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* Ratings pending – login to http://plus.mcmaster.ca/evidencealerts in a few days if interested.

**Abstract**

**Importance**: Limited evidence is available regarding long-term outcomes of opioids compared with nonopioid medications for chronic pain.

**Objective**: To compare opioid vs nonopioid medications over 12 months on pain-related function, pain intensity, and adverse effects.

**Design, Setting, and Participants**: Pragmatic, 12-month, randomized trial with masked outcome assessment. Patients were recruited from Veterans Affairs primary care clinics from June 2013 through December 2015; follow-up was completed December 2016. Eligible patients had moderate to severe chronic back pain or hip or knee osteoarthritis pain despite analgesic use. Of 265 patients enrolled, 25 withdrew prior to randomization and 240 were randomized.

**Interventions**: Both interventions (opioid and nonopioid medication therapy) followed a treat-to-target strategy aiming for improved pain and function. Each intervention had its own prescribing strategy that included multiple medication options in 3 steps. In the opioid group, the first step was immediate-release morphine, oxycodone, or hydrocodone/acetaminophen. For the nonopioid group, the first step was acetaminophen (paracetamol) or a nonsteroidal anti-inflammatory drug. Medications were changed, added, or adjusted within the assigned treatment group according to individual patient response.

**Main Outcomes and Measures**: The primary outcome was pain-related function (Brief Pain Inventory [BPI] interference scale) over 12 months and the main secondary outcome was pain intensity (BPI severity scale). For both BPI scales (range, 0-10; higher scores = worse function or pain intensity), a 1-point improvement was clinically important. The primary adverse outcome was medication-related symptoms (patient-reported checklist; range, 0-19).
**Results:** Among 240 randomized patients (mean age, 58.3 years; women, 32 [13.0%]), 234 (97.5%) completed the trial. Groups did not significantly differ on pain-related function over 12 months (overall P = .58); mean 12-month BPI interference was 3.4 for the opioid group and 3.3 for the nonopioid group (difference, 0.1 [95% CI, -0.5 to 0.7]). Pain intensity was significantly better in the nonopioid group over 12 months (overall P = .03); mean 12-month BPI severity was 4.0 for the opioid group and 3.5 for the nonopioid group (difference, 0.5 [95% CI, 0.0 to 1.0]). Adverse medication-related symptoms were significantly more common in the opioid group over 12 months (overall P = .03); mean medication-related symptoms at 12 months were 1.8 in the opioid group and 0.9 in the nonopioid group (difference, 0.9 [95% CI, 0.3 to 1.5]).

**Conclusions and Relevance:** Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

**Trial Registration:** clinicaltrials.gov Identifier: NCT01583985.

### Comments from Clinical Raters

**Family Medicine (FM)/General Practice (GP)**

More good evidence to demonstrate that opioids are not as good first-line treatments as analgesics for AO and low-back pain. How could we have ever thought so incorrectly in the past?

**Family Medicine (FM)/General Practice (GP)**

Finally, a study comparing long-term opioid treatment with non-opioid treatment of a pain condition (although the non-opioid group could be treated with Tramadol, but few were). As has been shown in RCTs comparing short-term pain treatment, no advantage of opioid treatment was shown. My only qualm is that the opioid dosing was capped at a rather low maximum dose of 100 Morphine Equivalent Milligrams. Nonetheless, unless NSAIDs are contraindicated, treatment with NSAID-based therapy is as effective as opioid-based therapy.

**General Internal Medicine-Primary Care(US)**

An important paper that finds no clear overall advantage to initiating opioid over nonopioid medications in chronic back pain or chronic pain from hip or knee osteoarthritis. I would have liked to know how many patients were taking a combination of acetaminophen and ibuprofen. At least for post-operative pain, we know this is a very effective combination that is as good or better than oxycodone. It would be interesting to know to what extent, if any, it may have driven the overall results. Also, I'd like to have seen more detail on how many patients in each arm progressed through each treatment step. Some outcome assessors were blinded, although primary outcomes were patient reported and patients were not blinded. Allocation was concealed, which makes up for some of this. Limitations noted and all things considered, this trial provides good support for moving away from opioids as first-line initiated therapy in these patients.