

# Duloxetine for Arthritis Pain

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## Question

Is duloxetine effective for pain caused by arthritis?

## Evidence-Based Answer

Marginally. Duloxetine (60 mg to 120 mg once daily) is slightly more effective than placebo at reducing osteoarthritis (OA) knee pain (SOR: **A**, meta-analysis of 3 good quality RCTs). Indirect comparisons suggest duloxetine is more effective in reducing osteoarthritis symptoms than tramadol and hydromorphone and comparable to ibuprofen, naproxen, celecoxib, and oxycodone (SOR: **B**, network meta-analysis with significant heterogeneity).

**TABLE: Network meta-analysis using Frequentist and Bayesian models to indirectly compare Duloxetine to comparator medications for the treatment of hip and knee osteoarthritis symptoms.**

Comparator Medication	# Trials	# Patients	I <sup>2</sup>	Analysis Type	MD	95% CI
Ibuprofen	2	423	0%	Frequentist	-1.9	-6.3 to 2.6
				Bayesian	1.9	-2.1 to 5.9
Naproxen	7	1,889	52%	Frequentist	-1.9	-4.7 to 0.8
				Bayesian	0.2	-2.4 to 2.9
Celecoxib	14	4,681	33%	Frequentist	0.7	-2.1 to 3.5
				Bayesian	0.8	-1.5 to 3.1
Tramadol	5	1,507	58%	Frequentist	2.4	-1.0 to 5.7
				Bayesian	3	<b>1.5 to 8.3</b>
Hydro-morphone	2	468	64%	Frequentist	4.4	-0.3 to 9.0
				Bayesian	8.2	<b>3.8 to 13</b>
Oxycodone	2	398	44%	Frequentist	-2.1	-11 to 7.0
				Bayesian	-4.7	-13 to 4.1

I<sup>2</sup>=Heterogeneity; MD=Mean difference; CI=Confidence interval

## Data Review

A 2015 meta-analysis (3 double-blinded RCTs, N=1,011) compared pain reduction in patients with OA of the knee taking duloxetine versus placebo.<sup>1</sup> Patients included were largely Caucasian (86%) females (64%) with a mean age of 62 years and mean disease duration of 9 years with an average baseline pain score of 6 out of 10 on the Brief Pain Inventory. The intervention groups received duloxetine titrated to either 60mg or 120mg daily for 10 to 13 weeks. Duloxetine led to slightly greater pain improvement compared to placebo (mean difference (MD) -0.88 ; 95% CI -1.1 to -0.65; I<sup>2</sup>=0%) but the clinical significance of this difference is unclear as the minimum clinically important difference in the 0 to 10 scale was reported to be 2 points. More patients taking duloxetine had at least a 50% pain reduction compared to those taking placebo (N=989; 35% vs 23%; risk ratio [RR] 1.7; 95% CI, 1.3 to 2.3; I<sup>2</sup>=56%).

A 2014 network meta-analysis (34 double-blinded RCTs, N=17,446) indirectly compared the efficacy of duloxetine to ibuprofen, naproxen, celecoxib, tramadol, oxycodone and hydromorphone in reducing hip and knee OA symptoms using the Frequentist and Bayesian statistical models by calculating the change in pre and post treatment Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).<sup>2</sup> The WOMAC assessed pain, stiffness, and physical function. Trials were 12 -26 weeks long and included patients had a mean age of 60 years old and a mean duration of osteoarthritis of 7 years.

Duloxetine (60mg-120mg total daily dose) was more effective at reducing OA pain compared to tramadol (200mg-300mg total daily dose) and hydromorphone (16mg total daily dose) using the Bayesian network analysis but not using the Frequentist analysis. There was no significant statistical difference in pain reduction between duloxetine and ibuprofen (2400mg total daily dose), naproxen (1000mg total daily dose), celecoxib (200mg total daily dose), and oxycodone (10-120mg total daily dose) using either the Frequentist or Bayesian analyses (TABLE). A difference of only 0.88 points on a 0-10 scale would be of questionable clinical significance.

## Summary

Duloxetine does improve osteoarthritis pain and symptoms compared to placebo and is comparable to certain opioids and NSAIDs in effectiveness of treating osteoarthritis symptoms.

## References

1. Zhao YW, Sheng YS, Shu JL et al. Efficacy and safety of duloxetine on osteoarthritis knee pain: a meta-analysis of randomized controlled trials. *Pain Medicine*. 2015; 16:1373-1385. **[STEP 1]**
2. Myers J, Wielage RC, Hand B, et al. The efficacy of duloxetine, non-steroidal anti-inflammatory drugs, and opioids in osteoarthritis; a systematic literature review and met-analysis. *BMC Musculoskelet Disord*. 2014; 15:76 **[STEP 2]**