The Osteopathic Approach to Pain Management: Evidence from Past, Present, and Future Research at the Osteopathic Research Center

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Professor and Osteopathic Heritage Foundation Richards-Cohen Distinguished Chair in Clinical Research
Department of Family Medicine
MEMORANDUM

April 8, 1996

TO: David Vick, D. O.
Chairman, Manipulative Medicine

FROM: Benjamin L. Cohen, D. O.
Vice President for Health Affairs and Executive Dean

Attached you will find the agenda for the April 17th retreat with your department. Dr. Raven, Dr. Licciardone and Dr. Gracy will attend the retreat. As you know, I will be out of town next week and Dr. Greg McQueen will represent me at the retreat.
Osteopathic Research Center

Historical Background

- Established in 2002 as the “profession-wide” research center
- Acquisition of $25 million in research grant funding ($40 million, including recent NIH collaborative grant for national LBP trial)
- National and international visibility relating to osteopathic medicine and treatment of chronic pain
  - Osteopathic health services
  - US Surgeons General
  - Evidence for osteopathy in NHS (UK)
  - Evidence for international licensing/regulatory issues (WHO)
  - Federal Pain Research Strategy (NIH)
Systematic Review and Meta-Analysis of OMT for Low Back Pain

American Osteopathic Association Guidelines for Osteopathic Manipulative Treatment (OMT) for Patients With Low Back Pain

Clinical Guideline Subcommittee on Low Back Pain


Is somatic dysfunction the cause or a contributing factor in the presentation of LBP? (Look for “RedFlags.”)

No

Identify cause of LBP and treat accordingly.

Yes

Contributing factor: Identify primary cause of LBP and treat accordingly. Treat contributing somatic dysfunction using the same decision making as followed if the LBP is solely the result of somatic dysfunction.

Cause:
A. Define type of dysfunctional mechanics and as appropriate define the dysfunctional barrier.

B. Determine why the dysfunction is present (eg, articular, muscular, myofascial, neuroreflex, membranous).

C. Determine the patient’s level of tolerance for OMT.

D. Decide upon the type of OMT to most effectively address the cause of the dysfunction with consideration for patient tolerance.

E. Apply OMT to accomplish the desired response.

F. Reassess the dysfunction and determine if and when follow-up evaluation is necessary. Follow up, if appropriate, and repeat steps A-F.
OMT during Pregnancy

OBSTETRICS
Osteopathic manipulative treatment of back pain and related symptoms during pregnancy: a randomized controlled trial
John C. Licciardone, DO, MS, MBA; Steve Buchanan, DO; Kendi L. Hensel, DO, PhD; Hollis H. King, DO, PhD; Kimberly G. Fulda, DPH; Scott T. Stoll, DO, PhD

OBJECTIVE: To study osteopathic manipulative treatment of back pain and related symptoms during the third trimester of pregnancy.

STUDY DESIGN: A randomized, placebo-controlled trial was conducted to compare usual obstetric care and osteopathic manipulative treatment, usual obstetric care and sham ultrasound treatment, and usual obstetric care only. Outcomes included average pain levels and the Roland-Morris Disability Questionnaire to assess back-specific functioning.

RESULTS: Intention-to-treat analyses included 144 subjects. The Roland-Morris Disability Questionnaire scores worsened during pregnancy; however, back-specific functioning deteriorated significantly less in the usual obstetric care and osteopathic manipulative treatment group (effect size, 0.72; 95% confidence interval, 0.31-1.14; P = .001 vs usual obstetric care only; and effect size, 0.35; 95% confidence interval, -0.06 to 0.76; P = .05 vs usual obstetric care and ultrasound treatment). During pregnancy, back pain decreased in the usual obstetric care and osteopathic manipulative treatment group, remained unchanged in the usual obstetric care and sham ultrasound treatment group, and increased in the usual obstetric care only group, although no between-group differences achieved statistical significance.

CONCLUSION: Osteopathic manipulative treatment shows promise to mitigate the deterioration of back-specific functioning during the third trimester of pregnancy.

Key words: back pain, osteopathic manipulative treatment, physical functioning, pregnancy, randomized controlled trial


Previous studies have found that a majority of pregnant women report low back pain during pregnancy. Other common neurologic/musculoskeletal problems during pregnancy include pubic pain, hip pain, low back pain, leg cramps, carpal tunnel syndrome, and DeQuervain’s tenosynovitis. When considering such neurologic/musculoskeletal aspects of pregnancy, virtually all women experience symptoms associated with pregnancy, an estimated one quarter having at least temporary disability. Moreover, pregnancy-related back pain is often associated with sleep disturbance and may affect activities of daily living or quality of life.

Complementary and alternative medicine (CAM) therapies may be considered as treatment options for back-related symptoms during pregnancy because of the real or unknown risks inherent with many drug therapies. A majority of pregnant women and prenatal health care providers alike report that they would consider using CAM therapies for low back pain during pregnancy, particularly manipulative and body-manipulating techniques such as massage and spinal manipulation. Osteopathic manipulative treatment (OMT) is a form of manual therapy provided by osteopathic physicians. An intriguing aspect of OMT is that during pregnancy, like massage therapy or chiropractic, it potentially could be integrated with the established prenatal visits provided by osteopathic obstetricians. However, relatively little research has been conducted on OMT during pregnancy. An observational study using medical records review at 4 sites found that prenatal OMT was associated with lower risk of perinatal delivery and meconium staining of amniotic fluid. Nevertheless, corroborating evidence of OMT benefits during pregnancy from prospective studies or clinical trials is lacking. The primary purpose of this randomized controlled trial was to explore the potential effects of OMT provided exclusively during the third trimester of pregnancy on maternal back pain and related physical functioning.

MATERIALS AND METHODS
This Phase II randomized controlled trial was conducted by the Osteopathic

Visit no.

<table>
<thead>
<tr>
<th>Treatment effect</th>
<th>Contrast</th>
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</thead>
<tbody>
<tr>
<td>Back pain (average pain level)</td>
<td>UOBC+OMT vs UOBC only</td>
</tr>
<tr>
<td>Back-specific functioning (Roland-Morris Disability Score)</td>
<td>UOBC+OMT vs UOBC+SUT</td>
</tr>
</tbody>
</table>

The OSTEOPATHIC Trial

• Supported in by the National Institutes of Health
• Conducted from 2006 through 2011
• Largest single-site efficacy trial involving spinal manipulation for low back pain (N=455)
• 2x2 Factorial design
• 17 publications have derived from the trial

Osteopathic Manual Treatment and Ultrasound Therapy for Chronic Low Back Pain: A Randomized Controlled Trial

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Catherine M. Kearns, BSc
Kearns P. Singh, PhD

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Department of Psychology, College of Science, University of Texas at Arlington, Arlington, Texas.

Department of Preventive Medicine, Department of Medicine, University of California at Los Angeles, Los Angeles, California.

ABSTRACT

PURPOSE: We studied the efficacy of osteopathic manual treatment (OMT) and ultrasound (UST) for chronic low back pain.

METHODS: A randomized, double-blind, sham-controlled, 2 × 2 factorial design was used to study OMT and UST for short-term relief of non-persistent chronic low back pain. The 695 patients were randomized to OMT and UST or sham OMT and sham UST. A 240-mm, 780-MHz ultrasound transducer was used to deliver 90 minutes of ultrasound exposure to each treatment group. The treatment sessions were provided four times weekly. Intention-to-treat analysis was performed to estimate the difference in post-treatment improvement in low back pain at week 12 (10% or greater in 50% or greater in patient self-report). Five secondary outcomes, safety, and treatment adherence were also assessed.

RESULTS: There was no statistically significant interaction between OMT and UST. Patients receiving OMT were more likely than patients receiving sham OMT to achieve moderate improvement in low back pain at week 12 (10% or greater in 50% or greater in self-report). Rates of P < .001 and reduction in visual analog scale (VAS) at 12 weeks were both 3.4% and 4.4% for both groups. Exclusionary criteria were met for the OMT treatment group. Overall, patients in the OMT group were more likely to be satisfied with treatment at the end of the study (P < .001). Patients receiving OMT had increased medication use for low back pain, but this difference was not statistically significant. The treatment adherence was similar between the two groups.

CONCLUSIONS: The OMT regimen used in this study was effective in reducing chronic low back pain. It was safe, practical, and well accepted by patients.

INTRODUCTION

Low back pain is the most common form of musculoskeletal pain and is the leading cause of disability. The economic burden of low back pain is estimated to be over $100 billion annually in the United States. When low back pain persists for 3 months, it is considered chronic and may cause progressive physical and psychological effects. Although previous guidelines recommend considering epidural injections for chronic or persistent low back pain, a Cochrane Collaboration review concluded that spinal manipulation is not more effective than sham interventions for short-term relief of chronic low back pain. The effectiveness of spinal manipulation remains controversial among family physicians. Osteopathic manual treatment (OMT) is delivered by osteopathic physicians in the United States, and by osteopaths in many other nations. No trial of

Table 2. Treatment Effects for Osteopathic Manual Treatment and Ultrasound Therapy in Chronic Low Back Pain

<table>
<thead>
<tr>
<th>LBP Reduction Threshold</th>
<th>OMT</th>
<th>UST</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intention-to-treat analysis (N = 455)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30%</td>
<td>1.38 (1.16-1.64)</td>
<td>1.02 (0.86-1.20)</td>
</tr>
<tr>
<td>≥50%</td>
<td>1.41 (1.13-1.76)</td>
<td>1.09 (0.88-1.35)</td>
</tr>
<tr>
<td>≥20 mm</td>
<td>1.47 (1.17-1.86)</td>
<td>1.01 (0.80-1.26)</td>
</tr>
<tr>
<td>≥40 mm</td>
<td>1.96 (1.18-3.24)</td>
<td>1.09 (0.68-1.75)</td>
</tr>
<tr>
<td>Per-protocol analysis (N = 362)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30%</td>
<td>1.42 (1.19-1.70)</td>
<td>1.03 (0.87-1.23)</td>
</tr>
<tr>
<td>≥50%</td>
<td>1.48 (1.18-1.86)</td>
<td>1.11 (0.89-1.38)</td>
</tr>
<tr>
<td>≥20 mm</td>
<td>1.44 (1.13-1.85)</td>
<td>1.05 (0.83-1.34)</td>
</tr>
<tr>
<td>≥40 mm</td>
<td>2.08 (1.21-3.58)</td>
<td>1.01 (0.61-1.67)</td>
</tr>
<tr>
<td>Patients with missed treatments considered nonresponders (N = 455)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30%</td>
<td>1.38 (1.13-1.69)</td>
<td>0.97 (0.80-1.18)</td>
</tr>
<tr>
<td>≥50%</td>
<td>1.43 (1.12-1.83)</td>
<td>1.05 (0.82-1.33)</td>
</tr>
<tr>
<td>≥20 mm</td>
<td>1.40 (1.07-1.82)</td>
<td>0.99 (0.77-1.28)</td>
</tr>
<tr>
<td>≥40 mm</td>
<td>2.01 (1.16-3.49)</td>
<td>0.95 (0.57-1.59)</td>
</tr>
</tbody>
</table>

Other Notable Findings:
- Greater satisfaction with OMT (P<0.001)
- Lesser use of prescription rescue medication with OMT (P=0.048)

Recovery from Chronic Low Back Pain with OMT

CONCORD Patient-Centered Research Fellowship Training Program for Mid-Career Physicians

Osteopathic Research Methods and Evidence

OVERVIEW OF OSTEOPATHIC MANIPULATIVE TREATMENT RESEARCH

The early development of osteopathic manipulation included the seminal work of Louis Winter and later R.R. Depew and D. Korn in Independence, Missouri. This work formed the foundation for much of the neurophysiological research relating to OMT. These and other aspects of basic research relating to osteopathic philosophy and OMT are described throughout this textbook, and detailed information may be acquired through such organizations as the American Academy of Osteopathy.

The principles and techniques used to conduct OMT research generally mirror those used elsewhere in medicine. However, the distinctive aspect of OMT provide unique challenges for investigators planning to conduct research as well as for osteopathic students, educators, and physicians working to integrate the findings into their clinical practice. This chapter focuses on the design of OMT clinical research that may be considered to be “patient oriented” or “patient centered.”

CLINICAL RESEARCH METHODS

A basic understanding of clinical research methods is needed to conduct rigorous studies of OMT that will yield actionable recommendations and clinical practice guidelines. The reader is referred to existing introductory textbooks in the fields of clinical research design, epidemiology, and biostatistics that provide detailed explanations of methodologies and analytical approaches (3-3). The objective of this chapter is to provide a broad overview of commonly used research methods in that osteopathic medical students, residents, and physicians may become more knowledgeable consumers and evaluators of reported research studies and their findings and use these skills to better care for their patients.

The osteopathic clinical research paradigm (Fig. 5.1) may be used to schematically depict the timeline of evidence according to the underlying research design. As in many medical disciplines, the use of available interventions and therapies often is based on expert opinion. Indeed, medicine has long been considered a cottage industry with practices trained under the apprenticeship model. This was particularly true in the osteopathic profession as it developed in the Midwestern United States and gradually spread to other regions of the country and internationally. However, this model also characterized each discipline's field of osteopathy and surgery. Today, much of the training of osteopathic medical students in osteopathic principles and practices, including OMT, remains largely driven by expert opinion. Such evidence may be based on both theoretical grounds or “first principles,” or it may be inferred by previous clinical experience. This knowledge continues to be passed down from one generation to another through the network of osteopathic physicians as well as in its current contemporary literature by publications and presentations and by use and adoption in the clinical setting. Consequently, at the core of the osteopathic clinical research paradigm virtually all osteopathic methods and a substantial body of osteopathic literature...
The Osteopathic Approach to Pain Management

Aim 1 - Processes of Medical Care for Low Back Pain
Are there differences in practice style between DOs and MDs that may be observed using patient-reported perceptions of their physician’s interpersonal manner, empathy, communication style?

Aim 2 - Clinical Outcomes of Medical Care for Low Back Pain
Are there differences between DOs and MDs in treating low back pain that may be observed using patient-reported clinical status measures at baseline and over 6 months of follow-up?

Aim 3 - Relationships Between Processes and Outcomes of Medical Care for Low Back Pain
Is the relationship between exposure to osteopathic medical care and low back pain outcomes mediated by physician characteristics such as communication style, empathy, or other factors that are considered uniquely “osteopathic,” including OMT?
Conducted within the PRECISION Pain Research Registry from April 2016 through December 2018

Included 313 adult patients with chronic (89%) or subacute low back pain

A total of 87 treated by DOs and 226 treated by MDs

Physician characteristics were reported by patients using the PSQ-18, CARE, and CBQ

Patients were characterized with the Pain Catastrophizing Scale and the Pain Self-Efficacy Questionnaire at baseline

Outcomes were measured with a numerical rating scale for pain (1°), Roland-Morris Disability Questionnaire (1°), and PROMIS-29 SPADE quality of life cluster (2°)
Aim 1 Results

Results are embargoed pending publication
Results are embargoed pending publication
Results are embargoed pending publication
Aim 2 Results

Results are embargoed pending publication
Results are embargoed pending publication
Results are embargoed pending publication
**Mediation Analysis**

**MODEL SPECIFICATIONS**

\[ X = \text{Osteopathic medical care (vs. allopathic medical care)} \]

\[ Y = \text{Outcome variable(s)} \]

- Pain Catastrophizing
- Pain Self-Efficacy
- Low Back Pain Intensity
- Back-Related Disability
- Quality of Life Deficits

\[ M = \text{Mediator(s)} \]

- Physician interpersonal manner
- Physician empathy
- Physician communication style
- OMT

Multiple mediation model using 10,000 bootstrap samples to determine osteopathic treatment effects and 95% CIs

Aim 3 Results

M = Mediator(s)
- Physician interpersonal manner
- Physician empathy
- Physician communication style
- OMT

Results are embargoed pending publication
University of Minnesota to lead $14M national NIH study of non-drug therapies to prevent chronic back pain

Wednesday, September 20, 2017

University of Minnesota will receive $11.2M, with an additional $2.8M awarded to the University of Washington
Pain Research in Concert with Federal Pain Research Strategy

A strategic plan for pain research across federal agencies.

The FPRS planning committee, which includes the NIH/NINDS Office of Pain Policy, members of the NIH Pain Consortium and members of the IPRCC, has assembled a diverse and balanced group of scientific experts, patient advocates, and federal representatives who are working to identify and prioritize research recommendations as a basis for a long term strategic plan to coordinate and advance the federal research agenda. The key areas of prevention of acute and chronic pain, acute pain and acute pain management, the transition from acute to chronic pain, chronic pain and chronic pain management, and disparities in pain and pain care will provide a framework for development of the strategy upon which important cross-cutting elements will be addressed.

Organizational Structure
Statement of the Problem
The paucity of large data sets and prospective registries of well-characterized patients has delayed our understanding of acute and chronic pain and development of safe and effective pain management. Such resources will allow researchers to follow prospectively, sizable patient populations, pool large data sets through standardized data-sharing repositories, and utilize “big data” approaches, including comparative and cost effectiveness analyses. Information generated from these resources will help to elucidate the complex heterogeneity of pain, identify populations vulnerable to developing chronic pain, and discriminate subgroups who benefit from different pharmacological and non-pharmacologic treatments and treatment algorithms. Furthermore, given the heterogeneity within and across chronic pain disorders and populations, large data sets will increase the likelihood of delineating the complex interplay among genetic, environmental, occupational, physiological, psychological and clinical characteristics that contribute to the risk of developing, clinical course, and treatment of chronic pain.

PRECISION Pain Research Registry Overview

Dallas-Fort Worth Metroplex

Patients with subacute or chronic low back pain

Epidemiological studies

PRECISION Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation

Interventional studies (including randomized controlled trials)

Clinical studies
The PRECISION Pain Research Registry is Expanding to Major Cities in Texas in 2019

“A future for all unbounded by pain”

The Pain Registry for Epidemiological, Clinical, and Interventional Studies and Innovation (PRECISION) was established at the University of North Texas Health Science Center in 2016. Over 2,000 participants in Dallas-Fort Worth have screened for eligibility and 500 have enrolled. Research focuses on the following topics.

- Use of precision medicine to advance chronic pain management
- Pharmacogenetics of pain and its management
- Biological markers of pain and response to therapy
- Pharmacological interventions, including safety issues relating to opioids
- Non-pharmacological interventions
- Biopsychosocial factors relating to pain
- Functioning and quality of life in relation to pain

The PRECISION Pain Research Registry enrolls participants with subacute or chronic low back pain and collects follow-up data on a quarterly basis. A biobank is available to enhance the collaborative research that may be conducted through the registry; however, no diagnostic testing or treatment is provided by the registry.

www.unthsc.edu/PRECISION
Why Focus on Low Back Pain in the Registry?

- **632 million persons** worldwide have low back pain.
- It is the **#1 cause of disability** worldwide.
- More than **100 million Americans** suffer from chronic pain (more than heart disease + cancer + diabetes combined).
- Pain is responsible for **$635 billion annually** in medical expenditures and lost productivity (~DoD budget).
- “... relieving pain should be a national priority.”


**Timetable for Longitudinal Data Collection**

Table 1. Three-year timetable of patient-reported data elements and survey instruments.*

<table>
<thead>
<tr>
<th>Data elements and survey instruments</th>
<th>Timetable</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institutes of Health minimum dataset for low back pain</td>
<td>0 Mo 1-4 Wk 3 Mo 6 Mo 9 Mo 12 Mo 15 Mo 18 Mo 21 Mo 24 Mo 27 Mo 30 Mo 33 Mo 36 Mo</td>
</tr>
<tr>
<td>History of medical conditions inventory</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Comprehensive pharmacologic treatments item</td>
<td>● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Low back pain-specific opioid use item</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Low back pain-specific nonsteroidal anti-inflammatory drug use item</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Drug Adverse Events Index</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>History of non-pharmacologic treatments for low back pain inventory</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Numerical rating scale for low back pain</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
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<tr>
<td>Roland-Morris Disability Questionnaire</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Patient-Reported Outcomes Measurement Information System (29-item)</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Pain Sensitivity Questionnaire</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Pain Catastrophizing Scale</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Pain Self-Efficacy Questionnaire</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Communication Behavior Questionnaire</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Consultation and Relational Empathy Measure</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Patient Satisfaction Questionnaire (18-item)</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
<tr>
<td>Scale of Patient Overall Satisfaction with Primary Care Physicians</td>
<td>● ● ● ● ● ● ● ● ● ● ● ● ●</td>
</tr>
</tbody>
</table>

*Saliva samples for DNA sequencing and blood samples for biomarker analysis are also collected at the baseline (0 Mo) visit.*
Clinical Research Fellowship Program for DO Students

• Program started in June 2018 with 7 students from TCOM Class of 2021
• The fellowship includes a 4-week summer didactic training component and ongoing mentorship while in TCOM
• Applications for subsequent classes are due in January of each year
• Program benefits for Class of 2021 include:
  • Stipend of $5,000 for participation in summer program and subsequent completion of research project during Fall 2018 and Spring 2019
  • Complimentary textbook and didactic materials for the summer program
  • Up to $1,000 to attend a national conference to present the research project
  • Paid poster upon completion of the research project
  • Paid costs, if any, for publication of a peer-reviewed journal article
  • Fellowship certificate upon completion of the summer program and research project
Clinical Research Fellow Projects (Class of 2021)


Apollo Tran. An analysis of the association between GDF5 polymorphisms and chronic low back pain.

Maryam Burney. Mediating effects of self-reported measures of pain sensitivity, catastrophizing, and self-efficacy on the association between COMT and BDNF polymorphisms and chronic low back pain.

Benjamin Romanowski. Genetic influences on opioid use in chronic low back pain: OPRM1 rs1799971 polymorphisms.

Monika Schmitt. The link between diabetes mellitus and comorbid chronic low back pain: gene-based association study within a pain research registry.
Study of Pharmacogenetics to Inform Opioid Prescribing for Chronic Pain

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Annual No. of Prescriptions*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>40,783,000</td>
</tr>
<tr>
<td>Codeine</td>
<td>18,181,469</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>11,099,465</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>70,063,934</strong></td>
</tr>
</tbody>
</table>

Opioids can provide short-term benefits for moderate to severe pain. Scientific evidence is lacking for the benefits to treat chronic pain.

IN GENERAL DO NOT PRESCRIBE OPIOIDS AS THE FIRST-LINE TREATMENT FOR CHRONIC PAIN (for adults 18+ with chronic pain > 3 months excluding active cancer, palliative, or end-of-life care).

BEFORE PRESCRIBING

1. **ASSESS PAIN & FUNCTION**
   Use a validated pain scale. Example: PEG scale where the score = average 3 individual question scores (30% improvement from baseline is clinically meaningful).
   Q1: What number from 0 – 10 best describes your PAIN in the past week? (0 = “no pain”, 10 = “worst you can imagine”)
   Q2: What number from 0 – 10 describes how, during the past week, pain has interfered with your ENJOYMENT OF LIFE? (0 = “not at all”, 10 = “complete interference”)
   Q3: What number from 0 – 10 describes how, during the past week, pain has interfered with your GENERAL ACTIVITY? (0 = “not at all”, 10 = “complete interference”)

2. **CONSIDER IF NON-OPIOID THERAPIES ARE APPROPRIATE**
   Such as: NSAIDs, TCAs, SNRIs, anti-convulsants, exercise or physical therapy, cognitive behavioral therapy.

3. **TALK TO PATIENTS ABOUT TREATMENT PLAN**
   • Set realistic goals for pain and function based on diagnosis.
   • Discuss benefits, side effects, and risks (e.g., addiction, overdose).
   • Set criteria for stopping or continuing opioid.
   • Set criteria for regular progress assessment.
   • Check patient understanding about treatment plan.
CYP2D6 Metabolizer Phenotypes

- Ultra-rapid (high risk)
- Extensive (low risk)
- Intermediate (high risk)
- Poor (high risk)

Codeine Metabolism


Pharmacogenetics

Precise Medicine

Models

Study Aims

Opioid Prescribing

Usual Care Model

90 patients exclusively using opioids for low back pain

270 patients exclusively using NSAIDs for low back pain

22 high-risk patients exclusively using opioids for LBP

22 high-risk patients exclusively using opioids for LBP

270 patients exclusively using NSAIDs for low back pain

66 low-risk patients exclusively using NSAIDs for LBP

66 low-risk patients exclusively using NSAIDs for LBP

264 patients exclusively using NSAIDs for LBP

22 high-risk patients exclusively using opioids for LBP

88 patients exclusively using NSAIDs for LBP

## Case-Control Study of Chronic Widespread Pain

Table 1. Comparison of baseline sociodemographic and clinical characteristics of patients with chronic localized or regional pain and patients with chronic widespread pain.*

<table>
<thead>
<tr>
<th></th>
<th>CLRP (n=183)</th>
<th>CWP (n=69)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.2 ± 0.8</td>
<td>54.1 ± 1.2</td>
<td>0.97</td>
</tr>
<tr>
<td>Female</td>
<td>115 (62.8%)</td>
<td>45 (65.2%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Current opioid user</td>
<td>50 (27.3%)</td>
<td>34 (49.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Self-reported depression</td>
<td>74 (40.4%)</td>
<td>43 (62.3%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Ever unable to do usual work for ≥1 month due to low back pain</td>
<td>51 (27.9%)</td>
<td>34 (49.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ever received disability or workers compensation benefits for low back pain</td>
<td>33 (18.0%)</td>
<td>27 (39.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever involved in lawsuit or legal claim related to low back pain</td>
<td>9 (4.9%)</td>
<td>12 (17.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Pain intensity (0-10 scale)</td>
<td>5.8 ± 0.1</td>
<td>7.2 ± 0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Back-related disability (RMDQ score)</td>
<td>12.1 ± 0.5</td>
<td>17.5 ± 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PROMIS quality-of-life scale score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>40.4 ± 0.5</td>
<td>34.5 ± 0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety</td>
<td>52.2 ± 0.7</td>
<td>59.0 ± 1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depression</td>
<td>51.0 ± 0.7</td>
<td>56.8 ± 1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatigue</td>
<td>55.5 ± 0.7</td>
<td>62.0 ± 1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>54.2 ± 0.6</td>
<td>58.3 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Participation in social roles</td>
<td>47.1 ± 0.6</td>
<td>39.8 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain interference with activities</td>
<td>60.2 ± 0.6</td>
<td>67.4 ± 0.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
**Genetic and Psychosocial Aspects of Chronic Widespread Pain and its Management**

**Aim 1 – Candidate Genes for Chronic Widespread Pain**
We aim to determine which of 40 high-priority candidate genes for human pain identified and validated by inclusion among 535 “pain genes” largely derived from the Pain Genes Database are associated with CWP using an allelic model with gene and gene-set testing.

**Aim 2 – Psychosocial Factors Associated with Chronic Widespread Pain**
We aim to determine if pain sensitivity and pain catastrophizing may promote CWP, and if pain self-efficacy may protect against the development of CWP.

**Aim 3 – Interaction of Genetic and Psychosocial Factors**
The biopsychosocial model posits that biological factors (e.g., genes and neurotransmitters that they control) and psychosocial factors are both important in contributing to the etiology and management of pain, including CWP. We aim to determine the relative importance of genetic and psychosocial factors using a multivariable model.
## Case-Control Study of Quality of Life Deficits

Table 1. Comparison of sociodemographic and clinical characteristics of PRECISION Pain Research Registry patients with chronic low back pain according to baseline SPADE cluster score.*

<table>
<thead>
<tr>
<th></th>
<th>SCS ≥ 55 (n=203)</th>
<th>SCS &lt; 55 (n=162)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.3 0.7</td>
<td>54.4 1.0</td>
<td>0.94</td>
</tr>
<tr>
<td>Female (%)</td>
<td>67</td>
<td>68</td>
<td>0.78</td>
</tr>
<tr>
<td>Current opioid user (%)</td>
<td>42</td>
<td>24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever unemployed or unable to do usual work for ≥ 1 month due to LBP (%)</td>
<td>52</td>
<td>19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ever received disability or workers compensation benefits for LBP (%)</td>
<td>31</td>
<td>14</td>
<td>0.001</td>
</tr>
<tr>
<td>SPADE cluster score</td>
<td>61.3 0.3</td>
<td>50.0 0.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOL-sleep disturbance score</td>
<td>59.2 0.5</td>
<td>51.2 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOL-pain interference with activities score</td>
<td>66.5 0.4</td>
<td>57.3 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOL-anxiety score</td>
<td>59.9 0.6</td>
<td>46.2 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOL-depression score</td>
<td>58.2 0.6</td>
<td>44.9 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QOL-low energy/fatigue score</td>
<td>62.9 0.5</td>
<td>50.3 0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain Catastrophizing Scale score (0-52 scale)</td>
<td>26.0 1.0</td>
<td>9.5 0.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain Self-Efficacy Scale score (0-60 scale)</td>
<td>26.8 1.0</td>
<td>44.2 0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain intensity score (0-10 scale)</td>
<td>6.7 0.1</td>
<td>5.4 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Roland-Morris Disability Questionnaire score (0-24 scale)</td>
<td>17.0 0.3</td>
<td>10.1 0.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Is there a bidirectional relationship between pain/functioning and quality of life, and can greater emphasis on QOL improve pain/functioning?
Using Health-Related QOL Measures to Optimize Chronic Pain Management through Patient Engagement

**Aim 1 – Assess Changes in SPADE Cluster Score and 5 Component QOL Scale Scores**

We hypothesize that patients allocated to the experimental group will experience better change scores over 3 months on the SPADE cluster and each of its five component QOL scales (1° outcomes) than patients allocated to the control group, with Cohen’s $d \geq 0.5$.

**Aim 2 – Assess Changes in Pain Intensity and Back-Specific Functioning**

We hypothesize that patients allocated to the experimental group will experience better change scores over 3 months on a numerical rating scale for pain intensity and on the Roland-Morris Disability Questionnaire relating to back-specific functioning (2° outcomes) than the control group, with Cohen’s $d \geq 0.5$.

**Aim 3 – Determine Patient Actions Based on QOL Report that Mediate 1° and 2° Outcomes at 3 Months**

We hypothesize that between-group differences in QOL, pain intensity, and back-specific functioning in the trial will be mediated by patient actions prompted by the QOL report.
Methodological features of the registry (eg, remote consenting and electronic data capture) represent a new clinical trial paradigm that holds the promise of enrollment of large numbers of representative patients to study real-world effectiveness at a reasonable cost.

Such aspects of “randomized registry trials” have led to speculation that they represent the next “disruptive technology in clinical research”

*New England Journal of Medicine*

Acknowledgments

• Current sponsors of Dr. Licciardone’s pain research
  • National Institutes of Health
  • Osteopathic Heritage Foundation
  • Institute for Patient Safety – SaferCare Texas
  • American Osteopathic Association
  • University of North Texas Health Science Center