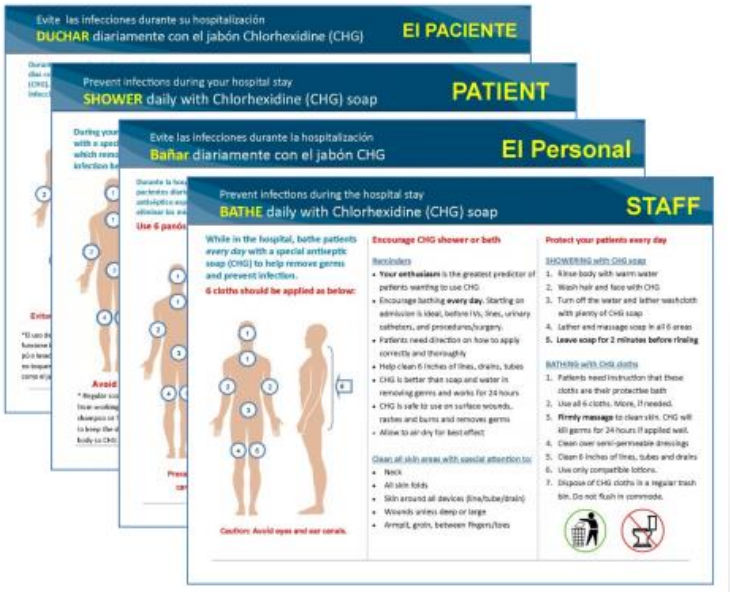
ABATE Infection Implementation

- Daily bathing of *all* patients!
- Median compliance with chlorhexidine bathing or showering across hospitals, 79% (IQR, 66%-79%)
- Compliance tracking:
  - Daily checks for all units until ≥ 85% compliance, then weekly checks
  - Quarterly staff and patient compliance assessments
- Healthcare system IT staff developed user-friendly reports to capture intervention administration and facilitate completion of compliance spreadsheets

ABATE Infection: Dissemination Tools Ready for Launch

Pragmatic trials can create ready implementation tools

- ABATE Infection tools ready for launch
  - Computer-based training for healthcare system
  - Flyers and training documents
  - FAQs
  - Training video



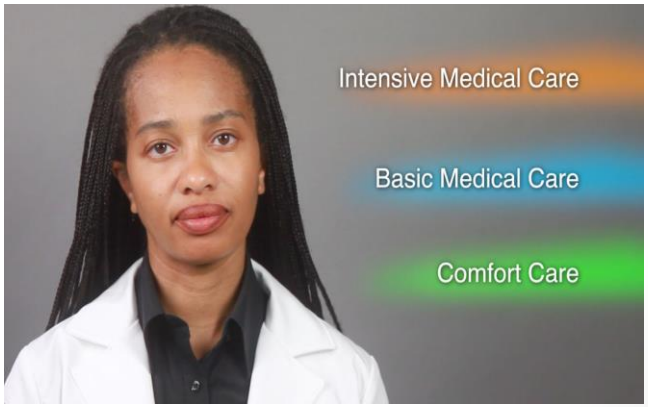
NIH Collaboratory Case Study: PROVEN

- Cluster randomized trial of advance care planning (ACP) video intervention in nursing home residents with advanced multiple comorbid conditions in 2 nursing home healthcare systems
- Video overcomes barriers of traditional ACP, which is ad hoc and perceived to take too long
- Randomized 360 nursing homes, 119 to intervention
- Primary outcome: hospital transfers of eligible patients with approximately 50% mortality at 1 year

PROVEN
PRagmatic Trial of Video Education in Nursing Homes

Video-Assisted Advance Care Planning

- Visualize treatments such as CPR
- Broad goals of care
  - Life prolongation, limited, comfort
- Specific conditions/treatments
- Adjunct to counseling
- 6 to 8 minutes
- Multiple languages
- Trained healthcare system staff to train facility champions, and jointly monitored implementation over 18 months of recruitment and 12 months of follow-up



ACP

Advance Care Planning

Making Decisions for People with Advanced Dementia

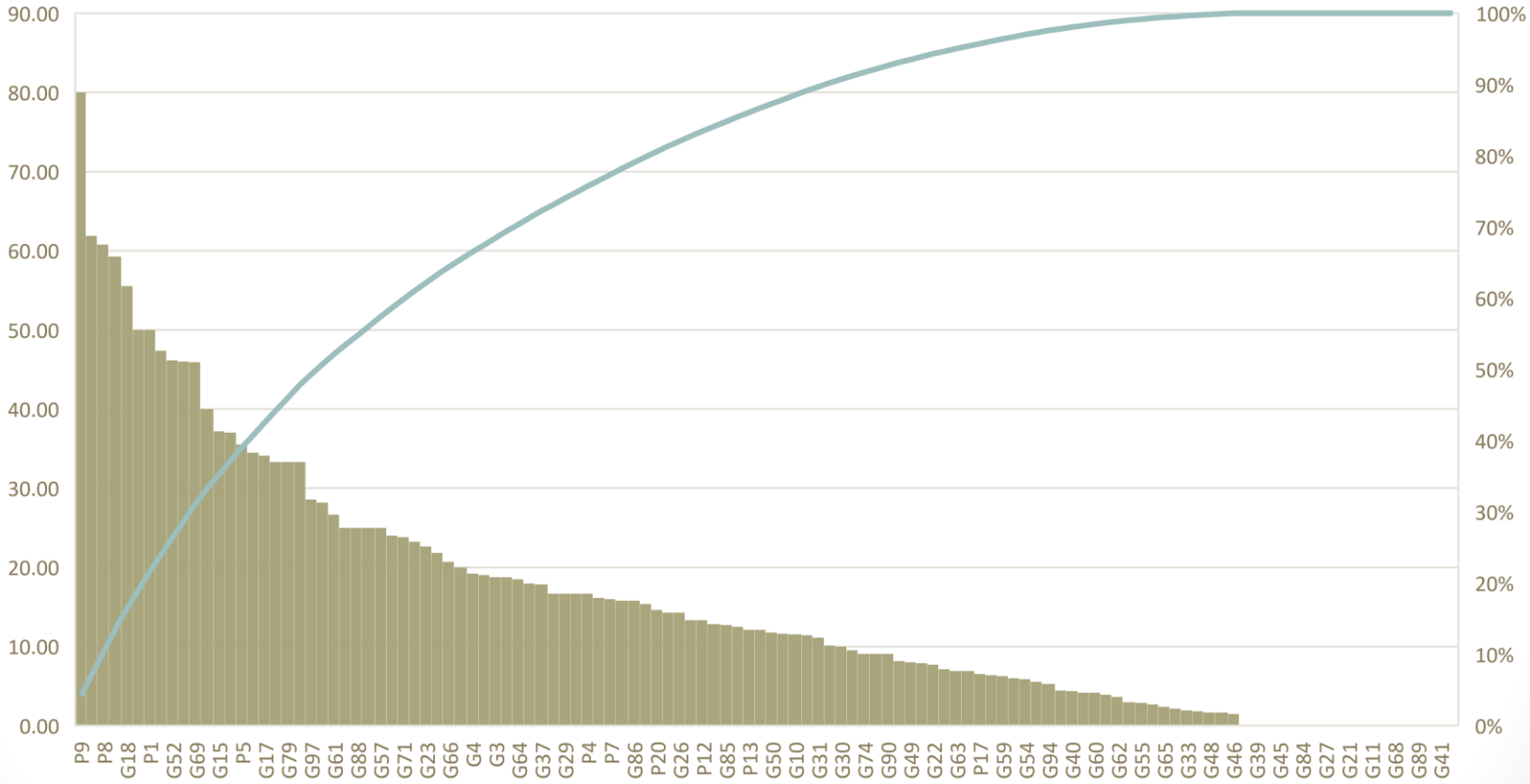
Why Should Advance Care Planning Affect Hospitalizations?

- Video sensitizes patients and families to poor prognosis of CPR for patients like them
- After video intervention, formal ACP discussions may be initiated with physician or nurse practitioner
- Preferences documented in DNR/DNH or other care restriction orders
- Next change in medical condition should not trigger a hospital transfer

Documenting the ACP Video Program

- A video status report (VSR) was programmed in the EMRs of healthcare system partners
- Each time a video is offered to a patient or his/her family, a VSR UDA was to be completed; documents whether shown or refused
- No. of patients offered video/No. of patients eligible
- Monthly reports generated for all intervention facilities
- Intended to identify limited implementation for retraining
- Documenting implementation has important lessons for future dissemination efforts

Variation in Facility Video Show Rate



Facilities in the Intervention Group

PROVEN Implementation Challenges

- Turnover of facility champions
- VSR record becomes one more “check box”
- High “offer rate” unrelated to high “show rate”
- Transfer of facility ownership
- ACP video program added to staff responsibilities
- Program became low priority at times of facility crisis
- Reducing hospital transfers is long-term goal; daily operating demands always a priority in an industry constantly in flux

Designing With Implementation and Dissemination in Mind

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rethinkingclinicaltrials.org

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Health Care Systems Research Collaboratory

Pilot and Feasibility Testing

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University of Washington Schools of Medicine and Public Health

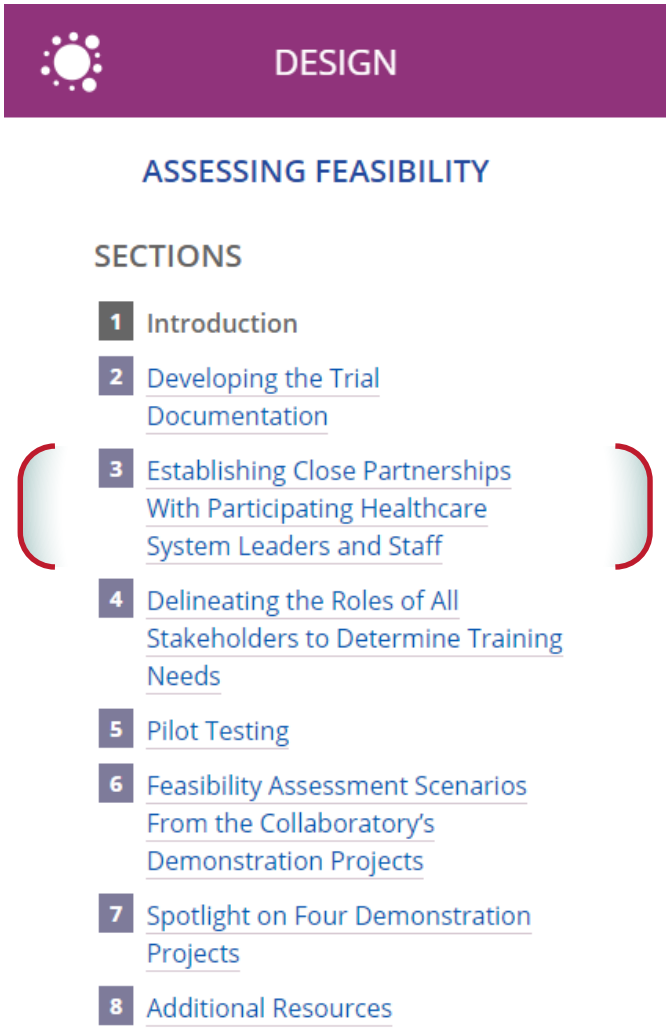
Important Things to Know

- Pilot testing the methods of your ePCT increases the likelihood of completing the trial and can prevent silly mistakes
- You need a biostatistician in the pilot/feasibility stage
- “Process issues” can derail an ePCT
- Use the pilot study to maximize acceptability, maintain affordability, and consider the scalability of your intervention

During the Pilot Phase

- Establish close partnerships with healthcare system personnel
- Test and validate EHR data collection and extraction
- Assess how well the intervention can be integrated into the clinical workflow
- Identify local champions at each study site

In the Living Textbook



Build Partnerships

- Is the intervention aligned with the priorities of the healthcare system partner?
- How ready is the partner?
  - Are extra resources needed to support the intervention, identify participants, and extract necessary data?
  - How many sites are available to fully participate?
  - How much provider training will be needed, and can training use the healthcare system's existing infrastructure?
- If the intervention proves successful, what adaptations would be needed to implement it in other healthcare settings?

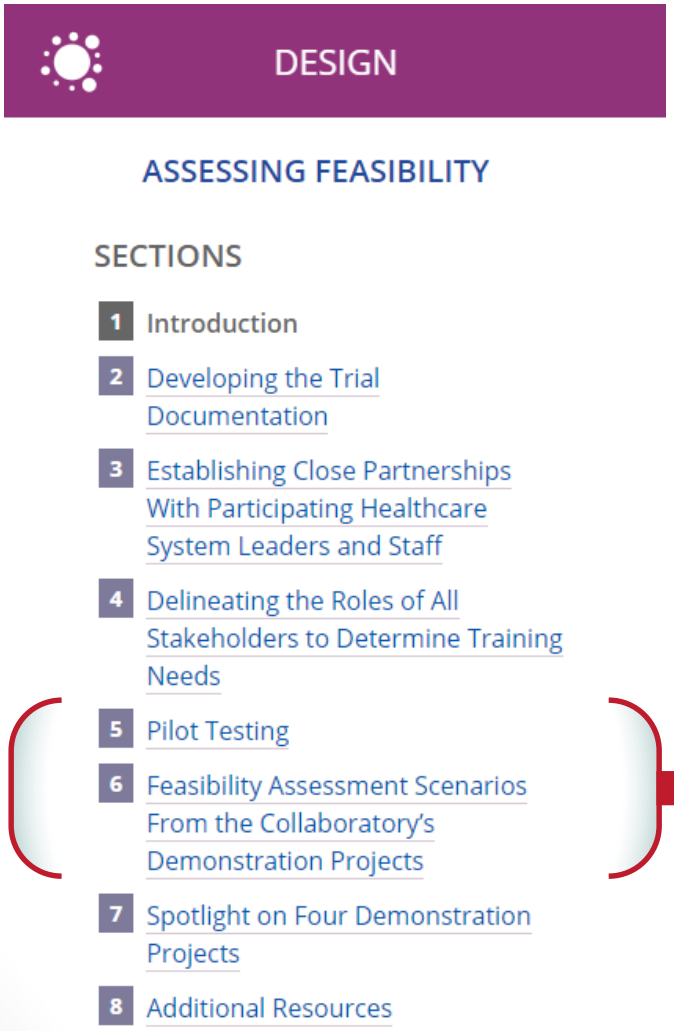
Aspects of Feasibility That Can Be Pilot Tested

- Verify that target population can be identified via the EHR
- Test phenotypes needed for sample identification
- Validate data collection & extraction methods
- Test data sample for quality & accuracy
- Coordinate processes with local champions
- Test the training materials for frontline providers & staff
- Evaluate informed consent materials

Quantify Feasibility for Pilot Aims

- Eligibility
- Recruitment
- Randomization
- Adverse events
- Retention
- Missing data
- Intervention fidelity

In the Living Textbook



- Biostatistical issues
- Secondary use of EHR data
- Capabilities and readiness of partner healthcare system
- Integrating the study into the clinical workflow

Quantifying Example 1

- Demonstrate effective recruitment and retention, which is defined as the ability to recruit an average of 10 patients per month per site and retain 80% of participants for final data collection at 6 months

Quantifying Example 2

- Determine whether the intervention can be delivered with reasonable feasibility, defined as 70% of the enrolled participants engaging in the intervention

Quantifying Example 3

- Demonstrate ability to collect primary outcomes and minimize missing data to less than 5% of primary outcome measures

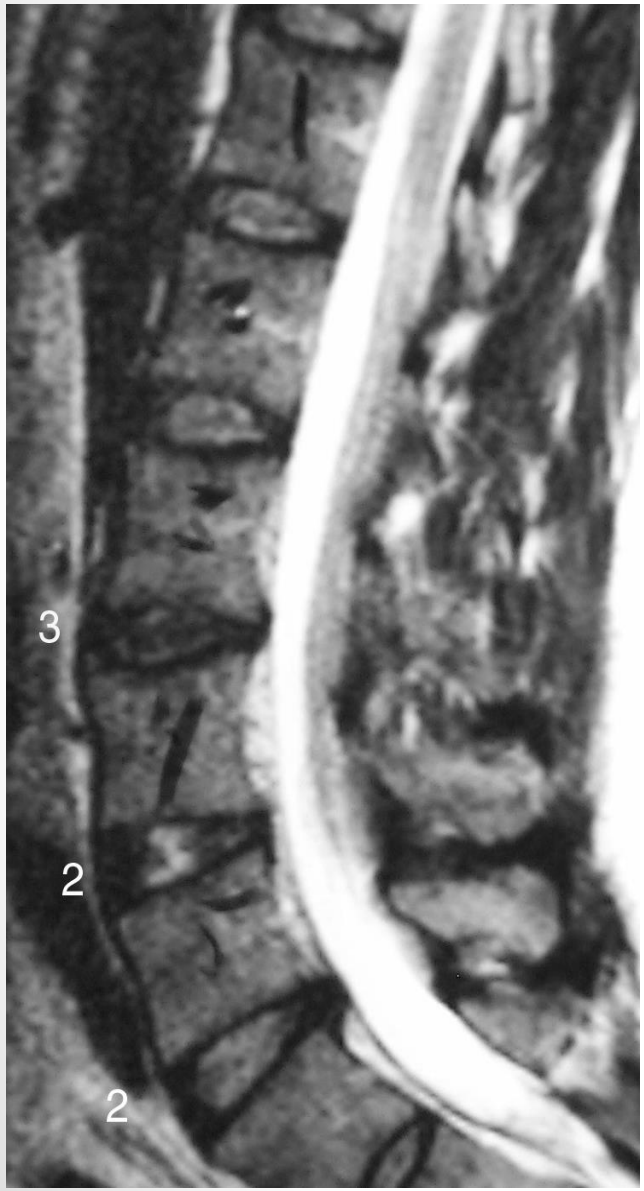
Evaluate Power Calculations

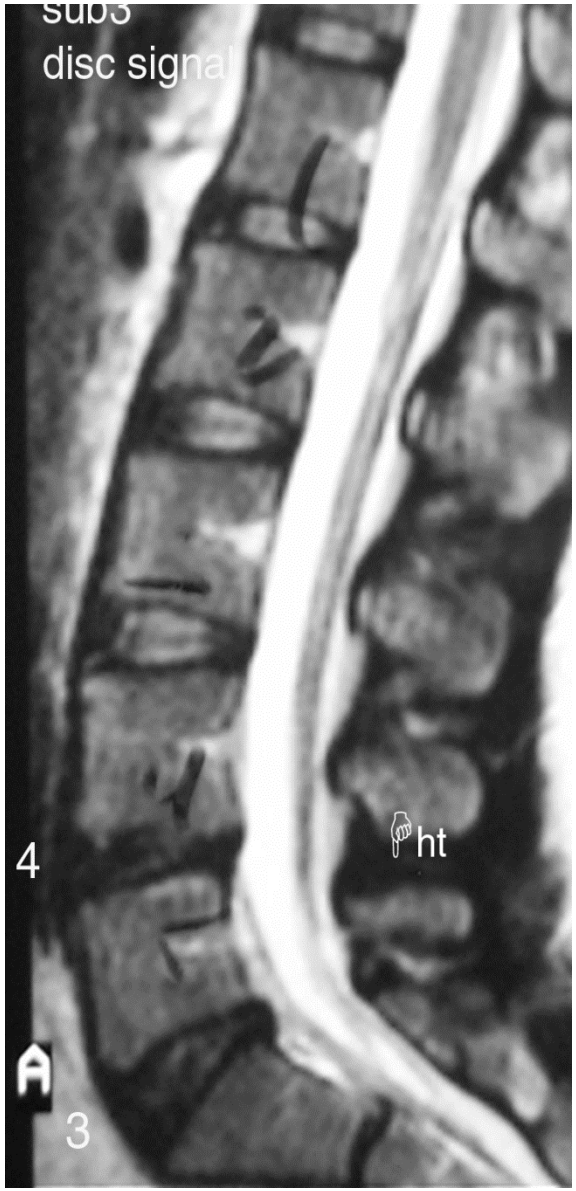
- If cluster randomization is involved, collect data to confirm estimate of intraclass correlation (ICC) for
power calculations

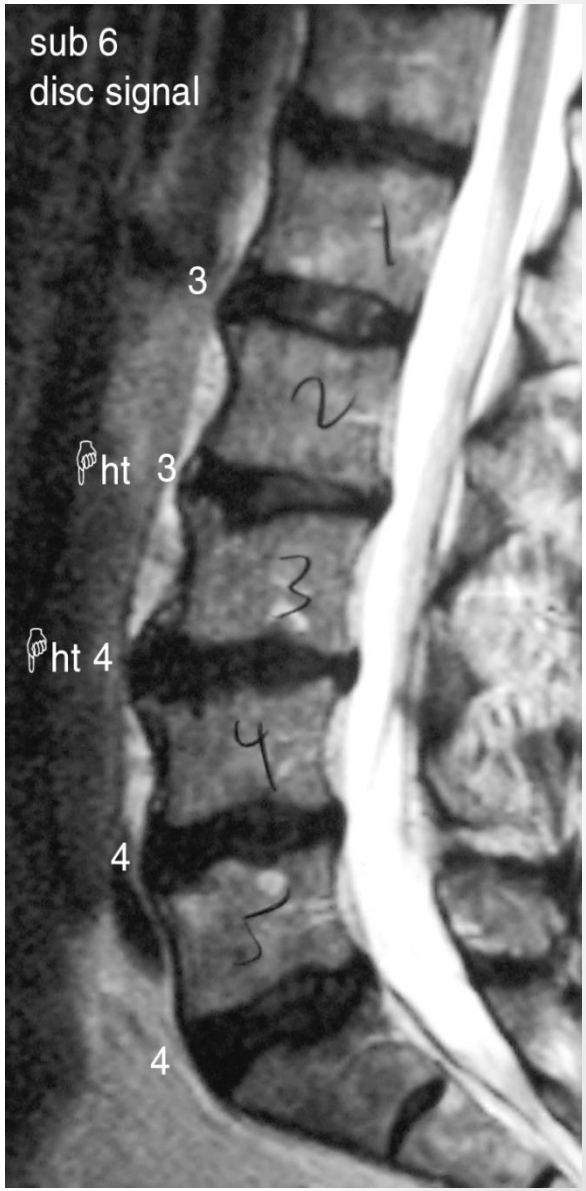
NIH Collaboratory Case Study: Lumbar Imaging with Reporting of Epidemiology (LIRE)

- Pragmatic trial of inserting benchmark rates of common spine imaging findings into routine spine imaging reports in people without symptoms
- Automatically enrolled primary care patients who had received a spine imaging test
- Randomly assigned clinics to receive or not receive the intervention text using a stepped-wedge randomization scheme
- Intent-to-treat analysis, regardless of intervention uptake or adherence

Disc Degeneration Without Back Pain







A Priori Limits on LIRE Intervention

- Minimal burden on healthcare system to deploy
- Centralized delivery by EMR
- Text understandable by healthcare providers and patients
- Data in intervention text current

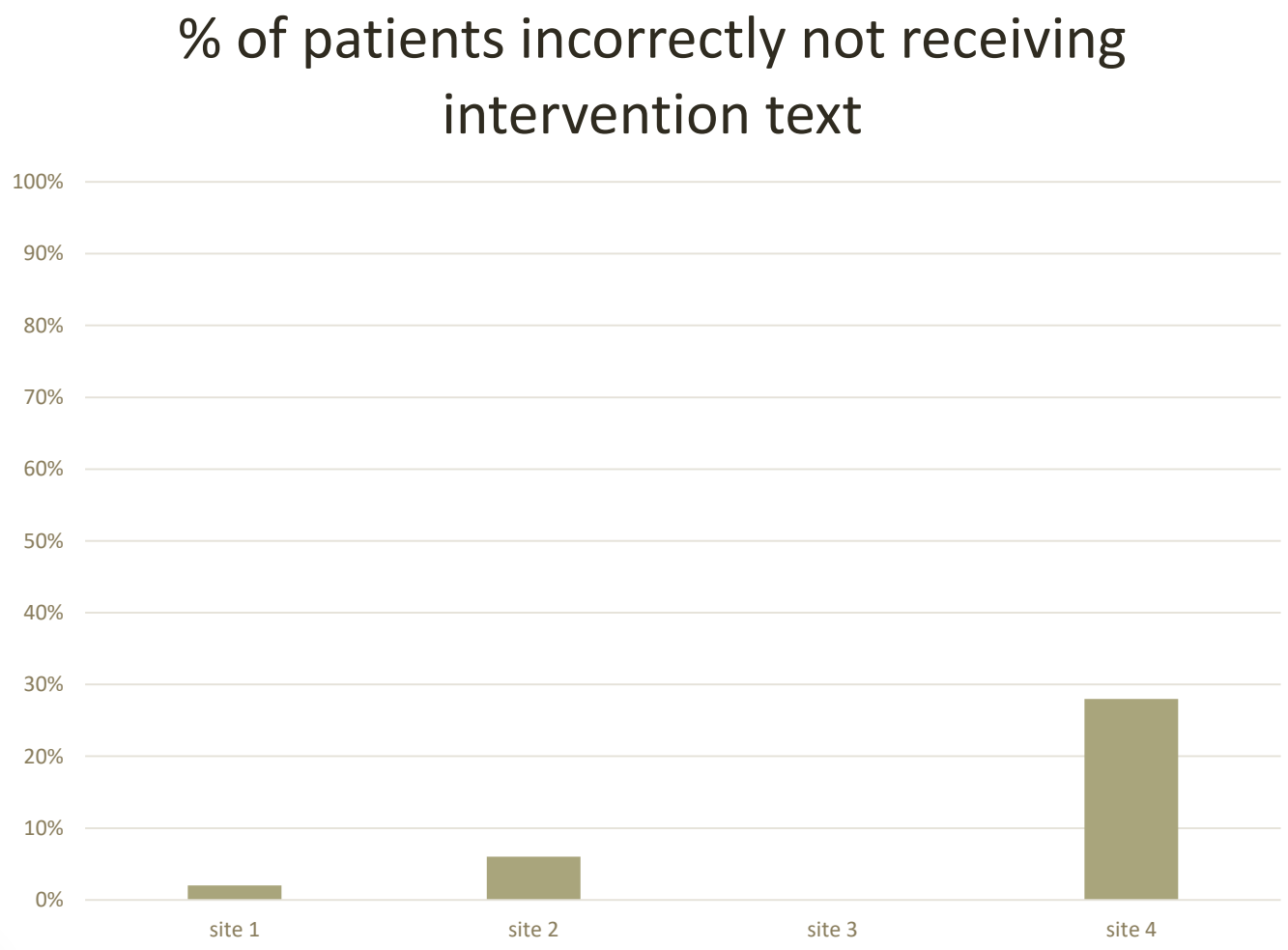
LIRE Pilot Study Process

- Technical ability to deploy the intervention
- Two types of data queries
  - “Index data pulls” to verify that intervention text was being inserted correctly
  - “Pilot EMR data pulls” to verify ability of sites to provide outcome data
- IRB grants waivers of consent and HIPAA authorization
- No ascertainment of patient-reported outcomes

LIRE Pilot Study Questions

- Success of intervention insertion (dichotomous)
- Completeness of outcome data retrieval
- Optimal wording of intervention text
- Success of obtaining consent and HIPAA waiver

Index Data Pull Example



Data Pull Allowed Troubleshooting

- “Problem with the clinic interface where we were given the incorrect provider IDs from the [radiological information system (RIS)] for a few providers.”
- “Handful of radiologists who just wouldn’t use the regional templates and insisted on using their own template.”

In the End, It's About…

- Avoiding silly mistakes
- Maximizing acceptability
- Maintaining affordability
- Remembering scalability

Ensuring Trial Readiness

- Troubleshooting and iterative testing
- Flexibility to accommodate local conditions and changes over time
- Continuous engagement with healthcare system
- Readiness tasks
  - Recruitment plans are finalized
  - Ethical/regulatory aspects are addressed
  - Intervention is fully developed and finalized
  - Data collection methods are adequately tested
  - Budget and timeline are realistic and feasible

In the Living Textbook: Readiness Checklist

DATA, TOOLS & CONDUCT

STUDY STARTUP

SECTIONS

1. Introduction
2. Implementation Readiness Checklist
3. Additional Resources

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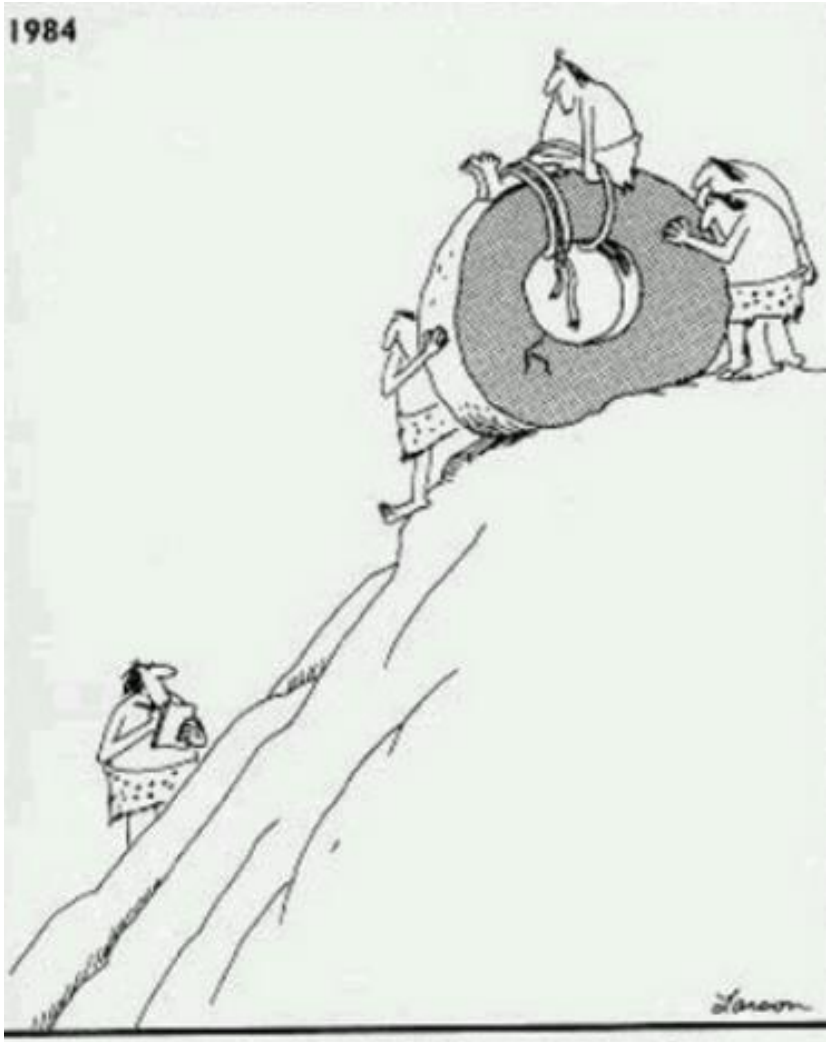
Implementation Readiness Checklist

Milestone	Completed
Recruitment plans are finalized	
All sites identified (documentation of site commitment)	
Methods for accurately identifying participants validated	
All agreements for necessary subcontracts in place	
Ethical/regulatory aspects are addressed	
Coordinated IRB oversight in place	
Finalized plans for informed consent or waiver of informed consent	
Finalized data and safety monitoring plan	
Intervention is fully developed and finalized	
Finalized intervention (including materials and training at sites) ready for site implementation	
Finalized protocol is IRB approved (informed consent and data collection forms, if applicable)	
Data collection methods are adequately tested	
Validated methods for the electronic health record information	
Validated study surveys, interviews, or other data collection modes	
Demonstrated quality assurance and harmonization of data elements across healthcare systems/sites	
Statistical and data analysis methods have been adequately developed	
Budget is realistic, feasible, and accounts for potential changes	

DeBar L, Jarvik JG, Tuzzio L, Vazquez M. Assessing Feasibility: Introduction. In: *Rethinking Clinical Trials: A Living Textbook of Pragmatic Clinical Trials*. Bethesda, MD: NIH Health Care Systems Research Collaboratory. Available at: http://www.rethinkingclinicaltrials.org.php56-29.ord1-1.websitetestlink.com/assessing-feasibility/assessing-feasibility-introduction/. Updated May 22, 2017.

Important Things to Do

- Conduct a pilot or feasibility study of the ePCT intervention
- Work with a great biostatistician and an informatician (if needed)
- Develop a partnership approach to working with your healthcare system
- Identify local champions for all your sites
- Anticipate, identify, and make a plan to address changes in the healthcare system



Early experiments in transportation

Assessing Feasibility

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