Reviewing the Evidence on Outcomes of Opioid Tapers

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Conflict of interest disclosure

- I have received research funding from the Agency for Healthcare Research and Quality, the Centers for Disease Control and Prevention, and the American Pain Society for topics related to opioids for chronic pain (including tapering)

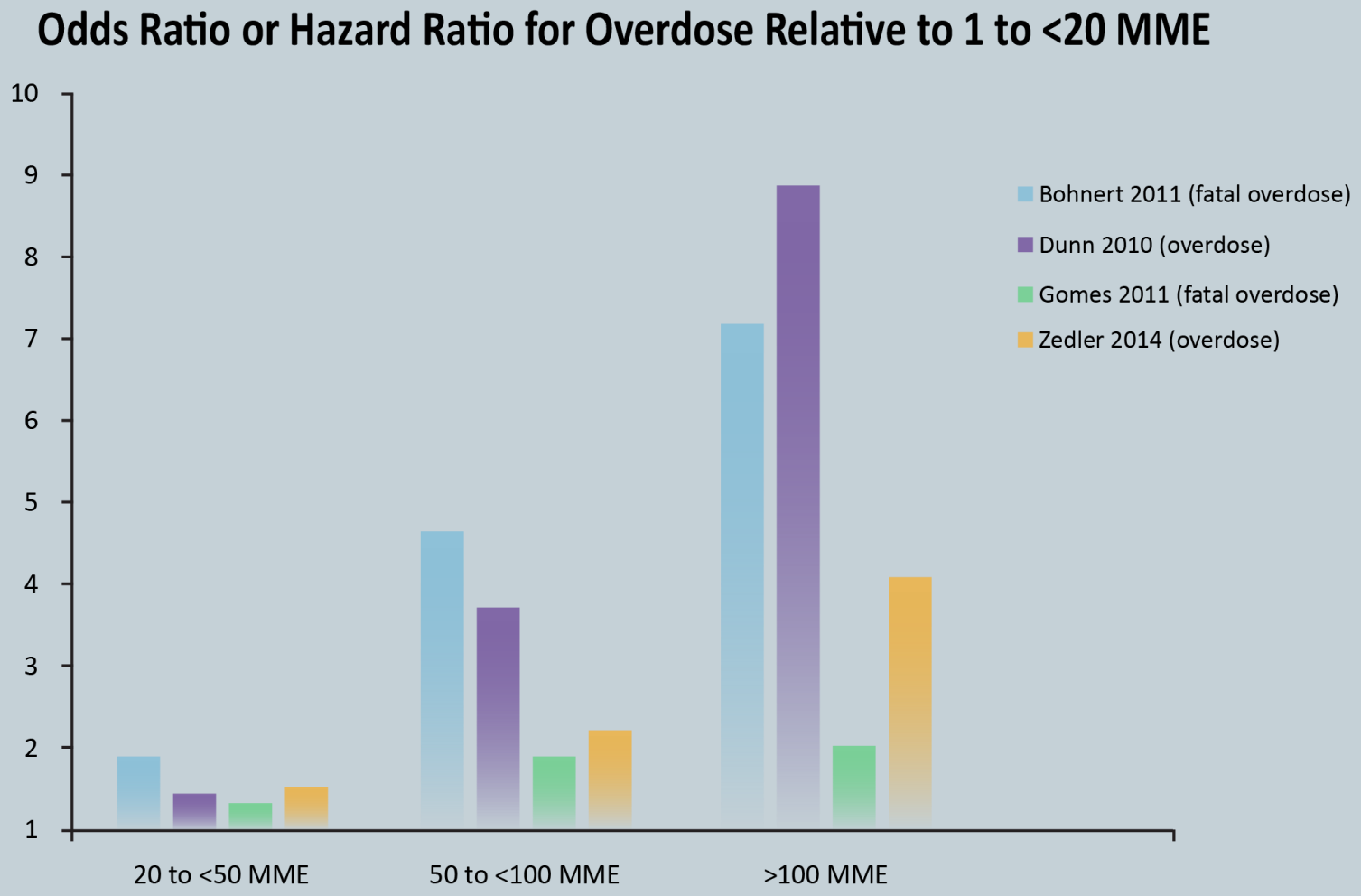
Case

- 53-year old female transferring care because her PCP is leaving practice
  - Shoulder and hip pain 2° avascular necrosis, s/p shoulder replacements, hip decompression, hip replacement
  - Fibromyalgia, non-radicular LBP, chronic headache
  - Depression, fatigue
  - Gastroparesis, irritable bowel syndrome
  - Morphine IR 30 mg 5 T (150 mg) q 8 hrs + oxycodone 5 mg 8 T (40 mg) q 6 hrs
    - MED/day: 690 mg
  - Modafinil 20 mg po qD
  - Pain 6/10 on average, with day to day fluctuation
  - Can carry out ADLs with pain, limited exercise, no aberrant behaviors

Background

- The expanded use of opioid for chronic pain has created a population of patients prescribed long-term opioid therapy for years or decades
- Doses are often above the 2016 CDC guideline suggested thresholds (>50 or >90 mg morphine equivalent dose/day)
- Long-term opioid therapy is associated with various side effects, morbidity, and overdose death; some risks are dose-dependent
- Evidence indicates that opioid therapy confers little benefit versus non-opioid therapy, particularly for function
- Opioid use disorder occurs in a subset of patients and quality of life may be adversely affected, despite perceived pain benefits

Prescribed opioid dose and overdose risk



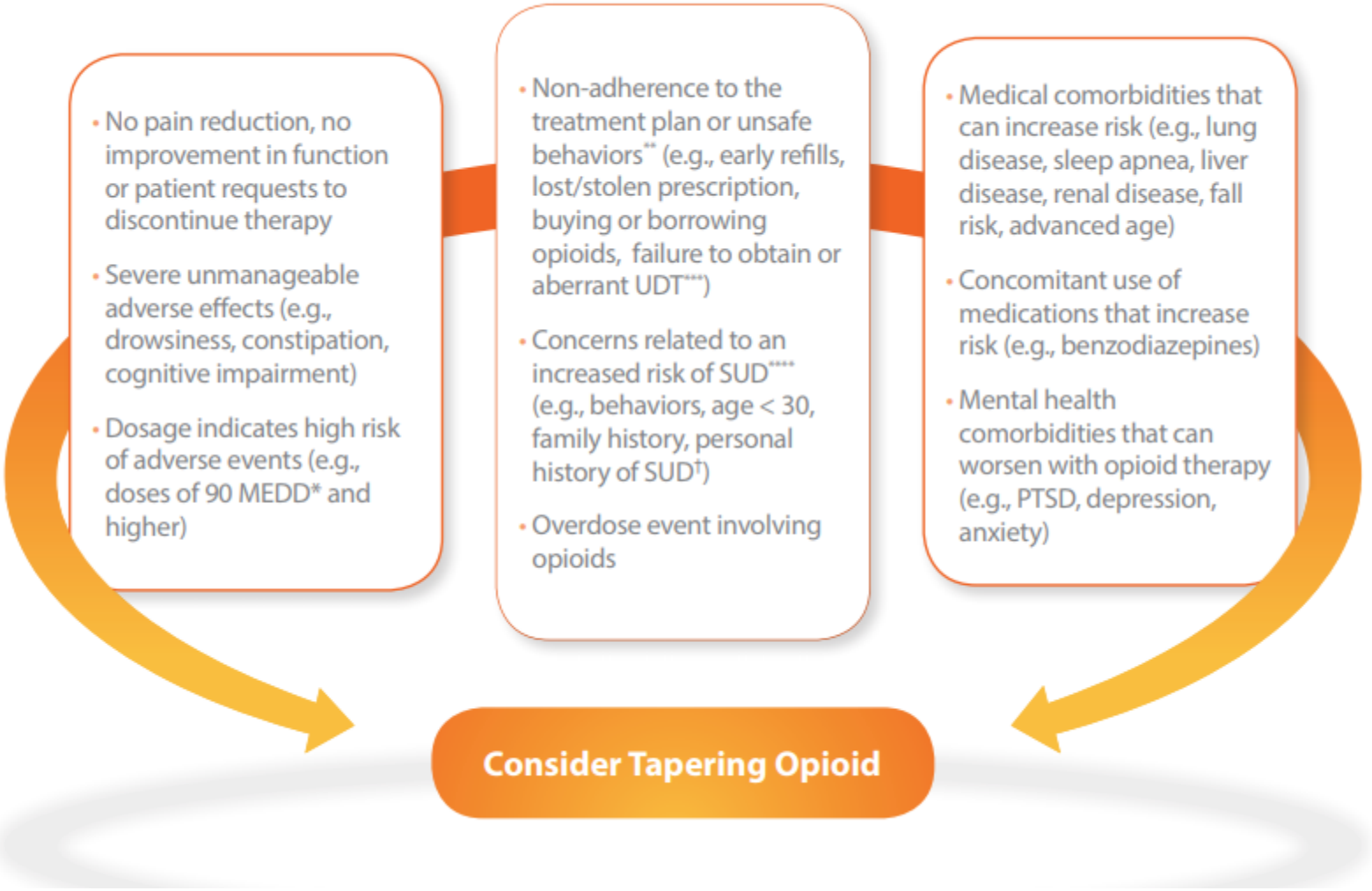
Tapering recommendations

- CDC: If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.
  - 10% reduction in initial dose per week (10 weeks to discontinuation) a "reasonable" starting point
  - AAFP: Decrease 10-20% every 1 to 2 weeks, adjust according to response
  - VA: "Most commonly, tapering will involve dose reduction of 5% to 20% every 4 weeks"
- What is the evidence on outcomes of tapering?

Tapering indications

- CDC guideline
  - No sustained clinically meaningful improvement in pain and function
  - Opioid dose ≥50 MME/day without benefit > risks
  - Concurrent benzodiazepines that can't be tapered off
  - Patient requests dose reduction or discontinuation
  - Patient experience overdose, other serious adverse events
  - ***Not:*** Taper all patients on higher doses or with specific pain conditions

VA Opioid Taper Decision Tool



Evaluating opioid tapers

- Comparisons
  - Taper vs. no taper/usual care
  - Slower vs. more rapid taper
  - Tapering with adjunctive treatment (pharmacological or nonpharmacological) vs. no or alternative adjunctive treatment
- Outcomes
  - Pain, function, QoL
  - Psychiatric outcomes, suicidality/suicide events
  - Opioid dose, discontinuation rates
  - Withdrawal symptoms, opioid-related adverse effects
  - Overdose events, opioid misuse, mortality
- Potential modifying factors
  - Demographics, pain type, opioid dose/type, indication for tapering, willingness to taper
  - Psychiatric comorbidities, substance use, medical comorbidities
  - Clinical context (care coordination, psychological support, taper protocols, etc)

Taper vs. no taper

- Small sample sizes, methodological limitations
- Kurita et al (2018): Patients (n=35) stabilized on high doses of opioids; taper by 10% weekly to cessation (clonidine for withdrawal) vs. maintenance of opioid doses
  - Mean opioid doses at baseline 367 vs. 221 mg MED/day
  - Planned to report outcomes at 6 mo, but only reported at 4 to 6 wk due to high attrition (1/15 completed follow-up in intervention group and 12/20 in control group)
  - Opioid dose (mg MED/day): 226.6 vs. 300.8 (p=0.45)
  - Pain (0 to 10): 6.5 vs. 5.1 (p=0.09)
  - HADS anxiety: 6.7 vs. 6.5, p=0.96; HADS depression: 6.4 vs. 6.0, p=0.86
- Blondell et al (2010): Patients (n=12) with prescription opioid dependence and chronic pain transitioned to SL buprenorphine; taper vs. maintenance
  - 5/6 in taper arm crossed over to maintenance and 1/6 had relapse; study terminated early without evaluation of planned outcomes
- Cowan et al (2005): Abrupt cessation of morphine associated with increased risk of withdrawal vs. continuation
  - No tapering protocol and only immediate (60 hour) outcomes evaluated

Taper support vs. opioid treatment as usual

- Sullivan et al (2017): n=35, 22 week taper support intervention (psychiatric assessment, weekly 30-minute motivational interviewing sessions, self-management training) vs. continued opioid treatment as usual
  - Baseline opioid dose: Mean 225.7 mg MED/day
  - BPI pain severity: Adjusted mean difference (MD) -0.68 (-2.01 to 0.64) on 0 to 10 scale
  - BPI pain interference: Adjusted MD -1.39 (-2.78 to -0.01) on 0 to 10 scale
  - Prescription Opioid Difficulty Scale: Adjusted MD -4.90 (95% CI -8.40 to -0.80) on 0 to 32 scale
  - Opioid dose (mg MED/day): Adjusted MD -26.7 (95% CI -83.0 to 29.6)
  - Effects on BPI pain interference and PODS persisted at 34 weeks

Slower versus more rapid taper

- Recommendations on taper speed almost entirely based on studies of patients with OUD related to heroin use (not patients with chronic pain)
- Mark et al (2019): Cohort study (n=494) of Medicaid beneficiaries in Vermont prescribed opioids at ≥120 mg MED/day for >90 days
  - Median time to discontinuation 1 day (86% discontinued within 21 days)
  - Each additional day to discontinuation associated with 1percent lower risk of an opioid-related ED visit or hospitalization (7% lower risk for each additional weed to discontinuation)
  - 60% of patients had substance use disorder prior to tapering but <1% received medication for OUD

FDA identifies harm reported from sudden discontinuation of opioid pain medicines and requires label changes to guide prescribers on gradual, individualized tapering

FDA Drug Safety Communication

Adjunctive varenicline versus placebo

- Hooten et al (2015): Cohort study (n=21) of patients undergoing tapering in an intensive outpatients interdisciplinary pain program randomized patients to varenicline versus placebo
  - Mean opioid dose at baseline 135 vs. 75 mg MED/day
  - No difference in median time to tapering completion (18 vs. 15 days), opioid withdrawal symptoms (COWS), pain, or depression

Taper plus counseling versus taper/maintenance

- Tennant et al (1982): Patients (n=42) who volunteered for withdrawing opioids; detoxification/counseling over 3 weeks vs. detoxification with maintenance if detoxification unsuccessful
  - Mean codeine doses 240 to 2400 mg/day
  - Completed 3 week intervention: 24% vs. 95%, RR 0.25 (95% CI 0.12 to 0.54)
  - Abstinent after 6 months: 9.5% vs. 19.0%, RR 0.50 (95% CI 0.10 to 2.44)

Outcomes of tapering/discontinuation

- Frank et al (2017): Systematic review with 67 studies
  - Mostly observational studies using pre-post design; methodological limitations (51 studies rated poor-quality); tapering not the purpose of many studies; evidence very low quality for all outcomes
  - Pain severity: 8 of 8 fair-quality and 21 of 28 poor-quality studies reported improved pain
  - Function: 5 of 5 fair-quality and 8 of 12 poor-quality studies reported improved function
  - QoL: 3 or 3 fair-quality and 4 of 9 poor-quality studies reported improved QoL
  - Opioid withdrawal symptoms: Rates ranged from 0% to 100%; 4 studies reported withdrawal symptoms in all patients
  - Substance use: 2 studies reported illicit substance use (63% and 64%); 1 study reported nonmedical use of prescription opioids (43%); 1 study reported illicit IV opioid use (<1%)
  - Adverse events: 1 opioid-related overdose in 5 studies
- Fishbain et al (2018): Systematic review with 20 observational studies
  - 85% of studies showed improved pain at tapering completion, 15% same pain

"Voluntary" tapering

- Darnall et al (2018): Patients (n=82) who received education about benefits of opioid reduction and agreed (volunteered) to taper over 4 months
  - Median opioid dose/duration at baseline: 288 mg MED/day and 6 years
  - Dose reduced up to 5% for up to 2 dose reduction in month 1; then up to 10% per week
  - 38% dropped out prior to 4 months
  - Median opioid dose at 4 months among completers: 150 mg MED/day
  - Pain intensity among completers: 5.0 at baseline vs. 4.5 at 4 months (p=0.29)
  - No change in pain interference or pain behavior
  - No change in anxiety, depression, sleep disturbance
- Patients in above study likely to be self-selected (volunteer bias)
  - No method for measuring "voluntariness" or assessing effects of "voluntariness" on tapering outcomes

BRAVO: Cardinal Principles of Tapering Patients

Figure 14-4: Discussing Prescription Opioid Dependence with Patients in the Primary Care Setting

B

- **Broaching the Subject**
  - Schedule enough time with your patient to have a discussion on this difficult topic
  - Anticipate the patient's strong emotional reaction
  - Identify the feelings, normalize those feelings, and express empathy with the concerns the patient may have

R

- **Risk-Benefit Calculator**
  - When assessing benefits, weigh the patient's pain relief against their functionality
  - Involve family members for more objective views on a patient's opioid use
  - Track common risks such as tolerance and opioid-induced hyperalgesia
  - Include all of these factors when discussing reasons for tapering off opioids

A

- **Addiction Happens**
  - Addiction is defined by the "Four C's": out-of-Control use, Compulsive use, Craving, and Continued use despite consequences
  - Dependence happens when the body relies on a drug to function normally
  - Dependence and Addiction are not equivalent

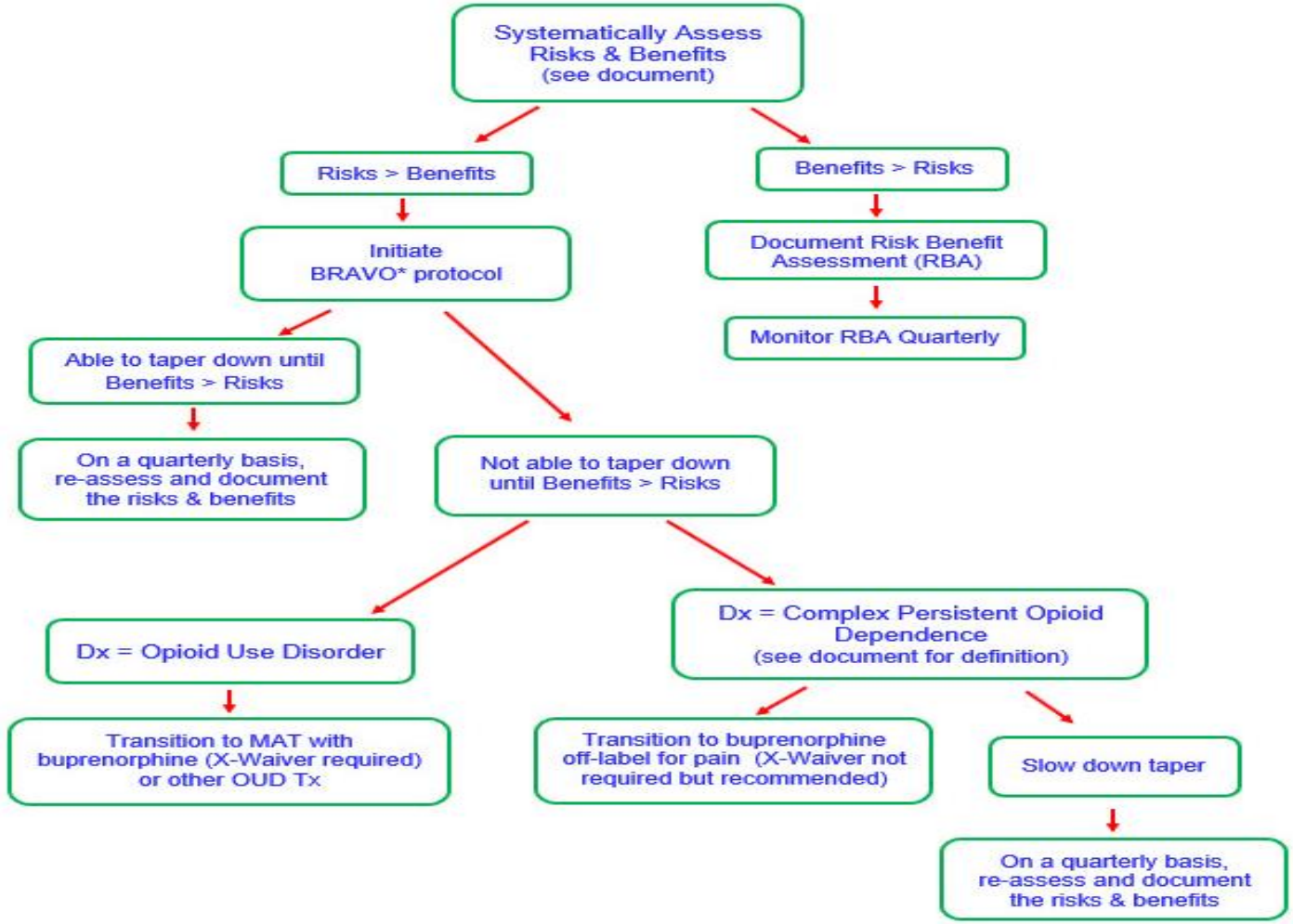
V

- **Velocity Matters - and So Does Validation**
  - Go slowly, take the necessary time to ease your patients down on their doses
  - Let the patient be involved when deciding how much to decrease and at what time
  - It is OK to take breaks in lowering the dosage
  - Never go backwards; your patient's tolerance will increase and progress will be lost

O

- **Other Strategies for Coping with Pain** – teach patients these 3 Dialectical Behavioral Therapy (DBT) practices:
  - STOP: **S**top, **T**ake a breath, **O**bserve internal and external experiences, and **P**roceed mindfully
  - Opposite Action Skills: acting opposite to a negative emotional urge in the service of pursuing values goals
  - Radical Acceptance: accepting reality as it is and not as we wish it to be

Oregon Pain Guidance Tapering Flowchart



https://www.oregonpainguidance.org/guideline/tapering/

Case

- Unclear if benefitting from high doses of long-term opioid therapy, ?worsening of GI symptoms; psychological comorbidities; polypharmacy; no signs of aberrant behaviors
- Slow taper initiated; over ~2.5 year period
  - Morphine 450 mg/day→ 75 mg/day
  - Oxycodone 160 mg/day→40 mg/day (60 mg MED)
    - MED/day: 690 mg→135 mg/day
- Added non-opioid medications
  - Duloxetine 20 mg qD
  - Buspirone 30 mg bid
- Pain and function no worse than when on high doses, no serious withdrawal

Conclusions

- Evidence on effects of opioid tapering in persons with chronic noncancer pain remains limited
- Some evidence to support taper support intervention
- Abrupt discontinuation associated with worse outcomes; data on optimal taper speed otherwise not available
- Very low quality evidence that patients who taper opioids experience improved pain and function
- Studies not designed to evaluate effects of tapering on overdose risk, use of illicit opioids, suicidality/suicide events
- Research needed on effectiveness of adjunctive treatments; buprenorphine taper vs. maintenance; effects of patient and clinical factors on taper outcomes

Thank You!