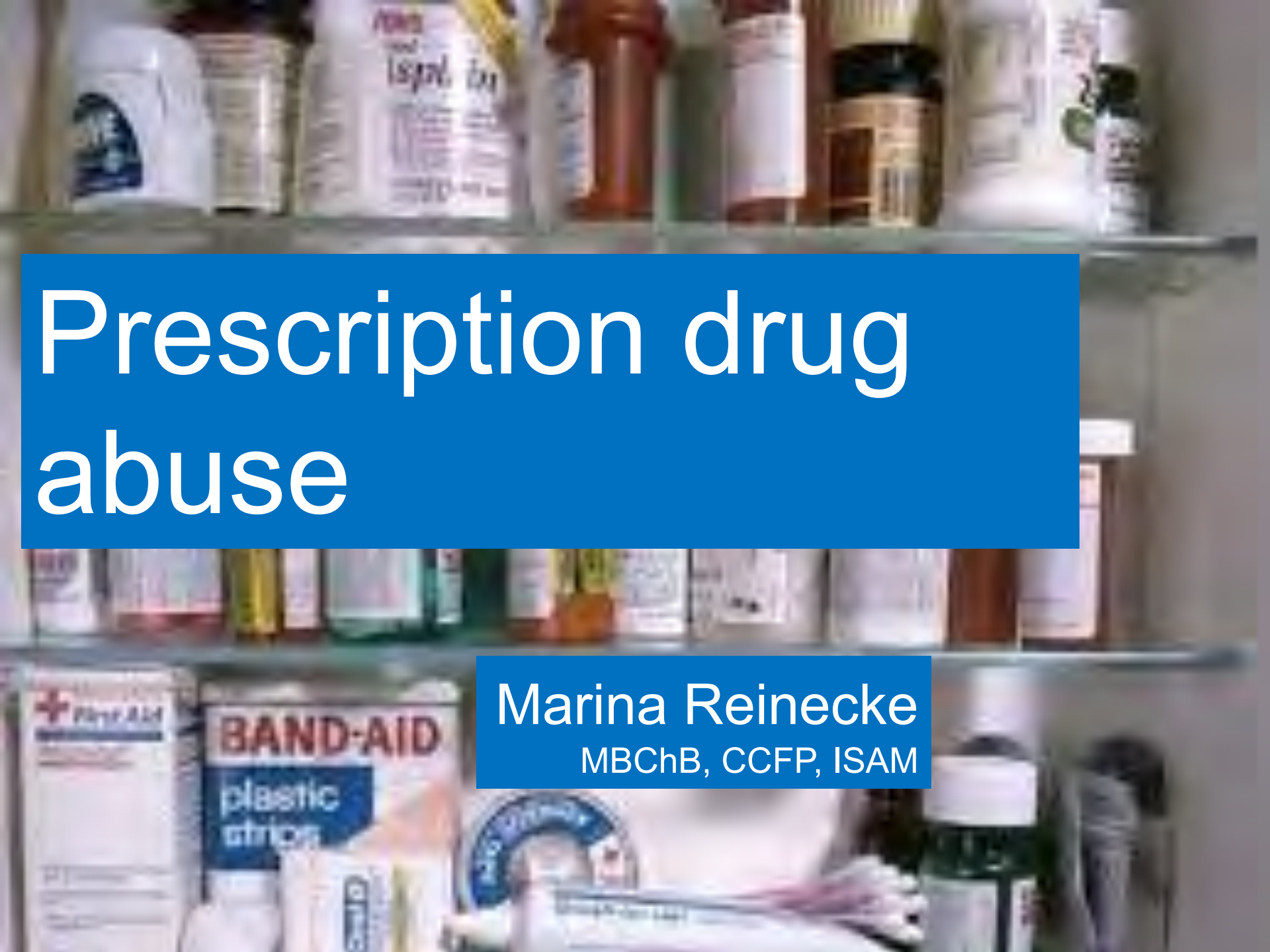


Prescription drug abuse

Marina Reinecke
MBChB, CCFP, ISAM

Conflict of interest…None

Thanks to:
Dr. Lindy Lee
Dr. Jim Simm
Dr. Joss Reimer
And Shelley Marshall, RN

Learning Objectives

- The scope of the problem and which drugs are involved
- How did we get here and what is our role moving forward:

- Safe opioid prescribing principles
  - A responsible approach to benzodiazepines
  - Recognize problems (including addiction) early
  - Review opioid use disorder
  - Treatment - what works and what doesn't

- A word from the CPSM

Rx drugs often abused

- Opioids
- Benzodiazepines
- Other..

Case discussion - Joe

- DPIN:
- Tylenol #3 120 tabs q 30 days
- Alprazolam 1mg 90 tabs q 30 days
- Temazepam 30mgs 30 tabs q 30 days
- Cyclobenzaprine 10mgs 90 tabs q 30 days
- Quetiapine 200mgs 60 tabs q 30 days
- Nystatin, esomeprazole and ferrous gluconate

Joe…

- 44 y/o male
- Hx of prescription drug abuse, treated tuberculosis, esophagitis and heavy smoking
- Known to have had an argument with his common law partner the night before..
- Found unresponsive face up on his bed.

ME's report:

- COD: Acute multidrug toxicity
- Manner of death: Undetermined
- Tox: codeine (free) 2310 ng/ml (10 - 100)
  morphine (free) 22 ng/ml
  temazepam 3180 ng/ml (600 - 900)
  ethanol 0 mg/dl
  cyclobenzaprine 510 ng/ml (3-23)
  norcyclobenzaprine 120 ng/ml

What's not present?

Opioid Addiction in Canada

Until 1990's, heroin was the major opiate – mainly in coastal cities

Around 1990 - Pain clinics were gaining acceptance for more opioid prescribing for pain

Then….

Mid 1990's – oxycontin produced, with major marketing campaign

Newfoundland had major "epidemic" of oxycontin addiction, which travelled westward

Many **aboriginal communities** were particularly affected


Swing Is Alive
Swing in the right direction with
Q12h
OxyContin
(OXYCODONE HCl CONTROLLED-RELEASE) TABLETS

Canada

2nd Highest dispenser of prescribed opioids per capita in the world (INCB, 2013)

England ½ our use

Japan 1/30 our use

Cuba 1/300 our use

Where Are These Drugs Going?

A significant amount is diverted and abused

“A Flood of Opioids, a Rising Tide of Deaths”……”
(New England Journal of Medicine Nov 18, 2010)

Opioid Overdose in Context

- Manitoba ~100 deaths/year
  - 7.9/100,000
  - Motor vehicle collisions: 8.8/100,000
- Non-fatal overdose ~3x as high
  - Methadone protective
- Prescriptions:
  - 2nd highest opiates globally
  - 200% increase since 2000
  - Benzodiazepine - 15x that of U.S.
- Dual concern - pain management:
  - 50% had to wait ≥ 6 months

Rx Opiates & Opioids

Codeine (Tylenol 1, 2, 3, 4)

Morphine

Hydromorphone (dilaudid)

Oxycodone (percocet, oxycontin)

Fentanyl patches

Methadone

Buprenorphine

Illegal opioids….

Opium products

“fentanyl powder”

heroin

Codeine

Canada sold ”over the counter” codeine (Tylenol 1) until Feb 1st, 2016

Usually women with difficult early life – try T1’s or T3’s and get more energy, and less anxiety

After 5-10 years, using 50-100 T1’s a day, increasing dysfunction at work and home

Percocet

5 mg oxycodone

Swallow, chew, or snort – use 10-20 tabs/day

Gateway to oxycontin

Oxycontin

Oxycontin: comes in 10, 20, 40, 80 mg strengths. Meant to be long-acting, however it can be chewed, snorted, or injected – then it is a high-dose, rapid acting drug…”hillbilly heroin”

Addicts use 80-600 mg/day

Cost $1 per mg…stealing, dealing, prostitution

Oxy-Neo – to decrease abuse

Hard shell is difficult to crush

If crushed and snorted…..”jellynose”

Not popular with addicts

When oxycontin was taken away…

More IV drug use - dilaudid, fentanyl, increased deaths, more medical illness

More heroin use in some communities

(oxycontin is back…..cheaper than before)

Morphine and Dilaudid

Injection use is more common with these

Fentanyl patches (meant to last 3 days)

Often cut up into “chiclets” and used orally

Or, to inject, extract the gel by mixing with vinegar or acetic acid

Many patients report near-deaths or knowing of friends who died

Street Methadone

Bought to experiment or to treat withdrawal

Can be lethal - someone tries methadone, falls asleep, found dead in the morning

Where do people get their drugs?

Local prescribers

“I rolled my truck – I didn’t break anything but talked my doctor into 600 mg oxy a day”

“I think one couple was making $14,000 month selling their opiates”

“I gave my friend $150 and he came back with an oxycontin script for me”

What do Opioids do?

1. they treat acute pain
2. they help **some** people with chronic pain
3. **they make some people feel very good…addiction**
4. **they can cause sedation/coma/death**

Risk – Different Response to Opioids

Many people– dull response to opioids – dislike the side effects

Our opioid patients – confidence, relief of anxiety, energy

Often against backdrop of family history of addiction; high incidence of childhood or early adulthood trauma

Opioid Addiction in Winnipeg

Manitoba traditionally used abstinence-based treatment – small methadone program

Dr Lee at AU (HSC) 2005 – assessed about 10 patients with opioid problems

2009 – assessed over 300 patients with prescription opioid addiction

Typical Patients

Wave 1: Suburban

Middle-class male age 17-30, support from family, educated, social skills

Using oxycontin, snorting - in trouble after 6-24 months with debt, crime, furious family, failing at school or work

Wave 2 : inner city – more use of morphine and dilaudid - more injection use – multiple family members may use together

The Teenager - Oxy Fixed Me

I was a nerdy procrastinator in a family of achievers. I was fourteen and found a percocet in the medicine cabinet – I took it and went to a party – I was funny, danced with any girl I liked, and felt high, confident and energetic.

I knew I had found the answer to my problems.

4 years later – debt, crime, despair

a professional…rx oxy

I loved my job, my family, sports. Then I had a car accident and hurt my foot –

These drugs do so much for me, I can't believe that everyone who uses them doesn't get addicted…….

If Opioids Make Them Feel Better…

Intermittent use becomes daily use

They want higher doses

They start to experience withdrawal

Now they have to use drugs just to feel normal and try to keep going – drug-sick, draggy

They hate their habit but can’t stop – all that matters is opiates and money for opiates

Tolerance

- Neurobehavioural adaptation
- Tolerance to analgesic effects develops slowly
- Rapid tolerance to psychoactive effects
- Highly tolerant patients can function on massive amounts of opioids
- Tolerance disappears within days

Question…

- Does opioid withdrawal pose a medical risk to the sufferer?

Withdrawal

- Usually mild, transient in patients on moderate doses for analgesia
- More severe in patients taking higher doses for psychoactive effects
- Addicted patients fear withdrawal and will do anything to avoid it
- No serious medical complications, except in **pregnant women, neonates** and those already **medically compromised**

Opioid Withdrawal: Time Course

On average (depending on half-life of opioid):

- Begins 6-24 hours after last use
- Peaks at 2-3 days
- Physical symptoms largely resolve by 5-10 days
- Insomnia and dysphoria may last weeks to months (prolonged psychological withdrawal)…high relapse rate with abstinence based treatment attempts

Opioid Withdrawal: Symptoms

Psychological

- Intense anxiety
- Craving for opiates
- Restlessness, insomnia

Physical

In pregnancy: uterine irritability

- Myalgias, sweats, chills
- Nausea, vomiting, cramps, diarrhea
- Signs of severe w/d (rarely seen): Dilated pupils, yawning, goosebumps

Diagnosing Opioid Use Disorder

Key messages

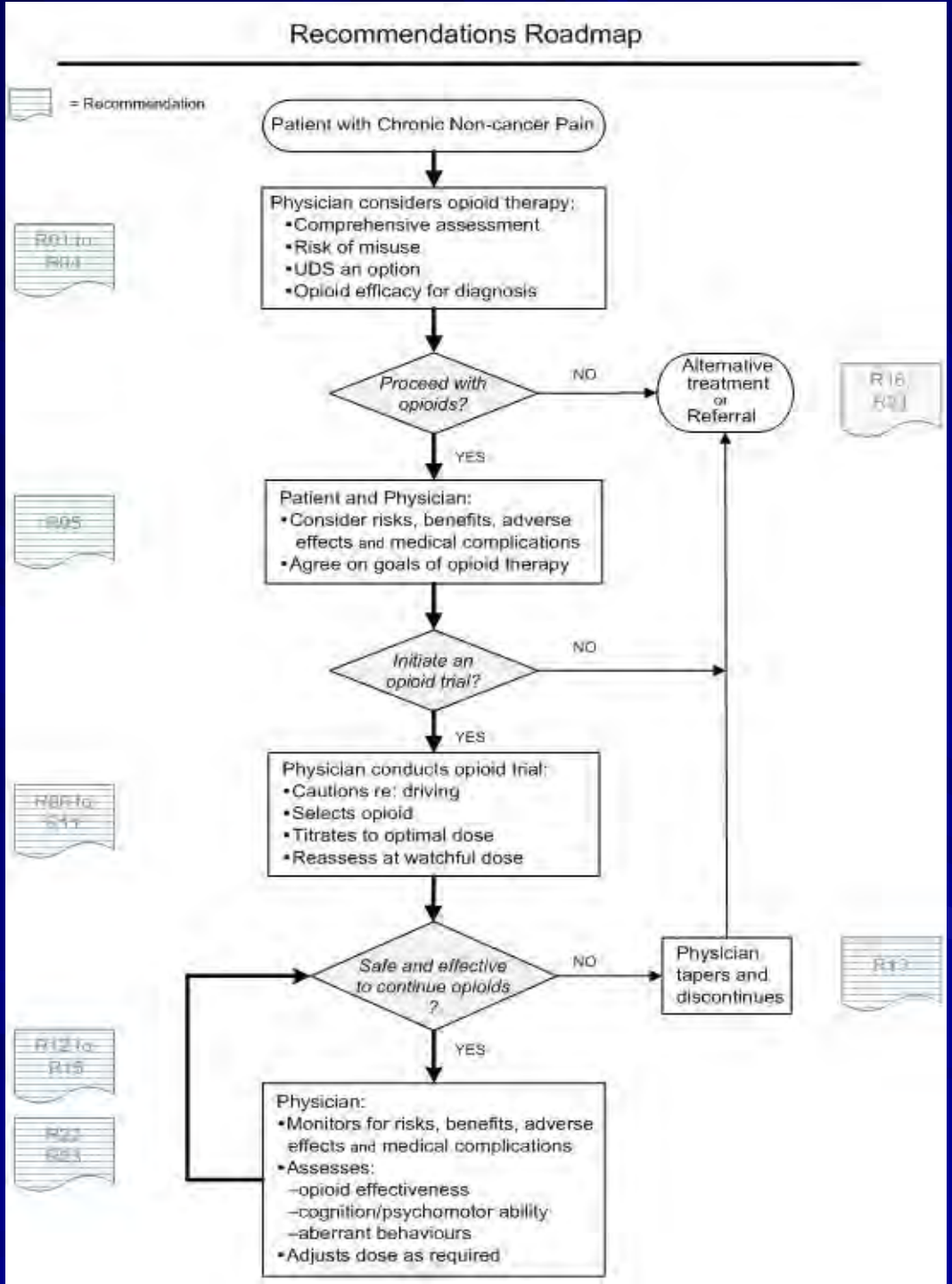
- **History** most important
- May need **collateral** information from other sources
- **UDS** is helpful when used in context of other information and when interpreted appropriately
- Certain **behaviours** maybe suggestive of problematic use, abuse or dependence

Treating Opioid Use Disorder

- Education re survival + reducing overdose risk
- Treat the abnormal brain
- Treat the broken life
- Repeat….

Survival and reducing overdose risk begins with safe prescribing….

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain 2010, http://nationalpaincentre.mcmaster.ca


Recommendations Roadmap
= Recommendation
Patient with Chronic Non-cancer Pain
Physician considers opioid therapy:
•Comprehensive assessment
•Risk of misuse
•UDS an option
•Opioid efficacy for diagnosis
R01 to R04
Proceed with opioids?
NO
Alternative treatment or Referral
R16 R21
YES
Patient and Physician:
•Consider risks, benefits, adverse effects and medical complications
•Agree on goals of opioid therapy
R05
Initiate an opioid trial?
NO
YES
Physician conducts opioid trial:
•Cautions re: driving
•Selects opioid
•Titrates to optimal dose
•Reassess at watchful dose
R06 to R11
Safe and effective to continue opioids ?
NO
Physician tapers and discontinues
R13
YES
R12 to R15
Physician:
•Monitors for risks, benefits, adverse effects and medical complications
•Assesses:
–opioid effectiveness
–cognition/psychomotor ability
–aberrant behaviours
•Adjusts dose as required
R22 R23

Definitions

- Chronic Non-Cancer Pain (CNCP)- Pain lasting greater than 6 months not due to cancer, or lasting longer than expected given the injury and degree of tissue damage.

- Addiction- Pattern of ***c***ompulsive use of a substance with loss of ***c***ontrol, ***c***raving and ***c***onsequences (medical, social, employment, legal)

Our Biases…

- It is not an emergency to prescribe opiates for chronic non-cancer pain.
- It is much easier to start opiates than to stop them.
- If no relief is seen at doses of 120 mgm morphine or equivalent, unlikely to see relief at higher doses and risk of overdose , addiction or death increase substantially.
- I have seen many young patients that abuse prescription opioids and later seen their obituaries.

Patients with chronic pain are challenging…

- Most patients who present with chronic pain:

– consulted with a number of physicians

– variety of diagnoses (sometimes vague)

– multiple failed treatments

- Fatigue, irritability, resentment, rejection, hopelessness, and despair are all common emotions that can negatively affect these patients
- One reason why this population has historically been difficult to treat has been inadequate communication between clinician and patient
- Whitten CE, et al. Perm J. Spring 2005;9(2):41-8.

Pain Management Dichotomies

- Benefit/Risk to patient

ASAM policy statement 2004: “Addiction to opioids may occur despite appropriate opioid therapy for pain in some susceptible individuals.”

- Duty to Patient vs Duty to Society

- Caregiver vs Enforcement

Pain vs Chronic pain disorder

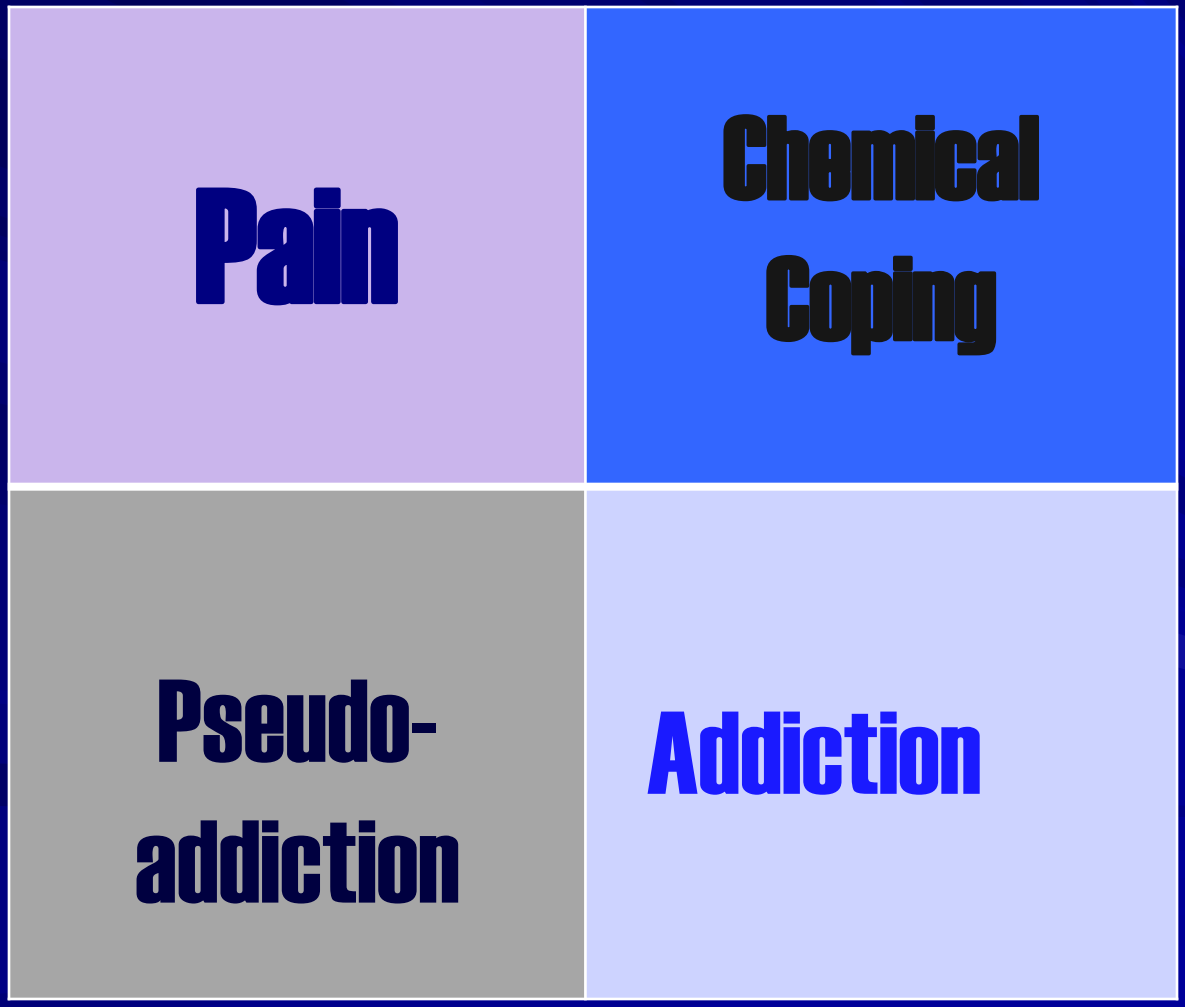
Chronic Pain

- Persistent or recurrent pain of nociceptive or neuropathic origin.
- Life still goes on despite limitations.

Chronic Pain Disorder

- Persistent or recurrent pain present most or all the time.
- Underlying pathology often has healed or may be minimal.
- Sadness, hopelessness, social isolation, failed treatments, multiple doctors, demoralization.

The diagnosis is not always clear at the first appointment…



What should you do before prescribing an opioid?

- Complete a thorough assessment to understand the pain problem.
- Templates may be useful.
- Make an informed decision about opioids as a reasonable treatment choice.

Evidence of Opioid Efficacy

Examples of CNCP conditions for which opioids were shown to be effective in placebo-controlled trials*

Weak or strong opioid

- 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

*A limitation of these trials was that the duration of opioid therapy was a maximum of three months.

Examples of CNCP conditions that have NOT been studied in placebo-controlled trials

Weak or strong opioid

- Headache
- Irritable bowel syndrome
- Pelvic pain
- Temporomandibular joint dysfunction
- Atypical facial pain
- Non-cardiac chest pain
- Lyme disease
- Whiplash
- Repetitive strain Injury

Opioid Efficacy – The Evidence

Nociceptive pain and osteoarthritis:

- Medium effect for pain and small effect for function with opioids
- Side effects like nausea & sedation are very common
- Many patients find side effects outweigh modest benefits, & drop out of treatment
- Opioids not recommended for routine use
- Document significant pathology: history, exam, imaging
- Start with: NSAIDs or acetaminophen, exercise, physical modalities
- 1 st line opioids: codeine, tramadol, tapentadol, buprenorphine patch

Neuropathic pain:

- Start with: TCA, SNRI, anticonvulsants. □
- 1st line opioids: codeine, tramadol, tapentadol, buprenorphine patch.
- Medium effect for pain and a small effect for function

Opioid Efficacy – The Evidence

Widespread soft tissue pain (fibromyalgia):

- **Caution with opioids**
- High prevalence of mood, anxiety disorders
- 1st line: Exercise, TCAs
- Only tramadol has been studied
- Potent opioids not recommended

Visceral Pain:

- Opioids not indicated for common abdominal pain complaints (e.g. IBS)
- Useful for severe organic pain (e.g. chronic pancreatitis, Crohn's)

What should you do before prescribing an opioid?

- Consider screening tools to help identify patients at risk of opioid misuse or addiction.

OPIOID RISK TOOL

		Mark each box that applies	Item Score If Female	Item Score If Male
1. Family History of Substance Abuse	Alcohol	[ ]	1	3
	Illegal Drugs	[ ]	2	3
	Prescription Drugs	[ ]	4	4
2. Personal History of Substance Abuse	Alcohol	[ ]	3	3
	Illegal Drugs	[ ]	4	4
	Prescription Drugs	[ ]	5	5
3. Age (Mark box if 16 – 45)		[ ]	1	1
4. History of Preadolescent Sexual Abuse		[ ]	3	0
5. Psychological Disease	Attention Deficit Disorder, Obsessive Compulsive Disorder, Bipolar, Schizophrenia	[ ]	2	2
	Depression	[ ]	1	1
		TOTAL	_____	_____

Total Score Risk Category
Low Risk 0 – 3
Moderate Risk 4 – 7
High Risk ≥ 8

What should you do before prescribing an opioid?

- Manage expectations by setting function-improvement and pain-reduction goals with the patient — these become the outcomes for measuring opioid effectiveness.

What should you do before prescribing an opioid?

- Ensure informed consent by reviewing with the patient: potential benefits, risks, side effects, and complications of opioid therapy.
- ‘This is a trial’
- Use a treatment agreement
- Set clear limits from the beginning
- Safety talk


PAUSE

OPIOID MANAGER

The Opioid Manager is designed to be used as a point of care tool for providers prescribing opioids for chronic non cancer pain. It condenses key elements from the Canadian Opioid Guideline and can be used as a chart insert.

Before You Write the First Script

Patient Name: _____

Pain Diagnosis: _____

Date of Onset: _____

Goals decided with patient:

_____

_____

_____

_____

_____

_____

_____

Initiation Checklist

	Y	N	Date
Are opioids indicated for this pain condition			
Explained potential benefits			
Explained adverse effects			
Explained risks			
Patient given information sheet			
Signed treatment agreement (as needed)			
Urine drug screening (as needed)			

Opioid Risk Tool

By Lynn R. Webster MD

	Items score if female	Items score if male
Items (circle all that apply)		
1. Family History of Substance Abuse:		
Alcohol	1	3
Illegal Drugs	2	3
Prescription Drugs	4	4
2. Personal History of Substance Abuse:		
Alcohol	3	3
Illegal Drugs	4	4
Prescription Drugs	5	5
3. Age (needs box if 16-45)	1	1
4. History of Preadolescent Sexual Abuse	3	0
5. Psychological Disease: Attention Deficit Disorder, Obsessive-Compulsive Disorder, or Bipolar, Schizophrenia	2	2
Depression	1	1
Total		

Total Score Risk Category:
Low Risk: 0 to 3, Moderate Risk: 4 to 7, High Risk: 8 and above

Overdose Risk

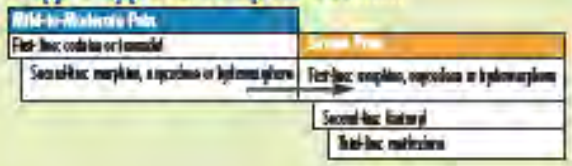
Patient Factors
- Elderly
- On benzodiazepines
- Mental impairment
- Hepatic impairment
- COPD
- Sleep apnea
- Sleep disorders
- Cognitive impairment

Provider Factors
- Incomplete assessment
- Rapid titration
- Combining opioids and sedating drugs
- Failure to monitor closely
- Insufficient information given to patient and/or relatives

Opioid Factors
- Codeine & Tramadol - lower risk
- CR formulations - higher dose than IR

Prevention
- Assess for Risk Factors
- Educate patients /families about risks & prevention
- Start low, titrate gradually, monitor frequently
- Consult with benzodiazepines
- Higher risk of overdose - reduce initial dose by 50%; titrate gradually
- Avoid parenteral routes
- Adolescents: elderly - may need consultation
- Watch for Abuse

Stepped Approach to Opioid Selection



Initiation Trial

A closely monitored trial of opioid therapy is recommended before deciding whether a patient is prescribed opioids for long term use.

Suggested Initial Dose and Titration (Modified from Weaver M, 2007 and the e-CPS, 2008) Notes: The table is based on oral dosing for CINCP. Brand names are shown if there are some distinct features about specific formulations. Reference to brand names as examples does not imply endorsement of any of these products. CR = controlled release, IR = immediate release, NA = not applicable, ASA: Acetylsalicylic Acid

Opioid	Initial dose	Minimum time interval for increases	Suggested dose increases	Minimum daily dose before converting IR to CR
Codeine (alone or in combination with acetaminophen or ASA)	15-30 mg q.4 h. as required	7 days	15-30 mg/day up to maximum of 600 mg/day (acetaminophen dose should not exceed 3.2 grams/day)	300 mg
CR Codeine	50 mg q.12 h.	2 days	50 mg/day up to maximum of 300 mg q.12 h.	NA
Tramadol (37.5 mg) + acetaminophen (325 mg)	1 tablet q.4-6 h. as needed up to 4/day	7 days	1-2 tab q. 4-6 h. as needed up to maximum 8 tablets/day	3 tablets
CR Tramadol	a) Zytrex XL®: 150 mg q. 24 h. b) Tridural®: 100 mg q. 24 h. c) Tridural®: 100 mg q. 24 h.	a) 7 days b) 2 days c) 5 days	Maximum doses: a) 400 mg/day b) 300 mg/day c) 300 mg/day	NA
IR Morphine	5-10 mg q. 4 h. as needed maximum 40 mg/day	7 days	5-10 mg/day	30-60 mg
CR Morphine	10-30 mg q.12 h. Kadian®: q.24 h. Kadian®: should not be started in opioid-naive patients	Minimum 2 days, recommended 7-14 days	5-10 mg/day	NA
IR Oxycodone	5-10 mg q. 4 h. as needed maximum 30 mg/day	7 days	5 mg/day	20 mg
CR Oxycodone	10-20 mg q.12 h. maximum 80 mg/day	Minimum 2 days, recommended 7-14 days	10 mg/day	NA
IR Hydromorphone	1-2 mg q. 4-6 h. as needed maximum 8 mg/day	7 days	1-2 mg/day	6 mg
CR Hydromorphone	8 mg q. 12 h. maximum 9 mg/day	Minimum 2 days, recommended 7-14 days	2-4 mg/day	NA

Initiation Trial Chart

Date					
Opioid prescribed					
Daily dose					
Daily morphine equivalent					
	More than 200				
	Less than 200				
Goals achieved → Yes, No, Partially					
Pain intensity					
Functional status → Improved, No Change, Worsened					
Adverse effects	Nausea				
	Constipation				
0 = None 1 = Limits ADLs 2 = Prevents ADLs	Drowsiness				
	Dizziness/Vertigo				
	Dry skin/Pruritis				
	Vomiting				
	Other?				
Complications? (Reviewed: Y/N)					
Aberrant Behaviour (Reviewed: Y/N)					
Urine Drug Screening (Y/N)					
Other Medications					

To access the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-cancer Pain and to download the Opioid Manager visit http://nationalpaincentre.mcmaster.ca/opioid/

Feb 2011

How do I titrate the opioid dose?

- Start with a low dose, increase gradually and monitor “opioid effectiveness,” i.e., an improvement in function or a reduction in pain intensity of at least 30%.

How do I titrate the opioid dose?

- Track the daily dose in morphine equivalents and flag the “watchful dose.” i.e., over 200 mg morphine or equivalent per day
- Most patients can be effectively managed below this.
- If you determine the dose required is beyond the watchful dose: reassess the pain problem to ensure opioids are the right therapy, reassess risk of misuse, and increase monitoring vigilance.

Morphine Equivalence Table

Opioid	Equivalent Doses (mg)	Conversion to MEQ
Morphine	30	1
Codeine	200	0.15
Oxycodone	20	1.5
Hydromorphone	6	5
Meperidine	300	0.1
Methadone & Tramadol	Dose Equivalents unreliable	
Transdermal fentanyl	60 – 134 mg morphine = 25 mcg/h 135 – 179 mg = 37 mcg/h 180 – 224 mg = 50 mcg/h 225 – 269 mg = 62 mcg/h 270 – 314 mg = 75 mcg/h 315 – 359 mg = 87 mcg/h 360 – 404 mg = 100 mcg/h	

Switching Opioids:	
If previous opioid dose was:	**Then, SUGGESTED new opioid dose is:**
High	50% or less of previous opioid (converted to morphine equivalent)
Moderate or low	60-75% of the previous opioid (converted to morphine equivalent)

How do I titrate the opioid dose?

- Recognize the “optimal dose” is reached with a BALANCE of three factors:
- 1) effectiveness: improved function or at least 30% reduction in pain intensity
- 2) plateauing: effectiveness plateaus—increasing the dose yields negligible benefit, and
- 3) adverse effects/complications: adverse effects or complications are manageable.

What should I do to ensure patient safety?

- Use the function-improvement and pain-reduction goals set with the patient to monitor opioid effectiveness — structured assessment tools could also help.
- Page 2 opioid manager

Brief Pain Inventory

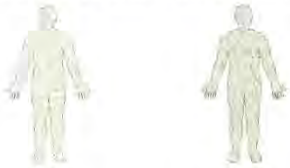
Date: _____ Time: _____

Name: _____

1) 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?

1. Yes 2. No

2) On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



front back

3) Please rate your pain by circling the one number that best describes your pain at its **worst** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10

No pain — *Pain as bad as you can imagine*

4) Please rate your pain by circling the one number that best describes your pain at its **least** in the last 24 hours.

0 1 2 3 4 5 6 7 8 9 10

No pain — *Pain as bad as you can imagine*

5) Please rate your pain by circling the one number that best describes your pain on **average.**

0 1 2 3 4 5 6 7 8 9 10

No pain — *Pain as bad as you can imagine*

6) Please rate your pain by circling the one number that tells how much pain you have **right now.**

0 1 2 3 4 5 6 7 8 9 10

No pain — *Pain as bad as you can imagine*

7) What treatments or medications are you receiving for your pain?

_____

_____

_____

_____

8) In the past 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% 10 20 30 40 50 60 70 80 90 100%

No relief — *Complete relief*

9) Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

B. Mood

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

D. Normal work (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

F. Sleep

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

G. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

H. Ability to concentrate

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

I. Appetite

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — *Completely interferes*

What should I do to ensure patient safety?

- Watch for aberrant drug-related behaviours that could signal opioid misuse

Indicator	Examples
Altering the route of delivery	❑ Injecting, biting or crushing oral formulations ❑ Biting, chewing, swallowing or injecting topical preparations (e.g., sustained-release analgesic patches)
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 rather than scheduled use
Drug seeking	❑ Recurrent prescription losses ❑ Aggressive complaining about the need for higher doses ❑ Harassing staff for faxed scripts or fit-in appointments ❑ Nothing else "works"
Repeated withdrawal symptoms	❑ Marked dysphoria, myalgias, GI symptoms, craving
Accompanying conditions	❑ Currently addicted to alcohol, cocaine, cannabis or other drugs ❑ Underlying mood or anxiety disorders 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

What should I do to ensure patient safety?

- Assess factors that could impair cognition and psychomotor ability, possibly making driving unsafe.

What should I do to ensure patient safety?

- Use available consultation as needed, e.g., pain condition unresponsive;
- Opioid misuse or addiction suspected;
- Special populations pregnant, psychiatric co-morbid conditions, elderly, or adolescent.

Withdrawal-mediated Pain

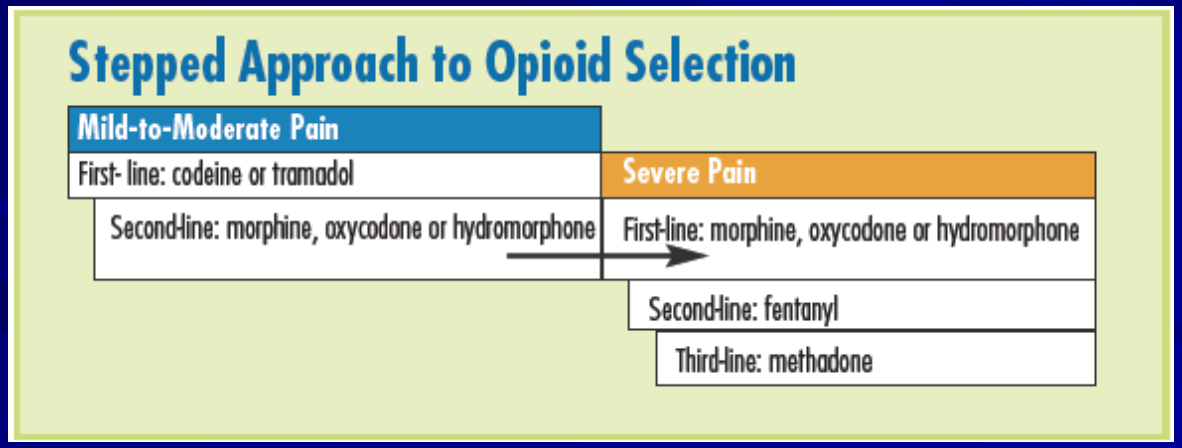
- Pain magnified as opioid wears off
- Pain “all over” or worsening of pain in location of prior pain condition
- Symptoms quickly relieved with opioids
- Resolves as withdrawal improves
- Often misidentified by patient as underlying pain condition

What should I do to ensure patient safety?

- Collaborate with pharmacists to improve patient education and safety.
- Fax cover sheet; DPIN checks
- Control dispensing
- Encourage feedback

When do I stop the patient's opioids?

- Stop or ***switch opioids*** when side effects or risks are unacceptable or opioid effectiveness is insufficient.
- Opioid manager: Switching Opioids



Morphine Equivalence Table

Opioid	Equivalent Doses (mg)	Conversion to MEQ
Morphine	30	1
Codeine	200	0.15
Oxycodone	20	1.5
Hydromorphone	6	5
Meperidine	300	0.1
Methadone & Tramadol	Dose Equivalents unreliable	
Transdermal fentanyl	60 – 134 mg morphine = 25 mcg/h 135 – 179 mg = 37 mcg/h 180 – 224 mg = 50 mcg/h 225 – 269 mg = 62 mcg/h 270 – 314 mg = 75 mcg/h 315 – 359 mg = 87 mcg/h 360 – 404 mg = 100 mcg/h	

Switching Opioids:	
If previous opioid dose was:	Then, SUGGESTED new opioid dose is:
High	50% or less of previous opioid (converted to morphine equivalent)
Moderate or low	60-75% of the previous opioid (converted to morphine equivalent)

When do I stop the patient's opioids?

- Page 2 Opioid Manager
- Discontinue opioids with a tapering protocol — avoid sedative-hypnotic drugs, especially benzodiazepines, during the taper.

Survival and reducing overdose risk begins with safe prescribing….

OVERDOSE RISK:

Patient Factors:

- Elderly
- **On benzodiazepines**
- Renal impairment
- Hepatic impairment
- COPD
- Sleep apnea
- Sleep disorders
- **Cognitive impairment**

OVERDOSE RISK

Provider Factors:

- Incomplete assessments
- Rapid titration
- Combining opioids and sedating drugs
- Failure to monitor dosing
- Insufficient information given to patient and/or relatives

All within our control….

OVERDOSE RISK

Opioid Factors:

- Codeine & Tramadol - lower risk
- CR formulations - higher doses than IR

Prevention:

- Assess for Risk Factors
- Educate patients /families about risks & prevention
- Start low, titrate gradually, monitor frequently
- Careful with benzodiazepines
- Higher risk of overdose - reduce initial dose by 50%; titrate gradually
- Avoid parenteral routes
- Adolescents; elderly - may need consultation
- Watch for Misuse

Treating Opioid Use Disorder

- Education re survival + reducing overdose risk
- Treat the abnormal brain
- Treat the broken life
- Repeat….

Fixing the Problem….

1. Crime approach – lock them up
2. Social philosophy – just say no!
3. Abstinence-based addiction care
4. Medication-assisted recovery (methadone, Suboxone)

Taper VS maintenance opioids from a Doctor

- Tapers don't work if the patient is addicted and can return to street access of drugs
- It keeps it a secret – it has no recovery work attached;
- It may be risky and may in fact prolong active addiction since no motivation to change, especially if maintenance doses are prescribed
- They often try to get extra to divert/sell – they start street use again – they manipulate the doctor; It often escalates conflict with family.
- Tight contract and daily dispensing; document why prescribing outside of guidelines!!

Abstinence

It’s the obvious solution!

Is it? Success rates are problematic and death rates are higher

Abstinence and Success Rates

Doctors, Pilots – 90% abstinent

Long term, street-hardened – 3%

The “new wave” of 1-2 years prescription opioid abuse – minimal success in Manitoba with abstinence

Treatment Options

Abstinence-based Treatment

"mild" Opioid Use Disorder

- Non-medical withdrawal management
- Medical withdrawal management
  - clonidine, simple analgesics, fluids etc…

PLUS

Relapse Prevention

- Long term therapeutic community
- Mutual support groups
- Counseling
- Residential or outpatient treatment programs
- **Comprehensive management approach is needed**

OR

Opioid Agonist Treatment

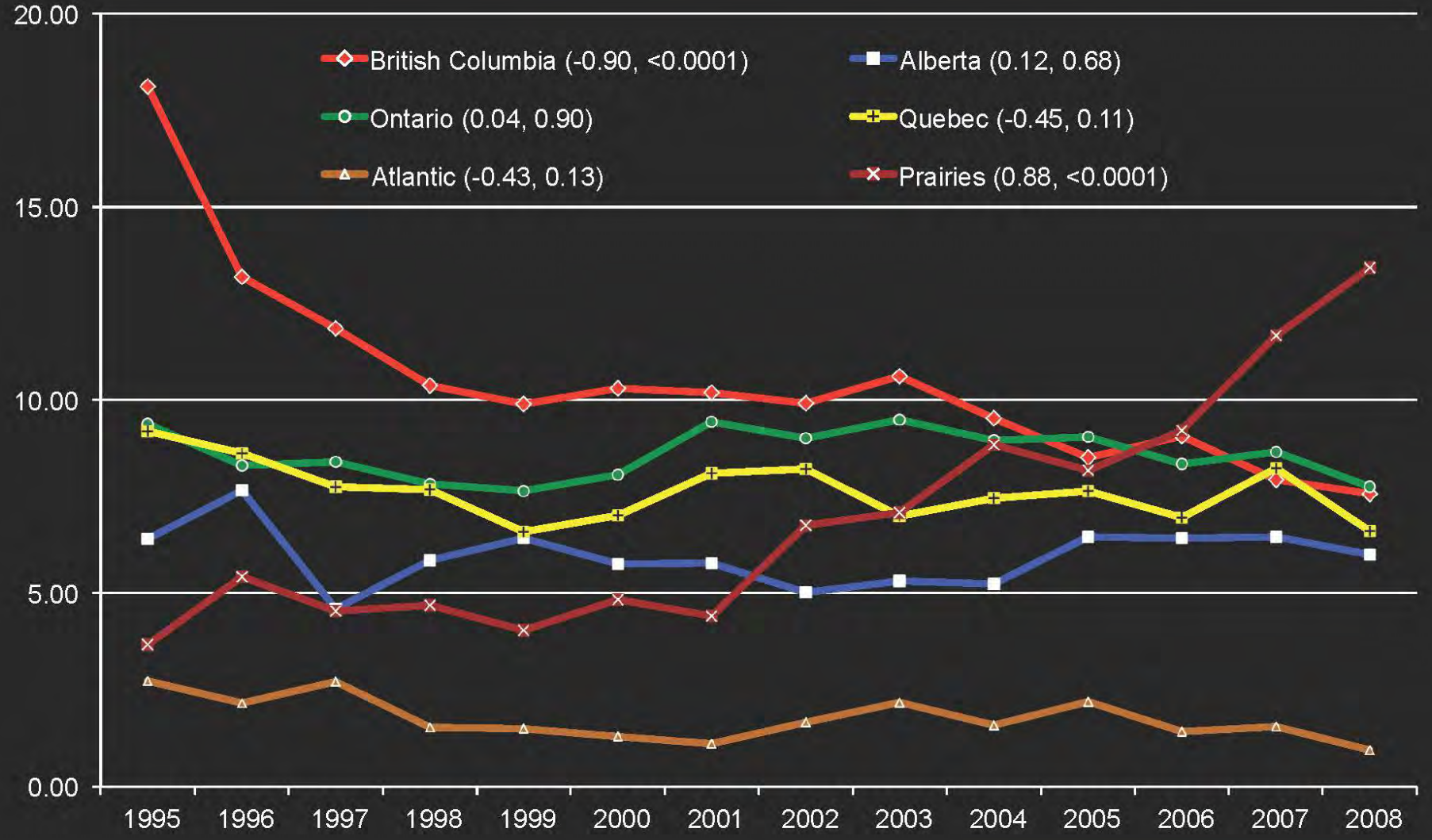
- Buprenorphine
- Methadone

"moderate or severe"

Opioid Agonist Treatment

- Diagnosis of opioid use disorder
- Failed other forms of treatment (abstinence-based) ????
- Now reasonable first line option!!!
- Injecting use/more consequences – more urgent need for harm reduction

HIV+ tests by region by year (rate)



Modified from PHAC, Feb 2011

Hazeldon Program

Major abstinence-based program in Minnesota

Looked at their relapse and death statistics in their opioid-addicted patients

Now offering Suboxone

Methadone Maintenance Therapy

- Slow onset, long duration of action
- Relieves withdrawal, cravings without sedation or euphoria
- Can be monitored with UDS
  - Distinct from other opioids
- Hard to double doctor
- Relationships with clinic staff – honesty, hope, humor - longterm program, time to grow up

MMT: Components

- Daily dispensing supervised
- Gradual introduction of take-home doses (contingency management)
- Regular UDS's
- Ideally, prescribed in the context of comprehensive addiction care, including:

Counselling	Housing
Family therapy	Food support
Parenting planning	Medical care

Methadone - Goals

1. Survival and stability
2. Stop opioids, stop injecting
3. Stop other drugs
4. Grow emotionally, develop success with work, family, school, life
5. Consider weaning off, if appropriate

Limitations of Methadone Treatment

- High risk of overdose early in treatment
- Very long half life, bioaccumulation
  - Optimal candidate is using higher doses opioids, is highly tolerant
  - Reaching stable dose takes time++
- Not all communities have methadone providers
- Major commitment of time for patient and provider
- Analgesic duration only 8 hours

Methadone - Outcomes

Almost all stop opioids. Most stop other drugs (except marijuana). Most return to productive lives (and start paying taxes!).

They keep their treatment a secret
Stigma and social judgment are big problems.

Some wean off after 2-5 **years.**

$$$

Cost of methadone treatment for 1 year - $5,000

Cost of untreated heroin addict in BC - $44,000

(crime, health, children in care)

Cost of 1 week hospital detox over $5,000

Cost of 1 month residential treatment (often not effective for opioid addiction) $5,000-$30,0000

Cost of HIV & Hep C treatment…huge…..prevention is essential

What do you think doc?

Consider abstinence when:

- Pt young
- Oral use, no IV use
- Use < 18 mnths
- Stable, supportive family/work
- Patient's choice
- Circumstances (finances, rural location)

What do you think doc?

Consider maintenance therapy when:

- Relapses after previous treatment
- IV use
- Polysubstance abuse
- Social stressors/instability
- Chronic pain + addiction
- Patient's choice/circumstances
- Physical health problems from addiction
- Pregnancy

Unless..

- Pregnancy is the exception!
- Opioid dependence during pregnancy has been associated with numerous adverse fetal outcomes secondary to the drug itself, as well as, secondary to poor nutrition and inadequate prenatal care
  - Poor neonatal outcomes such as:
  - Intrauterine growth restriction
  - Lower birth weight
  - Preterm prelabour rupture of membranes

Pregnancy

- If mom is in withdrawal, the fetus is as well!!
- Present standard of care for opioid use disorder in pregnancy is methadone maintenance treatment (MMT)
- Methadone-maintained pregnancies have reduced obstetrical complications and improved outcomes
- What if mom does not want methadone or does not have access?

Buprenorphine: Pharmacology

Key principle

Unique pharmacological properties…

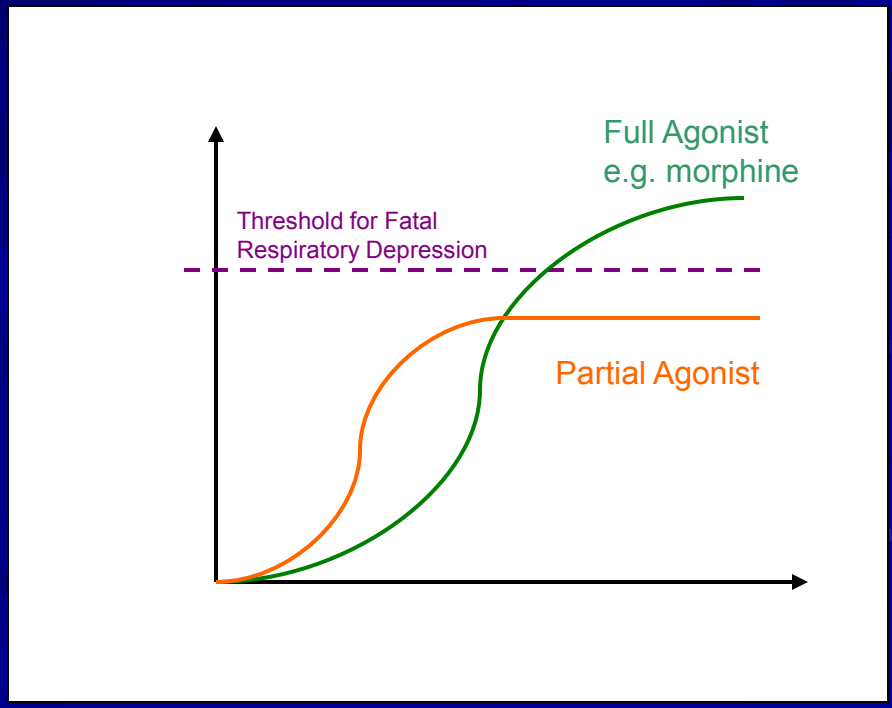
1. Much *safer* with respect to risk of overdose and respiratory depression
2. *Long duration of action* thus possibility of less-than-daily dispensing
3. *High affinity for* (i.e. binds tightly to) *opioid receptor*, thus blocking the effect of illicit and other opioids

Pharmacology: Safer

- Mu receptor partial agonist ("turns on")
  - Ceiling effect for respiratory depression and it's other opioid agonist properties
- Kappa receptor antagonist (blocks or "turns off")
  - Could be what offsets the respiratory depression effect at higher doses

Mu receptor – analgesia, euphoria, resp. depression, pupilary constriction, dec. bowel mobility, sedation

Kappa receptor – analgesia, dysphoria, diuresis



Johnson et al., Buprenorphine: how to user it right. Drug and Alcohol Dependence 70 (2003) S59-S77

Pharmacology: Safer

- Overdose with buprenorphine *alone* is very rare
  - Increased lethality if combined with benzodiazepines and other sedatives or if used intravenously
  - In a French study (2001), only two cases (of 78 fatalities) of overdose deaths due to buprenorphine alone (asphyxiation due to aspirating vomitus)

Kintz, P., 2001. Deaths involving buprenorphine: a compendium of French cases. *Forensic Sci. Int.* 121, 65-69.

Pharmacology: Naloxone in Suboxone®

Suboxone® = Buprenorphine + Naloxone

- Suboxone only formulation of buprenorphine available in Canada
- **Naloxone:** opioid receptor antagonist, i.e. binds opioid receptor, but doesn't activate it
  - Will cause withdrawal if patient physically dependent on opioids
- Naloxone only effective if Suboxone® used IV
  - 0-10% sublingual & little to no oral bioavailability

Chiang, NC, 2003. Pharmacokinetics of the combination tablet of buprenorphine and naloxone. Drug and Alcohol Dependence, 70: p. S39-S47

A system responding…

- Fight stigma
- Make treatment available (Train methadone and Suboxone providers…? Separate exemptions)
- Change physician prescribing – Education + Monitoring duplicate Rx'ing + Support (Mentoring)
  - MMDRC
  - CPSM review panel
  - MPEAP
  - ME death reviews and prescriber feedback
- Change attitudes of public towards these drugs

Reducing overdose risk..
Naloxone Distribution Programs

What do they look like?

- Common in dense urban heroin markets
- Target people who inject drugs
- Lay responder training: 15-20 min
  - Reduce overdose risk
  - Recognize overdose
  - Respond to overdose
  - Storage of drug and refills
- Various models of prescribing and dispensing

Naloxone Distribution Programs

How well do they work?

- Knowledge uptake and perceived comfort 6 months post training is good
  - comparable to health professionals
- Continued reluctance to call 911
- No increase in overdose risk taking behaviour
- Impact on fatal overdose rates is modest
  - Coffin and Sullivan (2013) prospective estimate: 1 life saved q 227 kits, 6% OD death reduction
  - Bennett & Holloway (2012) retrospective review: 27 OD reversals for 521 kits, 1 q19 kits

Our Plan for a Pilot Naloxone Program

- Funding for take-home-naloxone kits from Street Connections
  - HR (nursing) reallocated
- Pilot: people who inject opiates
- Training also offered to partners, friends, family, etc.
- 60-80 clients/year
  - based on Edmonton uptake
- Nurse run program –
  - by drop in at 496 Hargrave

Kit Components

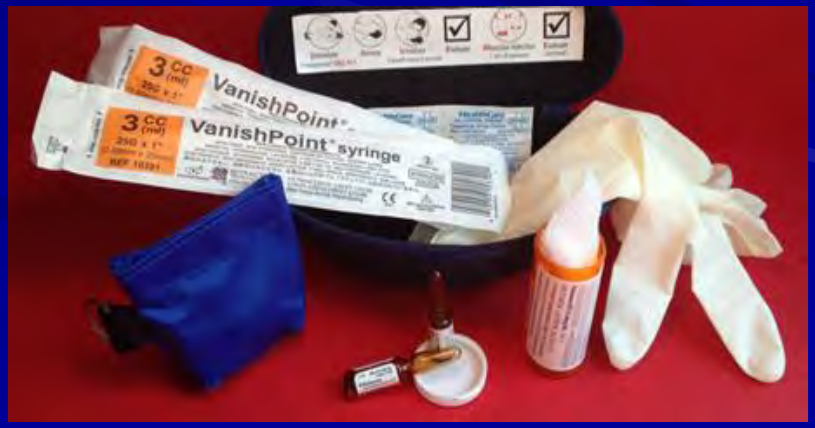
2 ampules naloxone in pill bottle, gauze wrapped, 2 VanishPoint 3 cc 25g 1”

2 swabs, 2gloves

One-way rescue breathing mask

Administration information form – kit identifier

Overdose recognition – overdose response steps



Evaluation

1. Consultation in 2014 (n=20)
   - Most had experienced or witnessed overdose
   - Overdose response training and naloxone valued
2. Combination of program tracking and survey
3. Demographic questionnaire
4. Pre-post training questionnaire
5. Naloxone tracking and administration form

Urine Drug Testing

Urine Drug Screening

- Chronic pain patients have high prevalence of unauthorized drug use on UDS (approx 15%)[1]
- Patients usually don't object if it's routine clinical policy
- Used for detection of:
  - Diversion and non-compliance
  - Double-doctoring
  - Abuse of other drugs e.g. cocaine, benzodiazepines

[1] Manchikanti et. al, 2006. Pain Physician. 9:123

Urine Drug Screening

- Regular UDS are often a component of long-term treatment programs (such as methadone programs for opioid use disorder patients)
  - UDS help physicians prescribe methadone safely
  - Many programs give take-home doses to patients with UDS free of addicting drugs; this acts as a motivation for patients to stop using

Benzodiazepines

Anxiety and mood disorder prevalence

- Approx 24% of population will be diagnosed over a 5 year period in Manitoba*
- 20% dissatisfied with sleep, 13.4% Canadians met all criteria for insomnia**

***2013 RHA Indicators Atlas**

Morin et al Can J Psy Sep 11

Class

- As sedative-hypnotics
- “perfect sedative’ should calm and reduce anxiety with minimal effect on alertness and motor functions
- Hypnotic- induce sleep, onset and maintain as close to natural sleep state as possible
- Difference is usually dose-dependent


KEEP
CALM
AND
CARRY
ON

Benzodiazepines

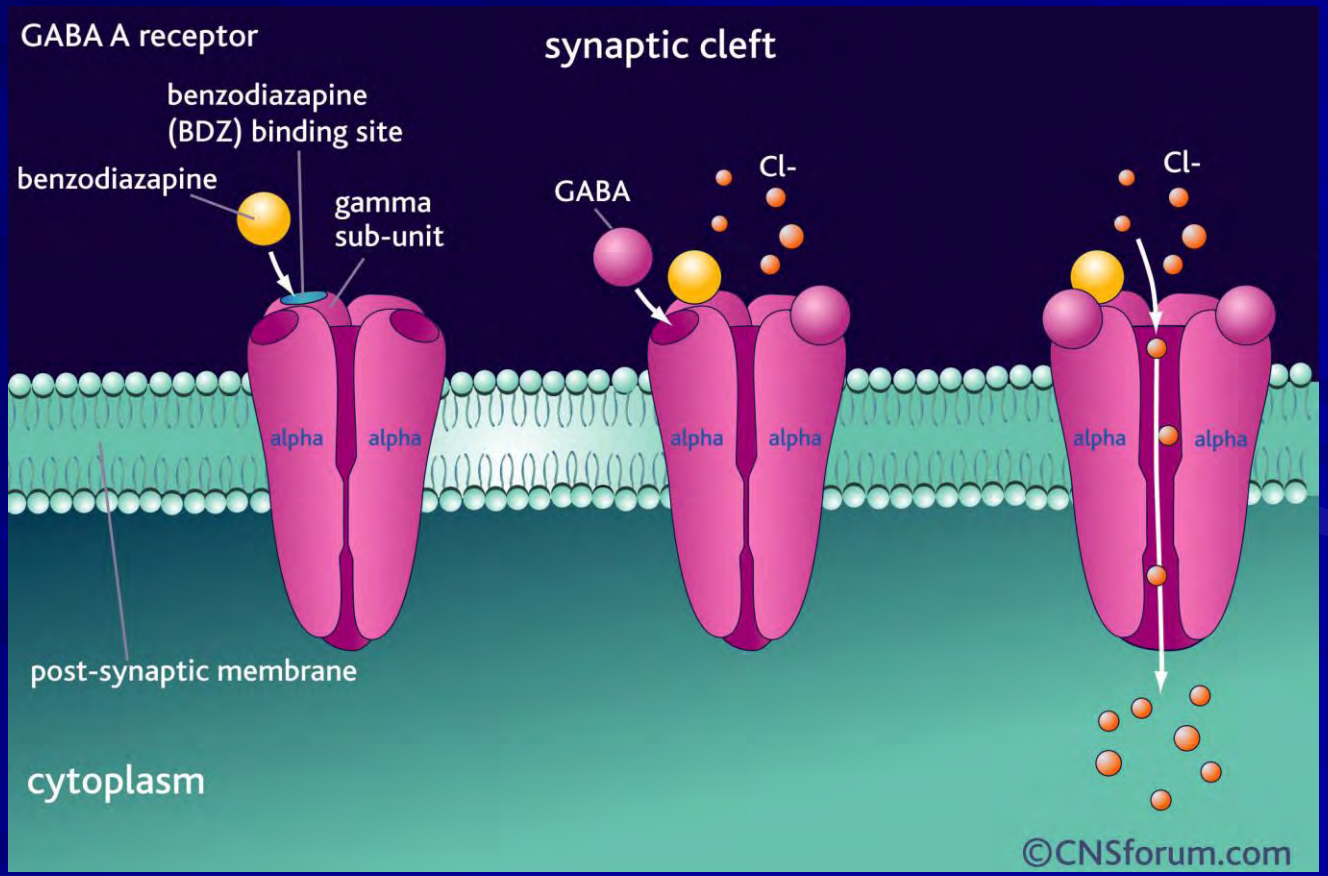
History

- BZ's Replaced barbiturates, which more likely to cause, anaesthesia, coma, respiratory depression and death.

- BZ's definite improvement over barbituates but continue to have problems with addictive properties and significant side-effects.

Mechanism of action

- Potentiate GABA which is an inhibitory neurotransmitter



UNIVERSITY OF NEWCASTLE

Neurology, Neurobiology & Psychiatry

Professor Heather Ashton

ASHTON MANUAL

INDEX PAGE

BENZODIAZEPINES: HOW THEY WORK AND HOW TO WITHDRAW

(aka The Ashton Manual)

- PROTOCOL FOR THE TREATMENT OF BENZODIAZEPINE WITHDRAWAL
- Medical research information from a benzodiazepine withdrawal clinic

Professor C Heather Ashton DM, FRCP

Revised August 2002

Therapeutic actions (short-term use)

Action	Clinical Use
Anxiolytic - relief of anxiety	- Anxiety and panic disorders, phobias
Hypnotic - promotion of sleep	- Insomnia
Myorelaxant - muscle relaxation	- Muscle spasms, spastic disorders
Anticonvulsant - stop seizures	- Seizures due to drug poisoning, some forms of epilepsy
Amnesia - impair short-term memory	- Premedication for surgeries, sedation for minor surgical procedures

Other clinical uses, utilising combined effects:

- Alcohol detoxification

Prof. Heather Ashton

History…

- This new group of drugs was initially greeted with optimism by the medical profession, but gradually concerns arose… in particular, the risk of dependence became evident in the 1980s.

Benzodiazepines have a unique history in that they were responsible for the largest-ever class action lawsuit against drug manufacturers in the United Kingdom, involving 14,000 patients and 1,800 law firms that alleged the manufacturers knew of the dependence potential but intentionally withheld this information from doctors.

Guidelines issued by the UK-based National Institute for Health and Clinical Excellence (NICE)

- Carried out a systematic review….
- Based on the findings of placebo-controlled studies, they “do not recommend use of benzodiazepines beyond two to four weeks, as tolerance and physical dependence develop rapidly, with withdrawal symptoms including rebound anxiety occurring after six weeks or more of use”.

Beers List

- All BZ's listed in Beer's list
- Beers Criteria for Potentially Inappropriate Medication Use in Older Adults, commonly called the Beers List

Abuse/Dependence patterns

- **Therapeutic dose dependence: doses of less than 30 mg diazepam, patient seems unable to function without but minimal side-effects**
- **Rule of thumb dependence can develops on over 40 mg diazepam (or equivalent) daily**
- **Prescribed more to women**
- **Problematic in Seniors "In Manitoba, 21% of Metis woman over age 90 and 14% of 'others' received repeated prescriptions for benzodiazepines in 06/07"**

***Metis Health Status Report**

Risky business…for the addicted brain

- The addicted brain loves shortacting, potent agents (Xanax)…readily available and CHEAP
- “Escape into oblivion” binge use
- Alternate with stimulants…”to come down”
- Enhance effects of other drugs such as opioids….

Different name…different strength

	Approximately Equivalent Oral dosages (mg)[3]
Diazepam (Valium)	10
Alprazolam (Xanax)	0.5
Clonazepam (Rivotril)	0.5
Lorazepam (Ativan)	1
Temazepam (Restoril)	20
Triazolam (Halcion)	0.5
Zopiclone (Imovane)	15
Eszopiclone (Lunesta)	3

Side effects

- Oversedation (dose related)
- Overdose deaths (Potentiating other sedative Rx meds/alcohol)
- Delirium and confusion
- Increased risk of accidents/falls at home/MVA's
- 'Anterograde amnesia'
- Memory impairment: "episodic memory", "blackouts", impaired learning of new information and coping techniques, unresolved grief
- Paradoxical stimulant effects
- "Emotional anaesthesia"
- Depression, Emotional blunting (precipitating suicide)
- "Pseudodementia" in the elderly

Why are they still used

- They do work, especially early on…
- Least resistance; “easy” treatment for anxiety
- Patients request them (hhm…)
- Side-effects are often more distressing to others (families) than the patient

Why are they still used

- MD's convince themselves of benefit….
- Harm reduction (despite a lack of evidence)
- Compassion
- Justified by end goal
- "My patient population is unique"
- "But he/she may seizure"

The evidence….

- **There is evidence that benzodiazepines increase opioid toxicity and risk of overdose.**
- Concurrent prescribing of opioids and benzodiazepines is common.
- Cross-sectional studies suggest that pain patients may be more likely to be prescribed opioids and to receive higher doses if they abuse alcohol, are on benzodiazepines, or are depressed (Hermos 2004, Sullivan 2005).
- Most opioid overdoses involve multiple drugs in addition to opioids (Mirakbari 2003); benzodiazepines and alcohol are most commonly implicated.

The evidence…

- The serum concentration of opioids is lower in mixed overdoses than in pure overdoses, suggesting that other drugs significantly lower the lethal opioid dose (Cone 2004).

Prescribing? Use caution

- Screening, Screening, Screening
- Don’t jump to rxing, should actually be 2nd or 3rd line treatment
- Be prepared to stick to your guns about short term use
- Limit dosing
- New patients, access medical records, DPIN
- Monitor, Comprehensive UDS

Non-addictive alternatives

- SSRIs, Tricyclic antidepressants, others (e.g. mirtazapine)
- Buspirone,
- Clonidine
- Antipsychotics
- Psychotherapy (preferably CBT in Group setting)
- Exercise (?Aerobic exercise better)
- Mutual help agencies such as ADAM
- Yoga, meditation etc

The CPSM

- No physician or patient is above the guidelines
- If deviate from guidelines..good documentation of rational
- Recognize that bad outcomes/deaths occur in context of good and bad prescribing
- Expected: documentation of comprehensive assessment, careful risk screening, appropriate prescribing for the diagnosis made, and ongoing monitoring of response to treatment, function, compliance, adverse events and red flags for abuse/diversion.
- Physicians are guardians of public health….

Stopping BZ'z

- Not obligated to prescribe them
- Generally, switch to long-acting, diazepam or clonazepam, bid at most tid dosing
- Avoid prn's
- Taper about 10% a month
- More rapid often backfires
- Need to be firm
- Ashton manual

Benzodiazapine withdrawal

insomnia, irritability, increased tension and **anxiety, panic attacks**, hand tremor, sweating, difficulty with concentration, confusion and cognitive difficulty, memory problems, dry retching and nausea, weight loss, palpitations, headache, muscular pain and stiffness, a host of perceptual changes, hallucinations, **seizures,** psychosis, and suicide

Benzodiazapine withdrawal

- Vital signs generally not as elevated as in alcohol withdrawal
- Seizures not uncommon
- Quick onset with shorter acting BZ's such as alprazolam, lorazepam, temazepam
- Longer acting Bz's such as clonazepam and diazepam may not see withdrawal symptoms for a week, on occasion, person may appear well and have a seizure "out of nowhere"

Benzodiazepine withdrawal

Generally withdrawal symptoms can be treated with tapering dose of diazepam over 2 - 4 weeks

…..but there is a small percentage of patients that have “protracted withdrawal” (post-acute BZ withdrawal) with odd symptoms such as movement disorders, perceptual changes, chronic depression, psychosis.

Postulated to be due to long-term down regulation of GABA receptors

RESOURCES

- BOOKS

– "Feeling Good" Dr Burns

– "Mind over Mood" D. Greenberg

– "Anxiety and Phobia Workbook" E. Bourne

– "Dying of Embarrassment" Marway et al

- Community Resources

– Anx. Disorders of Manitoba www.adam.mb.ca

– Canadian Mental Health Ass. www.cmha.mb.ca

– Dual Recovery Anonymous www.draonline.org

Other..

- **Bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban)**
- Gabapentin
- *Cyclobenzaprine (Flexeril)*

Gabapentin (*Neurontin*)

- Neuropathic pain affects up to 8% of the population
- increasing prevalences of age-related causes of neuropathic pain (including postherpetic neuralgia and diabetic neuropathy)
- “gabapentin is a mainstay of treatment and now a prevalent drug of abuse”

Gabapentin (*Neurontin*)

- Varying experiences with abuse including: euphoria, improved sociability, a marijuana-like 'high', relaxation and sense of calm, although not all reports are positive (for example, 'zombie-like' effects).
- UK police report indicates increasing tendency to use gabapentin as a 'cutting agent' in street heroin.
- Like opiates, gabapentin is fatal in overdose; unlike opiates, there is no antidote and the long half-life instils the need for prolonged, intensive management of overdose.
- NHIB has variety of restrictions re coverage of this agent (max 5000mgs per day; one Rx'er if on methadone)

- "Substance misuse of gabapentin"; Br J Gen Pract. Aug 2012; 62(601): 406–407.

Bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban)

- A lot cheaper than cocaine
- Pharmacists in Ontario sell Zyban OTC without a prescription.
- Spring, 2013 Ontario's interim chief coroner: - at least six deaths in the province in the past two and a half years that were at least partly caused by bupropion abuse.

http://www.ctvnews.ca/health/health-headlines/doctors-warn-of-potentially-fatal-abuse-of-wellbutrin-antidepressant-1.1383282#ixzz2xMgM52xN

Bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL , Zyban)

- crushed and smoked/snorted/injected
- high compared to stimulants (methamphetamines or crack cocaine)
- Fillers can cause embolisms/abscesses at injection sites
- ERP in North Bay, Ontario reported: “it appears that when bupropion enters the bloodstream, it leads to a necrotizing, or tissue-destroying effect”
- “Chronic drug user tried to inject the drug into his jugular vein. He missed the site and likely hit his vertebral artery, causing the drug to enter his spinal column. His brain stem slowly necrotized and the man was eventually taken off life support and died”.

Thank you!

Questions?