PEER simplified decision aid: neuropathic pain treatment options in primary care

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This decision aid is for clinicians for discussion of treatment options for patients living with neuropathic pain. It is derived from our accompanying systematic review of randomized controlled trials (RCTs; **e130**).[1] Effectiveness data were generated from RCTs comparing active treatment to control. The evidence focuses on the proportion of patients achieving a clinically meaningful reduction in pain, generally defined as a 30% or more reduction in pain.

How was this tool was developed?

Icon arrays were developed using risk ratio estimates from meta-analyses of patients attaining a clinically meaningful improvement in pain. The control response rate was standardized to 29%, the approximate control response rate averaged for all included studies. The risk ratio for each intervention was applied to the average 29% control rate to attain the estimated benefit of that intervention. Standardizing control rates allows for easier comparison of estimated benefits of differing interventions. The estimates are from placebo-controlled trials and are not direct comparisons, so differences between interventions are approximations with some uncertainty.

Our systematic review identified the best available evidence for most interventions.[1] For anticonvulsant medications, we included evidence for gabapentin, pregabalin, oxcarbazepine, and topiramate, with 90% of the studies examining gabapentin or pregabalin. All 4 anticonvulsant medications demonstrated similar efficacy; more adverse events were seen with oxcarbazepine and topiramate. For serotonin-norepinephrine reuptake inhibitors, we included duloxetine, venlafaxine, and desvenlafaxine, with 75% of the literature focused on duloxetine. Efficacy and adverse events were similar, regardless of the drug. To improve quality, we excluded partially reported crossover trials. This worked for other therapies, but in the case of tricyclic antidepressants, it left only 2 very low-quality RCTs with conflicting results. For clarity, we used a recent systematic review of tricyclic antidepressants[2] and meta-analyzed responder data, including partially reported crossover trials (meta-analysis available from authors on request). We did not identify any relevant RCTs for exercise or topical lidocaine.

The decision aid

The tool is a 1-page summary (2-sided) of estimated effectiveness of treatment options for neuropathic pain; a printable version is available from **CFPlus**.* Accompanying the icon array (**Figure 1**)[3] is a blue arrow that indicates the level of evidence associated with each of the listed interventions, based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) working group criteria,[3] which reflects confidence in risk ratio estimates. **Figure 2**[1,2,4] includes classification of therapies by benefits and harms, withdrawals due to adverse events, typical adverse events, prescribing considerations, and estimated costs.

We did not report on cannabinoids for neuropathic pain, as we have done so before.[5] While this previous icon array does address neuropathic pain, it includes other types of neuropathic pain not included in this analysis, so effect estimates are not directly comparable. The tool is not a guideline, and the evidence was not assessed by an independent guideline committee. Information presented here will be combined with similar systematic reviews and tools on other types of chronic pain to inform future guideline development.

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Competing interests
None declared

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*Easy-to-print versions of **Figures 1** and **2** are available at **www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

Figure 1

PEER SIMPLIFIED DECISION AID / NEUROPATHIC PAIN

How many people will have their neuropathic pain meaningfully improved (≥30%) by different treatments?

* Anticonvulsants included pregabalin, gabapentin, oxcarbazepine and topiramate

**SNRIs included duloxetine, venlafaxine and desvenlafaxine

Figure 2

Treatment Options for Neuropathic Pain

BENEFITS AND HARMS	TREATMENT	NUMBER NEEDED TO TREAT (NNT)	WITHDRAWALS DUE TO ADVERSE EVENTS* (TREATMENT VS PLACEBO)	ADVERSE EVENTS (EXAMPLES)	COST	PRESCRIBING COMMENTS
☺ Benefits likely exceed harms	**Pregabalin**	7	11% vs 5% NNH 17	Dizziness, peripheral edema, weight gain, ataxia, somnolence	$$	Doses ranged from 75 mg to 600 mg daily (most commonly studied dose was 300 mg daily).
	Gabapentin	7	13% vs 8% NNH 22	Dizziness, somnolence, peripheral edema	$ to $$	Doses varied, with the most commonly studied dose ranging from 900-3600 mg per day.
	SNRIs	8	13% vs 5% NNH 13	Dizziness, nausea, somnolence	$ to $$$	Studied drugs included duloxetine (40-120 mg), venlafaxine (75-225 mg), and desvenlafaxine (50-400 mg).
	Rubefacients (Capsaicin)	10	6% vs 2% NNH 25	Application site redness, burning, pain, pruritus and swelling	$ to $$	Benefit seen with both 0.075% cream and 8% high concentration patch (8% Patch Not Available in Canada).
☺ Benefits may not exceed harms in some patients	**Opioids**	10	14% vs 6% NNH 12	Somnolence, pruritus, nausea, vomiting, constipation, dizziness	$$ to $$$	While 13% of patients improved above placebo, many adverse events were reported. Approximately 3% of patients with chronic pain will develop opioid use disorder over 2 years.[5]
☹ No benefit	**Acupuncture**	No difference from placebo	No difference from placebo	Not reported	$$$ to $$$$	Types of acupuncture included traditional, auricular and electroacupuncture. Patients were followed for 8-10 weeks.
☹ Harms likely exceed benefits	**Oxcarbazepine**	7	26% vs 7% NNH 6	Somnolence, back pain, nausea, dizziness, serious adverse events	$$	Effects were no different than placebo, however high withdrawals due to adverse events were seen.
😐 Unclear Benefits/ Harms	**TCAs (Amitriptyline)****	4	16% vs 7% NNH 12	Dry mouth, dizziness, drowsiness	$ to $$	RCTs are small and at high risk of bias. Most commonly studied dose was 25-75 mg daily.

*Statistically significant findings reported
Cost approximates dollars per month: $ = <25, $$ = 25-50, $$$ = >50-100, $$$$ = >100
SNRI: Serotonin Norepinephrine Reuptake Inhibitors, **TCAs:** Tricyclic Antidepressants, **NNH:** Number Needed to Harm
Note: No responder data identified for exercise and lidocaine.
**Due to an inconsistent estimate of effect and statistical significance, uncertainty existed in our analysis of TCAs. To clarify the potential estimate of effect, TCA data was pulled from a previously published Cochrane review[2]