MRI for Low Back Pain: Comparative Effectiveness Research & Pragmatic Clinical Trials

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Talk Outline

• Study design basics
• CER observational study example: BOLD
• CER pragmatic randomized trial example: LIRE

Efficacy vs. Effectiveness

• Efficacy: can it work under ideal conditions
• Effectiveness: does it work under real-world conditions

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Talk Outline

• Study design basics
• CER observational study example: BOLD
• CER pragmatic randomized trial example: LIRE
Design: So Many Choices

<table>
<thead>
<tr>
<th>Observational vs Experiment</th>
<th>Observational</th>
<th>Experimental</th>
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<tbody>
<tr>
<td>Observational</td>
<td>Case series</td>
<td>Non-random allocation</td>
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<tr>
<td>Cross-sectional</td>
<td>Case-control</td>
<td>RCT</td>
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<tr>
<td>Case-control</td>
<td>Cohort</td>
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Timing      | Goal    | Goal
---|---|---
Prospective | Descriptive | Explanatory
Retrospective | Analytic | Pragmatic

Case-Control

- 2 groups defined by outcome
- Observational
- Retrospective - outcomes need to have occurred
- Descriptive or analytic
- Good for rare outcomes

RCT

- Experiment
- Groups created randomly
- Prospective
- Analytic
- Best design for eliminating bias

RCT

- Only design that controls for unknown biases
- Cohort and case-control designs can control for known biases

BOLD Aim 1

- To establish cohort to evaluate effectiveness, safety, and cost-effectiveness of interventions for pts ≥ 65 with back pain
- Setting: 3 HMOs
- Sites
  - Kaiser Northern CA
  - Henry Ford Health System Detroit
  - Harvard Pilgrim/Vanguard Boston

Back pain Outcomes using Longitudinal Data (BOLD)

Comparative Effectiveness, Cost and Outcomes Research Center (CECORC)
Depts. of Radiology and Health Services
**Aim 2: Early Imaging Cohort**

- Prospective observational cohort
- Compare effectiveness of early imaging to no early imaging in elderly with new episode of LBP
- Outcomes
  - Disability (RMDQ)
  - Pain
  - Subsequent resource utilization

**Primary hypothesis**
-Pts receiving early imaging will have worse RMDQ scores at one year c/w those who do not receive early imaging
-Will control or match for baseline back-related disability, pain severity, duration and co-morbidities

**Early Imaging Study- Key Aspects**

- **Design:**
  - Prospective observational cohort study
  - Propensity score matching of demographic and clinical characteristics
- Exposure: Diagnostic imaging (plain films, CT or MR) of lumbar or thoracic spine within 42 days of a new primary care visit for back pain.
- Primary Outcome: Roland-Morris Disability Questionnaire

**Think of an Older Adult**

76 year old male 78 year old female

Imagine they have acute LBP
Think of an Older Adult

76 year old male
78 year old female
Imagine they have acute LBP: one gets imaged immediately and the other waits 8 wks

Possible Older Adult with LBP

- Who will have a better outcome?
- Who will use more resources?

Early Imaging and Outcomes

Original Investigation
Association of Early Imaging for Back Pain With Clinical Outcomes in Older Adults


Baseline Demographics Virtually Identical

Baseline LBP-related Characteristics Virtually Identical
No Difference in Primary Outcome (RMDQ) Over Time

Secondary Measures Over Time

Large Differences in 12 Month RVUs

Mixed model difference estimate (95% CI) = 22.3 (12.3-32.3) P<0.001

BOLD Early Imaging Results

- Early imaging group no better outcomes than similar older adults who did not get early imaging.
- Early imaging group had greater use of healthcare services, such as visits, injections, etc.

Outcomes and Costs?

- Outcomes?
  - Similar regardless of early imaging
  - Resource use?
  - > for early imaging group
### Pragmatic vs. Explanatory Trial

<table>
<thead>
<tr>
<th>Explanatory trials</th>
<th>Pragmatic trials</th>
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</thead>
<tbody>
<tr>
<td>Examine efficacy</td>
<td>Determine comparative effectiveness (CER)</td>
</tr>
<tr>
<td>Conducted under ideal conditions</td>
<td>Routine practice</td>
</tr>
<tr>
<td>Explain mechanisms</td>
<td>Aim to help providers, patients, and policy makers choose between interventions</td>
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</table>

### Pragmatic Trials

**Large Simple Trials**

**Effectiveness Trials**

### Explanatory Trials

- If and how an intervention works
- Control for as many biases and confounders as possible
- Maximize intervention’s effect

### Pragmatic Trials

- Size: huge $n \rightarrow$ robust estimates, heterogeneity
- Endpoints: patient oriented with minimal adjudication
- Setting: integrated into real world
  - Non-academic centers
  - Leverage digital data
  - Patients as partners

### Key features of most PCTs

- **Use of electronic health records (EHRs)**
  - EHRs allow efficient and cost-effective, recruitment, participant communication & monitoring, data collection, and follow up
- **Randomization at clinic or provider level**
  - Protocols can be tailored to local sites and can adapt to changes in a dynamic health care environment

### But EMRs Have Their Limitations
Example: Data Quality Issues with Death

• Unambiguous—should be easy
• BUT in LIRE
  – Pts died prior to index visit
  – Pts had visits after death
  • 1.4% of those who died subsequently had visits

Example of Pragmatic Trial—Lumbar Imaging with Reporting of Epidemiology (LIRE)
LIRE Funded by NIH Health Care Systems Research Collaboratory
• Supported by the NIH Common Fund
• Goal: improve the way (pragmatic) clinical trials conducted
• Build infrastructure for CER

Background and Rationale
• Lumbar spine imaging frequently reveals incidental findings
• These findings may have an adverse effect on:
  – Subsequent healthcare utilization
  – Patient health related quality of life

Disc Degeneration in Asx

Hypothesis
• Inserting benchmark info will influence subsequent management of primary care patients with LBP
  – Fewer subsequent imaging tests
  – Fewer referrals for minimally invasive pain treatment
  – Fewer referrals to surgery
  – Less narcotic use

LIRE PRECIS

The Intervention

Comment
The following findings are as common in normal, pain-free volunteers that while we report their presence, they must be interpreted with caution and in the context of the clinical situation. Among people between the age of 40 and 50 years who do not have back pain, a plain film x-ray will find: 1 out of 10 have minimal degeneration
- 6 out of 10 have disc height loss
Note that even 3 in 10 means that the finding is quite common in people without back pain.
Participating Systems

- Kaiser Perm N. California
- Henry Ford Healths System, MI
- Kaiser Perm WA (formerly Group Health Coop) WA & ID
- Mayo Health System, MN & WI

LIRE: Enrollment

<table>
<thead>
<tr>
<th>Site</th>
<th>Clinics (n=98)</th>
<th>PCPs (n=3304)</th>
<th>Pts (n=250,876)</th>
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<tr>
<td>HFHS</td>
<td>n=98</td>
<td>n=3304</td>
<td>n=250,876</td>
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<tr>
<td>KP NCAL</td>
<td>11%</td>
<td>71%</td>
<td>6%</td>
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<tr>
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<tr>
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<td>7%</td>
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<tr>
<td>Mayo</td>
<td>21%</td>
<td>11%</td>
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LIRE- Primary Outcome

- What we want to know: how patient’s back pain is doing
  - Back pain-related disability: Roland-Morris Disability Questionnaire
  - Back and leg pain: pain NRS
  - HRQoL
- How do we get this data?
  - Ask the patient: Pt Reported Outcome

Are PROs Pragmatic?

- Barriers:
  - Time to get
  - # of personnel
  - Finding and contacting
  - $$
- For 100s- 😊
- For 1,000s- 😞
- For >100,000s- 😞

LIRE- Primary Outcome= Spine-related RVUs

- A single metric of overall intensity of resource utilization for spine care based on CPTs converted to RVUs
- Passively collected from EMR

Key Pragmatic Aspects of LIRE

- Broad inclusion criteria
- Waiver of consent/minimal risk
- Simple, easily implementable intervention
- Passive collection of outcomes
Impact of Design on Policy

- Many entities using GRADE (Grading of Recommendations, Assessment, Development and Evaluation)
- Developed by Guyatt et al.

GRADE and Dx Tests

- Cross sectional or cohort studies can provide high quality evidence of test accuracy
- However, test accuracy is a surrogate for patient-important outcomes, so such studies often provide low quality evidence about diagnostic tests

Observational vs. Randomized

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<th>Obs</th>
<th>RCT</th>
<th>PCT</th>
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<td>Confounding</td>
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<td>Pt/Provider acceptance</td>
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<tr>
<td>Generalizability</td>
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Take Home Points

- Both observational (case-control, cohort) & experimental designs important for CER, each has (+)s/(-)s
- Pragmatic vs. Explanatory trials and the PRECIS tool
Explanatory vs. Pragmatic Trials

The Great Zefforelli’s choir worked a lot better in controlled conditions.

BOLD Team

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