CUE Update in Pain Medicine
2010 SGIM 33rd Annual Meeting
Friday, April 30 2:00PM – 3:30PM
Minneapolis Convention Center
Minneapolis, Minnesota

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Update in Pain Medicine

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**Section 1: Collaborative Care**


**Background:**
- Evidence-based low back pain (LBP) guidelines are widely available, but not always followed.
- Involving nurses in disease management aspects of guidelines may improve their implementation.

**Aims/purpose:**
- To compare effects of different guideline implementation methods on patient LBP outcomes. Three groups were compared: 1) physician education alone (3 seminars and 2 academic detailing visits), 2) physician education plus nurse education in motivational counseling (2 full-day seminars and 1-3 supervised practice sessions), and mailed guidelines (control).

**Methods:**
- German clinical trial with randomization at the practice level
- Inclusion criteria were ≥ 1 family physician and ≥ 1 nurse willing to participate
- Participating physicians recruited consecutive patients presenting for LBP
- A sample of 1874 patients was estimated to detect a small effect (0.10)

**Results:**
- 118 practices (126 physicians) and 1378 patients (avg. 12/practice) enrolled
- Patients’ average age was 49, 58% were men, and 55% were employed
- 80% of patients in the physician plus nurse group received ≥ 1 motivational counseling session (avg. 1 session, range 1-4)
- On the primary outcome (a functional capacity scale) at 6 months, the physician plus nurse group had a small improvement compared with control (p=0.032); the physician only group had a small improvement that was not statistically significant (p=0.120).
- Compared with control, patients in the physician plus nurse group had 18 fewer days in pain over 6 months (p=0.001); those in the physician only group had 16 fewer days in pain (p=0.002).
- 49% of intervention and 40% of control patients were pain-free at follow up.

**Author conclusion:**
- Intensive physician education had only a small effect on patient LBP outcomes. Effects were slightly more pronounced when nurse training in motivational counseling was added.
- The primary outcome may have been insensitive to change because patients were not very disabled at baseline and many had no pain at follow-up.
- The interventions also improved processes of care (fewer inappropriate imaging and injection procedures)

**Importance for Internists:**
- Training nurses to use guideline-directed motivational counseling may improve clinical outcomes.
- Nurse training is an investment, but skills could be applied to many other conditions requiring patient behavior change.
Collaborative care for chronic pain in primary care: a cluster randomized trial.  
Dobscha SK et al. JAMA. 2009; 301(12): 1242-1252.

Background:
- Adhering to pain guidelines is challenging in busy primary care settings
- Collaborative approaches many improve patient care through clinician education, patient activation, and system support.

Aims/purpose:
- To determine effects of a pain collaborative care intervention on patient outcomes, compared with usual care. The intervention included educational workshops for primary care clinicians, psychologist care manager visits and phone follow up, educational workshops for patients, and tailored recommendations to clinicians.

Methods:
- VA clinical trial with randomization at the primary care clinician level
- Inclusion: musculoskeletal pain ≥ 3 months, moderate intensity/disability
- Patients recruited by mail and posted flyers
- A sample of 400 patients was estimated to detect a medium effect (0.36)

Results:
- 42 clinicians (5 practices) and 401 patients enrolled
- Patients’ average age was 61, 92% were men, and 32% were employed
- The mean pain duration was 10 years
- On the primary outcome (Roland disability scale) at 12 months, intervention patients improved significantly more than controls (change -1.4 vs. -0.2, p=0.004). 22% of intervention vs. 14% of control patients had a 30% improvement (p=0.04), for a NNT of 12.7.
- Intervention patients also had significantly better pain intensity; those with depression had improved depression severity
- Intervention patients received more antidepressants, non-opioid analgesics and physical therapy appointments than controls
- Mean intervention phone contacts=5.4; <50% of patients went to 1 workshop
- Cost was ~ $1200 per intervention patient (including salary for 1 full-time psychologist and 20% of 1 internist, training, and materials)

Author conclusions:
- Collaborative care had a statistically significant but modest effect on pain and disability outcomes
- Improvements are meaningful, especially considering the population (older veterans with longstanding pain and high baseline disability)
- A more intensive intervention may have improved efficacy, but would be more expensive and less feasible in practice

Importance for Internists:
- Collaborative care may improve chronic pain care and clinical outcomes, even among highly disabled chronic pain patients
- This intervention may be best suited for clinics that are part of integrated systems, such as the VA, academic centers, or managed care organizations
Section 2: Assessment

Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. 

Background:
- Single item “pain screening” does not adequately measure pain.
- Multi-dimensional pain scales such as the Brief Pain Inventory (BPI) are widely used in specialty pain clinics and research settings, but are impractical for use in primary care.

Aims/purpose:
- To develop an ultra-brief pain measure derived from the BPI.

Methods:
- Used data from study 1 - a longitudinal study of 500 primary care patients with chronic pain (SCAMP) - to develop and initially validate the ultra-brief measure.
- Used data from Study 2 - a cross-sectional study of 646 veterans recruited from ambulatory care (HELP-vets) - to confirm reliability and validity in an independent patient population.
- Used consensus process to select items from the BPI.
- Assessed reliability (Cronbach’s alpha) and construct validity (Pearsons correlation coefficient for comparison to multiple other measures of pain intensity and function).
- Assessed responsiveness to change using comparison to participants’ global assessment of change and to change in serial Chronic Pain Grade scores. Measured with change score, effect size, and standardized response mean (SRM).

Results:
- Selected 3 items for the PEG: “Pain average,” “interference with Enjoyment of life,” and “interference with General activity.”
- Reliability of the PEG was 0.73 in Study 1 and 0.89 in Study 2.
- Construct validity of the PEG was good (r=0.60–0.89 in Study 1 and r=0.77–0.95 for pain-specific measures in Study 2).
- PEG showed responsiveness to change. Confidence intervals for the improved and unchanged groups did not overlap, but the unchanged and worse groups were not statistically different from each other. The improved group according to global rating of change had a mean improvement of 3.0 points (SD 2.5) on the PEG. The SRM among participants who improved at 6 months were similar for the PEG (1.20, 95% CI 0.96, 1.44), BPI severity (1.04, 95% CI 0.80, 1.28), and BPI interference (1.13, 95% CI 0.89, 1.37).

Author conclusions:
- The PEG, an ultra-brief three-item scale derived from the BPI, is a reliable and valid measure of pain among primary care patients with chronic musculoskeletal pain and diverse VA ambulatory patients.
- The PEG appears comparable to the BPI in terms of responsiveness to change.
- The PEG may be both useful and practical for chronic pain assessment in primary care and other ambulatory care settings.

Importance for internists:
- The PEG is a particularly appealing instrument for use by internists. It provides a feasible way to quickly measure not only pain intensity, but also interference with physical and emotional functioning.
Background:
- Clinicians vary widely in how frequently they obtain imaging tests for assessment of low-back pain.
- Several guidelines recommend against lumbar imaging in the first month of acute back pain, but these guidelines were based on data from observational studies.
- Since the publication of these guidelines, several RCTs have been published showing small favorable effects of routine lumbar imaging, but results have not always been statistically significant.

Aims/purpose:
- To investigate the effects of routine, immediate lumbar imaging versus usual clinical care without immediate imaging on clinical outcomes in patients with low-back pain and no indication of serious underlying conditions.

Methods:
- Systematic review and meta-analysis.
- Analyzed randomized controlled trials that compared immediate lumbar imaging (radiography, MRI, or CT) versus usual clinical care without immediate imaging for low-back pain.
- These trials reported pain or function (primary outcomes), quality of life, mental health, overall patient-reported improvement (based on various scales), and patient satisfaction in care received.
- Six trials (n=1804) met inclusion criteria.
- Study quality was assessed by two independent reviewers with criteria adapted from the Cochrane Back Review Group.
- Meta-analyses were done with a random effects model.

Results:
- There were no significant differences between immediate lumbar imaging and usual care without immediate imaging for primary outcomes at either short-term (up to 3 months, standardized mean difference 0·19, 95% CI –0·01 to 0·39 for pain and 0·11, –0·29 to 0·50 for function, negative values favor routine imaging) or long-term (6–12 months, –0·04, –0·15 to 0·07 for pain and 0·01, –0·17 to 0·19 for function) follow-up. Other outcomes did not differ significantly.
- Trial quality, use of different imaging methods, and duration of low-back pain did not affect the results, but analyses were limited by small numbers of trials.

Author conclusions:
- Immediate, routine lumbar-spine imaging in patients with low-back pain and no features suggesting serious underlying conditions did not improve clinical outcomes compared with usual clinical care without immediate imaging.
- Based on lower limits of 95% CIs, maximum plausible benefits on pain or function with routine imaging would be small or trivial.

Importance for Internists:
- This meta-analysis provides additional evidence that clinicians should refrain from routine, immediate lumbar imaging in patients with acute or sub-acute low-back pain and without features suggesting a serious underlying condition.

**Background:**
- Long-term opioid therapy is being prescribed with increased frequency (>3% of adults) for chronic non-cancer pain in community practices
- Death rates from opioid analgesic overdose have increased
- The extent that overdose risks are elevated among patients receiving medically prescribed long-term opioid therapy is unknown

**Aims/purpose:**
- To estimate overdose rates (nonfatal and fatal) among patients receiving long-term opioid therapy for their chronic non-cancer pain and compare risks among patients receiving different doses.

**Methods:**
- NIDA funded CONsortium to Study Opioid Risk and Trends (CONSORT)
- Observational study cohort persons enrolled in a Group Health Cooperative who started use of opioids for non-cancer pain between 1997-2005
- Obtained medication data from automated pharmacy files and calculated total morphine equivalents
- Obtained opioid-related overdoses from electronic medical record reviews
- Cox proportional hazards model were use to estimate overdose risk as a function of average daily opioid dose (morphine equivalents) received at the time of overdose

**Results:**
- 9940 patients who received long-term opioids for chronic non-cancer pain followed for a mean of 42 months (range <1-119 months) from initial 90-day exposure
- 61% of cohort had complete follow-up data
- 51 opioid-related overdoses were identified including 6 deaths
- Compared with patients receiving 1-20 mg/d of opioids (0.2% annual overdose rate), patients receiving 50-99 mg/d had a 3.7-fold increase in overdose risk (95% CI 1.5-9.5) and a 0.7% annual overdose rate.
- Patients receiving 100 mg/d or more had an 8.9-fold increase in overdose risk (CI, 4.0-19.7) and a 1.8% annual overdose rate

**Author Conclusions:**
- Patients receiving higher doses of prescribed opioids are at increased risk for overdose
- Further research on overdose risk and approaches to reduces associated risk is needed No significant differences were seen in pain, physical functioning, or contact with primary care

**Importance for Internists:**
- Long-term opioids should be prescribed with awareness of the risks and close patient monitoring especially in patients on high-dose opioids

Background:
- Long-term opioid therapy for non-cancer pain has increased
- The efficacy and risks of long-term opioids in patients with substance abuse histories are poorly understood
- Caution is advised in prescribing to person with substance use disorders, but little is known about actual health plan practices

Aims/purpose:
- To examine the extent to which persons with a history of substance abuse are receiving long-term opioids for chronic non-cancer pain
- Report trends and characteristics of long-term opioid use in these persons

Methods:
- NIDA funded CONsortium to Study Opioid Risk and Trends (CONSORT)
- Using 2 health plan (Kaiser Permanente of Northern California [KPNC] and Group Health Cooperative [GH] of Seattle Washington) data (1997-2005), the study compared age-sex-standardized rages of incident, incident long-term and prevalent long-term prescription opioid use, and medication use profiles in those with and without substance use disorder histories
- Data retrieved from automated administrative databases

Results:
- At KPNC prevalence of long-term opioid use increased from 11.6 to 17% with substance use disorder histories and from 2.6 to 3.9% for those without substance use history
- Respective rates at GH increased for 7.6 to 18.6% and from 2.7 to 4.2%
- Among patients with opioid disorder, KPNC rates increased from 44.1% to 51.1% and GH rates increased from 15.7 to 52.4%
- Patients with prior substance use diagnosis received higher dosage levels and were more frequent users of sedative-hypnotics.

Author Conclusions:
- Increased use of long-term opioids in higher risk patients suggests the importance of improved understanding of the benefits and risks of opioid therapy among persons with a history of substance abuse and the need for more careful screening for substance abuse history than in the usual practice

Importance for Internists:
- With evidence lacking to support the efficacy of long-term opioids for chronic non-cancer pain in general, extreme caution must be used when treating patients with a history of substance use as previous observational studies have consistently demonstrated high rates of opioid misuse is this population

Background:
- Use of chronic opioid therapy for chronic non-cancer pain has increased
- Prescription opioid misuse and mortality has increased

Aims/purpose:
- Review evidence and formulate evidence-based guidelines on use of chronic opioid therapy for chronic non-cancer pain

Methods:
- Multidisciplinary expert panel conducted systematic review commissioned by the American Pain Society (APS) who funded the guideline and the American Academy of Pain Medicine (AAPM)
- Literature search through November 2007 with 8,034 abstracts reviewed, with 14 systematic reviews and 57 primary studies (no included in the previously published systematic reviews) included
- Panel met 3 times from September 2006-January 2008 and used methods adapted from the GRADE working group and multi-stage Delphi process
- Final guideline was approved by APS and AAPM executive committees

Results:
- Evidence is limited, but chronic opioid therapy can be an effective therapy for carefully selected and monitored patients with chronic non-cancer pain.
- Opioids are associated with potentially serious harms, including opioid-related adverse effects and opioid misuse
- Recommendations provide guidance on patient management including: patient selection and risk stratification; opioid management plans; initiation and titration of chronic opioids; monitoring strategies; indications for discontinuation; prevention and management of opioid-related adverse effects; and when to obtain consultation

Author Conclusions:
- Safe and effective chronic opioid therapy for chronic non-cancer pain requires clinical skills and knowledge in both the principles of opioid prescribing and on the assessment and management of risks associated with abuse, addiction and diversion.
- Although evidence is limited, guidelines are offered

Importance for Internists:
- With evidence lacking to support the use of long-term opioids for chronic non-cancer pain these guidelines provide a reasonable standard of care for primary care providers offering this treatment for their patients.
Section 4: Antidepressants

Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis.

Background:
- Prior meta-analyses on antidepressants for Fibromyalgia Syndrome (FMS) suggest benefit in pain reduction with tricyclic antidepressants but have not evaluated newer classes of antidepressants

Aims:
- Conduct meta-analysis on treatment of FMS with anti-depressant
- Examine differences in efficacy for the different classes of anti-depressant

Methods:
- Researchers reviewed all articles (1966-2008) in all languages found from multiple search tools that performed a Randomized Controlled Trial of antidepressant for FMS defined using standard criteria.
  - Comparison group included pharmacological placebo
- Outcomes included pain, fatigue, sleep quality, depressed mood, HRQOL
- Weighted mean differences (WMD) or standardized mean differences (SMD) between study medicine and placebo determined effect size.

Results:
- 18 studies that met study criteria. Duloxetine trials included the largest number of subjects (n=1081)
- Impact of Antidepressants on
  - PAIN: small effect size -0.43 (-0.55 to -0.30, p<0.001)
  - FATIGUE no effect size -0.13 (-0.26 to -0.01, p=0.04)
  - DEPRESSED MOOD small effect size -0.26 (-0.39 to -0.12, p<0.001)
  - IMPROVED SLEEP small effect size -0.32 (-0.46 to -0.18, p<0.001)
  - HRQOL small effect size -0.31 (-0.42 to -0.20, p<0.001)
- Tricyclic Antidepressants showed large effect sizes for pain, fatigue, and sleep disturbances while showing small effect for HRQOL, and no impact on depressed mood.
- SSRIs showed small effect size for pain, depressed mood and HRQOL and no impact on fatigue or sleep.
- SNRIs showed strong evidence for small effect size for pain, sleep, depressed mood and HRQOL and no impact on fatigue.
- MAO inhibitors showed moderate effect for pain, but none on fatigue, sleep or depressed mood.

Author conclusion:
- Antidepressants as a class show small effect on treatment for FMS outcomes of pain, sleep, depressed mood and HRQOL but not fatigue.
- As a class, TCA show large effect on these same outcomes, whereas SSRI, SNRI show small effect.

Importance for Internists:
- Amitriptyline and duloxetine have the strongest evidence for improvement in symptoms related to FMS and should be first line agents.

Background:
- Prior meta-analyses on antidepressants for Fibromyalgia Syndrome (FMS) suggest benefit in pain reduction with tricyclic antidepressants but have not evaluated newer classes of antidepressants for all end points

Aims/purpose:
- Conduct systematic review on treatment of FMS with anti-depressant
- Account for individual outcomes (pain, sleep, mood) and composite outcomes

Methods:
- Researchers reviewed all articles in all languages found from multiple search tools that performed a clinical trial of antidepressant for FMS defined using standard criteria. Comparison group could include placebo, usual care or other treatment. Outcomes were symptom-specific measures.
- Studies were graded on quality

Results:
- 26 studies that met study criteria came from North America (46%), Western Europe (27%), and Turkey (25%). The methodological quality varied greatly.
- TCA (mostly amitriptyline) in 11 studies showed improvement in pain (90% of studies), fatigue (80%), and sleep (100%), reduction in depressive symptoms (60%) and improved quality of life (75%)
- SSRIs in 12 studies showed improvement in pain (83%), fatigue (50%), sleep (75%), depressiveness (70%), and quality of life (70%), although citalopram did not show any analgesic effect compared to placebo in two small studies
- SNRIs in 3 studies showed improvement in pain (100%), sleep (67%), depressiveness (67%), and quality of life (67%).
- Studies comparing outcomes classes of anti-depressants did not show superiority of one class, and no statistical difference exists between grouped findings as shown above. One study found amitriptyline plus fluoxetine better than either alone.

Author Conclusions:
- Amitriptyline, the best studied antidepressant for FMS, improves pain, fatigue, sleep and mood. Apart from citalopram, SSRI and SNRI also show improvement in outcomes.
- Studies of longer duration need to examine durability of improvements.
- Improvement in pain, sleep and fatigue appear to be independent of mood changes.

Importance for Internists:
- Most TCA, SSRI, SNRIs can be used for treatment for FMS.
- Due to overall effectiveness and cost, Amitriptyline at 10-25 mg/day can still be used as a first line treatment for FMS. Addition of fluoxetine to amitriptyline may be a reasonable next clinical step.

Background:
- Pain complaints account for 40% of all outpatient visits, and depression is present in 10-15% of all patients attending primary care. Pain and depression, furthermore, frequently coexist (30-50%)
- Quality of life and disability are frequently affected by pain and depression which in turn increases health care costs

Aims:
- To evaluate if a combined pharmacological and behavioral intervention improves pain and comorbid depression in primary care patients

Methods:
- Prospective, randomized controlled trial of 250 patients at 6 community-based clinics and 5 VA general medicine clinics
- Intervention group (n=123) had 3 months of optimized antidepressant therapy (algorithm-based), 3 months of self-management program (increasing self-efficacy and social support) and a continuation phase of 6 months. Usual care (n=127) had no specific intervention.
- 12 month follow-up with Depression (20-item Hopkins Symptom Checklist), pain severity and interference (Brief Pain Inventory) as main outcome measures. Other secondary measures including Roland Pain disability, Graded chronic pain scale, Generalized anxiety disorder (GAD-7) scale, and Short-Form 36 were also used.

Results:
- At 12 mos, 46/123 (37%) intervention patients versus 21/127 (16%) usual care were a depression responder (>50% decrease in HSCL-20 from baseline), RR 2.3 (1.5-3.2) with NNT 4.8.
- Importantly, with just anti-depression optimization, 51/123 (41.5%) intervention patients versus 22/127 (17%) were ‘pain responders’ (>30% decrease in BPI total from baseline), RR 2.4 (1.6-3.2), NNT 4.1
- At 12 mos, Secondary measures also showed better Roland Pain disability score, improved GCPS pain scores, GAD-7 scores, and SF-36 bodily pain and vitality scores.

Author Conclusions:
- Optimized antidepressant therapy along with a pain self management program produced significant reductions in depression severity and moderate reductions in pain severity and disability at 12 months.
- Reductions in depression and pain were seen early (1 mos) and sustained

Importance for Internists:
- Patients with chronic pain should be screened for comorbid depression and vice-versa
- Treatment with optimized antidepressant therapy and cognitive behavioral therapies may produce substantial clinical benefits in patients with dual comorbidities of pain and depression
Section 5: Nonopioid Treatments


**Background:**
- Neuropathic pain (mostly diabetic neuropathy and post-herpetic neuralgia) has historically been treated with tricyclic antidepressants (TCAs), and more recently gabapentin
- Comparisons between TCAs and gabapentin to determine superiority were primarily based on their individual responses versus placebo, and determined indirectly (i.e. TCA vs placebo VERSUS gabapentin vs. placebo)

**Aims/Purpose:**
- To determine the effect of gabapentin vs TCAs in both direct head-to-head comparisons and indirect analyses
- To determine any differences between the (TCA vs placebo) and (gabapentin vs placebo) trials

**Methods:**
- Literature search of randomized trials meeting inclusion criteria (RCT, adults with diabetic neuropathy or postherpetic neuralgia, gabapentin, TCA or placebo use, and reporting of outcome measures)
- Direct and indirect meta-analysis of all trials, and quality analysis (randomization, allocation concealment, masked patients, masked outcome assessor, intention-to-treat analysis) of all trials

**Results:**
- In 3 head-to-head trials, no difference between gabapentin and TCAs, RR 0.99 (0.76-1.29) for pain relief.
- In indirect comparisons, gabapentin were slightly worse than TCAs, RR 0.41 (0.23-0.74) for pain relief, although both were effective (gabapentin vs placebo RR 2.2 (1.8-2.7), TCA versus placebo RR 5.3 (3.1-9.1)
- No trial met all quality criteria, most trials were relatively short-term, and published in essentially different decades.

**Author conclusions:**
- No difference was detected between gabapentin and TCAs in head-to-head trials, but some favoring of TCAs in indirect trials.
- However, the methodology of the indirect trials were very disparate with poor quality criteria for the TCA trials (patient characteristics, regimens, assessment of outcomes, and design)
- Placebo response rate in the gabapentin trials was 24% and TCAs was 6%
- All clinical trials were relatively short-term with the longest trial only for 12 weeks

**Importance for Internists:**
- Direct (head to head) and indirect comparisons (A versus placebo VERSUS B versus placebo) may produce disparate results
- The quality of trials including patient selection, outcome definitions, design and conduct may greatly influence results and comparisons

Background:
- Back pain is the leading reason for visits to acupuncturists
- Several recent, European trials have suggested that real acupuncture and “sham” acupuncture are equally effective

Aims/purpose:
- To determine if acupuncture is more effective than usual medical care alone.
- To determine if real acupuncture is more effective than simulated (noninsertive) acupuncture.
- To determine if individualized acupuncture is more effective than standardized acupuncture.

Methods:
- 4-arm randomized controlled trial comparing the effectiveness of individualized acupuncture, standardized acupuncture, simulated acupuncture, and usual care.
- 638 adults with mechanical low back pain from Group Health Cooperative (Seattle, Washington) and Kaiser Permanente (northern California)
- 10 treatments delivered over 7 weeks by experienced acupuncturists
- Primary outcomes were Roland-Morris Disability Score (0-23) and symptom bothersomeness (0-10) and assessed at baseline, 8, 26, and 52 weeks.

Results:
- At 8 weeks, mean disability scores improved by 4.4, 4.5, and 4.4 points with individualized, standardized, and simulated acupuncture, respectively
- For usual care patients, disability scores improved by 2.1 points (p <.001)
- Clinically meaningful improvements in disability were seen in 60% of patients receiving acupuncture vs. 39% (P <.001) in the usual care arm
- Symptom bothersomeness improved by 1.6 to 1.9 points in the treatment groups vs. 0.7 points in usual care (P <.001)
- Improvements in functioning persisted at 1-year from acupuncture treatment vs. usual care

Author conclusion:
- Compared with usual care, acupuncture (individualized, standardized, and simulated) demonstrated clinically meaningful improvements in back-pain related function at 8 and 52-weeks
- Tailoring needling sites to each patient and penetration of the skin appear unimportant for facilitating the therapeutic effect of acupuncture.
- Acupuncture’s purported mechanism of action remains in question.

Importance for Internists:
- Given the large sample size included, minimal attrition, and rigorous design the study inferences are more robust than most acupuncture trials.
- Acupuncture, no matter what technique is used, appears safe and effective and a reasonable treatment option for patients with chronic low back pain.
Systematic review and meta-analysis of cannabis treatment for chronic pain.

Background:
- Cannabis has been used for the treatment of various conditions including muscles strains, seizures, asthma, depression, and pain.
- Clinical use of cannabis has been tightly restricted for ethical and legal reasons, and a lack of evidence demonstrating benefits.
- Animal and early clinical studies have suggested cannabis has analgesic properties and potential benefits for pain sufferers.

Aims/purpose:
- To assess the efficacy and harms of cannabis preparations for the treatment of chronic pain

Methods:
- Systematic review and meta-analysis of double-blind randomized controlled trials of cannabis preparations vs. placebo among patients with chronic pain.
- Search of Medline/Pubmed, Embase, and The Cochrane Controlled Trials Register of all literature published until February 2008
- Search terms included: “cannabis,” “cannabinoids,” “marijuana,” “THC,” “tetrahydrocannabinol,” “pain,” and “chronic pain.”
- Study quality assessment was performed independently by two authors

Results:
- The search yielded 229 studies; 18 trials included in review
- For efficacy, cannabis reduced pain intensity compared to placebo. The standardized mean response for cannabis was -0.61 (-0.84 to -0.37).
- For harm, the Odds Ratios (OR) was 4.51 (3.05-6.66) for altered perceptions (blurred vision, visual hallucinations, tinnitus, disorientation, confusion, dissociation, and acute psychosis) and a number needed to harm (NNH) = 7 (6-9);
  - For events affecting motor function (speech disorders, ataxia, muscle twitching, and numbness) OR=3.93 (2.83-5.47) and NNH = 5 (4-6);
  - For events altering cognitive function (impaired memory, altered attention) OR = 4.46 (2.37-8.37) and NNH = 8 (6-12).

Author conclusion:
- Treatment of chronic pain with cannabis formulations entails more risk than benefit
- However, the analgesic properties of cannabis deserve further study

Importance for Internists:
- In contrast to this study, previous systematic reviews of cannabis for pain conditions have not used meta-analytic methods.
- Most of the included trials were small and used a cross-over design which may not allow adequate wash-out of cannabis and potentially leading to bias.
- The average duration of trials included in the review were 25 days--too short to report about the potential addictive effect of cannabis.