CDC Recommendations for Nonopioid Treatments in the Management of Chronic Pain

Clinician Outreach and Communication Activity (COCA) Call

July 27, 2016

Office of Public Health Preparedness and Response
Division of Emergency Operations

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Planners have reviewed content to ensure there is no bias.

This presentation will include discussion of non-FDA approved nortriptyline for the treatment of fibromyalgia.

Objectives

At the conclusion of this session, the participant will be able to:

- State the evidence related to effectiveness and potential risks associated with nonopioid treatments for chronic pain.
- Outline nonpharmacologic and nonopioid pharmacologic treatment options for various chronic pain conditions.
- Review patient evaluation methods that can be used to identify the most appropriate treatment options for chronic pain.
- Describe the role of patient beliefs and expectations, and value of exercise, education, and nonopioid drug treatments in the management of musculoskeletal pain complaints.

Save-the-Dates

Mark your calendar for the upcoming opioid prescribing calls

Call No.	Date	Topic
1	June 22	Guideline for Prescribing Opioids for Chronic Pain
2	July 27	Non-Opioid Treatments
3	August 3	Assessing Benefits and Harms of Opioid Therapy
4	August 17	Dosing and Titration of Opioids

TODAY'S PRESENTER

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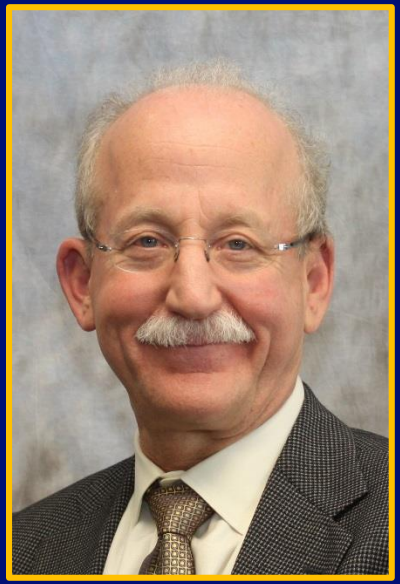
TODAY'S PRESENTER



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Disclaimer

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry

CDC Guideline for Prescribing Opioids for Chronic Pain:

Nonopioid Treatments for Chronic Pain

Deborah Dowell, MD, MPH

July 27, 2016

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Continuing Education Examination available at http://www.cdc.gov/mmwr/cme/conted.html.

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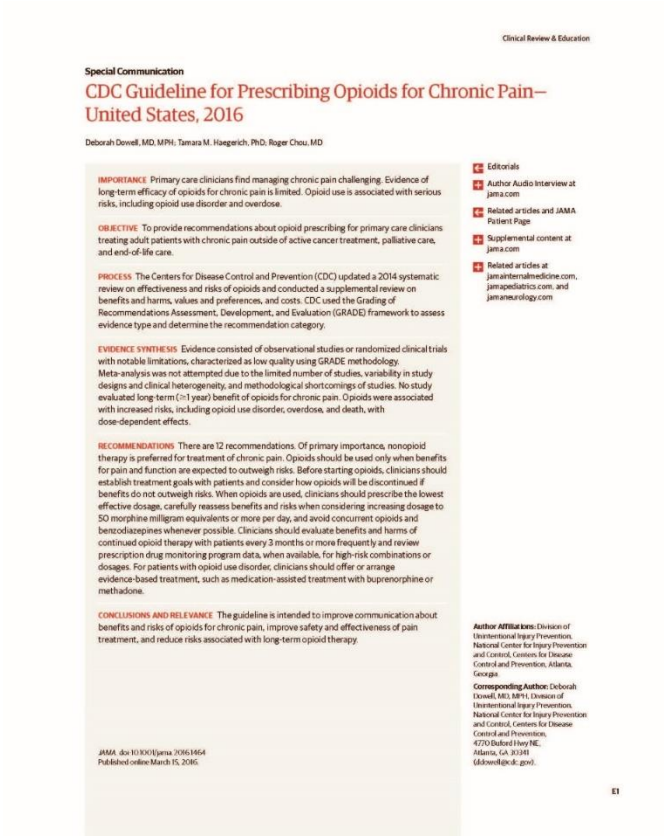

Clinical Review & Education

Special Communication

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

Deborah Dowell, MD, MPH; Tamara M. Haegerich, PhD; Roger Chou, MD

IMPORTANCE Primary care clinicians find managing chronic pain challenging. Evidence of long-term efficacy of opioids for chronic pain is limited. Opioid use is associated with serious risks, including opioid use disorder and overdose.

OBJECTIVE To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

PROCESS The Centers for Disease Control and Prevention (CDC) updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs. CDC used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to assess evidence type and determine the recommendation category.

EVIDENCE SYNTHESIS Evidence consisted of observational studies or randomized clinical trials with notable limitations, characterized as low quality using GRADE methodology. Meta-analysis was not attempted due to the limited number of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of studies. No study evaluated long-term (≥1 year) benefit of opioids for chronic pain. Opioids were associated with increased risks, including opioid use disorder, overdose, and death, with dose-dependent effects.

RECOMMENDATIONS There are 12 recommendations. Of primary importance, nonopioid therapy is preferred for treatment of chronic pain. Opioids should be used only when benefits for pain and function are expected to outweigh risks. Before starting opioids, clinicians should establish treatment goals with patients and consider how opioids will be discontinued if benefits do not outweigh risks. When opioids are used, clinicians should prescribe the lowest effective dosage, carefully reassess benefits and risks when considering increasing dosage to 50 morphine milligram equivalents or more per day, and avoid concurrent opioids and benzodiazepines whenever possible. Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently and review prescription drug monitoring program data, when available, for high-risk combinations or dosages. For patients with opioid use disorder, clinicians should offer or arrange evidence-based treatment, such as medication-assisted treatment with buprenorphine or methadone.

CONCLUSIONS AND RELEVANCE The guideline is intended to improve communication about benefits and risks of opioids for chronic pain, improve safety and effectiveness of pain treatment, and reduce risks associated with long-term opioid therapy.

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Effectiveness and harms of nonopioid treatments for chronic pain

Table 3. Effectiveness and Harms of Nonpharmacologic and Nonopioid Pharmacologic Treatments[a]

Source	Topic or Intervention	Participants or Population	Primary Outcomes	Key Findings	Study Quality
Busch et al,[45] 2007	Exercise training vs untreated control or nonexercise intervention	Systematic review of 33 RCTs with fibromyalgia patients	Global well-being, selected signs and symptoms, and physical function	Exercise training improves global well-being and physical function. Supervised aerobic exercise training has beneficial effects on physical capacity and fibromyalgia symptoms.	Four studies were classified as high quality, 15 as moderate quality, and 14 as low quality
Chaparro et al,[46] 2014	Noninjectable opioids vs placebo or other treatments	Systematic review of 15 RCTs with patients with chronic low back pain	Pain	One trial found tramadol similar to celecoxib for pain relief. Two trials did not find a difference between opioids and antidepressants for pain or function.	Low- to moderate-quality evidence
Collins et al,[50] 2000	Antidepressants vs placebo; anticonvulsants vs placebo	Systematic review of 19 RCTs for diabetic neuropathy or postherpetic neuralgia	Pain	For diabetic neuropathy, the NNT for ≥50% pain relief was 3.4 for antidepressants (12 trials, 10 evaluated TCAs and 3 SSRIs) and 2.7 for anticonvulsants (3 trials). For postherpetic neuralgia, the NNT was 2.1 for antidepressants (3 studies evaluating TCAs) and 3.2 for anticonvulsants (1 study evaluating gabapentin).	The mean and median quality score for included studies was 4 on a scale of 1-5
Fransen et al,[51] 2015	Exercise vs nonexercise group (active or no treatment)	Systematic review of 54 RCTs or quasi-randomized trials for knee osteoarthritis	Reduced joint pain or improved physical function and quality of life	Exercise reduced pain, improved function, and improved quality of life immediately after treatment; in studies providing posttreatment follow-up data, improved pain and function were sustained for 2-6 mo.	High-quality evidence for reduced pain and improved quality of life and moderate-quality evidence for improved function
Fransen et al,[52] 2014	Exercise vs nonexercise group (active or no treatment)	Systematic review of 10 RCTs or quasi-randomized trials for hip osteoarthritis	Reduced joint pain and improved physical function and quality of life	Exercise reduced pain and improved function immediately after treatment; in studies providing posttreatment follow-up data, improved pain and function were sustained for at least 3-6 mo.	High-quality evidence for reduced pain and improved function
Häuser et al,[53] 2013	Duloxetine vs placebo; milnacipran vs placebo	Systematic review of 10 RCTs for fibromyalgia patients	Benefits and harms	Duloxetine and milnacipran reduced pain by a small amount compared with placebo.	Risk of bias in included studies was low
Hayden et al,[54] 2005	Exercise therapy vs no treatment, other conservative treatments	Systematic review consisting of 61 RCTs for low back pain	Pain, function	Exercise therapy reduces pain and improves function with small magnitudes of effect. Effectiveness of exercise therapy appears to be greater in populations visiting a health care provider compared with the general population.	Only a small number of studies rated as high quality; potential publication bias
Lee et al,[55] 2014	CIM therapies vs single self-care CIM, non-self-care CIM, usual care/no treatment, other multimodal program, or other control	Systematic review of 26 RCTs for management of chronic pain	Pain symptoms	Integrative multimodal therapies resulted in positive, but sometimes mixed, effects on pain symptoms compared with active controls or single self-care modalities. More studies are needed to make strong conclusions about effectiveness.	Large majority of poor quality, including weaknesses in randomization and allocation concealment
Lunn et al,[56] 2014	Duloxetine vs placebo or other controls	Systematic review of 18 RCTs for neuropathic pain, chronic pain conditions without identified cause, or fibromyalgia	Benefits and harms of duloxetine	Duloxetine at 60 mg and 120 mg daily, but not lower dosages, were effective in reducing pain in diabetic peripheral neuropathy pain and in fibromyalgia.	Moderate-quality evidence for diabetic neuropathy; lower-quality evidence for fibromyalgia; some risk of bias
Moore et al,[57] 2009	Pregabalin vs placebo or any active control	Systematic review of 25 double-blind RCTs for postherpetic neuralgia, painful diabetic neuropathy, central neuropathic pain, or fibromyalgia	Analgesic efficacy and associated adverse events	Pregabalin was effective in patients with postherpetic neuralgia, diabetic neuropathy, central neuropathic pain, and fibromyalgia at doses of 300 mg, 450 mg, and 600 mg (but not at 150 mg) daily. NNTs were generally ≤6 for moderate benefit in postherpetic neuralgia and diabetic neuropathy but ≥7 for fibromyalgia.	Studies all had Oxford quality scores based on randomization, blinding, and reporting of dropout ≥3 (out of maximum of 5)
Moore et al,[58] 2014	Gabapentin vs placebo	Systematic review of 37 RCTs for neuropathic pain or fibromyalgia	Analgesic efficacy and adverse effects	Gabapentin was significantly more effective than placebo in reducing pain in diabetic neuropathy and postherpetic neuralgia. Evidence was insufficient for other conditions.	"Second-tier" evidence (some risk of bias, but adequate numbers in the trials)
Roelofs et al,[59] 2008	NSAIDs and COX-2 inhibitors vs control	Systematic review of 65 RCTs for nonspecific low back pain	Acute low back pain	NSAIDs are more effective than placebo for acute and chronic low back pain without sciatica, but have more adverse effects. NSAIDs are not more effective than acetaminophen but had more adverse effects. No type of NSAIDs, including COX-2 inhibitors, was found to be more effective than other NSAIDs.	Mixed high- and low-quality studies
Saarto et al,[60] 2010	Antidepressants vs placebo or other controls	Systematic review of 61 RCTs for neuropathic pain	Pain	TCAs and venlafaxine have low NNTs (3.6 and 3.1, respectively) for at least moderate pain relief.	Study quality limited by insufficient reporting detail
Salerno et al,[61] 2002	Antidepressants vs placebo	Systematic review of 9 RCTs for chronic back pain	Back pain	Antidepressants were associated with small but significant improvement in pain severity; improvements in function were not significant. Most (6) studies evaluated TCAs.	Moderate-quality studies
Staiger et al,[62] 2003	Antidepressants vs placebo	Systematic review of 7 RCTs in patients with chronic low back pain	Back pain	Four of 5 studies evaluating TCA and tetracyclic antidepressants found significant improvement in chronic low back pain. Other antidepressants studied (2 studies evaluating SSRIs and 1 evaluating trazodone) did not show significant pain improvement.	Mixed quality (quality scores ranged from 11-19 out of 22)
Trelle et al,[63] 2011	NSAIDs vs other NSAIDs or placebo	Meta-analysis of 31 RCTs comparing any NSAID with other NSAID or placebo for any medical condition	Myocardial infarction, stroke, cardiovascular death, death from any cause	Compared with placebo, NSAIDs were associated with increased risk of myocardial infarction, stroke, and cardiovascular death.	Generally high
Welsch et al,[64] 2015	Opioids (including tramadol) vs nonopioids (including acetaminophen, NSAIDs/COX-2 inhibitors, mexiletine, anticonvulsants, antidepressants, and muscle relaxants)	Systematic review of 10 RCTs in patients with neuropathic pain, low back pain, or osteoarthritis	Efficacy (including various pain measures), tolerability, and safety	There was no significant difference between opioids and nonopioid analgesics in pain reduction; nonopioids were superior to opioids in improving physical function and were better tolerated. When patients from tramadol trials (n randomized = 2788) were removed from results of the review, results for pain and function for patients receiving opioids (morphine) compared with alternative drugs (n randomized = 223) had wide, overlapping confidence intervals. Improved tolerability for alternative drugs vs morphine remained significant.	One study had a high, 2 studies a moderate, and 7 studies a low study quality
Wiffen et al,[65] 2014	Carbamazepine vs placebo or other active control	Systematic review consisting of 10 RCTs in adults with chronic neuropathic pain or fibromyalgia	Pain relief	Carbamazepine provided better pain relief than placebo for trigeminal neuralgia, diabetic neuropathy, and poststroke pain for ≤4 weeks. Dizziness and drowsiness were commonly reported with carbamazepine. In 4 studies, 65% of patients receiving carbamazepine vs 27% receiving placebo experienced ≥1 adverse event. In 8 studies, 3% of patients receiving carbamazepine withdrew because of adverse events (vs 0% taking placebo).	Third-tier evidence (trials involving small numbers of participants; considered likely to be biased, with outcomes of limited clinical utility, or both)
Williams et al,[66] 2012	Cognitive behavioral therapy or behavioral therapy	Systematic review of 42 RCTs for patients with nonmalignant chronic pain except headache	Pain, disability, mood, and catastrophic thinking	Cognitive behavioral therapy was found to have small to moderate effects on pain, disability, mood, and catastrophic thinking immediately after treatment when compared with usual treatment or deferred cognitive behavioral therapy, but only effects on mood persisted at follow-up. Behavioral therapy had a positive effect on mood immediately after treatment.	Mean quality of study design, 15.8 out of 26 (SD 4.3; range, 9-24 out of 26)

(continued)

Abbreviations: CIM, complementary and integrative multimodal; COX-2, cyclooxygenase 2; NNT, number needed to treat; NSAID, nonsteroidal anti-inflammatory drug; RCTs, randomized clinical trials; SSRIs, selective serotonin reuptake inhibitors; TCA, tricyclic antidepressants.

[a] All the studies in this table were included in the contextual evidence review.

From: **CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016.** JAMA. 2016;315(15):1624-1645.

Overview of findings from the evidence reviews

- Insufficient evidence to determine whether pain relief, function, or quality of life improves with long-term opioid therapy (most RCTs <6 weeks)
- Long-term opioid use for chronic pain is associated with serious risks, including abuse, dependence and overdose
- Many non-opioid therapies can improve chronic pain with less risk for harm
- When opioids are used, they are more likely to be effective if combined with other approaches

Opioids not first-line or routine therapy for chronic pain

- Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain.
- Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient.
- If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.

(Recommendation category A: Evidence type: 3)

Effective treatments for chronic pain

- Nonpharmacologic therapies
  - Exercise therapy
  - Cognitive-behavioral therapy
- Nonopioid pharmacologic treatments
  - Acetaminophen
  - NSAIDs, and COX-2 inhibitors
  - Selected anticonvulsants (e.g., pregabalin, gabapentin)
  - Selected antidepressants (tricyclics, SNRIs)
- Interventional approaches
- Multimodal and multidisciplinary therapies

Nonpharmacologic therapies can

- Result in sustained improvements in pain and function without apparent risks
- Encourage active patient participation in the care plan
- Address the effects of pain in the patient's life

Exercise therapy

- High-quality evidence for reduced pain and improved function for hip or knee osteoarthritis
  - Immediately after treatment
  - Improvements sustained for at least 2–6 months
- Previous guidelines strongly recommended aerobic, aquatic, and/or resistance exercises for patients with hip or knee osteoarthritis
- Can reduce pain and improve function in low back pain
- Can improve global well-being, fibromyalgia symptoms, and physical function in fibromyalgia

Cognitive behavioral therapy (CBT)

- Addresses psychosocial contributors to pain and improves function
- Trains patients in behavioral techniques
- Helps patients modify situational factors and cognitive processes that exacerbate pain
- Has small positive effects on disability and catastrophic thinking

Access to nonpharmacologic treatments

- Access and cost can be barriers
- Aspects of these approaches can be used even when there is limited access to specialty care
  - RCT: no difference in reduced chronic low back pain intensity, frequency or disability between
    - Patients assigned to relatively low-cost group aerobics
    - Individual physiotherapy sessions
  - Low-cost options to integrate exercise:
    - Brisk walking in public spaces
    - Use of public recreation facilities for group exercise

Using CBT principles in primary care

- Encourage patients to take an active role
- Teach relaxation techniques
- Support engaging in beneficial but potentially anxiety-provoking activities, such as exercise
- Support patient coping strategies
- Refer patients to support, self-help, and educational community-based programs
- Refer patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, for formal therapy with a mental health specialist

Acetaminophen

- Multiple guidelines: acetaminophen first-line for
  - Osteoarthritis
  - Low back pain

- Can be hepatotoxic at > 3-4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease
  - Avoid in liver failure
  - Reduce dosage in patients with
    - Hepatic insufficiency
    - History of alcohol abuse

NSAIDs and cyclooxygenase 2 (COX-2) inhibitors

- NSAIDs first-line treatment for
  - Osteoarthritis
  - Low back pain

- NSAIDs and COX-2 inhibitor risks:
  - Gastritis, gastrointestinal bleeding or perforation
  - Fluid retention, renal and cardiovascular risks
  - Interference with platelet aggregation
  - Topical NSAIDs have less systemic risk than oral NSAIDs

Selected antidepressants

- Tricyclics (TCAs, e.g., amitriptyline) and SNRIs (e.g., duloxetine) are effective and recommended in multiple guidelines for
  - Neuropathic pain (e.g., diabetic neuropathy, post-herpetic neuralgia)
  - Fibromyalgia symptoms

- TCAs relatively contraindicated in severe cardiac disease, particularly conduction disturbances
- Start TCAs at low dosages, titrate up as needed and tolerated
  - Often effective at lower dosages than for depression
  - Anticholinergic effects include sedation--use at bedtime

Selected anticonvulsants

- Selected anticonvulsants (e.g., pregabalin, gabapentin) are effective and recommended in multiple guidelines for
  - Neuropathic pain (e.g., diabetic neuropathy, post-herpetic neuralgia)
  - Fibromyalgia symptoms

- Start pregabalin or gabapentin at low dose and increase gradually given dose-dependent dizziness and sedation

- Check baseline and periodic CBC and LFTs with carbamazepine

Interventional approaches

- Injections can improve short-term pain and function
  - Arthrocentesis and intraarticular glucocorticoid injection in rheumatoid arthritis or osteoarthritis
  - Subacromial corticosteroid injection in rotator cuff disease
  - Epidural injection for lumbar radiculopathy

- Potential risks
  - Articular cartilage changes (in osteoarthritis)
  - Sepsis
  - Rare but serious adverse events associated with epidural injection: loss of vision, stroke, paralysis, death

Multimodal and multidisciplinary therapies

- Can reduce long-term pain and disability more effectively than single modalities
- Involve coordination of medical, psychological, and social aspects of care
- Are not always available or reimbursed by insurance
- Can be time-consuming and costly for patients
- Should be considered for patients not responding to single-modality therapy, or who have severe functional deficits
- Combinations should be tailored depending on patient needs, cost, and convenience

Selection of therapy: evaluation

- Evaluate patients, establish or confirm diagnosis
  - Focused history, including
    - History and characteristics of pain
    - Contributing factors (psychosocial stressors, sleep)
  - Physical exam
  - Imaging *only if indicated*, e.g., if
    - Severe or progressive neurologic deficits are present or
    - Serious underlying conditions are suspected
- For complex pain syndromes, consider pain specialty consultation to assist with diagnosis as well as management

Selection of therapy: role of pain mechanism and diagnosis

- NSAIDs for nociceptive pain (e.g., osteoarthritis, muscular back pain)
- Selected antidepressants or anticonvulsants for neuropathic pain (e.g., diabetic neuropathy, postherpetic neuralgia) or fibromyalgia); topical lidocaine for localized neuropathic pain
- Physical or occupational therapy can address posture, weakness, or repetitive motions contributing to musculoskeletal pain
- Surgical intervention can relieve mechanical/compressive pain
- Glucose control can prevent progression of diabetic neuropathy
- Immune-modulating agents useful in rheumatoid arthritis

Selection of therapy: role of risk factors for harm

- Use medications only after determining expected benefits outweigh risks given patient-specific factors
- Consider falls risk when selecting and dosing potentially sedating medications (e.g., tricyclics, anticonvulsants, opioids)
- Weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults, patients with hypertension, renal insufficiency, or heart failure, or those at risk for peptic ulcer disease or cardiovascular disease
- Consider topical NSAIDs over oral NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) in patients aged ≥ 75

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CDC Guideline for Prescribing Opioids
for Chronic Pain

NON-OPIOID MEDICATIONS & NONPHARMACOLOGIC TREATMENT

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PAIN MEDICINE

CASE LEARNING OBJECTIVES

1. Outline the differential diagnoses for this patient's symptoms, and the methods to choose among them.

2. Identify patient belief systems that might interfere with treatment, and strategies to address these.

3. Review the role of patient education in setting expectations when managing musculoskeletal pain.

4. Describe the rationale for exercise therapy, and how to overcome patient barriers to physical therapy.

5. Defend the rationale for use of a tricyclic antidepressant drug as the initial medication for this patient.

PATIENT HISTORY – 7/8/14

- Gender: Male
- Age: 38
- Symptoms
  - Non-radicular, aching, stabbing neck pain x 3 weeks
  - Intermittent neck pain/headaches starting in 2008. Also: headaches, diffuse bilateral upper extremity pain + thoracic & lumbar spine
- Electromyography (EMG) 6 years ago: normal
- Magnetic resonance image (MRI) 3 weeks ago:
  - Degenerative disc disease (DDD) + foraminal narrowing C5-6; C6-7

HISTORY CONTINUED

- Rx: oxycodone 5/325 twice daily; cyclobenzaprine 10 mg at bedtime
- Mood: “grumpy because of pain”
- Past medical history: Irritable Bowel Syndrome
- Smokes ½ packs per day; no illicit drugs
- Lives with girlfriend + 10 y/o daughter
- Job: builds cranes; can’t make it to work one day per week
- Activity: 3 hours in recliner after work

PATIENT REPORTED OUTCOME MEASURES

- **Pain, interference with Enjoyment, General function (PEG) tool**
  - ± Brief Pain Inventory (BPI)
  - ± Promise 10
  - ± Oswestry Disability Index (ODI)
  - ± Roland Morris Disability Questionnaire (RMDQ)
- **Personal Health Questionnaire PHQ-9 + General Anxiety Disorder GAD-7**
  - Or short version PHQ-4
  - When elevated ↑ : full PHQ-9, GAD-7 plus Primary Care-Post Traumatic Stress Disorder PC-PTSD
- **Alcohol Use Disorders Identification Test AUDIT-C**
- **ORT, SOAPP, COMM, or DIRE**
  - All of these misuse/addiction tools are widely used, though poor predictive validity
- **Prescription Drug Monitoring Program (PDMP)**
  - Important to check, he may request an opioid refill!

CDC RECOMMENDED ASSESSMENTS

Pain average, interference with Enjoyment of life, and interference with General activity (PEG) Assessment Scale

1. What number best describes your pain on average in the past week:

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

2. What number best describes how, during the past week, pain has interfered with your enjoyment of life?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

3. What number best describes how, during the past week, pain has interfered with your general activity?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

Krebs 2009, Kroenke 2009

Patient Health Questionnaire PHQ-4

- Combines Generalized Anxiety Disorder GAD-7 + PHQ-9
- Score ≥ 6 needs attention

Over the past 2 weeks have you been bothered by these problems?	Not at all	Several days	More days than not	Nearly every day
Feeling nervous, anxious, or on edge	0	1	2	3
Not being able to stop or control worrying	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Little interest or pleasure in doing things	0	1	2	3

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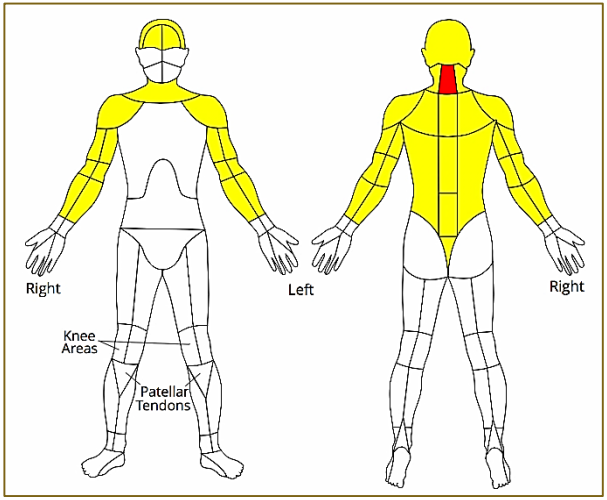
PATIENT REPORTED OUTCOMES (PROs)

- Pain intensity: 6/10
- Pain interference with:
  - General function: 7/10
  - Quality of life: 7/10
  - Sleep:
    - Initiation: 6
    - Maintenance: 6
- Mood: PHQ-4: 6/12
  - …so added, GAD-7: 6/21
  - …and, PHQ-9: 8/27



Patient self-selected important activity (“work”): 8

Oswestry Disability Index: 50
Opioid Risk Tool: 4

Satisfaction with pain treatment: 2/10

EXAM

- Height: 5’7” and Weight:119 lbs
  - Normal = 130 lbs; Body mass index (BMI) 18.6
- Vital Signs normal
- 14/18 “tender points”
- Limited range of motion – neck, lumbar
- Neuro –
  - Normal deep tendon reflexes (DTRs)
  - No long tract signs
  - Pain inhibited weakness both upper extremities (UEs)
  - Sensation normal

MAKE MULTIDIMENSIONAL ASSESSMENT

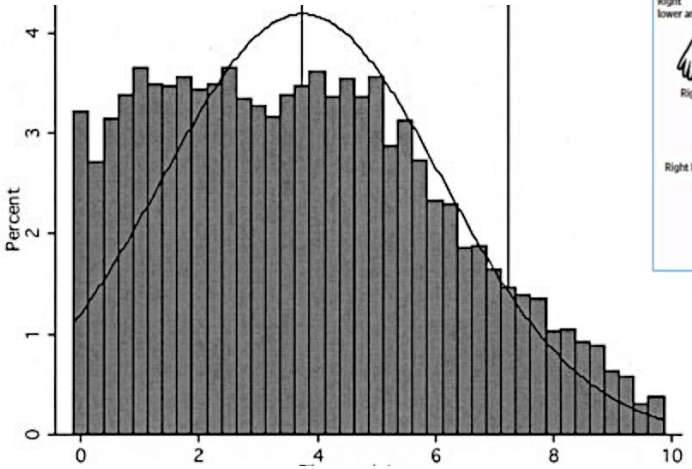
Diagnoses

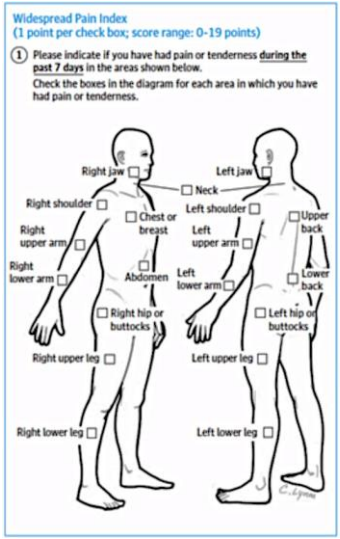
1. Axial neck pain (“cervicalgia”)
2. Fibromyalgia vs. inflammatory arthritis
3. Weight loss, unexplained
4. Long-term opioid therapy, low dose
5. Irritable bowel syndrome
6. Mild depression and anxiety
7. Moderate sleep disturbance

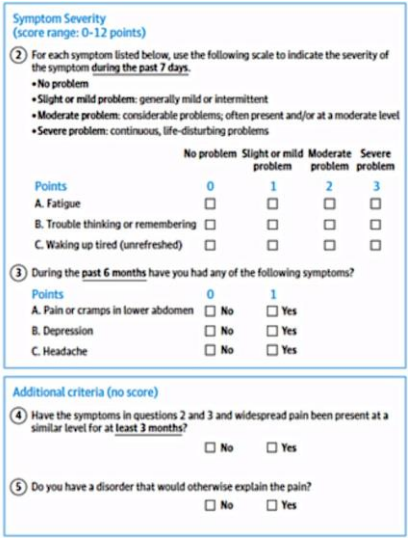
WIDESPREAD PAIN & CO-OCCURRING PAIN DISORDERS

"Fibromyalgia-ness"

Symptom Intensity Scale







Clauw 2014, Wolfe 2009

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ESTABLISH TREATMENT PLAN

Plan

1. Discuss likely diagnoses and treatment plan
2. Set up appropriate expectations
    - Records from current health care provider(s)
    - Intentions and plans regarding long-term opioids
3. Labs
    - C-reactive protein (CRP)
    - Anti-cyclic citrullinated peptide antibody (anti-CCP)
    - Anti-nuclear antibody (ANA)
4. Visit summary with links to info on Fibromyalgia

(e.g. fibroguide.com)

FOLLOW UP – 7/22/14

- Resists diagnosis of Fibromyalgia

  …“it is a ‘psychological’ condition”

- Continue discussion of Fibromyalgia pathophysiology
  - Offer brief education re pain mechanisms and treatment to help understand pain
  - Suggest educational materials
- Referral to physical therapy (PT) for neck range of motion (ROM)/strength + general conditioning

EXERCISE – GENERAL POINTS

1. **Exercise is good; PT is a means**

   "Closest thing to a wonder drug? Try exercise"

2. **Optimal exercise? No definite evidence**

3. **PT/exercise often "fails"**

   "…made my pain worse!"

4. **Clinician interventions**

   - Find PT who will work with complex pts
   - Ask about progress – have pt demonstrate
   - Basic concepts – baseline; "exchange list"; tolerance for flares

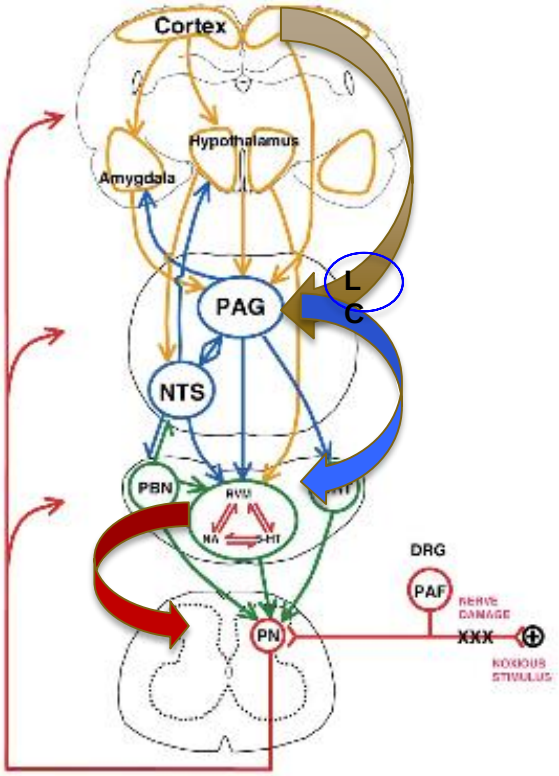
Carroll 2016, Hayden 2005

FOLLOW UP – 7/22/14 (2)

- Discontinue cyclobenzaprine, in favor of **nortriptyline** 10 mg
    - Slow managed titration to 50 mg qhs
- Off opioids because previous prescriber no longer in local practice
    - Consider periodic checking PDMP regardless

WHY NORTRIPTYLINE?

DESCENDING INHIBITORY CONTROL SYSTEMS



Norepinephrine is a principal neurotransmitter facilitating the "descending inhibitory systems"

Millan 2002, Ossipov 2014

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CLINICAL TRIALS FOR TCA EFFECTIVENESS:

Post Herpetic Neuralgia

NNT* 2.1-2.7

Diabetic Peripheral Neuropathy

NNT* 1.2-1.5

Atypical Facial Pain

NNT* 2.8-3.4

Fibromyalgia/Central Pain

NNT* 1.7

*NNT = Number needed to treat

Saarto 2007

FOLLOW UP, OVER MONTHS

8/27/14

1. Nortriptyline + PT – reduction in widespread pain
2. Neck pain/headaches still present, but less
   - Pain reduced 10%
   - Rest of PEG improved 40%
   - PHQ-4 = 4
3. Sleep better
4. Exam – reduced sensitivity of tender points

9/25/14

1. Nortriptyline – AM fatigue, some dry mouth
2. Pain still 6/10
3. Rest of PEG improved 60% from baseline
4. PHQ-4 = 2

NON-DRUG MULTIMODAL ANALGESIA

- **Cognitive:**
  - Identify distressing negative cognitions and beliefs
- **Behavioral approaches:**
  - Mindfulness, relaxation, biofeedback
- **Physical:**
  - Activity coaching, graded exercise land & aquatic with PT, class, trainer, and/or solo
- **Spiritual:**
  - Identify and seek meaningfulness and purpose of one's life
- **Education (patient and family):**
  - Promote patient efforts aimed at increased functional capabilities

"COMPARING" EFFECTIVENESS*

PAIN TREATMENTS	EXTRAPOLATED BENEFITS FOR VARIED PAIN OUTCOMES
Opioids	≤ 30%
Tricyclics/SNRIs	30%
Anticonvulsants	30%
Acupuncture	≥ 10%
Cannabis	10-30%
CBT/Mindfulness	15-50%
Graded Exercise Therapy	variable
Sleep Restoration	≥ 40%
Hypnosis, Manipulation, Yoga	"+ effect"

***NOTE**

- *Many studies low GRADE quality of evidence*
- *Most studies <3 months*
- *Rarely do studies compare one treatment with another*

See also: CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. JAMA. 2016;315(15):1624-1645.

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FOLLOW UP

11/5/14

1. Recent flare up of neck pain
2. Reviewed PT exercises – mainly stretching
3. Discuss neck/shoulder girdle strengthening
4. Sleep/fatigue – trazodone vs. more nortriptyline

2/10/15

1. Weight = 140 (BMI 22)
2. Sleep improved – nortriptyline, amitriptyline, trazodone
3. Worse UE sx's; possible C6 radic – work up?

SUMMARY

- Anticipate multiple symptoms
- Prepare for adversity
- Setting expectations is key
- Continuing re-evaluation
- *Always* consider psychosocial factors

Pain management takes time – many dimensions that evolve over time

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