Introduction to the Management of Opioid Use Disorder

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Conflict of Interest Declaration: Nothing to Disclose

Presenter: **Anne Robinson**

Title of Presentation:

Introduction to the Management of Opioid Use Disorder

I have no financial or personal relationships to disclose

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Learning Objectives

- List the key criteria for diagnosis of OUD.
- Define "pseudoaddiction".
- Describe the basic pharmacology of buprenorphine/naloxone (bup/nlx), its mechanism of action, and safety profile.
- Outline the approach to bup/nlx induction and the key elements of ongoing follow-up.
- Describe the process for establishing a treatment program in communities that do not have a pharmacy or on-site pharmacist.

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DSM 5 Criteria
≥ 2 within 12mos

1. Opioids often taken in larger amounts or over longer period of time than intended.
2. Persistent desire or unsuccessful efforts to cut down or control use.
3. Great deal of time spent in activities necessary to obtain opioid, use the opioid, or recover from its effects.
4. Craving or strong desire to use.
5. Failure to fulfill major role obligations at work, school, or home

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6. Continued use despite negative consequences (social or interpersonal).
7. Important social, occupational, or recreational activities are given up or reduced.
8. Use in situations in which it is physically hazardous.
9. Continued use despite knowledge of having a persistent/recurrent physical or psychological problem that is likely caused by or exacerbated by opioids.

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These criterion are not used for those who are medically supervised on prescribed opioids:

10. Tolerance (either of):
    a) Need for markedly increased amounts of opioid to achieve intoxication or desired effect
    b) Markedly diminished effect with continued use of same amount of opioid
11. Withdrawal (either of):
    a) Characteristic opioid w/d syndrome
    b) The same (or closely related) substance is taken to relieve or avoid w/d symptoms

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Determining Severity

Mild: 2 – 3 criteria

Moderate: 4 – 5 criteria

Severe: ≥ 6 criteria

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Could it be Pseudoaddiction?

Aberrant behaviour occurring due to undertreated pain.

Are the patient's "red flag" behaviours signs of desperation due to poorly controlled pain?

Requires careful consideration

Behaviours resolve when pain is effectively treated.

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Treatment Options

- Counseling**
- Detox
- Opioid antagonist (naltrexone)
- Opioid Maintenance Therapy

** *Counseling is a key component of all treatment plans.*

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BUPRENORPHINE	METHADONE
Partial μ agonist	Full μ agonist
LOWER risk of death by OD	HIGHER risk of death by OD
LONG half-life (36 – 48 hrs)	LONG half-life (24 -36 hrs)
Daily or alternate day dosing	Daily dosing
HIGH affinity for μ receptor	AVG affinity for μ receptor
LESS potential for abuse	MORE potential for abuse
K antagonist	K agonist
$$	$
May not need M.E. (varies by province)	M.E. required

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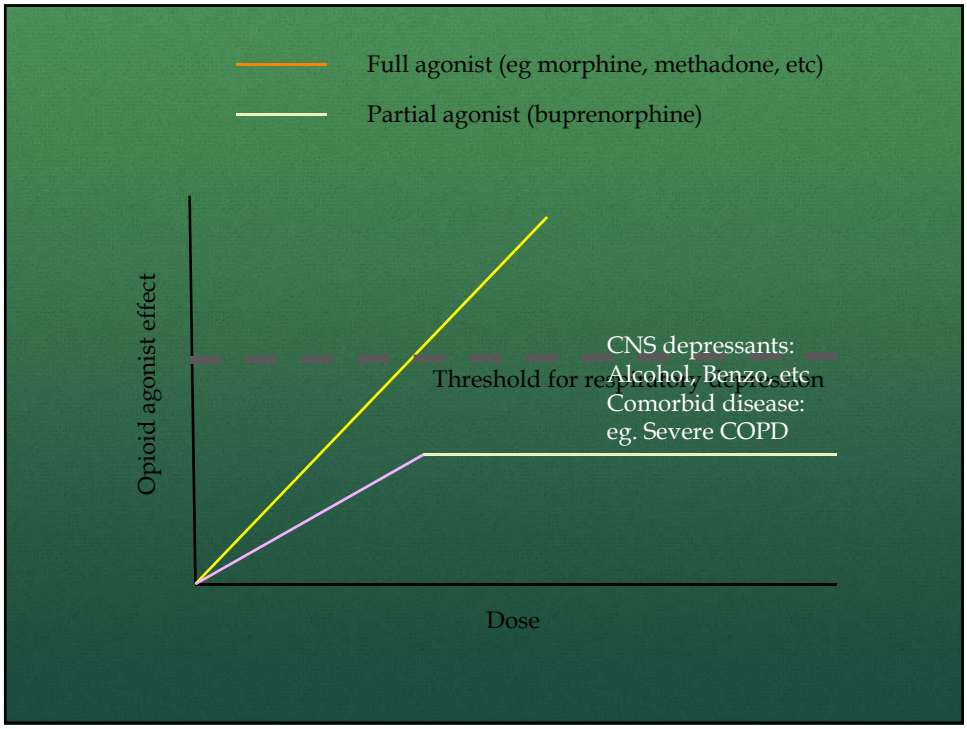
Full agonist (eg morphine, methadone, etc)
Partial agonist (buprenorphine)
Opioid agonist effect
CNS depressants:
Alcohol, Benzo, etc
Comorbid disease:
eg. Severe COPD
Dose

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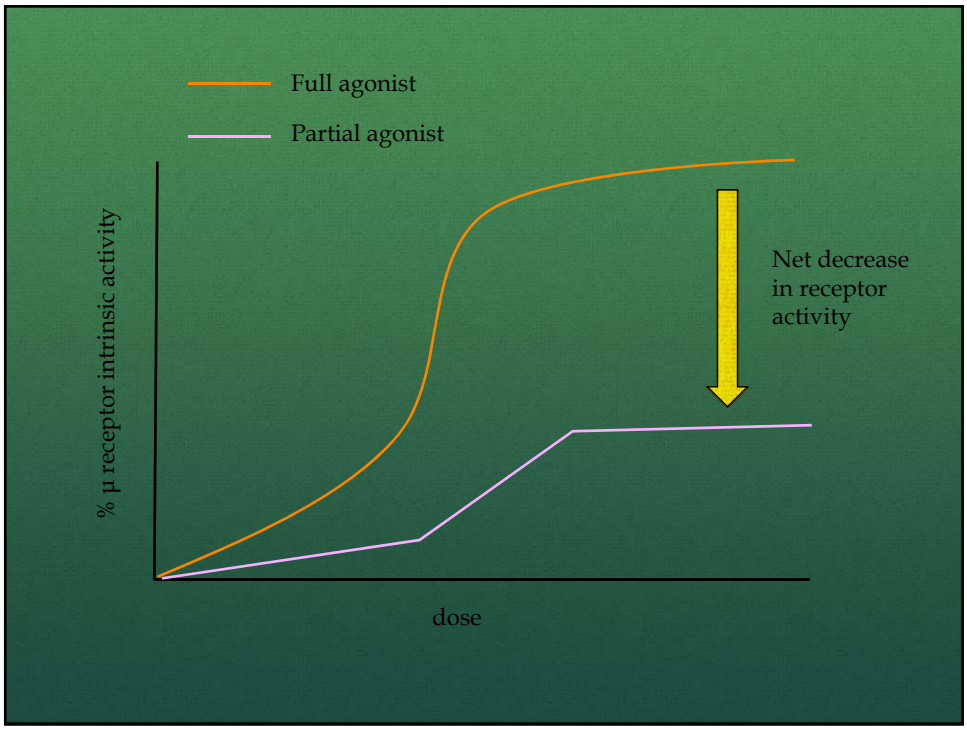
Full agonist
Partial agonist
% μ receptor intrinsic activity
Net decrease
in receptor
activity
dose

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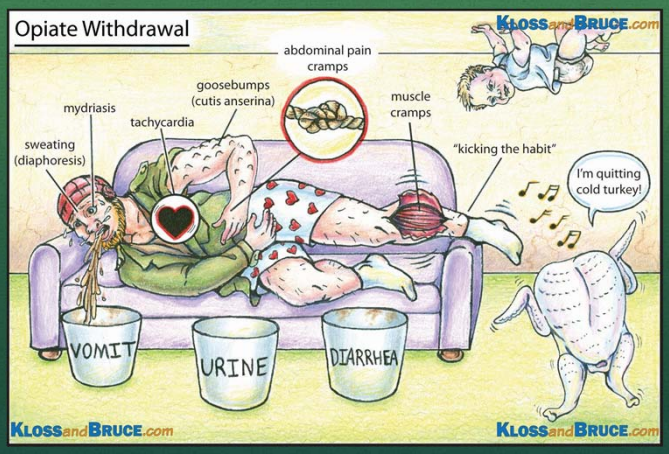
BEWARE! Precipitated Withdrawal!!!



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Why is naloxone added?

- Naloxone is a μ receptor antagonist
- Has very high affinity for the μ receptor
- It has extremely low bioavailability when taken SL or PO (must be given IV or IM to be effective)
- Added to Suboxone® as a deterrent to abuse by injection

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Initial Assessment

- ❑ Confirm diagnosis of OUD (DSM V)
- ❑ Complete history (deploy the medical student!)
- ❑ Assess for concurrent disorders (can be done at subsequent visit)
- ❑ Physical exam
- ❑ Laboratory investigations (can be deferred)
- ❑ Set goals & expectations of treatment plan

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History

- Drug use history (all substances) & Patient's goals
- PMHx
  - Medical, Surgical, OB, Injuries, Chronic Pain
  - Meds, allergies, immunizations, etc
- Mental Health
  - Emotional traumas, SI/SA, previous dx, Residential school, adverse childhood experiences, etc
- Social Hx
  - Work, housing, relationships, kids, DV, supports/stressors, criminal, etc
- Family Hx
- ROS

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Concurrent Disorders

- Timing of screening (may be better to delay)
- Various screening tools (PDSQ, MMS,etc)
- Mood disorders (depression, bipolar)
- Anxiety disorders (GAD, OCD, panic, social, PTSD)
- Psychotic disorders
- Personality disorders

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Physical Exam

- Vitals
- Skin (track marks)
- CVS, Resp, Abd
- As indicated by Hx

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Labs

- No specific labs are absolutely required prior to beginning bup/nlx (unless clinical S&S of significant medical impairment)
- General and preventive health (CBC, Renal fn, Liver fn, DM screen)
- I.D. screening (Hep, HIV, STI, TB)
- Pregnancy
- Baseline UDS

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UDS

- Therapeutic monitoring (analogous to BS logbook)
- Punitive consequences are NOT helpful
- Provide an opportunity for discussion and reflection
- Need to be knowledgeable about FPs and FNs
- POC testing allows timely feedback/discussion, but limited to a few selected substances and incr FP & FN
- Broad spec more detailed info, need knowledge of metabolites to interpret correctly

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UDS Collection

- Remove bulky clothing & no bags/purses in bathroom
- Consider: temperature, pH, Cr, sp gravity

T (within 4 min)	32 – 38 °C
pH	4.5 – 8.0
Cr	> 2.0 mmol/L
Specific gravity	> 1.003

- High level concern: bluing agent in toilet, tamper-evident tape, no soap, inspect room after, etc

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Treatment Agreement

- Patient Education
- Expectations, Rules
- Dose adjustments, Carries, Missed Doses, Diversion, etc
- UDS
- Discontinuing treatment

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Induction

- Completed pre-treatment assessment
- Assess for contraindications
- Ensure any full agonist opioids are adequately clear (need to be in at least mild w/d, check COWS)
  - 6 – 12 hr abstinence for short-acting opioids
  - 12 – 24 hr abstinence for delayed-release opioids
  - 3 – 5 days for methadone (after taper to < 30mg)
- Pregnancy test
- UDS
- Follow dosing protocol

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Contraindications

- Allergy
- *Severe* liver dysfunction
- Acute *severe* respiratory illness
- Paralytic ileus
- Medically debilitated patients

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Strong Precautions

- Acute alcoholism
- Current abuse or severe dependence on BZDs or other sedating substances
- *Severe* COPD, asthma
- Elderly

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General Cautions

- Severe renal insufficiency
- Hypotension
- BPH or urethral stricture
- Operating heavy equipment or driving during induction
- Biliary tract dysfunction
- Co-administration of other CNS depressants
- Pregnancy

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Serious Adverse Effects

- Hypersensitivity reactions
- CNS depression, respiratory depression
- Hepatic events (most assoc with IV abuse)
- Orthostatic hypotension
- NAS

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Common Side Effects

- Constipation
- Headache
- Nausea
- Hyperhidrosis
- Sedation
- Difficult urination
- Depression
- Anxiety
- Asthenia
- Elevated liver enzymes
- Xerostomia (possibly dental caries)

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Ongoing Care

- ❑ Frequency of visits
- ❑ UDS
- ❑ Assessing stability and progress
- ❑ Diversion
- ❑ Carries
- ❑ Dose adjustments, alternate dosing schedules, missed doses
- ❑ Relapse
- ❑ Counseling

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Frequency of Visits

- During induction, you may be seeing them daily for 3 – 5 days
- Every 1- 2 weeks until showing signs of stability
- As stability improves, every 1 – 3 months

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UDS

- Key part of therapy
- Frequency determined by level of stability
- Ideally, done randomly. Done in office (do not take home). Basic measures to avoid tampering etc.
- POC is great for allowing immediate feedback/discussion (but more FPs, FNs)
- Do broad spec for any unexpected POC results

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Counseling

- By who?
- You (MI, supportive counseling, UDS review)
- Self-directed (self-help books, online CBT, e-counseling)
- Community MH worker (variable skill level), Church-associated, Mentors/Elders, NA/AA
- Advanced MH counselor
- Consider psychiatry referral for patients with complex psychiatric co-morbidities

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Dose Issues

- Adjustments: up or down, tapering
- Missed doses:
- Guest dosing:
- Alternate schedules: double or triple dosing
- Discontinuation: plan for w/d symptoms

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Missed Doses

BUP Dose	# of Missed Doses	New Starting Dose
> 8mg	> 7 days	4mg
> 8mg	6 – 7 days	8mg
6 – 8mg	6 or more days	4mg
2 – 4mg	6 or more days	2 – 4mg

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Stability

- No evidence of ongoing problematic substance use (incl EtOH), no cravings, no w/d
- No acute or unstable psychiatric symptoms
- Stable behaviour and social situation
- No aberrant UDS results
- Frequency of missed doses
- Think of categories:
  - Unstable (or least stable)
  - Moderately stable (or more stable)
  - Stable (or most stable)

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Diversion

- A common, and even expected, behaviour
- Sign of instability
- Ensure there is a means for D.O.T. provider to report this information to you
- Use similar approach as per positive UDS
- Lose carries privileges, consider crushing dose
- Consider decreasing dose by 25 – 50%

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Carries

- Not until evidence of stability (no recent positive UDS, no diversion behaviour)
- Stable housing situation (need to have a safe place to keep meds)
- Establish rules/expectations (meds will not be replaced if lost/stolen etc)
- Start with only 1 – 2 doses/week and increase according to ongoing stability
- Generally, max carries for chronically stable patient would be 1 – 2 weeks of medication

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Relapse

- An expected part of recovery
- Do not catastrophize
- Reframe, reflect, restart

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Minimum Elements Needed for Bup/nlx Therapy

- ❑ DSM V diagnostic criteria
- ❑ Other treatment options considered
- ❑ Pretreatment Assessment
- ❑ Knowledge of Bup/nlx (pharmacology, contraindications, side effects)
- ❑ Access to some form of D.O.T. service
- ❑ Ability to provide at least MI or supportive counseling
- ❑ UDS (ideally POC)

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D.O.T. Service

- Ideally provided by regulated HCW (pharmacist, RN, etc)
- When no HCW available, the Narcotic Control Act allows a layperson to act as an agent of either the prescribing physician or the patient receiving treatment
  - This layperson would require appropriate training and oversight

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Most Important!

Compassion

Clinical Curiosity

BS Detector

Sense of Humour! 😄

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Buprenorphine/Naloxone Key Points and Handy Reference Materials

Anne Robinson MD CCFP (AM) at SRPC Conference April 2019
(highly recommend additional education such as CAMH courses)

DSM V Criteria for OUD: At least 2 of these symptoms within the past 12 months.		
1. Opioids often taken in larger amounts or over longer period of time than intended.		
2. Persistent desire or unsuccessful efforts to cut down or control opioid use.		
3. Great deal of time spent in activities necessary to obtain opioid, use the opioid, or recover from its effects.		
4. Craving or strong desire to use opioids.		
5. Failure to fulfill major role obligations at work, school, or home.		
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.		
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.		
8. Recurrent opioid use in situations in which it is physically hazardous.		
9. Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.		
10. Tolerance,* as defined by either of the following: a) Need for markedly increased amounts of opioids to achieve intoxication or desired effect. b) Markedly diminished effect with continued use of the same amount of opioid		
11. Withdrawal,* as manifested by either of the following: a) Characteristic opioid withdrawal syndrome. b) Same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms.		
* These criterion (items 10 & 11) are not considered to be met for those taking opioids solely under appropriate medical supervision.		
Mild: 2 – 3 symptoms	Moderate: 4 – 5 symptoms	Severe: 6 or more symptoms

"Where There is no Pharmacist" approaches to providing DOT
The Narcotic Control Act allows for a 3rd party to act as an agent of either the prescribing physician or the patient receiving treatment.
Key elements of training should include: • Confidentiality requirements • Documentation requirements • Reporting requirements • Exact procedures for observing patients during dosing • How to manage a suspected diversion attempt • Exact procedures for tracking medication (pill counting)

URINE DRUG TESTING

Punitive approach is not recommended (ie. do not stop therapy based on positive UDT).
Patient-centered approach allows for non-judgemental discussion of ongoing illicit drug use, relapses, and goals of harm reduction.

Type of Test	Point of Care	Lab Immunoassay	Broad Spectrum
Method	Enzyme Immunoassay	Enzyme Immunoassay	Chromatography +/- mass spectrometry
Advantages	Immediate results	Detects several classes of drugs Timely results (hrs)	Detects specific drug and/or metabolite Identifies drugs not detected by immunoassay Higher sens & spec
Disadvantages	Limited number of drugs detected High FP and FN rate	Only identifies class FN and FP for certain drugs	Takes much longer (days to weeks) Need knowledge of metabolites

RECOMMENDED RESOURCES

- McMaster PBSG Module (UDT – Interpreting Results, Feb 2017)
- LifeLabs® 2016.http://tests.lifelabs.com/Laboratory_Test_Information/Search.aspx enter Ontario, then "Drugs of abuse screen (urine)"; then click on "Forms"
- DynaCare® Labs 2016. https://www.dynacare.ca/healthcare-providers-and-hospitals/continuing-medical-education/interpretation-guides.aspx
- Rx Files: Q&A Summary. Urine Drug Screening (UDS). 2011. http://www.rxfiles.ca/rxfiles/uploads/documents/urine-drug-screening-uds-qanda.pdf

STANDARD BUP/NLX INDUCTION PROTOCOL

Patient must be in at least mild w/d prior to initiating and/or abstinent of full agonist opioid for at least 12 hrs (IVDU), 24 hrs (other routes), or 3-5 days if methadone use.

Day	Morning	Afternoon	Max Dose
1	Starting dose of up to 4mg	If in W/D, give up to 4mg as "top up"	8mg (usual) 12mg (in special circumstances)
2	No W/D? Give total Day 1 dose. W/D present? Give total Day 1 dose plus up to additional 4mg	If in W/D, give up to 4mg as "top up" (Day 2 afternoon assessment is often not necessary)	16mg
3	No W/D? Give total Day 2 dose W/D present? Give total Day 2 dose plus up to additional 4mg		20mg
4	No W/D? Give total Day 3 dose W/D present? Give total Day 3 dose plus up to additional 4mg		24mg

MISSED DOSES (give restart dose, then re-titrate as per induction protocol)		
Buprenorphine Dose	Number of Consecutive Days Missed	New Starting Dose
> 8mg	> 7 days	4mg
> 8mg	6 – 7 days	8mg
6 – 8 mg	> 5 days	4mg
adapted from Handford et al 2012		

BUPRENORPHINE	**METHADONE**
Partial *mu* agonist • LOWER risk of death if OD • Ceiling effect • May not be adequate for users of very large amounts of opioids	Full *mu* agonist • HIGHER risk of death if OD • No dose limit
25 -40 x the oral morphine equivalent	No applicable oral morphine equivalence
LONG ½ life (36 – 48 hrs) • Daily or alternate day dosing	LONG ½ life (24 – 36 hrs) • Daily dosing
VERY HIGH affinity for *mu* receptor • Blocks other opioids • Less reward of illicit opioid use • Difficult to manage acute pain	AVERAGE affinity for *mu* receptor • Can add other opoids
Can cause Precipitated Withdrawal • Due to high mu affinity combined with partial mu activation • Patient needs to be in w/d prior to induction	Does not cause Precipitated Withdrawal BUT, higher risk of death during induction
kappa antagonist • Less dysphoria	*kappa* agonist • Dysphoria side effects
Very few drug interactions	Numerous drug interactions
Little/no QT prolongation	QT prolongation
More difficult DOT	Simple DOT
$$	$

CLINICAL OPIATE WITHDRAWAL SCALE (COWS)

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Resting Pulse Rate: _____beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset**: *over last ½ hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 Multiple episodes of diarrhea or vomiting
Sweating: *over past ½ hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor** *observation of outstretched hands* 0 No tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 Unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/ muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Mild: 5-12 Moderately Severe: 25-36 Moderate: 13-24 Severe: more than 36

From: Wesson DR, LingW J Psychoactive Drugs 2003 Apr-June: 35(2):253-9