Doc, What Else Can I Do?
Learning the Evidence Behind Complementary and Alternative Chronic Pain Management for Chronic Nonspecific Low Back Pain
Part 1 of 2
Michael Saenger, MD, FACP
Karen Drexler, MD
APA PCSS-O; January 25, 2013

Conflicts of Interest
• No Financial Nor Academic Conflicts
• Biases, favorable toward:
  – Bio-psycho-social approach to health care
  – Self empowered Care / Self-Efficacy
  – Evidence Based Practice (EBP)
  – Systems of Care
    • Patient Centered Medical Home
    – Evidence is evolving, so learn for change

What is CAM?
• Complementary and Alternative Medicine
• All things “outside the box” of Bio-Medicine

• Complementary = “in addition to” Conventional “Scientific, Modern” Medicine
• Alternative = “in place of” Conventional

• Integrative = “combining the best of Conventional and CAM”

http://nccam.nih.gov/research/blog
NCCAM Summary

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Sorry, we can’t cover everything

• Goals: to Learn and Keep Learning
• Overview Part 1 (today):
  – CAM Popularity
  – How to Not be Fooled by the “Evidence”
  – Current CAM Evidence for:
    • Homeopathy
    • Mindfulness and Yoga
  – Now what?

Coming in Part 2

– Current CAM Evidence for:
  • Devil’s Claw
  • Spinal Manipulation, Massage, Acupuncture and Alexander Technique
  • Reiki
– Now what?
Complementary and Alternative Medicine (CAM) is Popular

- Over 1/3rd of all adults used CAM in 2007
  - Your patients are using CAM
- Ask them what:
  - On
  - Tried
  - Wanting to try


CAM is Popular for Women and Men
What we know about CAM

- Not much
- BUT, Chronic Opioid Therapy for CNCP is also based on Low Quality Evidence
  - “In the United States guideline, 21 of 25 recommendations were viewed as supported by only low-quality evidence.
  - In other words, the developers of the guidelines found that what we know about opioids is dwarfed by what we don’t know.”

Cautionary Tale – Use of “Evidence”

- “Despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.”
- NEJM; Letter to the Editor
- Retrospective review
- Inpatients

Cautionary Tale – Use of “Evidence”

- “Opioid maintenance therapy can be a safe, salutary and more humane alternative…”
- Retrospective Case Series, Single Center
- 38 patients – 2/3 on < 20 mg morphine daily
Case Presentation
Karen Drexler, MD

- 28 year old Afghanistan veteran with TBI & PTSD
  - In rehabilitation for alcohol, “bath salt” and “spice” dependence
  - Seeks treatment for low back pain
- Aware that history of TBI & substance use disorder increases risk of addiction to opioids,
  - Asks about natural treatment (herbal, exercise)
  - Energy therapies, “Reiki” or “Healing Touch.”
Assessing Clinical Effectiveness

- Treatment
  - Conventional
  - CAM
  - Usual Care

- Outcomes
  - Pain
  - Function
  - Side-effects

- Costs
  - Direct
  - Indirect


Evidence Based Practice


How Not to be Mis-led; How to Appraise the Evidence:

- Validity of Methods
  - Jadad Score
  - GRADE Score

- Results - Treatment Effect based on Intention to Treat Analysis (ITT)
  - Minimally Clinically Important Difference (MCID)
  - Number Needed to Treat (NNT)
  - Confidence Intervals (CI; not Standard Error of the Mean [SEM])
  - Forest Plot
    - Standardized Mean Difference (SMD)

- Applicability
  - Patient Values
  - Safety
  - Costs
Jadad Score of Methodological Validity of RCT

- 0-5 points
- 3 points = "High Quality", "Low Risk of Bias"
  - Is the study randomised? If yes, + 1 point.
    - Is the randomization procedure reported and appropriate?
      - If yes, + 1 point.
      - If no, delete all points awarded for randomization.
    - Is the study double blind? If yes, + 1 point.
      - Is the double blinding method appropriate?
        - If yes, + 1 point.
        - If no, delete all points awarded for double blinding.
      - Are the reasons for patient withdrawals and dropouts described, for each treatment group?
        - If yes, + 1 point.

GRADE Working Group evidence grades – Systematic Review: How Confident?

- High: Further research is very unlikely to change our confidence
  - Several high-quality RCTs with consistent results
- Moderate: Further research is likely to have an important impact
  - One high-quality RCT
  - Several RCT with some limitations
- Low: Further research is very likely to have an important impact
  - One or more RCTs with severe limitations
- Very low: Any estimate of effect is very uncertain.
  - Expert opinion
  - One or more RCTs with very severe limitations

http://www.gradeworkinggroup.org/index.htm
How to Measure “PAIN” and Changes?

• MANY options:
  – Numeric Rating Score (NRS) 0-10
  – Visual Analog Scale (VAS) 0-100 …

• How to combine results with different Scales?
  – Standardized Mean Difference (SMD)

Is the effect size important?

• “A difference is a difference only if it makes a difference”
  Darrell Huff. How to Lie with Statistics. 1954

• Statistical Significance is necessary but not sufficient for Clinical Significance

Significant Improvements in Pain

• Patients’ expectations: pain free
  – Impossible short of general anesthesia

• Minimum Clinically Important Difference
  – MCID = 30% reduction
    • > 2 points decrease on 0-10 scale
    • 0.5 change in SMD
    • < 0.7 or > 1.6 change in OR
Besides Pain
What Else Should Be Measured?

• Function
  — Meaningful
    • Patient-Centric
  — Measures:
    • Disease non-specific – SF 36
    • Disease specific – RDQ or ODI

Measures of Function

• Medical Outcomes Study Short Form 36: SF 36
  — 8 subscales; each scored 0-100
  — 20-30 point change is moderately significant
• Rowland [Morris] Disability Questionnaire: RDQ
  — 0-24 Scale
  — 2-3 point is Minimally Clinical Important Difference
  — 2-8 point change is needed for significant improvement
• Modified Oswestry Low Back Pain Disability Index: ODI
  — 10 questions scaled to 100 points
  — >10-20% change may be MCID

Lack of Safety & Side-effect Reporting

• Deficiency in:
  — CAM reporting
  — FDA oversight

• Remember additional risks, especially with:
  — Pregnancy
  — Drug – Drug Interactions
    • P450 concerns with many Botanical agents
      — E.g. St. John’s Wort
CAM Categories:

- Whole Medical Systems
- Mind-Body Medicine
- Natural, Biologically Based Products
- Manipulation and Body Based Practices
- Energy Medicine

Whole Medical Systems

- Traditional Chinese Medicine
- Ayurvedic Medicine
- Traditional Healers
- Homeopathy
- Naturopathy

Homeopathy

- “Law of similarities” = “Like cures like”
- “Remedies”
  - Considered drugs
    - Food, Drug and Cosmetic Act of 1938
  - “High Potency” = extremely dilute

Homeopathic Treatment of Patients With Chronic Low Back Pain: A Prospective Observational Study With 3 Years’ Follow-up
Homeopathy in LBP

- Prospective, multicenter, observational study
- 129 consecutive adults self entering treatment
- 144 Remedies used in 909 Prescriptions
  - Averaging 7 prescriptions per patient
- 34% remained in treatment through 2 years
  - Large numbers "Lost to Follow-up"

Number Needed to Treat (NNT)

- Number of patients who must be treated to avoid an outcome in one patient
- Big number = many patients are exposed to side-effects and cost without improvement

- NNT = 1 / Absolute Risk Reduction
- ARR = difference in outcomes

? Infinitely Large NNT in Homeopathy

- NRS (Numeric Rating Score, i.e. 0-10)
  - Decreased by 1.5 points (<2) at 12 months
  - Not Minimally Clinically Important Difference
- Reportedly significant improvement in SF 36 QoL (Quality of Life) scores
  - Increase in 5 points on 0-100 scale at 12 months
  - Not Minimally Clinically Important Difference
Safety in Homeopathy

- Dilutions of Remedies may not contain even one part of the substance

Cost of Homeopathy = ? $750

- Homeopath visit fees:
  - 1st visit for 60-90 minute interview
    - $100-300 MD
    - $50-250 non-MD
  - Following visits for 15-45 min; every 1-6 months
    - $50-100 MD
    - $30-80 non-MD
- Remedy
  - $4-10

Mind-Body Medicine

- Progressive Relaxation
- Deep Breathing Exercises
- Meditation and Mindfullness
- Prayer
- Music Therapy
- Yoga

- Remember that these elements may be part of larger Whole System of Health
Mindfulness Therapy for cLBP

• “Derived from Buddhist spiritual tradition, mindfulness has been secularized and integrated into behavioral treatment”
  – Mindfulness-based stress reduction
  – Mindfulness-based cognitive therapy

• Goal is “to accept all varieties of experience”
  – “Present focused, nonjudgmental”


Mindfulness-based stress reduction for low back pain. A systematic review

• 3 RCT; 117 patients
• Treatments: 8 weekly 1.5 hour sessions (½ teaching, ½ meditation) and meditation homework 45 minutes daily
• Control groups were “Waiting List” or “Health Ed

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Inclusion</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esmer</td>
<td>55</td>
<td>failed surgery</td>
<td>40 weeks</td>
</tr>
<tr>
<td>Morone</td>
<td>74</td>
<td>moderate cLBP</td>
<td>3 months</td>
</tr>
<tr>
<td>*Morone</td>
<td>78</td>
<td>moderate cLBP</td>
<td>4 months</td>
</tr>
</tbody>
</table>


Intention to Treat Analysis (ITT)

• Analyze outcomes based on
  – randomized assignment,
  – not based on the smaller group left after:
    • Cross-over
    • Lost to follow-up...
• ITT opposite of “Per Protocol Analysis"
Not Intention to Treat (ITT)

? Infinitely Large NNT Mindfulness Tx

- Esmer study after “failed” spinal surgery  
  - Reportedly small improvements but not ITT
- Morone studies of older patients with cLBP:  
  - No statistically significant change in pain  
  - Trend, but no clinically significant change in disability
- Improvements noted in “acceptance” scores
- Prior studies in anxiety noted small, lasting decrease in symptoms

Safety of Mindfulness Therapy

- No known adverse events
Cost Mindfulness Therapy? $400

• For 8 sessions
• Online programs available for anxiety...

https://www.tickets.umn.edu/CSH/Online/ accessed Jan 2013

Yoga in Chronic Low Back Pain
Systematic Review

• Yoga started within Ayurveda
  — “Ancient knowledge that aims to discover the true sense of human life and to find remedies for diseases.”
  — “[Yoga] creates inner, physical and emotional balance through the use of postures, called asanas, combined with breathing techniques or pranayama.”

• To study “Yoga” we focus on isolated parts not necessarily the Whole System


Yoga in Chronic Low Back Pain
Systematic Review

<table>
<thead>
<tr>
<th>Study (2007)</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Duration</th>
<th>Outcome Measures</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hurley (2005)</td>
<td>RTC with 3 parallel groups</td>
<td>32 patients with CLBP</td>
<td>24 weeks</td>
<td>Self care, MPQ</td>
<td>Low</td>
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<tr>
<td>Rafferty (2005)</td>
<td>RTC with 3 parallel groups</td>
<td>29 patients with isolated low back pain</td>
<td>12 weeks</td>
<td>Interscan</td>
<td>Medium</td>
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<tr>
<td>Green (2005)</td>
<td>RTC with 6 parallel groups</td>
<td>53 patients with CLBP</td>
<td>12 weeks</td>
<td>Interscan</td>
<td>Low</td>
</tr>
<tr>
<td>Hahn (2005)</td>
<td>RTC with 5 parallel groups</td>
<td>51 LTD adults</td>
<td>24 weeks</td>
<td>Interscan</td>
<td>Medium</td>
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<tr>
<td>Stenman (2005)</td>
<td>Single blind RTC with 2 parallel groups</td>
<td>40 patients with CLBP</td>
<td>12 weeks</td>
<td>Interscan</td>
<td>Low</td>
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<tr>
<td>Merton (2005)</td>
<td>Single blind RTC with 2 parallel groups</td>
<td>37 patients with CLBP</td>
<td>12 weeks</td>
<td>Interscan</td>
<td>Low</td>
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Yoga in Chronic Low Back Pain
Systematic Review

Table 2: Quality assessment of the included studies ( Jadad score).

<table>
<thead>
<tr>
<th>Study year</th>
<th>Random sequence</th>
<th>Allocation concealment</th>
<th>Blinding of participants or personnel</th>
<th>Blinding of outcome assessors</th>
<th>Withdrawals and dropouts</th>
<th>Sum (Jadad score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen et al. (2013)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Chettiar et al. (2010)</td>
<td>1</td>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
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<td>Garfield et al. (1996)</td>
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<td>0</td>
<td>1</td>
<td>3</td>
<td>5</td>
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<tr>
<td>Yamashita et al. (2006)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>4</td>
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<tr>
<td>Knecht et al. (2006)</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td>Newman (2006)</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Williams (2008)</td>
<td>1</td>
<td>0</td>
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<td>0</td>
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Points were awarded as follows: study described as randomized, 1 point; allocation concealment, 1 point; participants blinded to intervention, 1 point; evaluator blinded to intervention, 1 point; description of withdrawals and dropouts, 1 point.


Yoga in Chronic Low Back Pain
Single Blind RCT; Single Center

• Participants agreed to attend
  – at least 20 of 24 weeks and
  – at least 40 of 48 classes (90 min) and
  – to do 30 min sessions on non-class days

• Participants in the control group continued self-directed standard medical care

• Most were white, college graduated women

• Validity = 4 of 5 Jadad score

Pain - Yoga in Chronic Low Back Pain

Function - Yoga in Chronic Low Back Pain

? How Large a NNT for Yoga

- (slide 49) What do you see? What is implied?
  - See how the Per Protocol graph looks more impressive.
  - Look again at the VAS, in the ITT, Pain is statistically decreased but not quite to Minimally Clinically Improved Difference - Pain does not decrease by >2 points in 20mm - Could trend continue if study was extended?
- (slide 50) Also check out the whiskers depicting intervals for Function
  - These intervals are Standard Error of the Mean (SEM) and not Confidence Intervals (CI) - which would be approximately twice the width
  - Hence there is no statistical difference in the 24 week Functional assessment between experimental and control groups

- However, in selective, motivated patients, Yoga could be the start of a new approach to their complex pain with
  - Active, self empowered care
  - New thinking and behaving
Safety of Yoga

• Infrequent MSK injury
• Men may have greater risk:
  – 16% of Yoga practitioners are men,
  – but account for more injuries:
    • 30% fractures
    • 71% of nerve damage

Cost of Yoga = ? $750

• 4 introductory classes $50-90
• $115 monthly fee, unlimited group classes
• MUCH more if you go in for all the trends...

Summary of Part 1:
State of EBP for CAM for cLBP

• Low quality of evidence
• Short term, small benefit possible for:
  – ? Mindfullness Therapies
  – Yoga
  – [and more evidence coming in Part 2]
Duration of Therapy?

- Yoga
  - Growing trend of effect
  - Should treatment continue beyond 8 weeks?
    - What would the cost be?
    - Would the small benefit grow?

So What Do We Do?

- Standardize best care within Medical Home
  - Then individualize care
    - Rather than just variation in care

So What Do We Do?

- Remember limitations and benefits of all our therapies: Conventional and CAM
  - If we applied the same rigorous criteria opioids would FAIL for chronic pain
- Perhaps Yoga and other therapies have some benefit [Wait for Part 2]
  - Consider applying them within a package of step-wise options
So What Do We Do?

• Seek:
  – Safety
  – Clinically Important Differences in effect
  – Resource stewardship

So What Do We Do?

• Bio-Psycho-Social Approach
  Screen for and address all:
  – Mental Health needs
    • Anxiety including PTSD
    • Depression including Bipolar
  – Substance Use Disorders
  – Relational, Vocational needs

So What Do We Do?

• Bio-Psycho-Social Approach
  – Empower Self-Care and Self-Efficacy
    • Learn:
      – Motivational Interviewing
      – Coaching
    • Encourage starting with one healthier behavior:
      – E.g. Progressive Relaxation, or Deep Breathing...
      – Could include Yoga ...
Learn and Keep Learning

- Cochrane Collaboration
- PubMed Advanced Search
- Trip Database
  - http://library.medicine.yale.edu/guides/screencasts/finditfast/finditfast_9/PubMed Advanced

Questions?

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**NCCAM References/Resources**

- Subscribing to CAM newsletter
  https://nccam.nih.gov/tools/subscribe?digest=1
- Summary Table
  http://nccam.nih.gov/health/providers/digest/pain-science/chart

**For Patient Reference**

- 6 Tips for patients considering CAM
  http://nccam.nih.gov/health/tips/pain
- NCCAM Clinical Digest
  http://nccam.nih.gov/health/providers/digest/chronicpain.htm

**CAM Therapies/Diagnostic Techniques Not Supported by NCCAM for LBP**

- Glucosamine
- Prolotherapy
- Static Magnets
- Applied Kinesiology
- Iridology
Coming in Part 2

– Current CAM Evidence for:
  • Devil's Claw
  • Spinal Manipulation, Massage, Acupuncture and Alexander Technique
  • Reiki
– Now what?