The “Watchful Dose”

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Faculty/Presenter Disclosure

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Objectives

1. Understand scientific basis of “watchful dose”
2. Recognize that risk/benefit ratio of opioids may change at higher doses
3. Understand recent changes to CDC’s “watchful” opioid thresholds
4. Be familiar with strategies to increase safety & documentation in patients at or above the “watchful dose”
History of the “Watchful Dose”
History of the “Watchful Dose” (1)

- Late ‘90s: use of opioids for CNCP >3 mo discouraged*
- Pain advocacy groups begin lobbying to liberalize opioids*
- Washington State, 1999: “no disciplinary action will be taken against a practitioner based solely on the quantity or frequency of opioids prescribed.”**
- 2001: Pain as the “fifth vital sign” †
- Axiom: best treatment for opioid tolerance is to continue increasing opioid dose

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Increasing emphasis on opioids to treat chronic pain without clear evidence of safety or efficacy in CNCP

- Number of opioid-related deaths in US, 1999-2010: >100,000
  - Number of casualties, Vietnam War: 58,000*

- 2005: up to 4% (11.5 million adults) of US population prescribed long-term opioid therapy**

- 2010: Canadian guideline sets “watchful dose” at 200 MED†

- 2016: “…insufficient evidence to determine long-term benefits of opioids…though evidence suggests risk for serious harms that appear to be dose-dependent.”††

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† nationalpaincentre.mcmaster.ca/documents/opioid_guideline_part_b_v5_6.pdf
†† “CDC Guideline for Prescribing Opioids for Chronic Pain”, March 15, 2016
(MED= Morphine Equivalents per Day (mg/d))
Is there Evidence for Opioid Efficacy in the Long Term?
# Evidence Base for Opioids in Pain Management

## Table B-4.1 Evidence of Opioid Efficacy

<table>
<thead>
<tr>
<th>Examples of CNCP conditions for which opioids were shown to be effective in placebo-controlled trials*</th>
<th>Examples of CNCP conditions that have NOT been studied in placebo-controlled trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tramadol only</strong></td>
<td><strong>Weak or strong opioid</strong></td>
</tr>
</tbody>
</table>
| Fibromyalgia | • Diabetic neuropathy  
  • Peripheral neuropathy  
  • Postherpetic neuralgia  
  • Phantom limb pain  
  • Spinal cord injury with pain below the level of injury  
  • Lumbar radiculopathy  
  • Osteoarthritis  
  • Rheumatoid arthritis  
  • Low-back pain  
  • Neck pain |
| | • Headache  
  • Irritable bowel syndrome  
  • Pelvic pain  
  • Temporomandibular joint dysfunction  
  • Atypical facial pain  
  • Non-cardiac chest pain  
  • Lyme disease  
  • Whiplash  
  • Repetitive strain Injury |

*Please note that this table is a summary and does not cover all conditions or opioids. For a complete list, refer to the referenced document.
Long-term Opioid Use

- Meta-analysis of RCTs of opioids in CNCP:
  - 61/62 trials lasted ≤16wks
- Cochrane Review, 2010: “weak evidence” for clinically significant pain relief from opioids
- Danish Health Interview Survey (2000): 10,434 people
  - recovery from chronic pain 4x less likely in patients on opioids
  - use of strong opioids reduced function & quality of life

Is there Evidence for Opioid Safety in the Long Term?
Opioid Adverse Effects

- Most commonly-reported adverse effects:
  - constipation
  - nausea, vomiting
  - dizziness
  - drowsiness

- More serious long-term consequences:
  - hypogonadism, infertility
  - immunosuppression
  - falls & fracture risk (elderly)
  - prolonged QT (methadone & buprenorphine)
  - sleep-disordered breathing
  - opioid-induced hyperalgesia
  - nonfatal overdose
  - death
Opioids cause Respiratory Depression

- Disordered breathing during non-REM sleep increases with opioid dose†
- Tolerance to pain likely occurs before tolerance to respiratory depression††
- Hence patients develop progressive nocturnal respiratory depression while up-titrating opioids for pain relief

†† Dumas EO et al. AAPSJ. 2008 Dec; 10(4): 537.
Opioid Overdose

- Compared to risk of overdose at 20 MED:
  - Dose >50 MED, risk was 3.7-4.6x *,**
  - Dose >100 MED, risk was 9x *

- Patients aged 15-64 years, followed for up to 13 years:
  - 1 in 550 died from opioid-related overdose
  - However, 1 in 32 died if MED >200 †

** Bohnert AS et al. JAMA 2011;305:1315-1321.
What is the Future of the “Watchful Dose”? 
Future of the “Watchful Dose”

- 2007: Washington State establishes “yellow flag” dose at 120 MED*
- 2013: Ohio State Medical Board: “trigger point” at 80 MED*
- CDC: “carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 MED, and avoid increasing dosage to ≥90 MED” **

CDC Guideline

- Updated a 2014 systematic review by the Agency for Healthcare Research & Quality (4209 studies identified; 39 selected)*
- 7 additional studies were identified
- Study heterogeneity prevented meta-analysis
- Obtained input from:
  - Experts
  - Primary care professional society representatives
  - State agency representatives
  - The public
  - Peer reviewers
  - Federally-chartered advisory committee
- Recommendations are “voluntary, rather than prescriptive standards.” **

Future of the “Watchful Dose”

- April/May, 2016: British Columbia and Nova Scotia independently endorse CDC guidelines
- New Brunswick plans to incorporate CDC guidelines into a prescription monitoring system debuting next year
- Newfoundland & Labrador incorporating CDC guidelines into mandatory prescribing program for new doctors
- Ontario: ???

*theglobeandmail.com, May 8, 2016
"Physicians must:

4. Advise patients that LTOT is not indicated for certain medical conditions including headache disorders, fibromyalgia and axial low back pain.

9. Document the offer of a take-home naloxone prescription to all patients who are at risk of respiratory depression as a consequence of receiving opioid medications.

11. Order at least annual random urine drug testing and/or random pill counts for all patients on long-term opioids, sedatives or stimulants.

Physicians must not:

12. Prescribe benzodiazepines, or other sedative/hypnotic medications to patients on LTOT, other than as a documented taper.

13. Prescribe combinations of prescription drugs that are pharmacologically irrational, such as combinations of stimulants, opioids and/or sedatives.

14. Provide prescriptions allowing dispenses of opioids, sedatives and stimulants which exceed a one-month supply or 250 tablets, whichever is less."

* CPSBC Professional Standards & Guidelines, June 1 2016
(LTOT= Long-term Opioid Therapy)
Unintended Consequences of the “Watchful Dose”
Unintended Consequences

- Creates “culture of fear” among opioid prescribers
- Stigmatizes those patients who legitimately benefit from higher-dose opioids
Are Opioids Unfairly Targeted?

- Same level of watchfulness not applied to all potentially lethal medications
  - Benzodiazepines: 3.46x risk of death
  - Prednisone: 2.83x risk of death in RA patients
  - NSAIDs: risk of death 1.76x (1.39x celecoxib, 1.58x rofecoxib)
  - Gabapentin: increased suicide risk

How Would We Manage Pain if All Opioids Were Discontinued?
What if My Patient is At or Above the Watchful Dose?
Questions To Ask Yourself:

1. Do you think this dose of opioids is justified?

2. Can you justify this dose of opioids?
What Justifies a Given Opioid Dose?

❖ Some combination of function, symptom relief, and safety
  ❖ “High Dose = High Function”

❖ A stable patient:
  ❖ Behaviour (M-A-D, Urine Drug Screen results)
  ❖ Dose maintained over time

❖ Could the same result be obtained by:
  ❖ Rotating opioids to achieve a lower total MED?
  ❖ Adding a non-opioid therapy to reduce MED?
What Undermines a Given Opioid Dose?

- Frequent/Rapid Dose Increases
- Polypharmacy, esp. sedatives
- Aberrant Behaviours
- Lack of improvement in function or symptoms
- Lack of documentation
If You’re Uncertain
If You’re Uncertain

- Increase Safety
  - Tamper-resistant opioid
  - Shorten dispensing interval
  - Regular Urine Drug Screens
  - “Circle of Care”

- Increase Documentation
  - Baseline Function (Pain Disability Inventory)
  - Effectiveness Goals
  - Opioid Risk Tool
  - Treatment Contract
If You’re Uncertain

- **Increase Safety**
  - Tamper-resistant opioid
  - Shorten dispensing interval
  - Regular Urine Drug Screens
  - “Circle of Care”

- **Increase Documentation**
  - Baseline Function (Pain Disability Inventory)
  - Effectiveness Goals
  - Opioid Risk Tool
  - Treatment Contract
Rates of OxyContin Abuse Before and After OxyContin Reformulation

Reduction in Reports of Fatalities Involving ERO in Post-reformulation Periods

(ERO= Extended-Release Oxycodone)
## Tamper-Resistant Opioid Formulations

### Available in Canada

- CR oxycodone – resistant to crushing
- CR hydromorphone – tablet is nondeformable
- Oxycodone/naloxone CR tablet

### Not available in Canada

- ER oxycodone
- ER morphine sulfate/naltrexone hydrochloride
- ER oxycodone hydrochloride/naloxone hydrochloride
- ER hydrocodone bitartrate
- ER oxymorphone – reformulated
- IR oxycodone – new formulation
- CR morphine with a sequestered core of naltrexone

*CR= Controlled-Release; ER= Extended-Release; IR, Immediate-Release.*
“Circle of Care”

- Educate patients about the use or disclosure of their personal health information to:
  - Other members of the health care team
  - Pharmacists
  - Spouses/families
- Consider adding consent to speak with those within “circle of care” to treatment agreement

CMA: http://policybase.cma.ca/dbtw-wpd/PolicyPDF/PD11-03.pdf
Pharmacists can:

- Alert physicians of possible M-A-D or double-doctoring
- Reinforce patient education about:
  - Safe, appropriate use of opioids
  - Safe disposal for unused opioids
  - Patch return policies (e.g., Patch4Patch initiative)
- Suggest partial fill opioid prescriptions for patients having difficulty with control
- Observe aberrant behaviour or adverse effects
Aberrant Drug-related Behaviour Observed by Pharmacists

If You’re Uncertain

- Increase Documentation
  - Baseline Function (Pain Disability Inventory)
  - Effectiveness Goals
  - Opioid Risk Tool
  - Treatment Contract

- 2nd Opinion (even a colleague in the same office)
- Letter from Patient
- Trial Weaning or Rotating Opioids
  - Document change in function and symptoms
1. **Start with a comprehensive assessment** to ensure opioids are a reasonable choice and to identify risk/benefit balance for the patient.

2. **Set effectiveness goals** with the patient and inform patient of their role in safe use and monitoring effectiveness.

3. Initiate with a low dose; increase gradually; monitor ‘opioid effectiveness’ and recognize ‘optimal dose’. Track daily dose in morphine equivalents (MEQ) per day – flag the ‘watchful dose’ (200 mg MEQ).

4. Watch for any emerging risks/complications to **prevent unwanted outcomes** including misuse and addiction.

5. **Stop opioid therapy** if it is not effective or risks outweigh benefits.
Brief Pain Inventory

**Pain Assessment Tool**

**Brief Pain Inventory (Short Form) - Modified**

Date: __/__/__
Name: Patient Name Here

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?
- [ ] Yes  
- [ ] No

On the diagram below, shade in the areas where you feel pain. Put an "X" on the areas where it hurts the most.

XXX
XXX
XXX

What things make your pain feel worse?

- Exercise, standing, lifting, sitting for a long time

What things make your pain feel better?

- Rest, heat, a few beers

What treatments or medications do you receive for your pain?

Naproxen/esomeprazole, acetaminophen/codeine, muscle relaxant. Used to have physiotherapy.

### Opioid Risk Tool

<table>
<thead>
<tr>
<th>Select patient gender</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family history (parents and siblings):</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Illegal drug use</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Prescription drug abuse</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td><strong>Personal history:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drug use</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Prescription drug abuse</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>Mental health:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis of ADD, OCD, bipolar, schizophrenia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Diagnosis of depression</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Other:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age 16-45 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>History of pre-adolescent sexual abuse</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

**Scoring:** 0-3 → low risk  4-7 → moderate risk  ≥8 → high risk

Adapted from: Webster LR, Webster RM, Pain Med. 2005;6:432-442.1  
nationalpaincentre.mcmaster.ca/documents/practicetoolkit.pdf
Sample Opioid Treatment Agreement

I understand that I am receiving opioid medication from Dr. ________________ to treat my pain condition. I agree to the following:

1. I will not seek opioid medications from another physician. Only Dr. __________ will prescribe opioids for me.

2. I will not take opioid medications in larger amounts or more frequently than is prescribed by Dr. __________.

3. I will not give or sell my medication to anyone else, including family members, nor will I accept any opioid medication from anyone else.

4. I will not use over-the-counter opioid medications such as 222’s and Tylenol® No. 1.

5. I understand that if my prescription runs out early for any reason (for example, if I lose the medication, or take more than prescribed), Dr. ________________ will not prescribe extra medications for me; I will have to wait until the next prescription is due.

6. I will fill my prescriptions at one pharmacy of my choice; pharmacy name:

   __________________________________________

7. I will store my medication in a secured location.

I understand that if I break these conditions, Dr. ________________ may choose to cease writing opioid prescriptions for me.
General Tips for Patients on Opioids

❖ Track pain & function at every visit
❖ Document the daily MED from all sources at every visit
❖ Opioid Risk Tool & Treatment Contract upon initiation of any opioid
❖ Random urine drug screening (UDS) when on opioids
  ❖ Minimum q3 months, frequency according to risk
❖ “Circle of Care”, esp. family members & pharmacists
If You’re Uncertain

- Increase Documentation
  - Baseline Function (Pain Disability Inventory)
  - Effectiveness Goals
  - Opioid Risk Tool
  - Treatment Contract

- 2nd Opinion (even a colleague in the same office)
- Letter from Patient (indicating function gained due to opioids)
- Trial Weaning or Rotating Opioids
  - Document change in function and symptoms
Thank You