OPIOIDS

Pain + OUD: higher tolerance, more pain sensitive. While admitted consider: HM 4-6mg PO q3h +/- HM Contin 6 mg BID

Replacing illicit opioids during admission: higher tolerance, aim to keep pt in hospital, alleviate withdrawal if patient unable to use during admission

Relapse rate 90% at 2 months without OAT

CANCEL OUTPATIENT RX ON ADMISSION

All opioid orders: "Hold if sedated or RR < 10"

Dose equivalents

Hydromorphone 2mg = Oxycodone 5 mg = Morphine 10mg = Codeine 66mg;
MMT: SROM 1:4-8, dose dependent

OPIOID AGONIST THERAPY

METHADONE

Pharmacology

- synthetic, full mu agonist
- $t_{1/2}$=24-36h; 5 days until steady state
- 24-hour dosing is usual for OAT
- For analgesia it's often dosed every 8 hours
- Peak: 3hrs
- Metabolized through Cytochrome p450 into inactive metabolite *hepatic dose adjustment
- Excreted in urine
- No dose adjustment necessary for dialysis/renal impairment

Initiation

No tolerance	10 mg
Risk of sedation (EtOH/BNZ use)	20 mg
Tolerant, no RFs	30mg

RFs: >60 y.o., lung/liver disease, meds that interact with and ↑ methadone

Titration

0-80mg:

No tolerance	5 mg q5d
Risk of sedation (EtOH/BNZ use)	10 mg q3d
Tolerant, no RFs	15mg q3d

>80mg: 5-10mg q5-7d

3 consecutive days prior to dose increase

Missed doses
*MUST CONFIRM LAST DOSE

Wk 1-2 (<50mg)	2 missed	Restart
>50mg	3 missed	↓50%, incr by 10mg/d x 3
	≥4 missed	Restart

Pros

- No max dose
- Easier to initiate
- Health Canada approval for pain
- Full agonist

Cons

- Drug interactions
- QTc prolongation
- ↑ risk OD/resp depression
- Requires DWI initially
- Long titration (consider starting concurrent kadian to alleviate w/d symptoms)

SUBOXONE

Pharmacology

buprenorphine/naloxone

- Semi-synthetic partial mu agonist with high receptor affinity
  - This is why precipitated withdrawal can happen!
- Sublingual tablet, can take 10 min to dissolve
- $t_{1/2}$=24-60h, avg 37h; 5-7 days until steady state
- 24-hour dosing is usual for OAT; can dose q2d
- Peak: 1 hr
- Metabolized through Cytochrome p450 into active metabolite *hepatic dose adjustment
- Excreted in feces
- No dose adjustment necessary for dialysis/renal impairment

Precipitated withdrawal: BUP binds tightly to mu receptors but only partially activates them. If full agonists are occupying mu receptors, BUP will bind more tightly, kicking them off the receptors causing relative opioid deficiency. This causes sudden, severe withdrawal symptoms. Treatment: Give more BUP OR Treat with adjuncts (clonidine, gravol, ibuprofen, imodium)

Traditional Induction

(no opioids at time of first dose)

1. Once COWS > 12 (12h after SA opioids, 24h after LA, 5d after MMT)
2. First dose 2-4mg (can give 6mg if COWS >24)
3. R/a after 60 min,
   1. COWS worse: precipitated w/d
   2. Withdrawal resolved: no further doses on day 1. Give same dose on day 2.
   3. Improved but ongoing w/d: additional 4 mg q1-3h until w/d resolves, to a max of 12mg on day 1
4. Day 2: Give total day 1 dose as consolidated AM dose
5. R/a after 60 min, see step 3 up to max dose 16mg
6. Adjust by 2-4mg daily to effect. Max dose 24mg

Missed doses
*MUST CONFIRM LAST DOSE

≤8 mg	≥6 missed	4 mg, or prev dose, whichever is less
>8mg	6-7 missed	8 mg
	>7 missed	4 mg

Microinduction

(opioids @ time of first dose)

Day 1: 0.5 mg OD
Day 2: 0.5 mg BID
Day 3: 1 mg BID
Day 4: 2 mg BID
Day 5: 3 mg BID
Day 6: 4 mg BID
Day 7: 4 mg TID
Day 8: 12 mg OD (D/C opioids)

Rapid Microinduction

Day 1: 0.5 mg q3h, max 2.5 mg
Day 2: 1 mg q3h, max 8 mg
Day 3: 12mg daily (D/C opioids)

Pros

- More lenient carries
- Less OD/resp depr risk
- Milder S/E
- Easier transition to MMT
- Faster titration

Cons

- ?less treatment retention
- May be suboptimal if high tolerance
- Difficult to reverse BUP ODs

KADIAN/SROM

(slow release oral morphine)

Pharmacology

- Natural full mu agonist, capsule containing beads of coated morphine to slow release; given sprinkled in applesauce
- $t_{1/2}$=11h; 2 days until steady state
- 24-hour dosing is usual for OAT
- Peak: 10 hr
- Hepatic metabolism into active metabolites
- Excreted in urine primarily
- Caution in renal impairment d/t accumulation of metabolites
- 3rd line if failed MMT & suboxone
- Other long acting opioids (HM Contin) have not been studied and are not recommended

Dosing

More guidelines to come
Start: 30-60mg
↑ q 2days (no specified dose)
Max 1200mg

Switch from MMT
Convert MMT: SROM at 1:4
(eg. MMT 60=SROM 240)
↑ q2d (likely will require closer to 1:8-10

Missed doses
*MUST CONFIRM LAST DOSE

Day 2	↓ 40%
Day 3	↓ 60%
Day 4	↓ 80%
Day 5	Restart

Pros

- Vs. MMT:
  - Shorter QTc
  - Reduced cravings

Cons

- Less evidence
- UDS more challenging to interpret

CARRIES

- MMT:
  - 8 weeks on MMT & 1 week neg UDS
  - UDS 1-2x/wk
  - Incr by 1 day/wk qmonthly
- Suboxone:
  - Physician discretion, suggest DWI Mon-Fri with weekend carries x first 2 months, then increase gradually
- Kadian:
  - No formal guidelines in Ontario
  - BC guidelines: should be DWI indefinitely
    - If not, 16 weeks neg UDS & stable SROM dose x 4 weeks

In summary, opioid orders for INPATIENTS with OUD: 1. Some form of OAT (unless declines) 2. Additional opioids to cover for any ongoing illicit use and/or for acute pain

Created by Olivia Brooks, Alex Wilson, Sarah-Maude Rioux Updated: Aug 2020

ALCOHOL

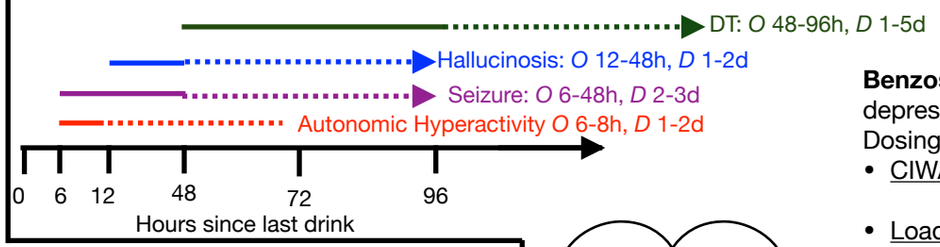
Standard Drinks: 13.6g of EtOH

BEER/COOLER/CIDER	WINE	LIQUOR
12 oz. 5%	5 oz. 12%	1.5 oz. 40%
x 1.5 for tall can	*5 SD/bottle*	*17 SD/ 26oz*
	10 SD/large bottle	

Must ask Q on history: last drink (determines anticipated course/current risks), hx of seizures/DT (load vs. CIWA only), cirrhosis (diazepam vs. Lorazepam)

ALCOHOL WITHDRAWAL SYNDROME

Timeline peak day 2-3



benzos

Treatment

Benzos: first line. Diazepam unless liver dysfn, age >65, risk of resp depression then Ativan (no active metabolites)
Dosing regiments:

- CIWA: symptom triggered; not validated in history of complicated w/d
  - eg. Diazepam 10mg if CIWA 10-20, 20mg if CIWA >20
- Loading: if hx of complicated w/d
  - Diazepam 20mg q1h x 3 or Ativan 4 mg q1h x 3
- Fixed: outpt w/d, inability to monitor pt (eg. Nonmed detox)
  - Diazepam 10mg QID, then 10mg TID, then 10mg BID, then 10mg OD, then d/c

Adjuncts: option to add phenobarbital, valproic acid, carbamazepine, gabapentin *benzo sparing approaches, not proven to reduce seizure risk

Anticraving Medications: see appendix for additional details on evidence for each med

Drug	MoA	Dose *I = initial; 🎯 target*	S/E	Monitoring *(M)*	Contraindications *(CI)*	NNT
Naltrexone	• Opioid antagonist, primarily mu • Reduces the pleasurable effects of EtOH	25mg daily x 3-7 d, then 50 mg daily	• GI: nausea, abdo pain, ↓ appetite, diarrhea • fatigue, headache, dizziness, syncope, arthralgias, myalgias	LFTs @ baseline & 6 wk; discontinue if >3x ULN	Liver dysfunction (balance against risks d/t ongoing drinking; can be used in cirrhosis pt if not in acute liver failure)	• 9 to reduce heavy drinking • No change in continued abstinence
Acamprosate (currently on backorder, Oct 2019)	• not fully understood, ? NDMA (glutamate) antagonist	• initially: 333mg TID x 1 week • therapeutic: 666 mg TID *dose reduction if CrCl 30-50ml/min	• diarrhea	Renal function	CrCl < 30 ml/min	9 to maintain abstinence • No effect on heavy drinking
Gabapentin	• vg Ca++ channels presynaptically, decrease excitatory NT secretion	• Initially 100mg TID • Incr by 300mg/day q 1-2d • Target: 1800mg/day *Renal dose adjustment	• dizziness • fatigue • ataxia	None	None	• 8 to improve abstinence • 5 to reduce heavy drinking

Other meds: Topiramate *i* 50mg/wk, ↑ 50mg/d q1wk, 🎯300mg/d, *S/E* dizziness, cogn. slowing, N/V/D/AP, *M* lytes, RFTs; Disulfiram: 🎯250-500mg/d, *MoA* blocks the oxidation of alcohol at the acetaldehyde stage, *S/E* Drowsiness, Rare but serious: hepatitis, neuropathy, optic neuritis, psychosis, confusion, *M* LFTs, CBC, RFTs, cardiac fn @ baseline, *CI* pregnancy, psychosis, severe CAD, using flagyl or alcohol containing substances (i.e. cough syrup), **Disulfiram rxn:* flushing, N/V, palpitations, CP, hypotension, resp depression, arrhythmia, only evidence in controlled settings; Baclofen: **[Cochrane 2018: ↑drinks/day, ↑ depression]** 5mg TID, 🎯10mg TID *renal adjustment, *MoA* agonist at GABA-B presynaptically, not fully understood, *S/E* headache, drowsiness, confusion, N/V, vertigo, parasthesias, muscle rigidity/spasms

Created by Olivia Brooks, Alex Wilson, Sarah-Maude Rioux Updated: Aug 2020

STIMULANTS

Crystal Meth, Cocaine/Crack

Complications: Cardiac (arrhythmias, MI), psychosis, seizures

Meds: Nothing great atm. Some evidence for topamax, bupropion, dexamphetamine, mixed amphetamine salts in cocaine and mirtazepine for meth in the chemsex population

So there's nothing we can do?! Good evidence for contingency management +/- CBT

Contingency management: patients awarded prizes of increasing value (i.e. Tim Hortons gift card for $2) for each appropriate UDS. The more appropriate UDSs a patient accumulates, the higher the prize value. Relapsed? Decreased prize value with more rapid escalation of prizes.

THC

Harm Reduction:

- Choose lower THC products
- Avoid if personal/family hx of psychosis, if pregnant or breastfeeding, if <16y.o.
- Avoid synthetic cannabinoids/dabbing (concentrated THC extracts)
- Avoid combustable routes of consumption (i.e. vape/edible > smoking)
    - High more intense with edibles; use no more than 2.5 mg THC per edible; high can take 4h to take effect, can last 12-24h
- Avoid deep inhalation/breath holding
- Use occasionally (e.g. max 1 day/week)
- No driving 6h post use

NICOTINE

Pharmacotherapy

1. NRT

- Long acting (patch)
    - 1 cigarette = 1 mg nicotine
    - Pack of cigarettes = 20-25 cig
    - ∴ 1 ppd = 21mg
    - Continue x 6 weeks, then ↓ by 7mg q2weeks
- Short acting (gum, lozenge, inhaler, spray)
- S/E: skin irritation, nightmares (remove patch at night)

2. Varenicline (Champix)

- Partial nicotinic receptor agonist
- Dosing: 0.5 mg OD x 3 days; 0.5 mg BID x 4 days; 1 mg BID x 12 weeks
- Stop smoking 7 days into pills
- S/E: Vivid dreams, insomnia, nausea, marginal incr CVD in pt with heart disease, neuropsyc s/e **disproven**

3. Bupropion (Zyban)

- NDRI
- Dosing: 150 mg OD x 3 days, 150 mg BID x 12 weeks
- S/E: Seizures, headache, anticholinergic, mood changes

E-cigarettes Harm Reduction

- Use Health Canada approved apparatus
- Avoid grazing, smoke at discrete times
- Be mindful of reducing amount smoked
- Reduce concentration of nicotine
- Do not use if do not currently smoke

BENZOS

	Benzo	Dose equivalent	Half life	Peak (PO)	Peak (IV)
	Clonazepam	0.25	34 h	1 hr	—
	Alprazolam	0.5 mg	12 h		—
Oral = IV	Lorazepam	1 mg	15 h		~ 5 min
Oral = IV	Diazepam	5 mg	100 h		
Oral = IV	*Phenobarb*	*15 mg*	*80 h*		

Benzo Taper

1. Switch to long acting benzo (especially if benzo misuse); not great evidence for this, but might make it more comfortable
2. Many approaches (eg. ↓25% q 2 weeks, then↓10% q 2 weeks after 15 mg diazepam)
    1. Warn patients about withdrawal symptoms, reassurance that symptoms are temporary
    2. Discuss risks of long-term benzo use
    3. Hospitalize if >100mg diazepam daily, illicit Benzos

Created by Olivia Brooks, Alex Wilson, Sarah-Maude Rioux Updated: Aug 2020

Substance use consultation

HISTORY

ID

HPI, PMHx, Meds, All, SocHx, FamHx

Substance use history: for all substances:

- Goal for substance use (abstinence, reduction, no change)
- First use, daily use, last use
- Amount used (current, max) $ spent if unable to quantify
- Route (IV, snort, PO, chew, smoke)
- Pattern of use (binge, daily, PM vs. Throughout the day)
- Complications
- Abstinence: last period, longest period
- Previous treatment (pharm, groups, residential tx)

DSM-V criteria for problematic substances

ID/OD RFs see right column

PHYSICAL EXAM

Signs of intoxication/withdrawal

- Pupils
- Skin (diaphoresis, piloerection, track marks)
- Tremor

Signs of complications

- Murmur (IE)…if you have a stethoscope
- Enlarged liver, sequelae chronic liver disease
- Skin ulcerations from cocaine adulterants/ methamphetamine parasitosis

INVESTIGATIONS

- UDS, HIV, Hep B/C, QTc
- Signs of chronic EtOH (↑ MCV, ↓ plat, ↑GGT)

Acronym when taking substance use hx:

Stimulants **T**HC **O**pioids **N**icotine **E**tOH **R**ecreational* **S**edative/hypnotics

Recreational: ketamine, MDMA, inhalants, PCP; Sed/hyp: benzos, barbituates, GHB

ID/OD RF

- Naloxone kit
- Use with others/at safe injection sites
- Recent ODs
- Test dose
- EtOH swabs prior to injecting
- Sharing/reusing needles

Terminology

- “point” = 0.1g
- “eighth”/“eight ball”= 1/8 oz = 3.5g
- “dime bag” /“10 paper”= $10 value
- “smash”= IV use
- “side”/“Tina”/“crystal”=meth
- “up”=cocaine
- “down”=fentanyl

UDS

Immunoassay

- “urine dip”, cheap, quick, available
- False + and -
- Opiates detects: morphine, codeine ONLY
  - Heroin metabolized into morphine
  - Will not detect fentanyl, hydromorphone, etc.
- Morphine is metabolized into hydromorphone, not the other way around
- Most substances detected within 3 d of use
- No false pos cocaine
- Cross reacting agents:
  - Amphetamines d/t bupropion, OTC cold meds, ranitidine
  - Benzos d/t sertraline

Mass Spectrometry

- Specific compounds
- Takes longer, more expensive
- Used to clarify unexpected results

Created by Olivia Brooks, Alex Wilson, Sarah-Maude Rioux Updated: Aug 2020

Drug	MoA	Dose	S/E	Monitoring	Contraindications	Evidence
Naltrexone	-Opioid antagonist, primarily mu -Reduces the pleasurable effects of EtOH	25mg daily x 3-7 d, then 50 mg daily	-GI: nausea, abdo pain, decr appetite, diarrhea -fatigue -headache -dizziness -syncope -arthralgias -myalgias	LFTs @ baseline & 6 wk; discontinue if >3x ULN	Liver dysfunction (balance against risks d/t ongoing drinking; can be used in cirrhosis pt if not in acute liver failure)	• Cochrane (2010): NNT=9 to prevent heavy drinking • Decr heavy drinking (5+ SD for men; 4+ SD for women) Decr drinking days Decr heavy drinking days Decr amount of EtOH No change in continued abstinence • *limited data on IM naltrexone
Acamprosate	-not fully understood -?glutamate antagonist@ NMDA receptor	-initially: 333mg TID x 1 week -therapeutic: 666 mg TID *dose reduction if CrCl 30-50ml/min	-diarrhea	Renal function	CrCl <30 ml/min	• Cochrane (2010): NNT=9 maintaining abstinence • Decr any drinking • Incr abstinence duration • No change on heavy drinking **vs. Naltrexone:** -no difference in sustained abstinence, return to heavy drinking
Gabapentin	-vg Ca++ channels presynaptically, decrease excitatory NT secretion	-Initially 100mg TID -incr by 300mg/day q 1-2d -therapeutic: 1800mg/day -renal dose adjustment	-dizziness -fatigue -ataxia	None	None	• Cochrane (2014), max dose 1500mg: Decr heavy drinking ?Decr amount of EtOH/drinking day No change in abstinence, craving • Mason (2014) 1800mg/d: Incr abstinence (NNT 8) Decr heavy drinking (NNT 5)
Topiramate	-inhib vg Ca++ -enhances GABA-A -antagonizes glutamate	-initially 50 mg/day -incr by 50 mg/wk -doses studied: 150-300mg/d (one study up to 400mg)	-dizziness; parasthesias; anorexia; drowsiness -abdo pain/nausea/diarrhea *teratogenic	Lytes Renal function	None	• Cochrane (2014): Decr amount of EtOH/drinking day Decr heavy drinking No change in abstinence, craving
Valproic Acid	-incr GABA activity -blocks vgNa+ channels	-initial 500mg BID -therapeutic 750mg BID	-headache; anxiety; fatigue -N/V/D -tremor -thrombocytopenia -hepatic failure (greatest in first 6 mo) -pancreatitis (can occur years into use)	LFTs CBC INR/PTT Valproic Acid Level	Liver disease Pregnancy	• Cochrane (2014): Decr amount of EtOH/drinking day No change in abstinence, craving Unclear effect on heavy drinking
Baclofen	-not fully understood -agonist at GABA-B presynaptically	-initial: 5 mg TID -therapeutic: 10 mg TID -renal dose adjustment	-headache; drowsiness; confusion -N/V -vertigo -parasthesias -muscle rigidity/spasms	None	None	• Cochrane (2018): No change abstinence, drinking days, heavy drinking days, craving, anxiety Increases drinks/drinking day Incr depression
Disulfiram	-blocks the oxidation of alcohol at the acetaldehyde stage	-250-500mg/day	-Drowsiness -Rare but serious: hepatitis, neuropathy, optic neuritis, psychosis, confusion	-LFTs (@ baseline and @ 2 weeks) -CBC, lytes, Cr -cardiac function at baseline if appropriate	-psychosis -severe CAD -using flagyl or alcohol containing substances (i.e. cough syrup)	• Kranzler (2018): Incr sustained abstinence in open label trials and in supervised settings