Exempted Codeine Products:
Perceptions, principles, & optimizing practice

CPhM Education Session
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A few perspectives on exempted codeine products

“...kind of useless”
- Ross Tsuyuki, editor of the CPJ & professor of pharmacy and medicine (U of A)

“... safe and effective for treatment of mild to moderate pain”
- Johnson & Johnson
After attending this part of the presentation, participants will be able to:

1. Assess the appropriateness of a patient’s request to self-medicate for a recognized medical or dental reason
2. Examine the appropriate use of opioids in chronic pain
3. Evaluate a patient's addiction potential
4. Summarize prevention tactics for diversion of exempted codeine preparations in primary care
Practice Direction: Exempted Codeine Preparations

2.3 A licensed pharmacist shall only prescribe an Exempted Codeine Preparation for a patient whom they have seen and assessed in person. The pharmacist’s assessment of the patient shall include, but is not limited to the following:

2.3.1 Signs and symptoms of the condition to be treated
2.3.2 Length and severity of present symptoms
2.3.3 Laboratory or other test results (if applicable)
2.3.4 Medical history
2.3.5 Allergies and/or sensitivities
2.3.6 Current medications (must include a review of the patient’s DPIN profile)
2.3.7 Extent and results of previous treatment for the current condition
2.3.8 Pregnancy and lactation status (if applicable)

2.3.9 Abuse risk

2.4 A licensed pharmacist shall only prescribe an Exempted Codeine Preparation when it is in the patient’s best interest, having considered the risks and benefits to the patient and other relevant factors specific to the patient’s care.

2.5 A licensed pharmacist shall issue a prescription only after advising the patient with the therapeutic alternatives and providing adequate information so the patient can make an informed decision.
Practice Direction
Prescribing

Documentation: A licensed pharmacist who issues a prescription must make and retain a record of:

2.9.1 The name and address of the patient
2.9.2 The date of birth of the patient
2.9.3 The name of the drug/device prescribed
2.9.4 The strength, if applicable, and quantity of the medication
2.9.5 The directions for use
2.9.6 The number of refills
2.9.7 the name of the licensed pharmacist issuing the prescription
2.9.8 the date of the prescription
2.9.9 the treatment goal, diagnosis or clinical indication for issuing the prescription
2.9.10 the rationale for the prescribing decision
2.9.11 the follow up plan
2.9.12 other health professionals notified
“Particularly striking to the panel was the realization that evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain…”


So, how do we deal with this?
Opioids: One of many tools

But they are usually blunt and may be dangerous
What about OTC codeine products?

➤ Chronic pain:

➤ *Statement of the obvious:* if there’s poor evidence support for the use of prescription-strength opioids, we can reasonably apply this to weaker opioid regimens as well

➤ Acute pain:

*Non-prescription (OTC) oral analgesics for acute pain - an overview of Cochrane reviews (Review)*

evidence). The lowest (best) NNT values were for combinations of ibuprofen plus paracetamol, with NNT values below 2. Analgesics with values close to 2 included fast acting formulations of ibuprofen 200 mg and 400 mg, ibuprofen 200 mg plus caffeine 100 mg, and diclofenac potassium 50 mg. Combinations of ibuprofen plus paracetamol had success rates of almost 70%, with dipyone 500 mg, fast acting ibuprofen formulations 200 mg and 400 mg, ibuprofen 200 mg plus caffeine 100 mg, and diclofenac potassium 50 mg having success rates above 50%. Paracetamol and aspirin at various doses had NNT values of 3 or above, and success rates of 11% to 43%. We found no information on many of the commonly available low dose codeine combinations.
Contemporized WHO pain ladder

Approach to Drug Tx in Pain

**ANALGESIC LADDER** (Adapted from WHO & Canadian Guidelines for CNCP)

- Used for both acute & chronic pain

Persistent or increasing pain

Opioid for Mild to Mod Pain:
- Codeine, Tramadol, Buprenorphine patch

Opioid for Mod to Severe Pain:
- Morphine, Hydromorphone, Oxycodone

Persistent or increasing pain

Non-opioids:
- Acetaminophen
- ASA / NSAID

Opioid for Mod to Severe Pain:
- Morphine, Hydromorphone, Oxycodone

Fentanyl Patch**
- If chronic stable pain; unable to take oral

Methadone**
- Useful in patients with pain &/or addiction; useful, complex drug & requires special license

Avoid Meperidine! DEMEROL; Poor analgesia, short acting, toxic metabolites, ↑ abuse risk.

rxfiles.ca
Generally recommended codeine dose for acute pain: 15-60mg q4-6h

To reach those doses with OTC codeine products →→

more ACETAMINOPHEN & CAFFEINE

- T1 X 2 tabs = T2 + 300mg more acetaminophen + 15mg more caffeine per dose --- OK

- T1 X 4 tabs = T3 + 900mg more acetaminophen + 45mg more caffeine per dose --- less OK/not OK

***Not to mention additional pill burden
An early bottom line (based on theory, safety concerns, & an absence of solid evidence):

- Use of OTC codeine products for **acute pain** might be appropriate if non-opioid options are contraindicated or have not been effective or tolerated

- **e.g.???

- Use of OTC codeine products for **chronic pain** may be an appropriate approach in a **VERY SMALL SUBSET** of patients

How do we decide who those appropriate cases are?
In the absence of clear direction...

Getting back to the basics

➡➡➡ Practice evolution
Back to the basics...

1. Nothing happens in isolation
   - i.e. pain is not an isolated disease

2. Be prepared
   - i.e. what happens upfront is essential

3. Use all the resources around you
   - i.e. pharmacological & non-pharmacological approaches
1. Nothing happens in isolation: Pain is not an isolated disease
Definitions

“**Acute pain** is a symptom that plays a functional role in body defenses and resolves with tissue recovery.

**...chronic pain** has no such functional role, does not resolve with tissue recovery, and can be a **primary diagnosis**. Chronic pain involves complex CNS signaling that can be amplified by stressors...

...a **biopsychosocial condition** that requires a comprehensive, **multidisciplinary approach”**
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Acute Pain</th>
<th>Chronic Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief of Pain</td>
<td>Highly desirable</td>
<td>Highly desirable</td>
</tr>
<tr>
<td>Dependence and tolerance to medication</td>
<td>Unusual</td>
<td>Common</td>
</tr>
<tr>
<td>Psychological component</td>
<td>Usually not present</td>
<td>Often a major problem</td>
</tr>
<tr>
<td>Organic cause</td>
<td>Common</td>
<td>May not be present</td>
</tr>
<tr>
<td>Environmental/family issues</td>
<td>Small</td>
<td>Significant</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Unusual</td>
<td>Common component</td>
</tr>
<tr>
<td>Treatment goal</td>
<td>Cure</td>
<td>Functionality</td>
</tr>
<tr>
<td>Depression</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
</tbody>
</table>
Impact of Chronic Pain

- Pain
- Depression, anxiety, inability to cope
- Sleep issues

https://www.youtube.com/watch?v=4b8oB757DKc
The Pain Experience

“A biopsychosocial condition”

J Prim Health Care 2012;4(3):254-8
2. Be prepared: What happens upfront is essential
a) Assessment

- Description of pain
- Function
- Individual’s risk of side effects
  - Considering age, comorbidities, and past experiences
- Individual’s risk of abuse/diversion
Pain Assessment

PQRST mnemonic

- **P**: provokes, precipitates
  - What brings it on and what takes it away?

- **Q**: quality
  - In the patient’s own words (prompt only if necessary – e.g. dull, sharp, stabbing, burning, etc.)

- **R**: radiation, referral
  - Does the pain move to another spot?
  - Are there other symptoms associated with the pain (e.g. nausea, shortness of breath)

- **S**: severity
  - How does the patient rate the pain?

- **T**: timing
  - When did the pain start?
  - Has it occurred before?
  - Is it constant or does it come and go?
Pain Severity Scales

UNBEARABLE  SEVERE  MODERATE  MILD  SLIGHT  NO PAIN

10  9  8  7  6  5  4  3  2  1  0
If you roll your ankle, what degree of pain severity have you experienced?

If you have “bone-on-bone” knee osteoarthritis, what degree of pain severity do you experience?

If you suffer from chronic low back pain, what degree of pain severity do you experience?

If you had a pain score of 2/10, would you use a pain reliever?

If you had a pain score of 5/10, would you use a pain reliever?

If you had a pain score of 8/10, would you use a pain reliever?

Would your answer change depending on what you had to do that day?
For many patients, especially those who have become dependent on opioids, maintaining low pain scores requires continuous or escalating doses of opioids at the expense of worsening function and QoL.

"Over time, pain intensity becomes linked less with nociception and more with emotional and psychosocial factors. Suffering may be related as much to the meaning of pain as to its intensity"

"Persistent helplessness and hopelessness may be the root causes of suffering for patients with chronic pain yet be reflected in a report of high pain intensity"

**i.e. Is a reduction in pain intensity the right goal for the treatment of chronic pain (or rather, is it the improvement of the pain experience)?**

"When we use exogenous opioids chronically and continuously, we sacrifice normal healthy motivational behaviors, socialization, and coping."

*Pain 2017, Aug 21 (same authors):*
MORE IMPORTANT questions: Pain Severity → FUNCTION

- How does the patient look and mobilize?
- Are they able to perform valued activities?
- Are they dysphoric and/or irritable?
- How are they sleeping?
- Do they feel well enough to socialize?
Brief Pain Inventory

1. Throughout our lives, most of us have had pain from time to time (e.g., headaches). Have you had pain other than these everyday types of pain?
   - Yes
   - No

2. On the diagram, shade in the areas where you feel pain.

3. Please rate your pain by marking the box beside the number that best describes your pain in the last 24 hours.
   - 0: No Pain
   - 10: Completely Interferes

4. Please rate your pain by marking the box beside the number that best describes your pain at least once during the last 24 hours.

5. Please rate your pain by marking the box beside the number that best describes your pain right now.

6. Please rate your pain by marking the box beside the number that best describes your pain the last time you woke up.

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:
   A. General Activity
      - 0: Does not Interfere
      - 10: Completely Interferes
   B. Mood
      - 0: Does not Interfere
      - 10: Completely Interferes
   C. Walking Ability
      - 0: Does not Interfere
      - 10: Completely Interferes
   D. Normal Work (includes both work outside the home and housework)
      - 0: Does not Interfere
      - 10: Completely Interferes
   E. Relations with other people
      - 0: Does not Interfere
      - 10: Completely Interferes
   F. Sleep
      - 0: Does not Interfere
      - 10: Completely Interferes
   G. Enjoyment of life
      - 0: Does not Interfere
      - 10: Completely Interferes
b) Information sharing

- The natural history and expected course of the pain condition
- Establish goals & expectations...
  - of treatment & the therapeutic relationship
  - yours and theirs (are they realistic?)
- Potential benefits of treatment (best estimates)
- Potential harms of treatment (best estimates)

Are you speaking the same language?
Iron out/avoid early misconceptions
Goals of therapy

- Pain reduction (realistic = 30-50%)
- Increased mobility (ADL)
- Exercise
- Sleep
- QOL
- Improved mood
- Minimal side effects
- Minimal cost
- Minimal pill burden

FUNCTION

Brief Pain Inventory
Now, how do we get there?

Need to look closely at:

Patient factors (past & present) +

Evidence for effect
3. Use all the resources around you: Pharm and non-pharm approaches
“Overall, currently available treatments provide modest improvements in pain and minimum improvements in physical and emotional functioning. The quality of evidence is mediocre and has not improved substantially during the past decade.”

ANALGESIC COMPARISONS FOR CHRONIC NON-CANCER PAIN

Pain Improvement (Δ in Pain Score on a scale of 0-10)

- no effect
- 0.5
- 1.0
- 1.5
- 2.0
- 2.5

NNT for 50% pain improvement

- TOPICAL NSAIDs for OA
- ACETAMINOPHEN for OA
- OPIOIDS for OA
- TRAMADOL for OA
- TRAMADOL for CLBP
- NSAIDs for CLBP
- ANTI-EPILEPTICS for NeP
- SNRIs for NeP
- TCAs for NeP
- OPIOIDS for NeP
- SNRIs for NeP
WHO ladder contemporized: the multipronged approach

Approach to Drug Tx in Pain

**ANALGESIC LADDER** (Adapted from WHO & Canadian Guidelines for CNCP)

- **Used for both acute & chronic pain**

**Taper**

**Titrate**

**Opioid for Mod to Mild Pain:**
- Codeine,
- Tramadol,
- Buprenorphine patch

**Opioid for Mod to Severe Pain:**
- Morphine,
- Hydromorphone,
- Oxycodone

**Persistent or increasing pain**

**Fentanyl Patch**
- if chronic stable pain; unable to take oral

**Methadone**
- useful in patients with pain &/or addiction; useful, complex drug & requires special license

**Non-opioids:**
- Acetaminophen
- ASA / NSAID
- +/- adjuvant*

**Avoid Meperidine!**
- Poor analgesia, short acting, toxic metabolites, ↑ abuse risk.

**Education** + **Non-pharmacological** +/-
Non-pharmacological approaches

- Heat and/or cold
- Physiotherapy
- Massage
- Chiropractic
- Acupuncture
- Counseling, CBT
- Exercise
- Music
- Yoga

*Likelihood of benefit dependent on type of pain being treated
“...encompasses behavioral, physical, and integrated medical approaches. It is not titrated to pain intensity but has a primary goal of reducing pain-related distress, disability, and suffering. When it does that successfully, a reduction in pain intensity might follow — or acceptance might make the intensity of pain less important to a person’s functioning and quality of life.”

Role of the pharmacist:
• Ensure safe and effective medication use
• Move patients away from a drug-centric approach to pain management
• Collaborate with others to reinforce positive approaches
How would you respond?

Case 1
Mr. Smith, 35 years old, is taking Tylenol #1 for low back pain which occurs once every 2 months or so. His pain is presently debilitating, but when he uses T1s for 3-4 days (8-10 tabs/day), he can function reasonably well until the episode resolves. He has some constipation when he uses them, but knows it is short-lived. He picks up a bottle of 100 every 3 months or so.

Case 2
Mr. Jones, 35 years old, is taking Tylenol #1 for chronic low back pain. He uses 4/day and has consistently done this for a few years. On occasional bad days (every few weeks), he will take 6-8/day. His use allows him to get to work every day at his construction company. On your advice, he has a warm bath at the end of the day to prevent having to use T1s after work. He picks up a bottle of 100 about every 3 weeks.

Case 3
Mr. Brown, 35 years old, is taking Tylenol #1 for chronic low back pain. He has been using them for 6 months and has escalated his dose from 4/day to 8/day to 12/day and now is asking for a bottle of 100 q1w.

Case 4
Mrs. White, 35 years old, is taking Tylenol #1 for headaches. She takes 3 tabs every morning plus another 3 tabs 2-3 X/day. She reports that she has headaches everyday, but T1s take the edge off the pain. If she doesn’t use T1s, she can’t get through a day.
The 6 A’s of Opioid Therapy

1) Analgesia
2) Activity
3) Adverse effects
4) Affect
5) Accurate records
6) Aberrant behaviour/Abuse risk

How is your patient’s picture shaping up?
Analgesia & Activity: e.g. Chronic Low Back Pain

Cochrane review (2013): n=15 trials, 5540 patients, duration = 4-12 wks

- Strong opioids vs. placebo:
  - NNT (≥30% pain relief) = 6
  - NNT (≥50% pain relief) = 7
  - Disability effect size = -0.26 (small)

- Strong opioid vs. TCA (n=56):
  - No difference in pain or disability outcomes

- Tramadol vs. placebo:
  - Pain intensity effect size = -0.55 (mod)
  - Disability effect size = -0.18 (small)

- Tramadol vs. celecoxib (n=1598)
  - NNT (≥30% pain relief) = 9 (for celecoxib)

Bottom line: very rarely would a patient with CLBP gain benefit from OTC codeine doses

Authors’ conclusions

There is some evidence (very low to moderate quality) for short-term efficacy (for both pain and function) of opioids to treat CLBP compared to placebo. The very few trials that compared opioids to non-steroidal anti-inflammatory drugs (NSAIDs) or antidepressants did not show any differences regarding pain and function. The initiation of a trial of opioids for long-term management should be done with extreme caution, especially after a comprehensive assessment of potential risks. There are no placebo-RCTs supporting the effectiveness and safety of long-term opioid therapy for treatment of CLBP.

What about Mr. Smith/Jones?
Abuse & Diversion Risk

- DPIN check +/- a phone call to your peer(s)
- What else are they asking for?
- What else is on their prescription profile?
- Other signs of current or future abuse?
- Utilize an Opioid Risk assessment Tool?

- Provide Small fills
  - How often?
- Discourage prn use → Why?
  - A reactive behaviour
  - Prevents development of active coping mechanisms and use of distractors
Now, what do we do with this? ➔ dependent on patient, relationship, comfort level, etc.

**Assessing abuse risk...**

**IF** we’re thinking about using opioids:

### Opioid Risk Tool

<table>
<thead>
<tr>
<th>Item</th>
<th>Mark each box that applies</th>
<th>Item score if female</th>
<th>Item score if male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family History of Substance Abuse:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>[ ]</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>[ ]</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>[ ]</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2. Personal History of Substance Abuse:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>[ ]</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>[ ]</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Prescription Drugs</td>
<td>[ ]</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3. Age (mark box if 16-45)</td>
<td>[ ]</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4. History of Preadolescent Sexual Abuse</td>
<td>[ ]</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>5. Psychological Disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia</td>
<td>[ ]</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>[ ]</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Score Risk Category:</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Low Risk:</td>
<td>0 to 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate Risk:</td>
<td>4 to 7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Risk:</td>
<td>8 and above</td>
<td></td>
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</tbody>
</table>

[http://nationalpaincentre.mcmaster.ca/opioid/](http://nationalpaincentre.mcmaster.ca/opioid/)
Opioid Adverse Events

“Short term” (i.e. they may go away):
- Most common & bothersome: nausea (28%), sedation (24%), dizziness (18%), cognitive impairment (<10%)

“Long-term”:
- Constipation (26%)
- Dependence, tolerance, addiction
  - With daily opioid use, can develop in days or weeks.
- Dental problems(?), hypogonadism
- How often do we tell this to our patients up front?

Unintentional overdose

* 80% of patients will have ≥1 side effect

Important:
We shouldn’t sacrifice function for pain reduction

www.agencymeddirectors.wa.gov
http://nationalpaincentre.mcmaster.ca/opioid/
www.britishpainsociety.org
### 3. Clinical Features of Opioid Use Disorder (OUD)*

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altering the route of delivery</td>
<td>• Injecting, biting or crushing oral formulations</td>
</tr>
</tbody>
</table>
| Accessing opioids from other sources | • Taking the drug from friends or relatives   
|                                  | • Purchasing the drug from the 'street'                                                   |
|                                  | • Double-doctoring                                                                         |
| Unsanctioned use                 | • Multiple unauthorized dose escalations                                                  |
|                                  | • Binge use rather than scheduled use                                                     |
| Drug seeking                     | • Recurrent prescription losses                                                           |
|                                  | • Aggressive complaining about the need for higher doses                                   |
|                                  | • Harassing medical office staff for faxed scripts or 'fit-in' appointments                |
|                                  | • Nothing else 'works'                                                                     |
| Repeated withdrawal symptoms     | • Marked dysphoria, myalgia, GI symptoms, cravings                                        |
| Accompanying conditions          | • Currently addicted to alcohol, cocaine, cannabis, or other drugs                        |
|                                  | • Underlying mood or anxiety disorders are not responsive to treatment                     |
| Social features                  | • Deteriorating or poor social function                                                   |
|                                  | • Concern expressed by family members                                                     |
| Views on the opioid medication   | • Sometimes acknowledges being addicted                                                  |
|                                  | • Strong resistance to tapering or switching opioids                                      |
|                                  | • May admit to mood-leveling effect                                                       |
|                                  | • May acknowledge distressing withdrawal symptoms                                         |

Case 3
Mr. Brown, 35 years old, is taking Tylenol #1 for chronic low back pain. He has been using them for 6 months and has escalated his dose from 4/day to 8/day to 12/day and now is asking for a bottle of 100 q1w.

Case 4
Mrs. White, 35 years old, is taking Tylenol #1 for daily headaches. She takes 3 tabs every morning and 3 tabs an additional 2-3 X/day after that. She reports that she has headaches everyday, but T1s take the edge off the pain. If she doesn’t use T1s, she can’t get through a day.
Hitting the Reset Button
Opioid Tapering

1. Educate on **why** (the purpose)
2. Educate on **what** you are doing (the physiological principles)
3. Educate on **how** (the process)
4. Emphasize that the process should go in **one direction**, even if it takes awhile
Basic follow-up checklist

- Established Goals: have they been accomplished?
- Re-educate: understanding pain condition and expectations of benefit and harm are essential
- Non-drug modalities: are they being pursued?
- Recovery & disposal: inquire if codeine no longer used
- Document: what is the specific plan for the future?
It’s time to suit up

Due to our:

1. Expertise
2. Positioning at key points in the health care system...

Pharmacists have tremendous potential to:

1. Take our place as a key player in the multimodal model of pain management
2. Promote and initiate effective pain management
3. Significantly minimize exempted codeine product use
Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Part A: Executive Summary and Background
Part B: Recommendations for Practice

Morbidity and Mortality Weekly Report (MMWR)

CDC > MMWR

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

Early Release / March 15, 2016 / 65

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Questions?
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