PCORI Workshop on Long-Term Opioid Treatment for Chronic Pain

Workgroup Discussion Questions - Group 1

Consolidated General Questions - Categories

1	**Pharmacologic Treatment Options (Drug vs. Drug Comparisons)**
2	**Dosing Strategies**
3	**Other**

Evidence Gap: The current evidence base for the use of long-term opioids (>3 months) for chronic pain and the effectiveness of different opioid dosing strategies is extremely weak, given the importance of this topic.

Objective: Identify, refine, and prioritize comparative effectiveness research questions that focus on long-term opioid treatment for chronic pain.

Considerations:

Comparisons of drugs in a randomized controlled trial design vs. an observational study
Patients with chronic noncancer pain >3 months Outcomes >1 year
Studies must be long enough to observe important outcomes.
Subgroups proposed and others to consider: • High risk patient populations • Low socioeconomic status or poor access to healthcare • Sex • Racial and ethnic minorities

Original (refined) Questions:

1	**Pharmacologic Treatment Options (Drug vs. Drug Comparisons):** In patients with chronic pain, what is the comparative effectiveness of opioids versus non-opioid medications or compared to other opioids on outcomes related to pain, function, quality of life, fractures, endocrine dysfunction, abuse, overdose, and death? *Potential patient populations may include:* patients with chronic low back pain, musculoskeletal pain, fibromyalgia, neuropathic pain; substance abusers, those recently incarcerated, pregnant women, cancer survivors etc. *Non-opioid therapies may include*: NSAIDS, Cox-II inhibitors, antidepressants, muscle relaxants, synthetic cannabinoids/medical marijuana, etc. *Subgroup Analysis:* How do harms vary depending on 1) type of pain, 2) patient demographics and clinical characteristics (including comorbidities, past or current substance abuse 3) Dose of opioids *Additional considerations:* Other unintended consequences

1.1	For patients with chronic pain, what are the comparative benefits and harms of the following analgesic combination regimens: 1) non-opioid analgesics (no opioids) vs. 2) non-opioid analgesics with limited as needed low-dose opioids vs. 3) non-opioid analgesics with daily opioid analgesics (up to 100 morphine-equivalent mg per day)? This study design should include flexible drug and dosing options within defined parameters for each arm and treatment to response targets (rather than fixed dose/drug targets).
1.2	What is the long-term benefit/risk profile of opioids (stratified by whether the drug is immediate- or extended-release and by low vs. high dose in morphine equivalents) compared to prescription NSAIDS, COX-II inhibitors, and acetaminophen, when used for >90 days to treat chronic non-cancer pain? This would require evaluation of a broad range of outcomes including pain, functional status, and quality of life, adverse events relevant to these drugs, abuse, overdose, death, and others pertinent to a full benefit-risk assessment.
1.3	For patients with chronic pain, what are the benefits and harms of tramadol vs. typical immediate-release opioid analgesics?
1.4	What is the comparative effectiveness of opioid analgesics versus transdermal medication therapy for individuals with chronic pain?
1.5	What are the comparative benefits and risks of using non pharmacological modalities and non opioid analgesics versus closely monitored long term opioid analgesics in chronic pain patients with a history of substance abuse and addiction disorder? Outcome measures include QOL indices (better mobility, sleep, mood, function), and decreased incidence of relapse.

2	**Dosing Strategies:** In patients with chronic pain on long-term opioid therapy, what is the comparative effectiveness of dose escalation versus dose maintenance or use of dose thresholds on outcomes related to pain, function and quality of life?
2.1	In patients on long-term opioid therapy, what are the effects of decreasing opioid doses or tapering off opioids versus continuation of opioids on outcomes related to pain, function, quality of life and withdrawal?
2.2	In patients with chronic pain, what is the comparative effectiveness of short- versus long-acting opioids or sustained release formulations on outcomes related to pain, function, quality of life, risk of overdose, addiction, abuse, misuse, or doses of opioid used?
2.3	For patients with chronic non-cancer pain, who have been on long-term opioid therapy, what are the comparative effectiveness of rotation to buprenorphine/naloxone and to methadone for outcomes of pain, function, misuse, overdose and addiction?
2.4	For patients with persistent chronic pain who are currently treated with opioids at ≥ 50 morphine-equivalent mg per day, what are the benefits and harms of opioid rotation with stable or increased dose vs. opioid rotation with dose reduction or tapering to discontinuation? To mirror realities of clinical practice and allow for individual patient differences in medication tolerance and efficacy, this study design should include protocols for co-treatment with non-opioid analgesics and flexibility in drug/dose options within defined parameters for each arm.
2.5	Do people with chronic pain require escalation of opioid dosing over time when these medications are taken for a year or longer compared to short term use of opioids for less than one year? The intended outcome: Indicate if chronic pain patients can utilize opioid medications without escalating dosage amounts over time, then these drugs could be

	prescribed with less concern and be construed as appropriate medications in the treatment of chronic pain by healthcare professionals.

3	**Other:** What is the comparative effectiveness of treatment strategies for managing patients with addition to prescription opioids on outcomes related to overdose, abuse, misuse, pain, function, quality of life? *Potential populations may include:* substance abusers, pregnant women, those recently incarcerated etc.
3.1	What is the comparative effectiveness of treatment strategies to reduce overprescribing of opiates (including Prescription Drug Monitoring Programs) in the Medicaid population?