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

Jerry Jarvik, M.D., M.P.H.
Professor of Radiology, Neurological Surgery and Health Services
Adjunct Professor Orthopedic Surgery & Sports Medicine and Pharmacy
Co-Director, Comparative Effectiveness, Cost and Outcomes Research Center (CECORC)
Director, UW Clinical Learning, Evidence And Research (CLEAR) Center
RSNA 2018

Acknowledgements

•NIH: UH2 AT007766-01; UH3 AT007766; P30AR072572
•AHRQ: R01HS019222-01; 1R01HS022972-01
•PCORI: CE-12-11-4469

Disclosures

Physiosonix (ultrasound company): Founder/stockholder
UpToDate: Section Editor
Evidence-Based Neuroimaging Diagnosis and Treatment (Springer): Co-Editor
GERRAF: Academic Advisory Board

Talk Outline

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

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- CER observational study example: BOLD
- CER pragmatic randomized trial example: LIRE

Efficacy vs. Effectiveness

Efficacy vs. Effectiveness

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

Design: So Many Choices

Observational vs Experiment	Timing	Goal	Goal
Observational • Case series • Cross-sectional • Case-control • Cohort	• Prospective • Retrospective	• Descriptive • Analytic	• Explanatory • Pragmatic
Experimental • Non-random allocation • RCT			

Case-Control

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

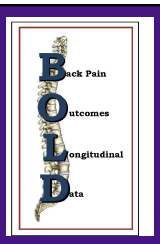
RCT

- 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

Back pain Outcomes using Longitudinal Data (BOLD)



Comparative Effectiveness, Cost and Outcomes Research Center (CECORC)

Depts. of Radiology and Health Services

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

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

Aim 2: Early Imaging Cohort

- 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

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

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

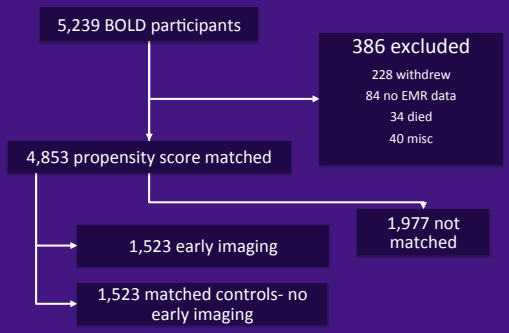
Research

Original Investigation

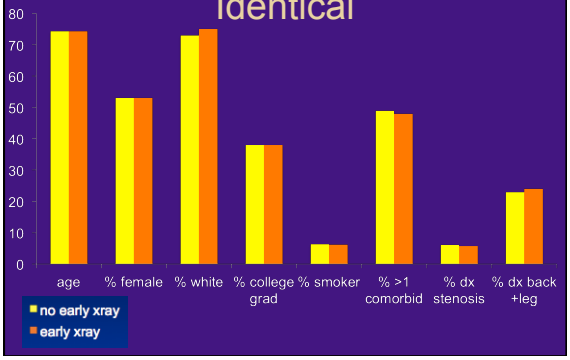
Association of Early Imaging for Back Pain With Clinical Outcomes in Older Adults

JAMA. 2015;313(11):1143-1153. doi:10.1001/jama.2015.1871

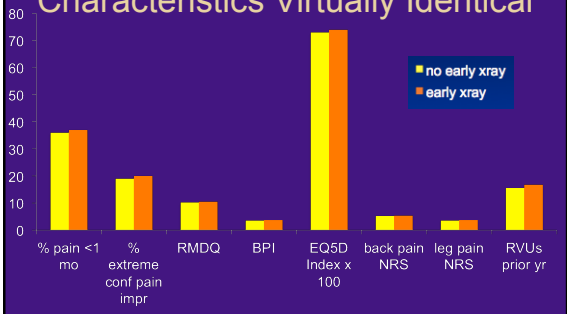
Early Imaging Study- Patient Flow

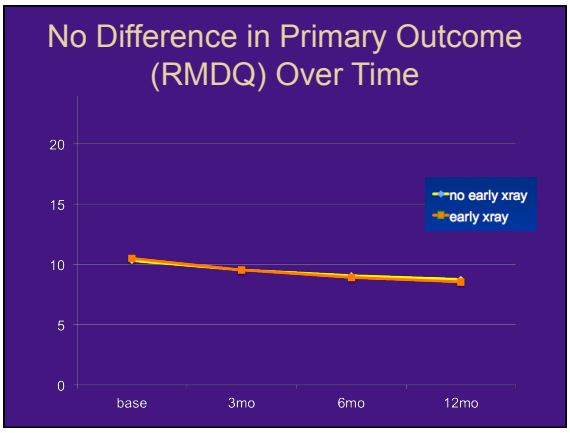


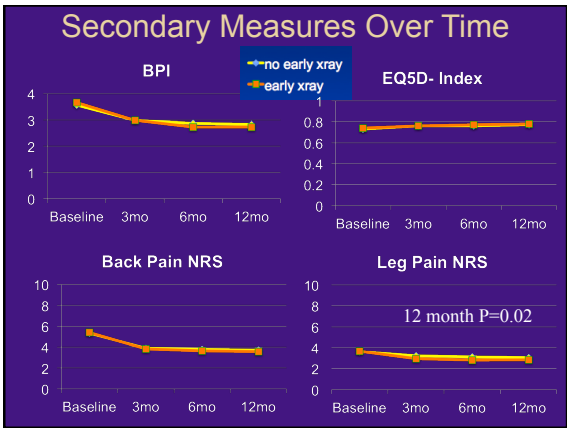
Baseline Demographics Virtually Identical

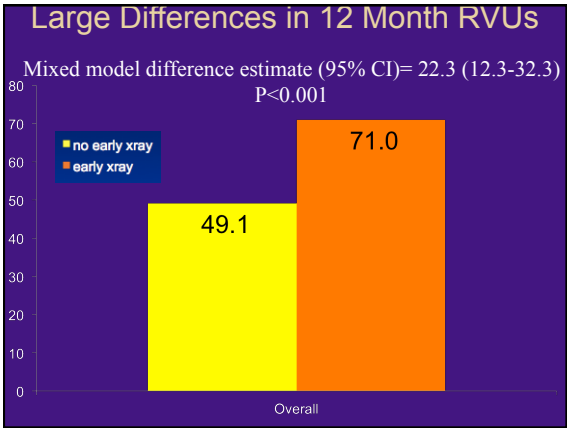


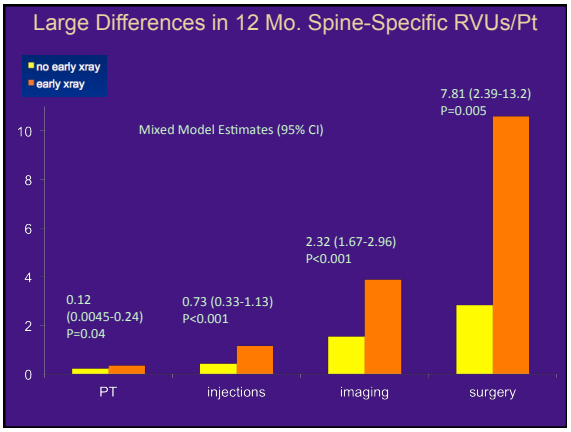
Baseline LBP-related Characteristics Virtually Identical











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

- Explanatory trials
  - Examine efficacy
  - Conducted under ideal conditions
  - Explain mechanisms
- Pragmatic trials
  - Determine comparative effectiveness (CER)
  - Routine practice
  - Aim to help providers, patients, and policy makers choose between interventions

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→ 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

NIH Collaboratory
Health Care Systems Research Collaboratory

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

Pragmatic vs. Explanatory Trials

CMAJ ANALYSIS

A pragmatic–explanatory continuum indicator summary (PRECIS): a tool to help trial designers

Kevin E. Thorpe MMath, Merrick Zwarenstein MD MSc, Andrew D. Oxman MD, Shaun Treweek BSc PhD, Curt D. Furberg MD PhD, Douglas G. Altman DSc, Sean Tunis MD MSc, Eduardo Bergel PhD, Ian Harvey MB PhD, David J. Magid MD MPH, Kalipso Chalkidou MD PhD

Published at www.cmaj.ca on Apr. 16, 2009. An abridged version of this article appeared in the May 12 issue of *CMAJ*. This article was published simultaneously in the May 2009 issue of the *Journal of Clinical Epidemiology* (www.jclinepi.com).

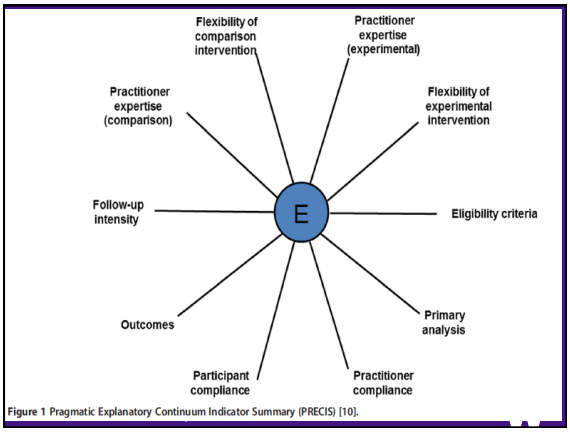
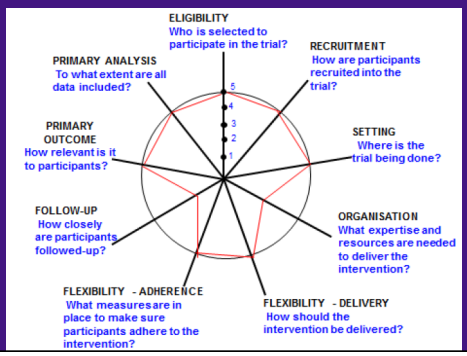


Figure 1 Pragmatic Explanatory Continuum Indicator Summary (PRECIS) [10].

Example from: Little P, Moore M, Kelly J, Williamson I, Leydon G, McDermott L, Mullee M, Stuart B: Ibuprofen, paracetamol, and steam for patients with respiratory tract infections in primary care: pragmatic randomised factorial trial. BMJ 2013, 347:f6041.



Example of Pragmatic Trial- Lumbar Imaging with Reporting of Epidemiology (LIRE)

LIRE (pronounced leer)- From the French verb, "To Read"

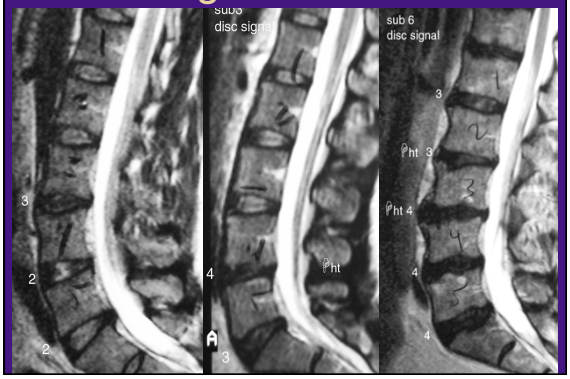
LIRE Funded by NIH Health Care Systems Research Collaboratory

- 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

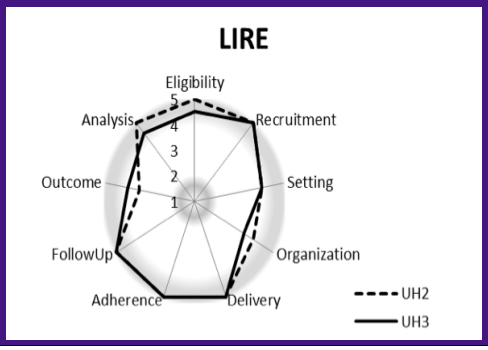
Disc Degeneration in Asx



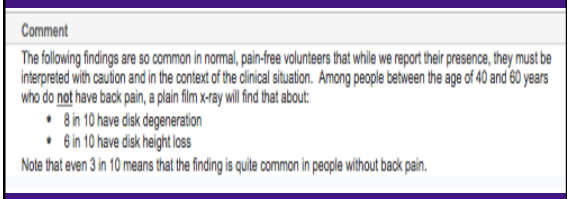
Hypothesis

- 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 so 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 60 years who do not have back pain, a plain film x-ray will find that about:

- 8 in 10 have disk degeneration
- 6 in 10 have disk height loss

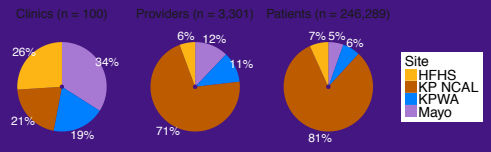
Note that even 3 in 10 means that the finding is quite common in people without back pain.

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

Clinics	PCPs	Pts
n=98	n=3304	n=250,876



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: Quality of Evidence
Putting it All Together

Step 1 Starting grade based on study design	Step 2 Reduce grade	Step 3 Raise grade High-quality observational studies	Step 4 Final grade
RCT - High	*Study quality (risk of bias)* Serious (-1) or very serious (-2) limitations	*Large magnitude of effect* Large effect (+1) RR > 2 or < 0.5, based on consistent evidence from two or more observational studies with no plausible confounders	High Further research unlikely to change confidence in the estimate of effect
Observational – Low Quasi-RCT Cohort Case-control	*Inconsistency* Important inconsistency (-1)	Very large effect (+2) RR> 5 or < 0.2, based on direct evidence with no major threats to validity	Moderate Further research likely to have an important impact on confidence in the estimate of effect and may change the estimate
All others – Very Low Case reports Case series	*Indirectness* Some (-1) or major (-2) uncertainty about directness	*Dose response gradient* (+1)	Low Further research very likely to have an important impact on confidence in the estimate and may change the estimate
	Imprecision Imprecise or sparse data (-1)	*All plausible confounders would have reduced the effect* (+1)	Very Low Any estimate of effect is very uncertain
	Publication bias High suspicion (-1)		

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Step 1 Starting grade based on study design
RCT - High
Observational – Low Quasi-RCT Cohort Case-control
All others – Very Low Case reports Case series

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

	Obs	RCT	PCT
IRB	☺☺☺	☹	☺
Cost	$$	$$$$$	$$$-$$$$$
Confounding	?????	_	_
Pt/Provider acceptance	☺☺☺☺☺	☹☹	☺☺
Generalizability	☺☺☺☺☺	☹☹	☺☺☺☺

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

BOLD Team

UW DCC

Jerry Jarvik, MD, MPH- PI
Zoya Bauer, MD PhD
Brian Bresnahan, PhD
Bryan Comstock, MS
Janna Friedly, MD MPH
Laurie Gold, PhD
Patrick Heagerty, PhD
Larry Kessler, PhD
Chris Nefcy
Sean Rundell, MS
Sean Sullivan, PhD
Judy Turner, PhD

Sites

Andy Avins, MD – Kaiser Permanente Northern CA
David Nerenz, PhD – Henry Ford Health System- Detroit
Srdjan Nedeljkovic, MD – Harvard Pilgrim/Harvard Vanguard- Boston
Rick Deyo, MD MPH– OHSU- Portland

LIRE Team

- Katie James, PA-C, MPH- PD
- Brian Bresnahan, PhD- Hlth Econ
- Bryan Comstock, MS- Biostats
- Janna Friedly, MD- Rehab
- Laurie Gold, PhD- Radiology
- Patrick Heagerty, PhD- Biostats
- Larry Kessler, PhD- HSR
- Danielle Lavallee, Pharm D, PhD
- Eric Meier, MS- Biostats
- Nancy Organ, MS- Biostats
- Kari Stephens, PhD- Informatics
- Judy Turner, PhD- Psychol/Psych
- Rick Deyo, MD, MPH- OHSU
- Dan Cherkin, PhD- GHRI
- Karen Sherman, PhD- GHRI
- Heidi Berthoud- GHRI
- Brent Griffiths, MD- HFHS
- Dave Nerenz, PhD- HFHS
- Dave Kallmes, MD- Mayo
- Patrick Luetmer, MD- Mayo
- Andy Avins, MD, MPH- KPNC
- Luisa Hamilton- KPNC