SUBSTANCE USE

in the time of COVID-19

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- No perceived potential conflicts of interest
- Relationship with commercial interests:
  - No interests in nor money received from a pharmaceutical, medical device or communications company
  - I do CFPF accredited talks for WorkSafeBC
  - No perceived bias from commercial entities

Disclaimer

- Please note the protocols shared in this presentation are suggestions only
- They do not take the place of clinical judgment
- I assume no liability for the use of these protocols
- Will not be covering toxidromes or ICU management

Objectives

1. Highlight key issues regarding substances use while physical distancing during the COVID-19 pandemic
2. Review assessment, and treatment protocols adapted for telemedicine
3. List the temporary changes to the national and BC provincial controlled substances act
4. Explore online resources for patients and clinicians

COVID-19

- New issues arise and long standing ones can be exacerbated during the COVID-19 pandemic and isolation protocols
- People may stock pile meds/substances and thus have more availability/access
- Supply chains may be cut off abruptly
- Quality of non-medical supply unreliable
- People may turn to non-beverage alcohol and non-medical substances to relieve withdrawal or to treat pain
- Social issues may complicate use patterns
- Some may want stabilization or reduction

Digital SUD Assess and Tx

- Care to underserved regions of need
- Facilitate use of validated tools to detect
- Introduce digital therapeutics
- Novel biomarkers (gait, speech, breathalyzer)
- Wearable sensors on mobile devices can help with medication adherence, relapse prevention, real-time interventions
- E.g. tracking visits to liquor stores, collecting breathalyzer information, and then counselor intervention

Assessment & Tx Protocols Adapted for COVID-19

- Caffeine
- Tobacco
- Alcohol
- Opioids
- Marijuana
- Benzodiazepines
- Stimulants

Where to start?

- First assess and make a diagnosis
  - Check Pharmanet, interview, examine
  - Screen (E.G. AUDIT, DAST, CRAFFT, DSM 5)
  - Substance Use or Substance Use Disorder?
  - Pain disorder? How functional?
- Is there physiologic dependence?
  - Is a withdrawal syndrome present?
  - How severe? Life threatening?
- What is the patient's circumstance?
  - Physical living situation? Others present?
  - Mental/physical health? Access to meds?
  - Domestic violence?

Caffeine

Caffeine and DSM 5

- Coffee, black & green tea, chocolate, colas, energy drinks – with lack of routine more use?
- Intoxication – 5+ below after 2+ cups coffee
  - Restlessness, nervousness, excitement
  - Insomnia, flushed face, diuresis, GI disturb
  - Muscle twitching, tachycardia/arrhythmia
  - Rambling thought/speech, inexhaustibility
  - Psychomotor agitation
- Must cause stress or impairment
  - Anxiety Disorder, Sleep Disorder, Withdrawal

Caffeine w/d Management

- ½ life = 4-6h (however,10 fold variation) so even just 1c/d can build up in a slow metabolizer and impact sleep and give headache on cessation
- Caffeine withdrawal (w/d) can include:
  - Headaches, irritability, impatience, restlessness
  - Sleep disturbance, dysphoria and fatigue
- Taper as tolerated by 1/2c – 2c every1-2d
- Most people no issues coffee 1-3 Cups/QAM
- Discuss this range with patients to help ease irritability, restlessness and insomnia

Why ask about caffeine?

- 37 year old female police officer, right knee cartilage defect, 2 surgeries, CNCP, isolated at home
- 6 months passive physio, T#3 1-2 q4h = 6-12/d
- ↑Anxiety with panic attacks and palpitations, insomnia, feels she is going "crazy", mood ↓
- For this ↑doses of duloxetine, and lorazepam
- Caffeine: coffee 5 cups/d + 4 energy drinks
- Each coffee = 3 shots espresso
- Caffeine= (15x160 mg/shot)+(4x160mg/edrink) +(12x15mg/T#3) = Total caffeine = 3,220 mg/d

Nicotine

Nicotine Replacement

- Nicotine patch 21,14, 7mg = 1, 2/3, 1/3 ppd
- Apply q am over muscle & hairless skin, rotate sites
- Take off if chest pain, light headed, N or V
- If nightmares occur >3 nights, remove patch at HS
- Use each patch strength for 2-6+ wks, longer best
- LR tip: At end of taper can leave on final patch 3d, or occlude half of 7mg patch to finish taper
- LR tip: If skin irritation - spray with steroid inhaler
- LR tip: If peels off - cover with transparent film
- Gum, inhaler, e-cigarette also effective
- Beware of vaping, especially in youth – high dose, anxiety, and lung issues requiring a ventilator (YIKES)

Nicotine - Antidepressant Tx

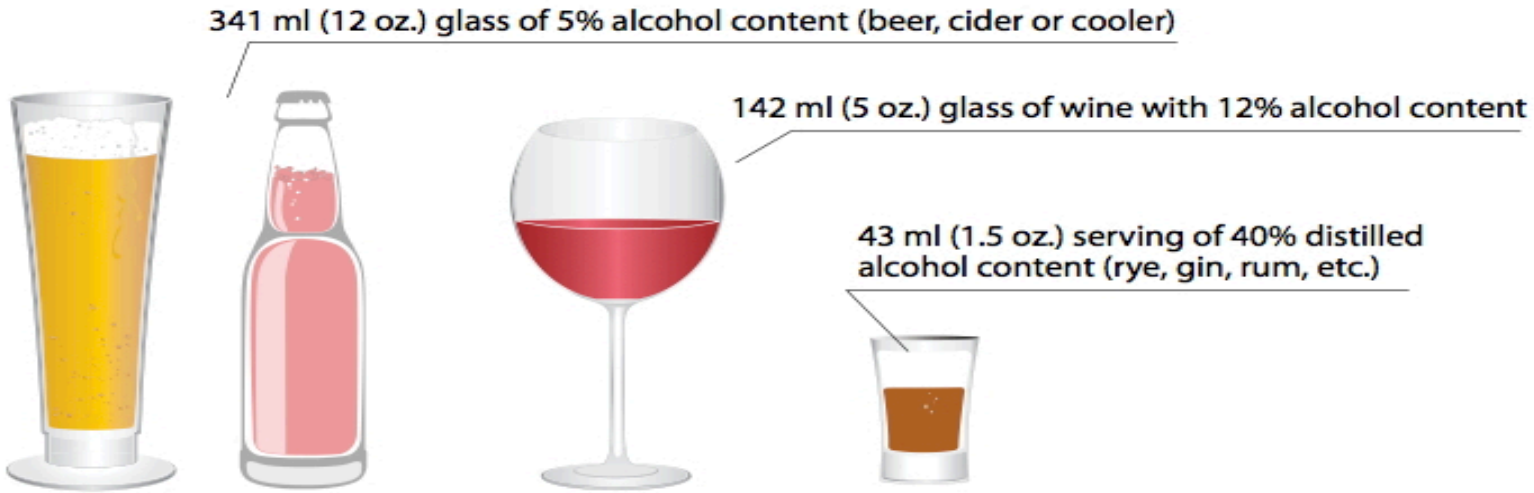
- Bupropion
  - DA and NOR reuptake inhibitor
  - Contraindicated with eating disorders, cocaine
- 150 mg/d same efficacy as 300 mg/d
- Stop smoking day 7(+ nicotine replacement)
- Can taper off bupropion after 3 months
- Some feel a bit squirrely on this medication
- 12 week quit rate 36%, 1yr quit rate 16.4%
- NB: ASAM guidelines use 2 agents at once, E.g. Bupropion plus nicotine patch

Nicotine Partial Agonist Tx

- Varenicline
- Partial nicotinic receptor agonist, ↑dopamine
- Contraindicated: renal impairment, pregnancy, suicidal or severe depression
- Dose: 0.5 mg/d x 3d, then 0.5 mg q12h
- 12 week quit rates ~44%, 1 yr quit rates same as bupropion or slightly better (22.1%)
- Dr. Rieb Tip: Ask patient not to smoke for 12+h prior to first dose, i.e. to be in withdrawal, then the medicine will relieve their withdrawal instead of precipitating it!

Alcohol

Age 18-65
Canadian low-risk drinking guidelines



- 0 if contraindicated, at least 2 days off/wk
- Females ≤ 10/wk, 2/d (rare event 3) max
- Males ≤ 15/wk, 3/d (rare event 4) max
- N.B. JAMA 2018 = increase morbidity with >1/d

Non-beverage Alcohol

Risk of use increases when…

- Supply chain is stopped of beer, wine, liquor:
  - Stores close, stop stocking or delivering
  - Other household members use the supply or cut off supply to a user
- Cost prohibitive due to gouging from stores or financial stress

Non-beverage Alcohol

- Hand sanitizer and rubbing alcohol contain isopropyl alcohol
  - 200+ ml toxic to adults, coma/death
  - If mixed with MAOIs particularly lethal

- Antifreeze contains propylene glycol, ethylene glycol and methanol
  - toxic by-products increase over 12 hrs
  - may appear increasingly drunk
  - Multiorgan failure, blindness

- Rice wine for cooking – high sodium
  - Seizure threshold is lowered

Mechanisms of Alcohol

- Acute consumption produces CNS sedation:
  - ↓ glutamate
    - Blocks postsynaptic NMDA glutamate receptor
  - ↑GABA
    - Binds to GABA1 receptors
  - Activates opioid system
    - ↑dopamine
  - ↑serotonin
- Withdrawal produces opposite - CNS activation
- Wernicke-Korsakoff Syndrome (WKS)
- Delirium tremens (DTs)
- Tremor = best predictor of impending seizure

Alcohol Withdrawal

- W/d = 2+ occurring hrs/days after cessation
  - Autonomic hyperactivity, eg. HR >100, sweat
  - Hand tremor, insomnia, N or V, anxiety
  - Hallucinations, illusions (visual, aud., tactile)
  - Psychomotor agitation, grand mal seizures
- Both use and withdrawal can be dangerous

Alcohol Lowering

- Home lowering reduces risk of sz if supply stops
- The patient is very unlikely to have a seizure if tapering by 1 to 2 drinks/d from any starting point
- If ≤ 7 drinks/d usually can stop "cold turkey"
  - i.e. otherwise healthy: No seizures, DTs, or head injury
  - However continue tapering if any of the above to 3/d
- Consider Residential detox if pt wants off and…
  - ≥8 drinks/d AND unsuccessful tapering/med mngt AND adverse consequences currently outweigh COVID risk
  - Seizure disorder, alcohol w/d seizures or DTs
  - Suicidal, psychosis, violence in w/d, pregnant
  - Unstable social situation (homeless, domestic violence)

Alcohol Lowering Strategies

- Is alcohol lowering/cessation right for this person?
- Metabolism by ALD = 1 oz pure ETOH/3h

= 1 standard drink per hour on average

- Keep a drinking diary
- Sip drinks, spread out drinking ≤1/hr
- Use a shot glass or measuring cup, pour your own
- Alternate alcoholic & non-alcoholic drinks
- Eat food and re-hydrate with water prior to ETOH
- Distract with other activities and interests
- Get help online – SMART recovery through CHCs have gone virtual as has AA and NA , WAGON and other private support networks

Home Alcohol Detox Protocol

- Ensure patient is physically dependent
  - Is drinking 6-8+ drinks/d, tremor
  - Must drink daily to alleviate symptoms (clear w/d)
  - Hasn't been abstinent 2+ days in the last 2 weeks
- Ensure patient is safe at home
  - Ideally to have a reliable caregiver with them x 72 hrs
  - No access to ETOH, no hx of seizure or delirium
- Ensure patient has not just ingested alcohol
  - Last drink should be 6-8pm night prior, check

Fixed Dose protocol

- Fixed dose schedules -no hx of seizure/delerium
- Scoring over 8 on CIWA-Ar
- Can have pharmacy deliver meds and video link with patient and observe dosing
- Diazepam 20 mg q1-2h x 3 doses
  - Stop if sedated, slurred speech, or RR < 10

Alternative medication:

- Lorazepam 2 mg dosed as above (elderly, liver problems or unknown LFTs, COPD/asthma)

Prevent WK syndrome: thiamine 250mg/d IM x 5d

Is impractical when in isolation, so oral 100 mg /d

Home-based Withdrawal Mngt

Another fixed dose schedule option:

- Diazepam 10 mg q6h x 4 doses
  - then 5 mg q6h x 8 doses
  - Start with pt in w/d in the morning - tremor
  - MD can witness first dose, reassess 2 hrs later, and adjust if needed, the rest take home
- Lorazepam 2mg x 4 doses then 1mg x 8 doses
- Use thiamine 250mg im x5d optimally, or oral 100/d
- Ideally reliable caregiver must administer meds
- Caregiver must stop if sedated or pt relapses

Home-based Withdrawal Management

- Gabapentin – Anticonvulsant
- Ca++ channel and GABA modulating
- 300 mg q6h = 1200 mg/d – days 1-3
- 300 mg q8h = 900 mg/d – day 4
- 300 mg q12h = 600 mg/d – day 5
- 300 mg hs = 300 mg/d – day 6
- May be better than benzodiazepines: Less sedation/drinking/craving at some time points, no increased adverse events for out-patients
- Exclude those with previous seizure or delirium

Follow-up of Home Detox

- Ideally see the patient every day through video link
- Initial load should be enough to prevent seizure in most cases (long half life)
- May need a benzo taper – for example:
  - lorazepam 2mg tid x3d, 2mg bid x1d, 2mg hs, off
- After benzo taper, then use trazodone, nortriptyline, or gabapentin to control sleep (off-label suggestion)
- Relapse? Review strengths and triggers. Try again.

Ongoing Management of AUDs

Q: Abstinence is a requirement of which medication used in the ongoing management of alcohol use disorders?

A) Acamprosate
B) Disulfiram
C) Naltrexone
D) Gabapentin
E) None of the above

Naltrexone for AUD

- 50 mg once daily (start with ½ tab x 3 days)
- Mu opioid receptor antagonist
- Blocks alcohol's pleasure/reinforcing effects
- Fewer slips, decreased amounts, (abstinence?)
- Must be opiate free 7-10 d for short acting opioid and for 2-3 weeks for long acting
- Contraindicated if LFTs over double normal
- Can be used while still drinking daily
- Naltrexone can reduce binge drinking episodes
- Use with binging can reduce amount consumed
- This is the safest drug to use with little monitoring

Acamprosate for AUD

- 333mg – start with 1 tab TID theb slowly increase to 2 tablets three times daily
- ↑GABA and ↓glutamate
- ↓craving, helps retain in treatment
- Dose response relationship, many trials
- Not advised to use while still drinking so taper off first
- Medication management important - tele

Gabapentin for AUD

- Gabapentin 600 mg q8h – depending on response start with 300 q8h
- Ca++ channel and GABA modulating
- Significantly improves abstinence and heavy drinking rates, dysphoria, insomnia, and craving over 12 weeks
- Potential side effects – potential sedation, memory impairment, word-finding difficulty, dangerous to drink with this med since it may increase risk of OD

Original Investigation

ONLINE FIRST

March 9, 2020

Efficacy of Gabapentin for the Treatment of Alcohol Use Disorder in Patients With Alcohol Withdrawal Symptoms

A Randomized Clinical Trial

Raymond F. Anton, MD[1]; Patricia Latham, PhD[1]; Konstantin Voronin, MD, PhD[1]; et al

» Author Affiliations

JAMA Intern Med. Published online March 9, 2020. doi:10.1001/jamainternmed.2020.0249

Findings In this randomized clinical trial, gabapentin compared with placebo significantly increased the number of people with total abstinence and reduced drinking. This effect was most significantly observed in those with greater pretreatment alcohol withdrawal symptoms—41% of participants with high alcohol withdrawal symptoms had total abstinence on gabapentin compared with 1% of participants in the placebo arm.

Disulfiram – not first line to initiate during isolation

- 250 mg once daily (range 125–500 mg)
- Aversion therapy – acetaldehyde build up
- Off alcohol 48 hrs prior, 1-14 d after pill
- With alcohol – flushing, n+v, ↑BP, ↑HR so can be dangerous to the medically unwell
- Contraindicated: MI+CAD, DM, epilepsy, cirrhosis, hypothyroidism, renal insuf.
- Commit to abstinence, assisted ingest
- Pharmacy can compound

12-step (AA)

Cochrane Library

Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

[Intervention Review]

Alcoholics Anonymous and other 12-step programs for alcohol use disorder

John F Kelly[1], Keith Humphreys[2], Marica Ferri[3]

Cochrane Database of Systematic Reviews 2020, Issue 3. Art. No.: CD012880. DOI: 10.1002/14651858.CD012880.pub2.

- High quality evidence that manualized AA/TSF interventions are more effective than other established treatments such as CBT for increasing abstinence...among patients with worse prognostic characteristics AA/TSF had higher potential cost savings than MET.

Opioids

Prescribing in a Pandemic

Health Canada Temporary Exemptions to the *Controlled Drugs and Substances Act (CDSA):*

- *Permit pharmacists to…*
  - *extend prescriptions (emergency supplies)*
  - *transfer prescriptions (between pharmacies)*
  - *deliver controlled medications (when safe)*
- *Permit prescribers to…*
  - *give verbal or faxed orders, but in BC…*
  - *send the original in the mail/courier, etc.*

Prescribing Resources

- College of Pharmacist's COVID-19 Response https://www.bcpharmacists.org/news/bc's-covid-19-response-–-temporary-authorizations-controlled-drugs-and-substances
- BC Centre on Substance Use COVID-19 information including Guidance: Risk mitigation in the context of dual public health emergencies; and a webinar on Substance use and safer supply
- https://www.bccsu.ca/covid-19/

Key Issues for Opioids

- Ensure stable supply of medications for chronic-non-cancer pain – e.g. longer scripts with part fill dispense, bubble pack
- Get as many people as possible off non-medical opioids and onto prescribed oral opioids
- Transition from injection use to oral route
- Keep users out of clinics and hospitals
- Prevent withdrawal and allow for steady supply of unadulterated medications

Opioids

Bind to opioid receptors

- Relieving pain (psychological and physical)
- ↑dopamine (DA) in pleasure centres (ventral tegmental area ➔nucleus accumbens)
- ↓ noradrenalin (NOR) in the fight or flight centres (locus coeruleus and amygdala), calming
- Affects brainstem (OD from respiratory depr.)
- Can produce dysphoria, sedation, impaired judgment, constipation, weight gain, erectile dysfunction (from decreased testosterone)

Opioid Use Can Cause Pain

Opioid Withdrawal

Withdrawal is not life threatening

- Unless patient has a history of seizures, is dehydrated, suicidal or pregnant

- Warn patients of OD risk post detox

Opioid Withdrawal

- DSM-5…3+ within minutes to days of stopping:
  - Dysphoria
  - N or V
  - muscle aches
  - lacrimation or rhinorrhea
  - diarrhea
  - yawning
  - fever
  - insomnia
  - Pupillary dilitation, piloerection or sweating

Opioids and the pandemic

- We want to maintain people with CNCP on a stable dose during the pandemic
- Bring non-medical opioid users (opium, heroin, fentanyl, street oxy, etc.) into care with designated oral prescription opioids
- Transition injection users (iOAT or illicit) over to designated oral opioids
- Urgent focus on sex trade workers
- Buprenorphine is opioid of choice


1887
Mrs. Winslow's
SOOTHING
SYRUP
FOR CHILDREN TEETHING

Opioid Lowering Options for those with CNCP who choose or need to lower:

1. Convert to long acting opioid – taper
2. Taper with short acting opioid
3. Withdrawal symptom management
4. Opioid substitution/rotation - taper

Typically…opioid tapering is not an emergency!

- As out patients most can drop 5-10% every 1-2 weeks, sometimes slowing to every 2-4 weeks for the last 20-30% of the opioid
- For patients on LOT for many years who have failed more rapid tapering, just slow it down to drop every 1-3 months
- Even if you drop the dose 5% every 3 months, in a year they will be down 20%, and by 2 years 40%. But this is ridiculously slow if they are on extremely high doses or have only been on a couple of years or less

Slow Taper by % - Example

- 100% of initial taper dose
- Drop 10% every 2 weeks to 50% of initial dose
- Then drop by 5% every 2 weeks to 30% of initial dose
- Then drop 2-5% every 2-4 weeks until off or at 90mg MEDD or below, adjusting to symptoms
- This means seeing them every 2-4 weeks
- Most can get down or off opioids
- Anecdotally, about 10% on LOT for CNCP will not be able to get down to 90 MEDD

Opioid Tapering - Long

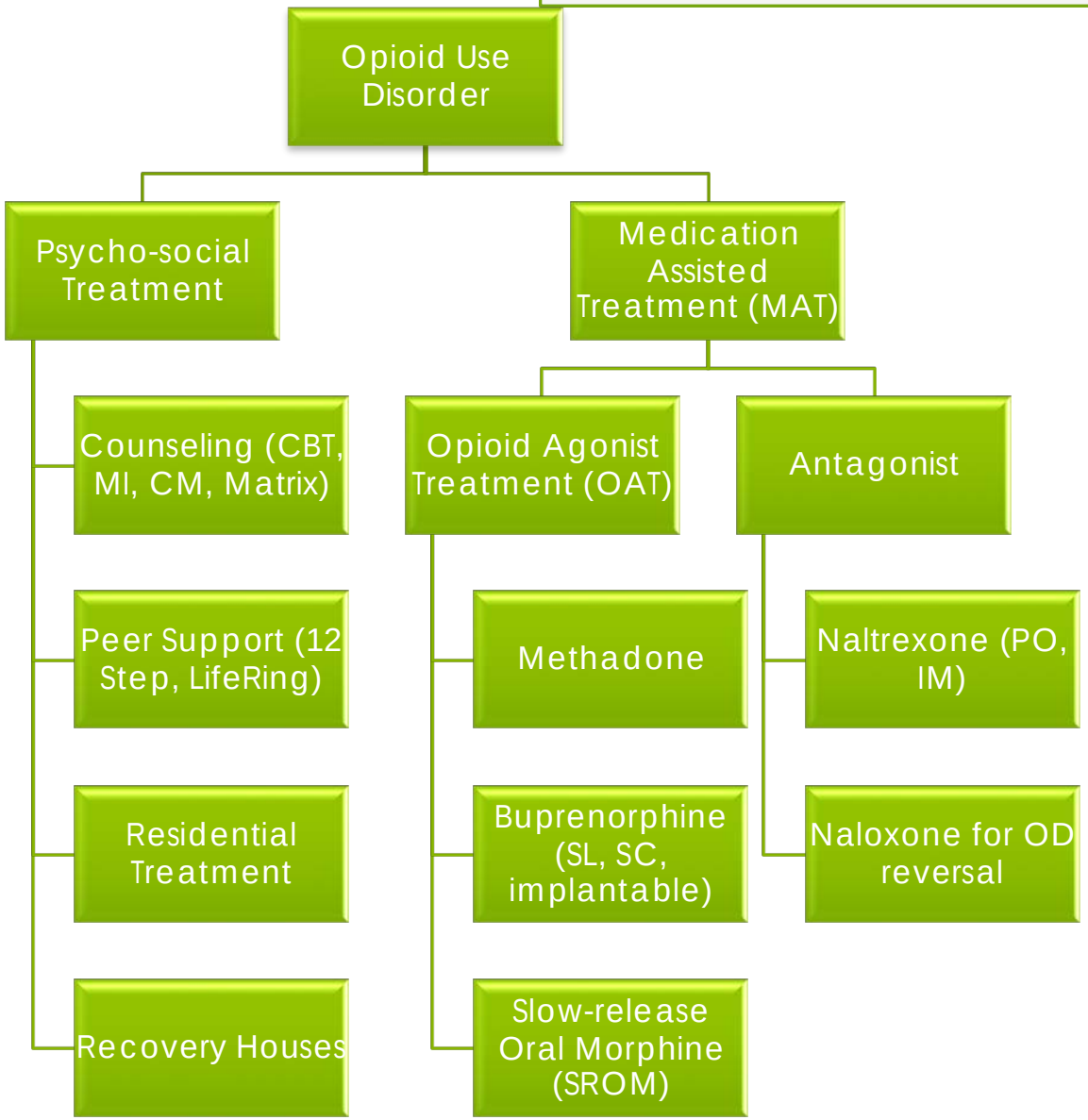
- Conventional wisdom is to convert short acting opioids to long acting then taper Sometimes short is needed to add back in at the end due to dose strength
- Convert to long acting (same drug less 25% - 50%, rest is given as short acting PRN, re-evaluate daily)
  - Once on just long acting: Taper ~5-10% per 1-14 d
  - Symptom management like the CINA protocol
- If rotating opioids beware of conversion
  - Lack of cross tolerance with some opiates

Opioid Tapering – Short

- Sometimes easiest to simply taper what the patient is currently using
  - E.g. Percocet 16-20/d, taken 6 tid +/- 2/d
- If it is a dual agent first switch to eliminate the ASA or acetaminophen (bloodwork?)
  - E.g. Oxycodone 5 mg 18/d
- Next spread out the daily dose evenly based on the ½ life of the medication
  - E.g. Oxycodone 5 mg 5/4/4/5 spread q6h

Opioid Tapering – Example

- Next taper the medication – drop can be q4-14d as out-pt, and drop daily as in-pt or faster if d/c needed (other symptom mngt may be needed)
- Oxycodone 5 mg 4/4/4/5 spread q6h
- Oxycodone 5 mg 4/4/4/4 spread q6h
- Oxycodone 5 mg 4/3/4/4 spread q6h
- Oxycodone 5 mg 4/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/4 spread q6h
- Oxycodone 5 mg 3/3/3/3 spread q6h…
- Continue this pattern until 0/0/0/1, then off


Opioid Use Disorder
Psycho-social Treatment
Medication Assisted Treatment (MAT)
Counseling (CBT, MI, CM, Matrix)
Peer Support (12 Step, LifeRing)
Residential Treatment
Recovery Houses
Opioid Agonist Treatment (OAT)
Antagonist
Methadone
Buprenorphine (SL, SC, implantable)
Slow-release Oral Morphine (SROM)
Naltrexone (PO, IM)
Naloxone for OD reversal

COWS

- COWS (Clinical Opiate Withdrawal Scale)

- Health practitioner administered
- Cows score above 13 can initiate meds – either a clonidine protocol or buprenorphine

- https://www.drugabuse.gov/sites/default/files/files/ClinicalOpiateWithdrawalScale.pdf

SOWS

- SOWS (Subjective Opiate Withdrawal Scale)
- Patient administered 16 questions, 4 pts each
- Withdrawal score: mild = 1 – 10;
  Moderate = 11 – 20; and Severe = 21 – 30
- Sows score above 11 can initiate meds – either a clonidine protocol or buprenorphine
- https://www.asam.org/docs/default-source/education-docs/sows_8-28-2017.pdf?sfvrsn=f30540c2_2


FARBENFABRIKEN
FRIEDR. BAYER & Co
ELBERFELD.
Heroin

Opioid w/d Management

- Clonidine protocol
- For use when you cannot (or will not) prescribe opioids, or if the patient stops abruptly:
- Often works best for short acting opioids like heroin, codeine, morphine, oxycodone, etc.
  - If outpatient and no reliable caregiver, then daily dispensed from a pharmacy usually, but with lockdown can bubble pack and dispense a week at a time

Opioid w/d Management

- Environment: Safe; minimal caffeine, exercise, and hot spices; no hot bath/shower/sauna
- Clonidine 0.1mg qidx4d, tidx1d, bidx1d, hsx1d prn
  - Test dose 0.1mg, BP pre & 1-2h post in the office can be done – OK if BP >90/60, OR if cannot leave home make sure no dizziness post dose
  - if BP lower or dizzy - give clonidine 0.05 mg tabs
  - Decreases temperature dysregulation (hot/cold flashes) insomnia & anxiety, and pain
  - Warn pts of postural hypotension, driving
  - Use with medications on next slide

Opioid w/d Management,

- Gabapentin 300 – 600 mg tid, prn for anxiety, insomnia, and pain *
- +/- Trazodone 50 mg 1-2 tabs hs for insomnia
- Loperamide 2 mg after loose stool, 8/d max
- Dimenhydrinate 25mg 1-2 tid N+V
- Ibuprofen 400 mg q 6-8h for pain
- Acetaminophen 500mg q6h for pain
- * Substitutions:
  - quetiapine 25 mg ½ -1 bid - tid and 1-2 hs
  - diazepam 5 mg qid x 4d, tid x1d, bid x1d (classic, but more dangerous if opioids continue, diversion)

METHADONE

Opioid Substitution: Methadone

- Methadone can be used for pts with an opioid use disorders and/or pain, and for detox
  - Dose once daily to eliminate withdrawal and block other opioids – may be sufficient
- Methadone used for pain dosed q6-8h
- If on methadone at admission to detox centre or hospital - Lower the dose by at least 25% and give the rest in 5 mg prn doses, witnessed ingestion, hold if sedated

Morphine to Methadone

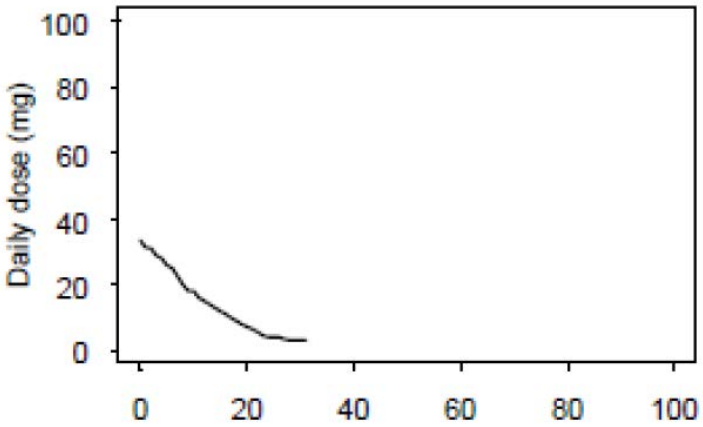
24 hour total oral morphine	Oral morphine to methadone conversion ratio
<30 mg	2:1
31-99 mg	4:1
100-299 mg	8:1
300-499 mg	12:1
500-999 mg	15:1
>1000 mg	20:1

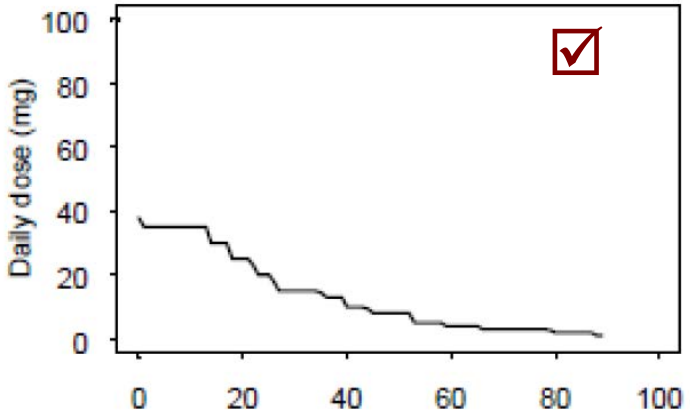
Managing Cancer Pain in Skeel ed. Handbook of Cancer Chemotherapy. 6th ed., Phil, Lippincott, 2003, p 663

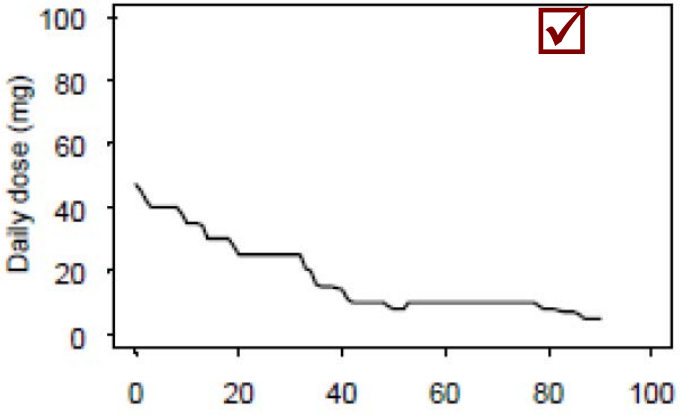
Methadone for Detox

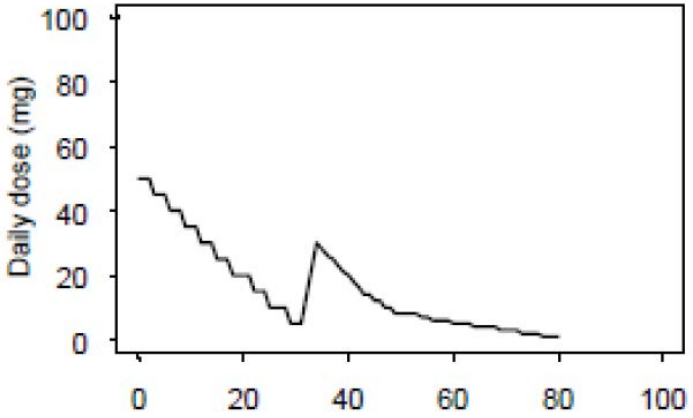
- MD must be trained – College course, license
- Only for highly tolerant patients on high dose opioids (not those on high dose methadone) in a supervised setting
- Methadone 20 mg with 5mg prn q4h up to 30mg max day 1 – witnessed, hold if drowsy or no w/d
- Then taper 5 mg daily until off
- LR Tips: Can taper last 5 mg by 1/d, and/or switch to buprenorphine patch at end of taper for sensitive individuals
- Or switch to bup/nx at end for maintenance

Patterns of Methadone Maintenance Dose Tapering (Most successful checked)









Modified from Nosyk et al, Addiction 2012; 107(9):1621-9.


Buprenorphine HCL
Sublingual Tablets
8 mg*
Midlothian

Opioid Substitution - Bup

- buprenorphine/naloxone (bup/nx) can be used for pts with an opioid use disorders or detox
  - Dose once daily to eliminate withdrawal and block other opioids – may be sufficient
- Bup/nx used for pain +/- SUD can be dosed q6-8h
- Bup/nx currently off label for pain alone though can argue physiologic dependence, tolerance

Buprenorphine/nx for Detox

- Ensure person is in w/d (SOWS≥11)
- 1-2mg test dose, if no precipitated w/d
- Then 2 mg q2h until symptoms abate
- Max 8 mg day 1, max 16 mg day 2
- Then taper by 1-2 mg /d
- E.g. 8/6/6/4/4/2/1 or 8/7/6/5/4/3/2/1
- Tip: Buprenorphine patching (20mcg/h) 1 d pre bup/nx can ↓ precipitated w/d
- LR Tip: Post bup/nx add patch, ↓w/d

Bup/nx and Pain

Pain Medicine

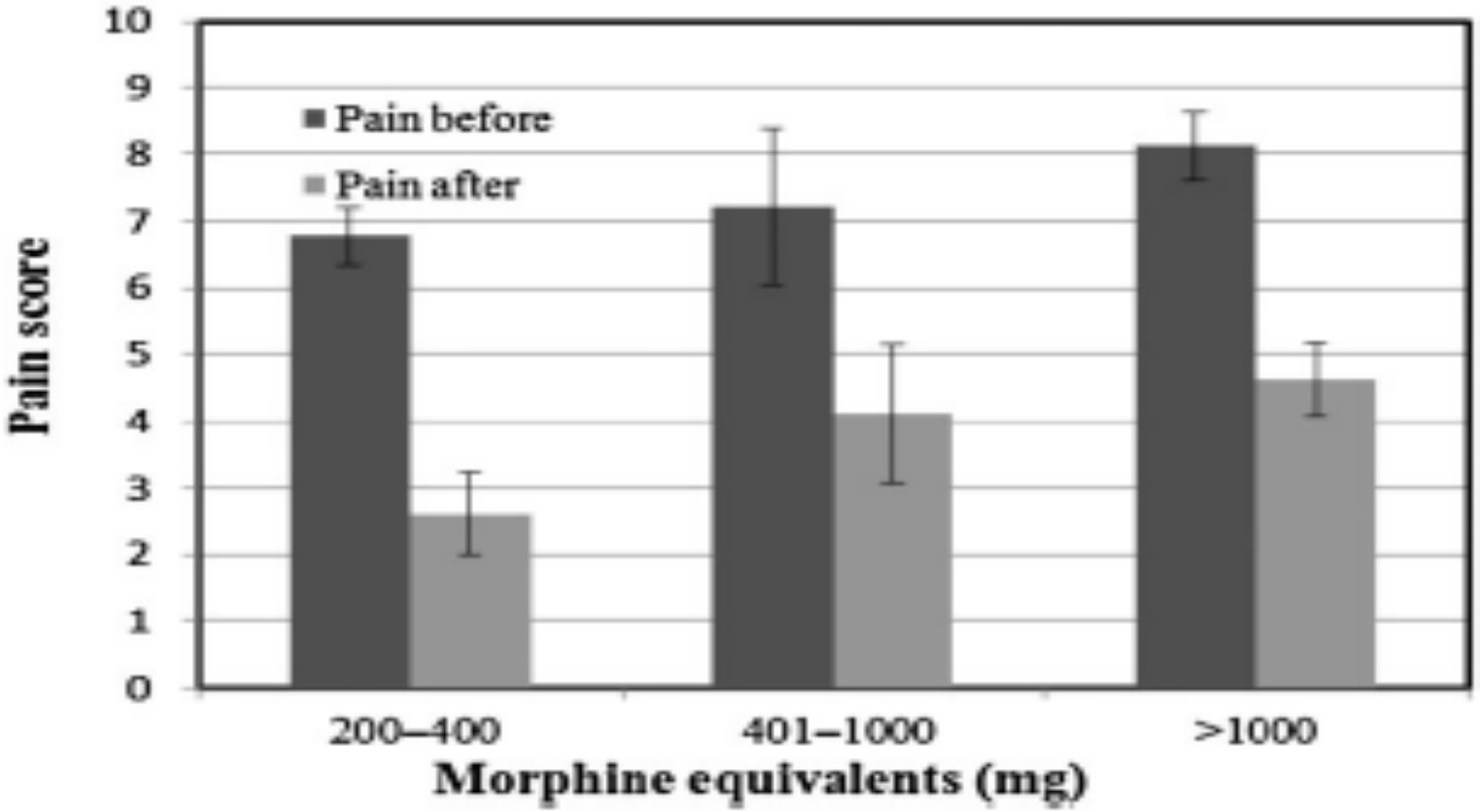
Pain Medicine 2014; *: **–**
Wiley Periodicals, Inc.

Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients

Daitch D et al. Pain Medicine. 2014

Retrospective chart review of patients on over 200 MEDD converted to Suboxone - pain scores dropped 51% on average, 8/10 to 4/10

Pre- and postconversion pain scores by preconversion morphine equivalents dosage



Average 4 point drop!

Daitch D et al. Pain Medicine. 2014

For those with OUD who are highly physiologically dependent and using high dose opioids – the following protocols have been shared…

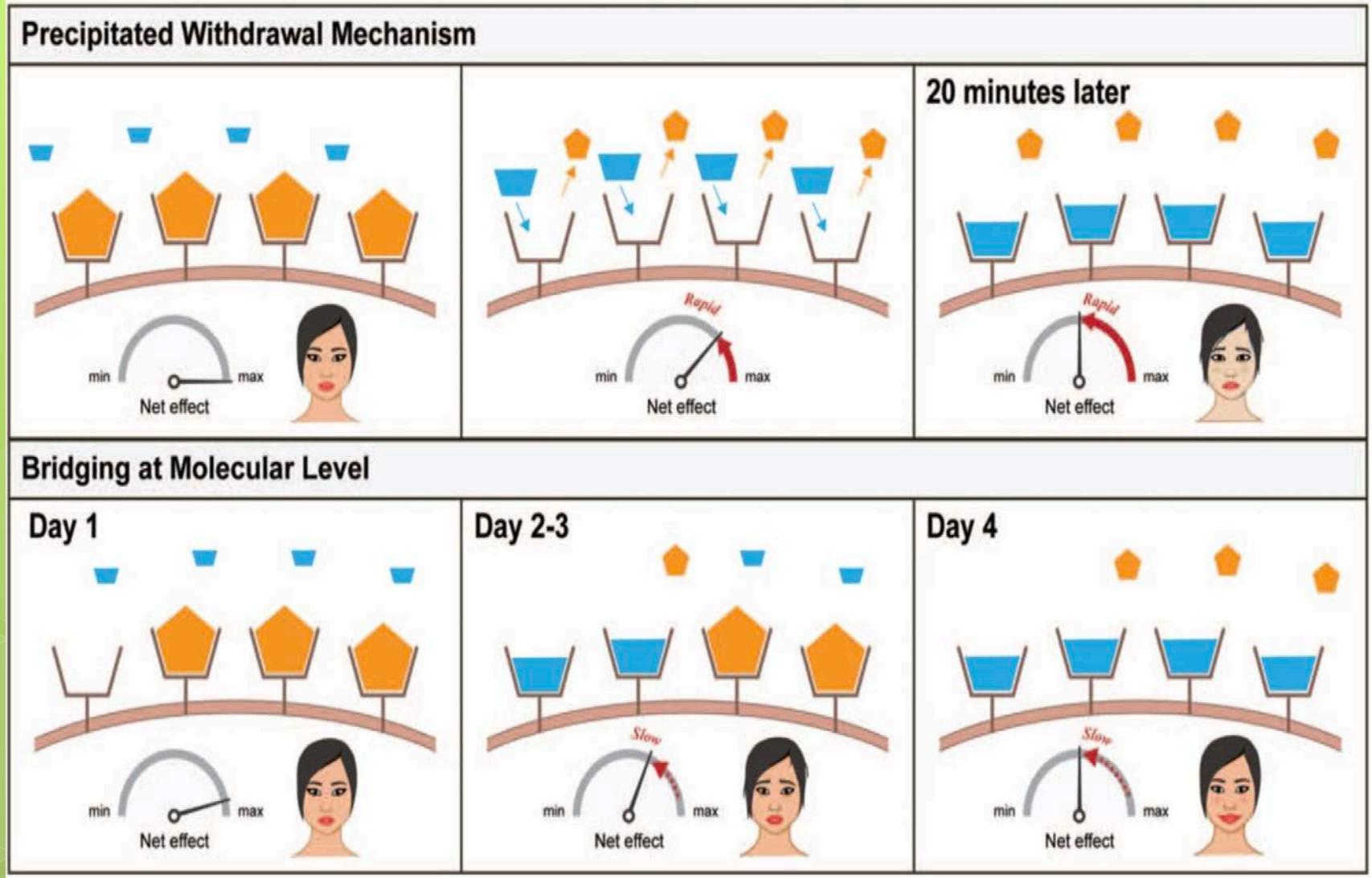
Buprenorphine Induction

REVIEW ARTICLE

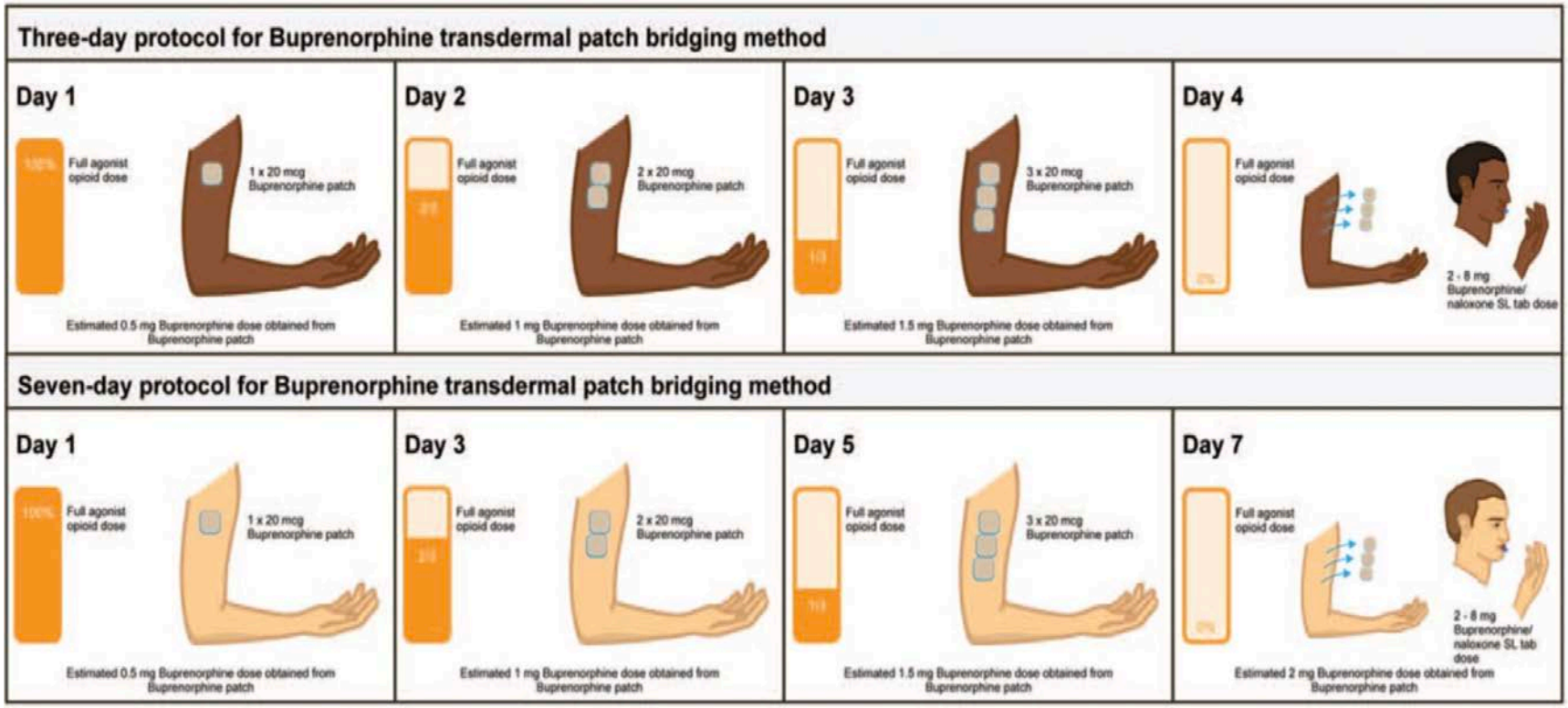
A Review of Novel Methods To Support The Transition From Methadone and Other Full Agonist Opioids To Buprenorphine/Naloxone Sublingual In Both Community and Acute Care Settings

Ghosh, Sumantra Monty MD, MSc, FRCPC, ISAM[1]; Klaire, Sukhpreet MD, CCFP[2]; Tanguay, Robert MD, FRCPC, ISAM[3]; Manek, Mandy MD, CCFP[4]; Azar, Pouya MD, FRCPC, ISAM[5] **Author Information**

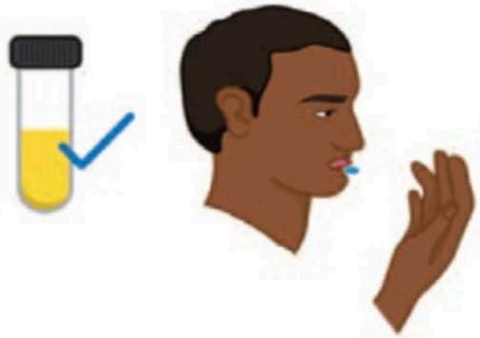
The Canadian Journal of Addiction: December 2019 - Volume 10 - Issue 4 - p 41-50
doi: 10.1097/CXA.0000000000000072



Mechanism behind precipitated withdrawal mechanism as well as bridging: Partial agonist opioid with high affinity for μ-receptors replaces the full opioid agonist rapidly over a short period of time causing a massive change in the net μ-receptor activation leading to rapid precipitated withdrawal. This can be mitigated by bridging, where the gradual introduction of higher affinity partial agonist opioids can help minimize withdrawal symptoms.



Three- and 7-day buprenorphine patch protocol.

At initiation 	If the methadone dose is: • > 60mg, reduce by ½ 2 days prior to start of buprenorphine/naloxone SL. • is < 60 mg, then the last dose should be given the morning prior to induction. Apply 40 mcg of transdermal buprenorphine (~1mg of buprenorphine/naloxone SL) for 3-6 days or until urine drug screen (UDS) is positive for buprenorphine.
Day 1 **Induction Day** 	Perform UDS. If urine screens positive for buprenorphine, stop the original opioid (ie. methadone). Administer 1mg SL Buprenorphine/naltrexone test dose. Observe 2 hours. If withdrawal symptoms emerge and COWS increases, hold further doses until COWS returns to baseline. Administer 1 mg test dose and observe two hours. Repeat if COWS increases. If COWS remains the same or decreases, administer 1-2mg SL buprenorphine, observe 2 hours. Repeat to a maximum of 8-12 mg buprenorphine SL on induction day, based on elimination of withdrawal symptoms Discontinue transdermal delivery.
Day 2	Administer induction day dose and up-titrate buprenorphine/naloxone SL up to 16 mg on Day 2 if pain or withdrawal symptoms persist.
Day 3	Administer Day 2 dose, up-titrate buprenorphine/naltrexone SL to 20-24 mg if pain or withdrawal symptoms persist.
Day 4	Continue established daily buprenorphine/naltrexone dose.

Bup. Induction by L. Rieb

- Stop full mu opioid and apply a buprenorphine transdermal 20 mcg/hr patch overnight (or Bup/nal 0.25 mg)
- Day 1 induction: Bup/nal SL 0.5 mg wait 1 hr: if no precipitated w/d then give 1 mg wait 1 hr: if no precipitated withdrawal then continue with standard induction 2 mg q 2-4 h up to max 8 mg-16mg.
- Day 2: give all previous day's dose then 2 mg q 2-4 h up to max 16-24 mg.
- If precipitated w/d at any point hold 3-4 h

Buprenorphine Injection

- Buprenorphine extended-release injection
- ”Sublocade”
- Excellent choice in the pandemic
- Titrate or taper Suboxone to 8 mg/d
- Loading doses: 300 mg SC x 2 months
- Maintenance dose: 100 mg SC q monthly
- Autotapers over months so little to no withdrawal even if supply chain disrupted

Buprenorphine - implant

- Implantable buprenorphine not yet approved by Health Canada
- Available in BC under federal special authority, other provinces can apply
- Clinician fills out a form
- Patient must pay company directly
- Shipped to a hospital pharmacy
- MD inserts 3 rods – last 6 months

ORT for pts failing bup, meth

Slow release oral morphine (SROM)

- Once daily witnessed ingestion
- Typically no take home doses

Heroin assisted therapy (HAT) AKA diacetyl morphine (DAM) therapy

- 3x/d witnessed injectable heroin, often supplemented with 30-40 mg methadone HS

Naltrexone – opioid antagonist

- Post detox use naltrexone 50mg/d po for those with OUD
  - can block 0.5+ gm of heroin IV or equivalent
- Start 1-2 wks after last short acting opioid (3-4 wks post methadone)
  - ¼ pill day 1; ½ pill day 2; 1 pill day 3 onwards
  - Witnessed ingestion is best
- Contraindicated cirrhosis, OD risk high once d/c
- Use for first 6-12 months of sobriety from OUD
- Analgesia with non-opioids or get consult

Naltrexone - injectable

- Monthly injectable IM naltrexone
- Not yet approved by health Canada, but in BC for OUD with special authority
- Other provinces/authorities can apply for this designation
- Practitioner fills out a form
- The patient must pay directly to US company
- Delivered to a hospital pharmacy, $$$
- Reduces relapses, days of opioid use, OD

Naloxone Take Home Kits

- Nasal or injectable naloxone kits given to people prescribed opioids for pain or addiction
- Train Pt and others living with them
- Can save lives in OD situations
- Sometimes Pt uses it on a friend
- Find out what is available/allowable in your area

Cannabis

Cannabis

- And new "Spice" = synthetic cannabinoids
- THC binds to CB1 and CB2 receptors
  - ↑DA, is a CNS stimulant and depressant
  - Changes perception, memory, motivation, movement, reflexes, BP, pain, appetite

- W/d reported <25%
  - Dysphoria, irritability, restlessness, insomnia, anorexia, anxiety, sweating, tremor & craving
  - Supportive care, drug free environment

Cannabis

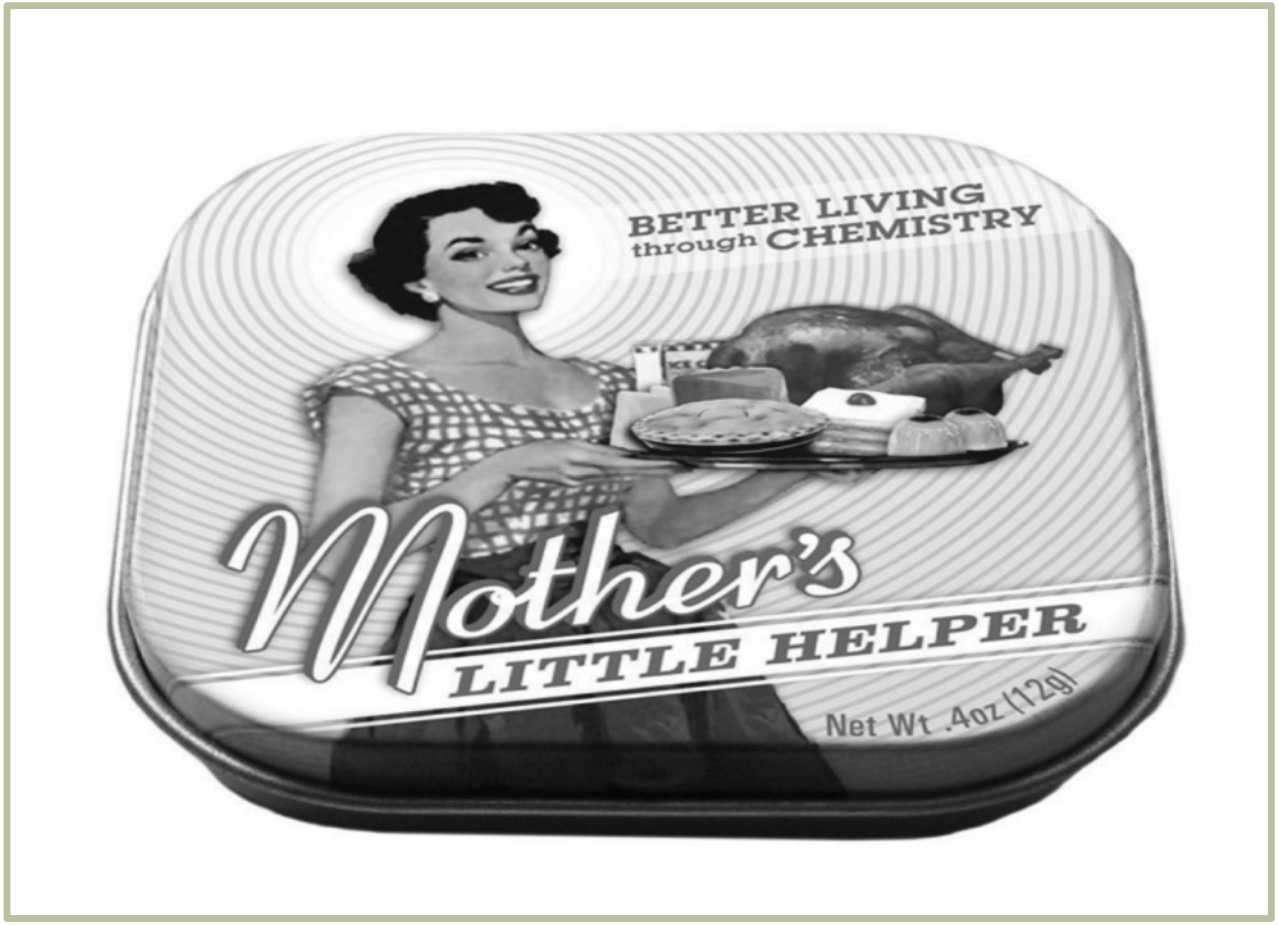
Can stop abruptly:

- Fat stores autotaper
- Depression, amotivation, lethargy, anxiety
- May come out of fog

Early data on treatments:

- NAC
- Nabilone and nabiximols
- Trazodone

Benzodiazepines



Unless High Risk or Impaired…

A pandemic is a poor time to taper a benzo!

If supply chain is unconcern tapering can occur faster than these protocols

Benzodiazepines

- Binds to GABA-BNZ receptors allowing chloride to enter
- Withdrawal criteria same as for alcohol
- Both use and w/d can be life threatening
- W/d may last weeks, occasionally months
  - High dose, long duration, short acting benzos, also high neuroticism, female gender, and mild to moderate alcohol use are all risks for difficult or prolonged w/d
  - Meta-analysis on tapering protocols inconclusive of the best rate – best to engage patients, some promise with substitute therapies

(Parr JM. 2008 and Schweitzer E. 1990)

Benzodiazepine – withdrawal

- Is this the best time to taper? Stabilize?
- Discuss with patients what to expect:
  - Anxiety symptoms – irritability, insomnia, panic attacks, poor concentration
  - Neurological symptoms – ringing in the ears, blurred vision, distorted perception, depersonalization
- Let them know if they get shaky to stop taper
  - Tremor is clearest sign pre-seizure
  - Need to reassess, perhaps take extra dose

Benzo Tapering - Long

- Abrupt cessation of > = diazepam 50 mg/d
  - Risk seizure, psychosis or delirium
  - Consider residential tx if abrupt cessation >80mg
- Home management: Convert to long acting benzo
  - Smooth blood level decreases symptoms
  - Diazepam can be used if young and healthy
  - Beware of daytime sedation, warn about driving
  - Clonazepam may be a good alternative for w/d from alprazolam or triazolam
  - Lorazepam if cirrhosis, elderly or unknown LFTs

Benzo Tapering - Long

- Give 75% in diazepam equivalent and divided q8h
  - Plus breakthrough prn doses of the original benzo
- Reassess in 1-2 days and at 1 week, establish dose
- Taper diazepam by 5-10% q 1-2 weeks
  - No regular breakthroughs
  - If short term use – faster, if long term – slower
  - Can initially drop faster if dose over 50 mg/d
  - Trazodone 50 hs or propranolol 10-20 tid may help decrease prolonged w/d symptoms, and off-label gabapentin may help

Benzo Tapering – Long

- Alternatively you can substitute in the diazepam 25% per week while decreasing the other benzodiazepine, then taper
- Since there may not be perfect cross tolerance some find this more comfortable
- Some find lorazepam more anxiolytic and diazepam more sedating
- Diazepam allows the dose to go lower before discontinuing since comes as 2 mg – can split

Ashton Protocol

- Dr. Heather Ashton from the UK
- Protocol for very slow benzo conversion and taper of diazepam (can apply the same principle to opioid tapering if needed)
- May use for highly sensitive patients
  - Those on for many years
  - Elderly
  - Failed conventional tapering

Benzo Taper - Short

- If the person has been on a short acting benzo for a long time, can taper this
- If highly sensitive/symptomatic, consider compounding the medication in a liquid vehicle as an inpatient:
- E.g. Lorazepam 1 mg/ml - 1 ml hs x 1d
  - 0.9 mg/ml – 1 ml hs x 1 d
  - 0.8 mg/ml – 1 ml hs x 1 d, etc. until off
  - Note – same volume taken each night
  - As an out patient can go slower

Benzo Withdrawal Management

- Some medications have been tried in withdrawal for symptomatic therapy:
  - SSRI for depressive symptoms
  - TCAs, melatonin, trazodone for insomnia
  - Propranolol for severe palpitations, gastric upset
  - ?Muscle relaxants
- No good evidence for this but is clinically relevant in engaging patients in withdrawal
- Novel studies being done with pregabalin, gabapentin, and other anti-epileptics

Off-label Pharmacological assisted benzodiazepine discontinuation

- Gabapentin 100 – 300 mg tid
- Pregabalin 50 – 75 mg qhs – tid

(Dr Mark Weiner, Ann Arbor, Mich., Pain Recovery Solutions)

Effects of pregabalin on subjective sleep disturbance during withdrawal from long term benzodiazepine use

- N = 282
- Pregabalin dose 315 mg/day (mean)
- Decrease in insomnia scores (week 12)

  Pregabalin 55.8 +/- 18.9

  Placebo 25.1 +/- 18.0
- Improvements in anxiety symptoms

(Rubio G et al, Eur Addict, Jun 2011)

Stimulants

Stimulants

- Can stop abruptly
- Cocaine (incl. "crack" and free "base") is a DA, 5HT, & NOR reuptake inhibitor
- Methamphetamine ("crystal meth", "jib"), amphetamine ("speed"), and PCP
  - direct agonists to these receptor sites and have a longer ½ life
- W/d includes 2+: Fatigue, vivid dreams, hypersomnia or insomnia, incr. appetite, psychomotor retardation or agitation
- 3 phase w/d: Crash, dysphoria, extinction

Stimulants, cont.

- Use can be life threatening, w/d is not
- Treatment is largely environmental support
  - Change of scene, rest, eat, calm, no triggers
  - No proven drug tx
- If agitated an atypical antipsychotic can be used
  - Eg Quetiapine 25 mg tid-qid, the dose can be titrated up to effect (caution – lower sz thresh.)
- Avoid benzos
- Generally avoid stimulant substitution

Designer Drugs and Inhalants

- MDMA "Ecstasy"- hallucinogen & stimulant +
  - Intox = bruxism & dry mouth (soother sign), ^HR, hyperthermia (dancing), rhabdomyolysis
  - Or water overload, hyponatremia, brain damage
  - w/d = like cocaine + muscle aches. No Rx.
- GHB – sed/hyp: w/d similar to benzo 3-15d
  - diazepam or phenobarbital to tx (monitor)
- Inhalants – Use dangerous w/d mild, rarely... disorientation, halluc., psychosis, seizures
  - Supportive care (no clear Rx - phenobarb?)

Treatment Options

Q: Which of the following is not considered "treatment" for alcohol dependence?

A) Medically supervised detoxification

B) Alcohol and drug counselors (1:1, group)

C) Residential recovery programs

D) Recovery houses, therapeutic communities

E) Self help groups (AA, Alateen, 16 step, RR)

Additional Resources

- Alcohol and Drug information and Referral Line
  - 24 hour service
  - Lower mainland 604-660-9382
  - BC Province wide 1-800-663-1441
- Inform Line 604-875-6381 or just 211
  - 24 hour service
  - Fraser Health and Vancouver Coastal Health Regions

Resources, cont.

- The Red Book Online
  - www2.vpl.vancouver.bc.ca/DBs/Redbook/htmlpages/home.html
  - Type in key words and pick “entire record”
  - Community, government, social services in LML
- Access Central 1-866-658-1221
  - Detox and addiction housing services for VCH
  - Calls returned same or next day, wait 1-7d
  - Vancouver detox, Cordova detox, Daytox

Resources, cont.

- Alcoholics Anonymous (search your city)
  - www.vancouveraa.ca
- Greater Vancouver Family Services
  - Youth detox, H-Art program, education Series
- Centre for Concurrent Disorders
  - 604- 255-9843
- All CHCs have Alcohol & Drug Counselors
  - Matrix, SMART, 1:1, referrals to residential

Treatment Centres - examples

Publically funded provincial facilities:

- Heartwood Centre: Highest detox, women
- Pacifica: men and women
- Maple Ridge Treatment Centre: M & W
- Peardonville House: takes women & children
- Burnaby Centre: Severe concurrent disorder
- Harbor Light – men – Salvation Army

Numerous private facilities in BC

Resources, cont.

- First Nations Residential Treatment
  - 15 centres, funded by Health Canada
  - Status Indian or spouse, Eg. Round Lake
- Recovery Houses
  - Provide 3-6 months of sober living
  - Varying levels of supported counseling
  - Examples – New Dawn, Turning Point
- Wet, Dry and Damp shelters & housing

Out of Province Resources

- Homewood in Guelph, Ontario
  - Concurrent eating disorder and SUD
  - Health Care professionals
- Bellwood in Toronto, Ontario
  - Sexual addiction +/- SUD
  - Gambling addiction
- For either you must write a letter to MSP in Victoria for special consideration

Online resources

- BCCSU Resources for patients, clinicians, families https://www.bccsu.ca/resources/
- Bounce Back BC – free online skill building for stress, and mild-mod anxiety/depression https://bouncebackbc.ca/
- Yoga with Adriene – free yoga + meditation https://www.youtube.com/user/yogawithadriene
- Beach Body - $99/year – hundreds of workouts https://www.beachbodyondemand.com/plans

Highlights

- Patients with physiologic dependence who need to stabilize or come down or off a substance can be assisted by a variety of approaches:
  - Replacement and/or tapering
  - Symptom management
  - Agonist therapy
  - Antagonist therapy
  - Education and non-pharmacologic options
  - Safety first in the time of COVID-19

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- This site calculates the CIWA – Ar online for you www.mdcalc.com/ciwa-ar-for-alcohol-withdrawal/
- Maldonado JR, et al. The "Prediction of Alcohol Withdrawal Severity Scale" (PAWSS): Systematic literature review and pilot study of a new scale for the prediction of complicated alcohol withdrawal syndrome. Alcohol 48 (2014) 375e390

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Thank you!