Management of Chronic Non-Cancer Pain

Appendix A: Non-pharmacological treatments

A) Physical activity/exercise therapies[1,2,3]

Exercise, regardless of form, is recommended for the management of chronic non-cancer pain.[2]
This table provides more details on evidence levels for specific exercises.

Type of activity/exercise	Benefits/role	Level of evidence	Type of pain
Aerobic exercise (e.g. walking)	Improved global well being and physical function, reduced pain (fibromyalgia[1])	●●	Fibromyalgia
Strengthening exercise (e.g. lifting weights)	Global well being, pain and physical function (fibromyalgia[1])	●	Fibromyalgia, non-specific low back pain
Core stabilising exercises (e.g. pilates)	Reducing pain (non-specific low back pain[2], fibromyalgia[1])	Not reported in guideline	Non-specific low back pain, fibromyalgia
Tai Chi	Reducing pain, improving disability (arthritis[2]), quality of life (fibromyalgia[1])	Not reported in guideline	Chronic arthritis, fibromyalgia
Yoga (any type)	Reducing pain and disability (headache, back pain, rheumatoid arthritis[3]). Improved quality of life, pain and function (fibromyalgia[1])	●●	Fibromyalgia, headache, low back pain, rheumatoid arthritis
Therapeutic aquatic exercise	Improved pain, quality of life, physical function, muscle strength (fibromyalgia[1], low back pain[2])	Not reported in guideline	Fibromyalgia, low back pain

B) Self-management programs[2,4]

Recommendations	Level of evidence	Type of pain	Benefits/ role	Harm
Self-management resources should be considered to compliment other therapies of patients with chronic pain	●●	Chronic musculoskeletal pain (osteoarthritis, rheumatoid arthritis, fibromyalgia, low back pain, neck pain, shoulder pain)	Reduced pain and disability (arthritis)[1]	Possible increased pain with exercise, resulting in drop out from programs: if this occurs, explore with the patient how best to help them cope.[3]

Self-management program characteristics

- Primarily educational using interactive and collaborative method often run by patients
- Focus on taking an active part in managing their pain
- Delivered as: individuals, face-to-face or electronically
- Content may include: education around goal setting, self-monitoring, psychological and rehabilitation interventions (e.g. exercise therapies)

C) Psychological therapies

Treatment	Recommendations	Level of evidence	Type of pain	Benefits/role	Harm
Cognitive Behavioural Therapy	Cognitive behavioural therapy should be considered for the treatment of patients with chronic pain	●●	Orofacial pain, low back pain, neck pain, rheumatoid arthritis, fibromyalgia	• Reduced pain (orofacial, low back pain, fibromyalgia)[2,5] • Reduced use of analgesics (low back pain) • Reduced disability (low back pain[2], fibromyalgia[5]) • Improved quality of life (low back pain) • Improved coping (low back pain, fibromyalgia) • Reduced depression (low back pain[2], fibromyalgia[5]) • Reduced physician visits (low back pain) • Improved sleep[2]	Rarely may include worsening of co-existing mental disorders
Mindfulness based interventions	No recommendations given in guidelines	●●	Fibromyalgia, low back pain, rheumatoid arthritis, musculoskeletal pain	Reduced pain, reduced depression and anxiety, improved quality of life	Not reported in guideline
Acceptance and Commitment Therapy	No recommendations given in guidelines	●●●	Osteoarthritis, neuropathic pain, low back pain	Improved depression and anxiety	Not reported in guideline
Respondent behavioural therapies	Progressive relaxation or EMG biofeedback should be considered for the treatment of patients with chronic pain	●●	Low back pain	Short term pain reduction, reduction in disability. No better than Cognitive Behavioural Therapy	Not reported in guideline

D) Physical therapies

Therapy type	Type of pain	Level of evidence	Recommendations	Benefits/role
Manual therapy	Low back pain, neck pain	●●●	Manual therapy should be considered for short term pain relief of patients with chronic low back pain	Short term: pain relief, functional improvement and cervicogenic headache[2]
			Manual therapy in combination with exercise should be considered for the treatment of patients with chronic neck pain	
TENS	Neuropathic pain, low back pain	●●●	TENS should be considered for the relief of chronic pain; either low or high frequency can be used	Pain (neuropathic pain)[2], improved function (low back pain)[2]
Low level laser therapy	Low back pain	●●●	Low level laser therapy should be considered as a treatment option for patients with chronic low back pain	Reduced pain[2]

	Non-opioid medications: general[2] (unless otherwise specified)						
	Drug/drug class	**Pain type**	**Level of evidence**	**Role in therapy**	**Potential harms**	**Dosage***	**Tapering****
General	**Acetaminophen**	Osteoarthritis (hip or knee), in addition to non-pharmacological treatment	●●●	• Should be considered for hip or knee osteoarthritis (alone or in combination with NSAIDs), in addition to non-pharmacological treatments	• Can be hepatotoxic at doses greater than 3-4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease[6] • Consider liver function tests if hepatic risk (history of liver problems or alcohol abuse, long-term use)[7] • Reduce dose in liver insufficiency or alcohol dependence[6] • Many medications (e.g. over-the-counter cough and cold and pain relief products) contain acetaminophen; read the label and avoid exceeding maximum dose[8]	• 1000-4000 mg/day[2] • Dose provided in product labelling (maximum 4000 mg/day) is for short-term treatment (5 days)[8] • There is greater risk (including gastrointestinal adverse events and multi-organ failure) from acetaminophen with extended duration of use, use conservative dosing and treatment duration[9]	Tapering not required
	Nonsteroidal anti-inflammatory drugs (NSAIDs): • celecoxib • diclofenac • ibuprofen • meloxicam • naproxen	Low back pain, osteoarthritis	●●●	• Should be considered for chronic non-specific low back pain • May have synergistic, dose-sparing effect when added to opioids[10]	• Risk of gastrointestinal bleeding/perforation, gastritis, and peptic ulcer disease[6,10] • Causes fluid retention[5] • Avoid in severe renal dysfunction (CrCl < 30 mL/min) or deteriorating renal disease; use caution if CrCl = 30-59 mL/min [11,12] • Avoid in severe hepatic impairment • Avoid during pregnancy (3rd trimester) or breastfeeding, severe uncontrolled heart failure, severe allergy to acetylsalicylic acid or NSAIDs, active peptic ulcer disease, cerebrovascular disease, inflammatory bowel disease, or known hyperkalemia[11] • Monitor blood pressure and signs of heart failure • Avoid in the elderly (consider topicals instead)[10] • Cardiovascular risks (heart attack and stroke)[6] • Ibuprofen (but not other NSAIDs) interacts with acetylsalicylic acid to make it less effective for cardioprotection and stroke prevention[13]	With all NSAIDs: • Allow 1-2 weeks for full effect[7] • Consider lower doses in the elderly[14] • Swallow whole, take with food[11,12,15,16] • Due to serious safety risks associated with oral NSAID use, use conservative dosing and treatment duration consistent with approved prescribing limits[9] • **Celecoxib**: 100 mg twice daily or 200 mg once daily (200 mg twice daily for rheumatoid arthritis, 200 mg/day for other type of pain)[15] • **Diclofenac regular-release:** 75-100 mg daily (divided into 3 daily doses; max 100 mg/day)[11] • **Diclofenac sustained release:** 75-100 mg once daily (max 100 mg/day)[11] • **Diclofenac + misoprostol:** 50 mg (diclofenac) + 200 mg (misoprostol) bid (max dose same as starting dose)[16] • **Ibuprofen regular-release formulation:** 200-400 mg q6-8h (max 1200 mg/day)[17,18] • **Ibuprofen 12-hour formulation:** 600 mg q12h (max 1200 mg/day)[17,18] • **Meloxicam:** 7.5-15 mg daily (max 15mg/day)[19] • **Naproxen (220 mg strength):** 220 mg q 8-12h (max 440 mg/day)[12] • **Naproxen** (125, 250, 375, and 500 mg strengths): Starting dose 250 mg bid may be increased to 375-500 mg bid, Usual max = 1000 mg/day (may be increased to 1500 mg/day for limited periods with careful monitoring)[20] • **Naproxen (275 and 550 mg strengths):** 275 mg q6-8h (max 1375 mg/day) or 550 mg bid[59] • **Naproxen (750 mg sustained-release strength)**: 750 mg once daily (max 750 mg/day)[20]	Tapering not required

LEGEND: CATEGORIES FOR LEVELS OF EVIDENCE (according to original guidelines' taxonomy)

- ••• Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
- •• Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
- • Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)

Non-opioid medications: anticonvulsants[2]						
	Drug/drug class	**Pain type**	**Level of evidence**	**Role in therapy**	**Potential harms**	**Dosage***	**Tapering****
Anticonvulsants	**Carbamazepine**	Trigeminal neuralgia (may also be used for general neuropathic pain)	•••	• Should be considered for neuropathic pain	• May cause blood dyscrasias and liver toxicity[10] • Monitor blood counts and liver function tests[11] • Enzyme inducer – may interfere with other drugs such as warfarin[21]	• **Starting dose:** 100 mg – 200 mg daily • **Titration:** increase biweekly by 100-200 mg/day • **Usual maintenance dose:** 200-800 mg per day (in 2 to 4 divided doses). Doses of up to 1200-1600 mg/day have been used[2,21]	• Every 3 months, consider discontinuing or reducing the dose[21] • Requires tapering: reduce dose by approximately 20% each week (faster if patient has reduced liver function)[22]
	Gabapentin	Neuropathic pain	•••	• Should be considered (at doses titrated up to at least 1,200 mg/day) for neuropathic pain • Generally 1st line gabapentinoid	• May cause dizziness, drowsiness, or confusion[7,10] • Potential for abuse-could lead to drug misuse or make the patient a target for drug abusers[14]	• **Starting dose:** 300 mg once daily at night • **Titration:** Increase weekly by 300 mg/day • **Usual maintenance dose:** 1,200-3,600 mg/day (divided into 3 doses)[2]	• Requires tapering: reduce dose gradually over at least 1 week[23,24]
	Pregabalin	Neuropathic pain	•••	• Should be considered (at doses titrated up to at least 300 mg/day) for neuropathic pain if other 1st and 2nd line pharmacological treatments have failed	• May cause sedation or dizziness[10]	• **Starting dose:** 75 mg twice daily • **Usual maintenance dose:** 300 mg/day (150 mg bid) • **Maximum:** 600 mg/day (300 mg bid)[2]	• Reduce dose gradually over at least 1 week[25]
		Fibromyalgia	•••	• Is recommended (at doses titrated up to at least 300 mg/day) for fibromyalgia			
Anticonvulsants with insufficient evidence to support use in chronic pain:[2] • Sodium valproate, lacosamide , lamotrigine, phenytoin, clonazepam, levetiracetam, topiramate							

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• Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)

Non-opioid medications: antidepressants[2]

	Drug/drug class	Pain type	Level of evidence	Role in therapy	Potential harms	Dosage*	Tapering**
Antidepressants	Tricyclic Antidepressants (TCAs): **amitriptyline,** nortriptyline, imipramine	Neuropathic pain	●●●	• Should be considered for neuropathic pain, except HIV-related neuropathic pain (imipramine or nortriptyline may be used if amitriptyline is ineffective)	• May cause sedation, dry mouth, confusion, constipation, urinary retention, prolonged QT interval, weight gain[7,10] • Many side effects may be tolerable with patient education, gradual dose titration and allowance for 1-2 weeks at a steady dose • Caution in elderly (nortriptyline preferred)[10]	**Amitriptyline:** • **Starting dose:** 10-25 mg/day • **Titration:** increase weekly by 10 mg/day • **Usual maintenance** dose: 25-125 mg/day[2] • **Imipramine or nortriptyline:** 25-75 mg/day[2]	Requires tapering: • Taper gradually over 4 weeks to 3 months or more (e.g. reduce dose by 25% every 4 weeks)[26] particularly if patient has been on the drug for 6 weeks or more • Doses should be decreased more slowly towards the end of the taper[27-39]
		Fibromyalgia	●●●	• Should be considered for fibromyalgia			
	Duloxetine (a selective serotonin norepinephrine reuptake inhibitor; SNRI)	Neuropathic pain due to diabetes	●●●	• Should be considered for diabetic neuropathic pain if other 1st or 2nd line pharmacological therapies have failed	• May cause headache, gastrointestinal upset, insomnia, drowsiness, constipation, fatigue, dizziness[10] • Contraindicated in hepatic or severe renal impairment[30]	• **Starting dose:** 60 mg once daily (30 mg starting dose may be used for tolerability reasons in some patients, with a goal of reaching 60 mg once daily within 1-2 weeks)[30] • **Usual maintenance dose:** 60 mg once daily (doses of up to 120 mg/day have been used)[2]	• Requires tapering if patient has been taking for more than 1 week[30] • Taper by switching to 30 mg strength or taking 60 mg on alternate days for at least 2 weeks[31]
		Fibromyalgia	●●●	• Should be considered for fibromyalgia			
		Osteoarthritis	●●●	• Should be considered for osteoarthritis			
	Fluoxetine (serotonin reuptake inhibitor; SSRI)	Fibromyalgia	●●●	• Should be considered for fibromyalgia	• May cause nausea, dizziness, headache, anxiety, nervousness, drowsiness, weakness, diarrhea, upset stomach, dry mouth, loss of appetite, excessive sweating, sexual dysfunction • May cause aggression or suicidal ideation/behaviour • May prolong QT[32]	• 20 mg/day (up to 80 mg/day)[2]	• Tapering generally not required (fluoxetine has a low risk of withdrawal symptoms due to its long half-life; active drug substances persist in the body for weeks)[27,32]

Non-opioid medications: topical[2] (unless otherwise specified)

	Drug/drug class	Pain type	Level of evidence	Role in therapy[2] (unless otherwise specified)	Potential harms	Dosage*
General	Topical NSAIDs: diclofenac solution[33] or gel[34]	Musculoskeletal pain[2] and osteoarthritis[35]	●●●	• Should be considered for musculoskeletal pain[2] or osteoarthritis,[35] in patients who cannot tolerate oral NSAIDs • Manufactured and compounded NSAID products may vary in potency	• Do not apply to skin with cuts or rashes • May cause skin blistering • Increases sun sensitivity (rare)[34]	**Solution:** 50 drops per knee 3 times a day, or 40 drops per knee 4 times a day[33] **Gel:** Apply 3-4 times daily (for lower strengths) or twice daily (for higher strengths)[34] Allow 1 week to reach full effects[7]
	Topical rubifacients (salicylate-containing; e.g. triethanolamine salicylate)	Musculoskeletal pain (if other drug treatments are not effective)	●●●	• Should be considered for musculoskeletal pain if other pharmacological therapies have been ineffective	• Skin reddening and irritation at application site	1 to 3 plasters (12 hours on, 12 hours off). Try for up to 4 weeks, then discontinue if no improvement.

* Titrate until efficacy or intolerance.[9,10] Counsel that side effects often diminish after 1-2 weeks.[7] Tapering is not required for topical medications.

** Tapering recommendations are intended as general guidelines only. Monitor the patient's response to dosage changes and use clinical judgment to base the pace of the taper on the patient's response to prior dosage reductions.[28]

	Non-opioid medications: medical cannabinoids						
	Drug/drug class	**Pain type**	**Level of evidence**	**Role in therapy**	**Potential harms**	**Dosage**	**Tapering**

General	**Cannabinoids:**
	• Synthetic tetrahydrocannabinol (nabilone-oral)
	• Nabiximols (buccal cannabinoids)[2,37]
	• Dried cannabis (taken by vaporizer or as an edible product)[38]
		Neuropathic pain[38]	• Oral/buccal cannabinoids: Evidence is weaker than for other drug treatments[38]
			• Dried cannabis: No research evidence to support use in other types of chronic pain (fibromyalgia, low back pain, osteoarthritis); only for neuropathic pain that has failed to respond to standard treatments[38]
				• Oral/buccal cannabinoids: In general, other pharmacological and non-pharmacological neuropathic pain therapies should be tried first[38]
				• Nabiximols are indicated as adjunctive treatment for neuropathic pain in patients with multiple sclerosis[37]
				• Dried cannabis: Do not use for neuropathic pain unless other pharmacologic therapies, non-pharmacologic therapies, and oral cannabinoids have failed[38]
				• Long-term benefits and harms in chronic non-cancer pain not well studied[37-39]
					• May cause drowsiness, euphoria, dry mouth, hallucinations
					• Even low doses of cannabis can cause cognitive impairment lasting up to 24 hours[38]
					• May cause physical or psychological dependence[37]
					• Dried cannabis is not appropriate for people:
					  • under 25 years of age
					  • with personal or strong family history of psychosis
					  • with current or past cannabis use disorder
					  • with cardiovascular disease
					  • who are pregnant, planning to become pregnant, or breastfeeding[38]
					• Caution (for oral cannabis) in liver dysfunction[39]
						• These substances are not covered by Ontario Drug Benefit (except for nabilone).
						• **Nabilone:** 1 or 2 mg bid; max 6 mg/day[39]
						• **Nabiximols:** 4 to 8 sprays/day (divided bid); max 12 sprays/day[37]
						• **Dried cannabis:** Dose is difficult to standardize due to limited dosing studies, differences in administration and cannabinoid content of different strains of cannabis, as well as interpatient variability. One study of vaporized cannabis used 800 mg placed in the vaporizer, with 8 to 12 inhalations taken over 2 hours. Inhale slowly over 5 seconds, hold breath for 10 seconds, then gently exhale.
						• For smoked cannabis (note: vaporization is generally preferred to smoking for safety reasons), the dose may range from 100-700 mg of no more than 9% THC cannabis daily. The upper safe level is approximately 3.0 g of dried cannabis per day (this upper limit would only be used for experienced cannabis users, not naïve patients, and would be gradually reached).[38]
						• There is some evidence for dry cannabis use with the bulk of the information on vaporized and smoked. Very little evidence exists in edible products. The upper safe limit is 3.0 g (this would only be used for experienced cannabis users).
							• Data not available on tapering.[38]
							• If patients using cannabinoids are also on high doses of benzodiazepines or opioids, consider lowering the dose of these medications.[38]

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Key points to discuss prior to an opioid trial	
Issue	**Talking points**[40,41]
Explaining an opioid trial	• "Opioids may or may not help you, and they have some risks. This is why we usually do what is called a 'trial'. We will start the medication slowly and gradually increase the dose to see if we can find a dose that improves your pain and function without causing side effects that you can't live with."

Establishing realistic goals of therapy for pain and function[5]	• "What do you hope that the opioid treatment will do for you? How important is this benefit to you?"[42]
	• "Goals may include reducing pain, improving function, or improving quality of life. Keep in mind that:
	  • Opioids have a medium effect on pain (10-20% difference on pain scale)
	  • Opioids have a small effect on function (<10% change on function scale)[40]
	  • Function can improve even when pain is still present.[5]
	  • However, there is no good evidence that opioids improve pain or function with long-term use".[6]
	• "It can also be helpful to think about what coping skills you may use to manage the pain. We can discuss non-drug methods of managing pain in more detail."

Patient's concerns about therapy	• "Is there anything that worries you about starting opioid treatment? What difficulties do you think you might have?"[42] • See the relevant rows in this table for talking points to address common concerns.
Possible risks of therapy	• **Common side effects:** nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting. "The most common side effects are nausea and constipation. These can usually be managed by using anti-nausea drugs and anti-constipation drugs while on an opioid. Anti-nausea drugs are generally used short-term until the nausea side effect wears off. Anti-constipation drugs are generally used long-term while you are on the opioid." • **Accidents:** See "Driving/operating machinery" row below in this table • **Overdose:** "Avoid mixing opioids with alcohol or sleeping pills because this increase the risk of overdose. Signs of overdose include slurred or drawling speech, becoming upset or crying easily, poor balance, or "nodding off" during conversation or activity." • **Addiction:** see "Addiction" row below in this table • **Long-term risks:** Long-term use of opioids can lead to serious side effects such as sleep disorders, increased sensitivity to pain, and hormonal effects (low testosterone, loss of sex drive, decreased fertility).[40]
Possible benefits of therapy	• **Reduced pain**: "With treatment, we hope to reduce your pain by a couple of points on the pain scale, for example, from a 7 to a 5 (out of 10)." • **Improved function:** "With treatment, we hope to improve your ability to do the activities that are important to you. However, the effect of the medication on function may be small. It's important not to overuse the medication, or function may actually get worse."
Safety	"Opioids can help but they do have risks – these can be managed if we work together." • **Driving/operating machinery:** "Don't drive while your dose is being gradually increased or if the medication is making you feel sleepy or confused." • **Withdrawal:** "If you stop taking your medication abruptly, you will experience withdrawal symptoms. This may feel like the flu: nausea, diarrhea, and chills. Withdrawal can be uncomfortable but it is not dangerous. It does not mean that you are addicted, just that you stopped the drug too quickly. If you stop your medication for 3 days or more, check with me before restarting it, because restarting opioids at your usual dose can have a significant risk of overdose and even death." • **Safe storage:** "Your body will get use to the dose that we set for you, but this same dose can be very dangerous for others. Store your medication safely at home; consider storing it in a lockbox, especially if there are children in the home. Do not store it in the medicine cabinet, as others will know to look for it there. Do not share your medication with others." • **Naloxone:** Naloxone is available to all patients prescribed opioids, (particularly important for patients on doses of 50 MME/day or greater; those with a history of overdose, or concurrent benzodiazepine use): "We recommend that you keep naloxone on hand in case of an accidental overdose. Naloxone is a medication that can reverse the effects of an opioid. You can get naloxone at your local pharmacy without a prescription. The pharmacist will show you and your family how to safely use and store it."[43]
Addiction	• "Addiction is a disorder where a person cannot control their use of a drug and continues to use it compulsively even if it leads to negative consequences in their life. Not all those suffering with addiction use the drug to 'get high'. When people take opioids for pain, there is a risk that some may develop an addiction to it: those at greatest risk have a history of addiction with alcohol or other drugs. However, we will make a plan to watch out for it to help keep you safe."
Treatment agreement	• "To help us tell whether the opioid trial is working for you, we will make a treatment agreement together. A treatment agreement helps outline our goals and expectations for the trial, and how the trial will work." https://link.cep.health/cncp43
Resources	• Prescription opioids: What you need to know: https://link.cep.health/cncp14 • Opioid information for patients: https://link.cep.health/cncp18

Putting the evidence in perspective:

While many opioid therapies have 2 or 3 dots under "Evidence level", denoting a good quality of evidence, this simply means that the studies were well-designed, not that the effect was large. Most of the studies were no more than 3 months long, and the overall effect size of opioids is only moderate for pain (corresponding to a 1 or 2 point decrease on a 10-point pain scale) and low for improved function (corresponding to a 10% or smaller improvement in function). Non-opioid treatments are considered 1st-line in managing chronic non-cancer pain. Opioids should be used only if non-opioid treatments have failed or cannot be used.[4]

	Opioids					
	Drug/drug class	**Pain type[2]**	**Level of evidence[2,40]**	**Role in therapy[41]**	**Potential harms[41]**	**Dosage[41**]**
Weaker opioids	**Codeine**	• Chronic low back pain • Osteoarthritis	●●●	• Use only if patient does not respond to non-opioid therapies • Among opioids, this is a 1st-line opioid for mild to moderate pain	• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting • Abuse/addiction (risk lower than with stronger opioids)	**Immediate release:** • **Start:** 15-30mg q4h prn • **Titration:** q7d, increase by 15-30mg/d • **Max:** 600 mg/d or acetaminophen 4g/d **Controlled release:** • **Start:** 50mg q12h • **Titration:** q2d, increase by 50mg/d • **Max:** 300 mg q12h **Pearls:** • When used with acetaminophen, limit max acetaminophen dose to 3.2g/day • Maximum duration of therapy for breastfeeding women = 4 days (some women rapidly metabolize codeine to morphine; causing neonatal toxicity)

	Tramadol	• Chronic low back pain
		• Osteoarthritis
			●●●	• Use only if patient does not respond to non-opioid therapies
				• Among opioids, this is a 1st-line opioid for mild to moderate pain
					• Seizure risk (in patients at high risk of seizure or patients on medications that increase serotonin, such as selective serotonin reuptake inhibitors [SSRIs])
					• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting.
					• Abuse/addiction: (risk may be lower than with other opioids)
						• **Tramadol/acetaminophen (37.5/325 mg):**
						  • **Start:** 1 tab q4-6h (max 4 tabs/d)
						  • **Titration:** q7d, increase by 1 tab q4-6h
						  • **Max:** 8 tabs/d
						• **Tramadol immediate release:**
						  • **Starting dose (days 1-3)**: 25 mg qam
						  • **Titration (as tolerated):**
						  • Day 4-6: 25 mg bid
						  • Day 7-9: 25 mg tid
						  • Day 10-12:25 mg qid
						  • Day 13-15: 50 mg tid
						  • Day 16 and thereafter: 50 mg qid
						• **Tramadol controlled release:**
						  • **Start:** 100-150 mg q24h (depends on brand)
						  • **Titrate:** q2-7d (depends on brand)
						  • **Max:** 300-400 mg/d (depends on brand)

	Opioids					
	Drug/drug class	**Pain type[2]**	**Level of evidence[2,40]**	**Role in therapy[41]**	**Potential harms[41]**	**Dosage[41]****

Stronger opioids	**Morphine**	• Chronic low back pain
		• Osteoarthritis (only continue if there is ongoing pain relief; regular review is required)
			●●	• Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain	• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting
					• **Abuse/addiction:**
					  • Use with caution in patients with high risk of opioid abuse
					  • Avoid in renal impairment (toxic metabolite can accumulate)
						• **Immediate release:**
						  • **Start:** 5-10 mg q4-6h (max 40 mg/d)
						  • **Titrate:** q7d, increase by 5-10 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day**
						• **Controlled release:**
						  • **Start:** 10-15 mg q12-24h
						  • **Titrate:** q14d, increase by 5-10 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥ 50MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day**

	Oxycodone	• Chronic low back pain
		• Osteoarthritis (only continue if there is ongoing pain relief; regular review is required)
			●●	• Use only if patient does not respond to non-opioid therapies. Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain	• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting
					• **Abuse/addiction:**
					  • Use with caution in patients with high risk of opioid abuse
						• **Immediate release:**
						  • **Start:** 5 mg q6h (max 30 mg/d)
						  • **Titrate:** q7d, increase by 5 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Manager for corresponding oxycodone dose.
						• **Controlled release:**
						  • **Start:** 10 mg q12h
						  • **Titrate:** q14d, increase by 10 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Manager for corresponding oxycodone dose.

	Hydromorphone	• Chronic low back pain
		• Osteoarthritis (only continue if there is ongoing pain relief; regular review is required)
			●●	• Use only if patient does not respond to non-opioid therapies
				• Among opioids, this is a 2nd-line opioid for mild to moderate pain and a 1st-line opioid for severe pain
					• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting
					• **Abuse/addiction:**
					  • Use with caution in patients with high risk of opioid abuse
						• **Immediate release:**
						  • **Start:** 1-2 mg q4-6h (max 8 mg/d)
						  • **Titrate:** q7d, increase by 1-2 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥ 50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Conversion Table for corresponding hydromorphone dose.
						• **Controlled release:**
						  • **Start:** 3 mg q12h (max 9 mg/d)
						  • **Titrate:** q14d, increase by 3 mg/d
						  • **Max:** Reassess benefit/risk of doses ≥50 MME/day, avoid or justify increasing dosage at doses ≥ 90 MME/day.** See Opioid Manager for corresponding hydromorphone dose.

	Fentanyl	• Chronic low back pain
		• Osteoarthritis (only continue if there is ongoing pain relief; regular review is required)
			●●	• Use only if patient does not respond to non-opioid therapies
				• Among opioids, this is a 2nd-line opioid for severe pain
					• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting
					• **Abuse/addiction**:
					  • Use with caution in patients with high risk of opioid abuse
					  • Avoid placing sources of heat on top of patch (e.g. heating pads)
						• Only use fentanyl in patients who have taken a morphine equivalent dose (MED) of at least 60-100 mg/day for at least 2 weeks
						• Use Opioid Manager to convert from other opioids.
						• Do not switch patients directly from codeine to fentanyl (10% of Caucasian patients lack the enzyme that metabolizes codeine to morphine; these patients may not have developed a tolerance to opioids).
						  • In Ontario, fentanyl patches must be prescribed and dispensed in accordance with the Patch For Patch program
						  • The Opioid Patch Exchange Disposal Tool can help assist with patch exchange

	Methadone	• Chronic low back pain
		• Osteoarthritis
			●●	• Use only if patient does not respond to non-opioid therapies
				• Methadone is primarily used for managing addiction but may sometimes be used to manage pain. Health Canada has removed the exemption on prescribing for methadone. For more information on the new requirements visit CPSO - Methadone Program
					• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting
					• **Abuse/addiction:**
					  • Use with caution in patients with high risk of opioid abuse
					  • Avoid in renal impairment (toxic metabolite can accumulate)
						• Methadone is not intended for initial titration in an opioid trial.
						• Consult a specialist with expertise in methadone treatment.

	Opioids					
	Drug/drug class	**Pain type[2]**	**Level of evidence[2,40]**	**Role in therapy[41]**	**Potential harms[41]**	**Dosage[41]****

Stronger opioids	**Tapentadol**	• Osteoarthritis (studied mainly in knee osteoarthritis)
		• Low back pain
			●●●	• Should be considered as an option for pain relief in patients with chronic low back pain and osteoarthritis	• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting, hypotension [44,45]
					• Abuse/addiction [44,45]
						• **Immediate release**
						  • **Start**: 50 mg q 4-6 h prn
						  • **Titrate:** 50 mg q 4-6 h
						  • **Max:** Not recommended daily doses >700 mg on the first day of therapy and 600 mg on subsequent days.
						• **Controlled release**
						  • **Start**: 50 mg bid (approximately every 12 hours)
						  • **Titration:** increase by 50 mg bid every 3 days
						  • **Usual dose:** 100-250 mg bid
						• The 50 mg extended-release tablets are intended for short-term use in the initial titration phase only.
						• **Patients currently taking other opioids:** Tapentadol has a dual mechanism of action: mu-opioid agonist plus norepinephrine reuptake inhibitor. Therefore caution is advised when switching to tapentadol from pure mu-opioids.[44,45]

	Buprenorphine (transdermal)	• Chronic low back pain
		• Osteoarthritis
			●●	• Useful if problems with oral administration.	• Nausea, constipation, drowsiness, dizziness, dry skin/itching, vomiting.
					• **Abuse/addiction**
					  • Allow 3 weeks before re-using the same patch site,[46] and avoid exposing the patch to direct sunlight (increases absorption).[47]
					  • Do not use in people weighing less than 40 kg.[46]
					  • May accumulate in severe hepatic impairment.[47]
						• May be used in opioid-naïve and opioid-experienced patients (in patients taking up to 80 mg oral MME/day.)[46] May cause opioid withdrawal symptoms in patients taking long-term or higher dose opioids before being switched to buprenorphine.[47]
						• **Opioid-naïve patients:**
						  • **Starting dose:** Start with the smallest patch: 5 mcg/hr; change patch every 7 days
						  • **Titration**: Remove current patch and replace with the next highest strength every 7 days as required. Patches available as 5, 10, 15, and 20 mcg/hr.
						  • **Tip**: *If pain occurs at the end of the dosing interval it is usually a sign that the dosage needs to be increased, not that the dosage interval needs to be decreased.*
						  • **Max dose:** 20 mcg/hr patch every 7 days.
						• **Opioid-experienced patients:**
						  • Start on 5 mcg/hr or 10 mcg/hr patch, provide adequate rescue medication, and titrate by 5 to 10 mcg/hr every 7 days as required (max 20 mcg/hr).[46,47]

	Buprenorphine/ naloxone	NA	NA	• Used for substitution treatment for adults with problematic opioid dependence. The naloxone component is to deter injection and intranasal use and abuse.[48]	• **Should only be prescribed by physician who:**
					  • Has experience in substitution treatment of opioid dependence
					  • Has completed a recognized education program.
					• Must be dispensed daily under healthcare professional supervision until patient is stable enough to safely store take-home doses.
					• Co-ingestion with alcohol or other CNS depressants could lead to a fatal overdose.
					• Accidental consumption of even one dose by an opioid-naïve person could lead to fatal overdose.
					• **Side effects:**
					  • After first dose: withdrawal effects (e.g. shaking, sweating, headache, pain, muscle aches, nausea)
					  • Other side effects: constipation, anxiety, tiredness, nausea/vomiting, dizziness, orthostatic hypotension.[48]
						• Do not use in opioid-naïve patients.
						• **When to start:**
						  • **Patients dependent on heroin or short-acting opioids:** Start when objective signs of withdrawal occur (Clinical Opioid Withdrawal Scale [COWS] score of 13 or greater), but not less than 6 hours after the patient last used opioids.
						  • **Patients receiving methadone:** First, reduce methadone to minimum dose tolerable by patient, then start buprenorphine/naloxone only when objective signs of withdrawal appear (COWS score of 13 or greater) and generally not less than 24 hours after the patient last used methadone.
						• **Starting dose:**
						  • **Day 1:** 4 mg, then an additional 4 mg dose if needed. Usual dose target for Day 1 is 8-12 mg.
						  • **Titration:** Increase by 2-8 mg to a level that holds the patient in treatment and prevents withdrawal effects
						• **Usual maintenance dose:**
						  • 12 mg to 16 mg once daily, maximum 24 mg daily
						  • Once stable, may give twice the patient's daily dose every other day (e.g. give 16 mg every other day for a patient stabilized on 8 mg daily) or 3 times a week (with twice the daily dose on Monday and Wednesday and three times the daily dose on Friday); do not exceed 24 mg on any one day.[48]

*Oral meperidine has no role in the treatment of chronic non-cancer pain (CNCP) because of its poor oral bioavailability and the accumulation of a toxic metabolite.[41]

****General dosage/administration tips:**

- Titrate oral opioids until efficacy or intolerance[10]
- Use the lowest effective dose[6]
- Benzodiazepines can considerably lower the lethal opioid dose; consider tapering off of benzodiazepines or starting with a lower dose of opioid
- Parenteral opioids are not recommended in CNCP (high risk of overdose, addiction, and infection)
- Use caution with controlled-release formulations: they can cause overdose if bitten/crushed (this converts them to immediate-release)[41]
- Titrate oral opioids until efficacy or intolerance[10]

Opioids are subject to restrictions around prescribing and dispensing:

- Be aware of the risk of prescription fraud - see the College of Physicians and Surgeons of Ontario (CPSO) resource on Prescribing Drugs[49]
- Refills are not permitted on opioid prescriptions. For more information, see the regulations summary chart[50]
- Patients must present valid photo ID (e.g. driver's license, photo health card, passport) when having an opioid prescription written by their prescriber and may also need to show ID when picking up opioid prescriptions at the pharmacy. To learn more, see this resource on Ontario's Narcotics Strategy[51]
- Effective January 1, 2017, Ontario Drug Benefit (ODB) does not cover certain high-dose opioid formulations: see this Ontario Ministry of Health Bulletin for more details[52]

WATCHFUL DOSE: Recommend reassessing the benefit/risk of doses ≥50 MME/day and to "avoid or justify increasing dosage" at doses ≥ 90 MME/day.

LEGEND: CATEGORIES FOR LEVELS OF EVIDENCE (according to original guidelines' taxonomy)

••• Highest level of evidence (meta-analyses; systematic reviews of RCTs; RCTs with varying levels of bias)
•• Mid-level evidence (systematic reviews of case studies; high quality case control or cohort studies; experimental studies w/o randomization; case reports or studies)
• Low-level evidence (expert opinion and/or clinical experiences of respected authorities/guideline development group)

Monitoring tips
• Monitor every 2-4 weeks for efficacy and tolerability • Continue until optimal dose is reached (see definition)[40] • Do a 3-day "tolerance check" for those at high risk of sedation (elderly, on benzodiazepines, renal or hepatic impairment, COPD, sleep disorders, cognitive impairment)[55] • Call the patient 3 days after initiation or dose change to ask about signs of sedation[40]

Optimal dose definition[40]
• Improved function (based on goals agreed upon with patient)* OR • At least a 30% pain reduction (2 points on a 0-10 scale) without loss of function[6] • No additional analgesic benefit for 1 or 2 additional dose increases • No serious side effects or complications *Can assess pain and function with Brief Pain Inventory scale

Talking Points[42,55]

Scenario:
You are concerned that your patient may be showing signs of addiction.

Open the discussion in a non-judgmental way:
"Is there anything about your use of pain pills that you are concerned about?"

Explore ambivalence by asking about pros and cons:
Pros: "What do you like about your way of using pain pills?"
Cons: "What do you not like about your way of using pain pills? What makes you think about stopping?"

Offer help:
"I can give you some information about addiction to pain pills. Would that be OK with you?"

Process for managing patients coming into your practice on opioids

i) Review appropriateness of therapy:

Patients entering your practice on opioids may not have received a proper opioid trial and may have inadvertently ended up on long-term opioid therapy for an acute condition that has since resolved.

Review and document[40]	
Pain condition diagnosis	• Is patient on the opioid for a pain condition for which opioids have been shown to be effective? (See Evidence for opioids in chronic non-cancer pain conditions table on p. 7)
Risk screening	• Assess patient's risk for abuse (may use Opioid Risk Tool) Opioids are not recommended for patients with an active substance use disorder. Facilitate treatment of the substance use disorder if not already addressed[56]
Goal setting	• Ask patient about their goals for therapy (pain reduction, function improvement), and whether they feel the opioid is helping them achieve these goals: "Realistically, what would living well look like for you?"
Informed consent	• Review risks/benefits/goals of therapy (see Talking Points in the Opioid Trial section p. 6). • Consider using an informed consent/treatment agreement (see sample treatment agreement).
Appropriateness of opioid and dose	• Ask patient whether their pain and function have improved (can assess pain and function with Brief Pain Inventory scale)
Adverse events of current opioid treatment	• Ask patient if they are having side effects and if so, the impact on their life.

ii) If opioid therapy is inappropriate, consider switching or discontinuing the opioid.

Discuss with the patient

Switch: "Sometimes a medication is appropriate when it is started but becomes less appropriate as time goes on and things change. I usually review my patients' pain medications regularly to make sure they are still on the best treatment for them. At this point, it seems that you might benefit from switching to a different opioid. How would you feel about that?"

If switching opioid, convert as described in the **Opioid Manager, Section D: Switching.**

Discontinuation: "Sometimes a medication is appropriate when it is started but becomes less appropriate as time goes on and things change. I usually review my patients' pain medications regularly to make sure they are still on the best treatment for them. At this point, it seems that your opioid medication is no longer giving you enough benefits to warrant the risks of using it. How would you feel about trying to slowly decrease the dose?"

If discontinuing opioid, taper as described in **Opioid Tapering Template.**

For support on prescribing and managing opioids for patients with chronic non-cancer pain please see the Opioid Manager
For support on discussing and executing an opioid taper please see the Opioid Tapering Template

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npao Nurse Practitioners' Association of Ontario