Substance Use Disorders

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01. **Introduction and Psychosocial Interventions**

02. **Nicotine**

03. **Alcohol**

04. **Opioids**

05. **Other substances**

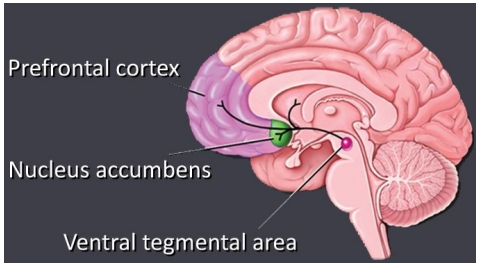
Stimulants, cannabis, etc.

01

INTRO

Addiction Neurobiology

- **Dopaminergic** projections from **ventral tegmental area** to **nucleus accumbens**
  - ***Meso-limbic pathway***



- Substances of abuse directly or indirectly affect the VTA firing
  - Benzodiazepines, alcohol, GHB → via GABA receptors
  - Nicotine → via nicotinic receptors
  - Opioids/opiates → via opioid receptors
  - Stimulants → directly affect dopamine levels
  - Cannabis → via endocannabinoid system
- Glutamate plays key role in mediating cravings

- Addiction risk factors:
  - Heritability 40-60%
  - Demographics – male, adolescents and young adults
  - Early exposure to substances
  - Permissive, high risk environments
  - Mental illness

Substance Use

CCHS 2012:
Lifetime prevalence

- Any SUD: 21.6%
- Alcohol: 18.1%
- Cannabis: 6.8%
- Other: 4.0 %

Table 1: Top five substances used in the past year by Canadians (2017)

	#1	#2	#3	#4	#5
General Population (15+)	Alcohol (78.2%)	Cannabis (14.8%)	Cocaine/Crack (2.5%)†	Hallucinogens and Salvia (1.5%)	Problematic Prescription Drugs (1.2%)†
Youth (15–19)	Alcohol (56.8%)	Cannabis (19.4%)	Hallucinogens and Salvia (2.8%)	Problematic Prescription Drugs (2.1%)†	Ecstasy (1.6%)† Cocaine/Crack (1.6%)†
Young Adults (20–24)	Alcohol (83.5%)	Cannabis (33.2%)	Cocaine/Crack (6.2%)	Hallucinogens and Salvia (5.1%)	Problematic Prescription Drugs (3.6%)†
Adults (25+)	Alcohol (79.4 %)	Cannabis (12.7%)	Cocaine/Crack (2.2%)†	Number suppressed	Number suppressed

Source: CTADS 2017[11]
Note: Figures identified with a cross (†) should be interpreted with caution because of the small sample size.

Concurrent disorders → <u>common</u>

- MDD, bipolar disorder, anxiety disorders , PTSD → lifetime prevalence 40-60%
- SCZ, ADHD, eating disorders, personality disorders

Substance Use Disorder – DSM-5 Criteria

Substance use, leading to significant impairment or distress, as evident by 2+ sx over 12-month period:

Impaired Control

- Takes the substance in larger amounts or over a longer period than originally intended
- Persistent desire to cut down use and/or multiple unsuccessful efforts to decrease use
- Great deal of time obtaining/using/recovering from substance
- Cravings

Social Impairment

- Failure to fulfill major role obligations at work, school, or home
- Persistent or recurrent social or interpersonal problems
- Important social, occupational, or recreational activities are given up or reduced

Risky use

- Recurrent substance use in situations in which it is physically hazardous
- Continues use despite physical or psychological problems

Pharmacological criteria

- Tolerance
- Withdrawal

Remission specifiers:

- In early remission
- In sustained remission

In a controlled environment

Severity specifiers:

- Mild (2-3 sx)
- Moderate (4-5 sx)
- Severe (6+ sx)

Substance-Induced Mental Disorder – DSM-5 Criteria

A. Clinically significant symptomatic presentation of relevant mental disorder
B. Evidence from history, physical exam, or lab investigations that:
    - Disorder developed during or within 1 month of substance intoxication/withdrawal
    - Substance is capable of producing the mental disorder
C. Not better explained by independent mental disorder, as evidenced by:
    - Disorder preceded onset of substance intoxication/withdrawal
    - Full mental disorder persists for at least 1 month after cessation of acute withdrawal or severe intoxication
D. Not during delirium
E. Clinically significant distress or impairment

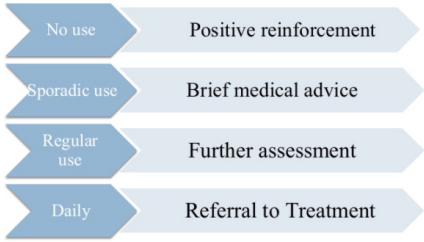
Clues to a primary mental disorder

- FMH of the primary mental disorder
- Age of onset
- Specific signs/symptoms e.g. flashbacks for PTSD, agoraphobia
- Severity, comorbidities
- Treatment response

Approach to Addiction Care - SBIRT

- Evidence-based

- **S**creening – validated tools to identify risk
  - CAGE
  - AUDIT (Alcohol Use Disorder Identification Test)
  - DAST-10 (Drug Abuse Screening Test – for all substances except ETOH)
  - ASSIST (Alcohol, Smoking and Substance Involvement Screening Test)



- **B**rief **I**nterventions – 5-15 minutes – "FRAMES"
  - Applicable to sporadic and regular substance users
  - May utilize Motivational Interviewing techniques

Table 2. Components of Brief Interventions (FRAMES)

Feedback is given to the individual about risk or impairment
Responsibility for change is placed on the participant
Advice to change is given by the clinician
Menu of alternative self-help or treatment options is offered to the participant
Empathic style is used by the counselor
Self-efficacy or optimistic empowerment is engendered in the participant

- **R**eferral to **T**reatment
  - Acute Care → detox, stabilize, engage in rehab
  - Rehabilitation → sustain abstinence, encourage self-management skills, relapse prevention
  - After care → monitor and support abstinence, relapse prevention

Evidence-based Psychosocial Interventions

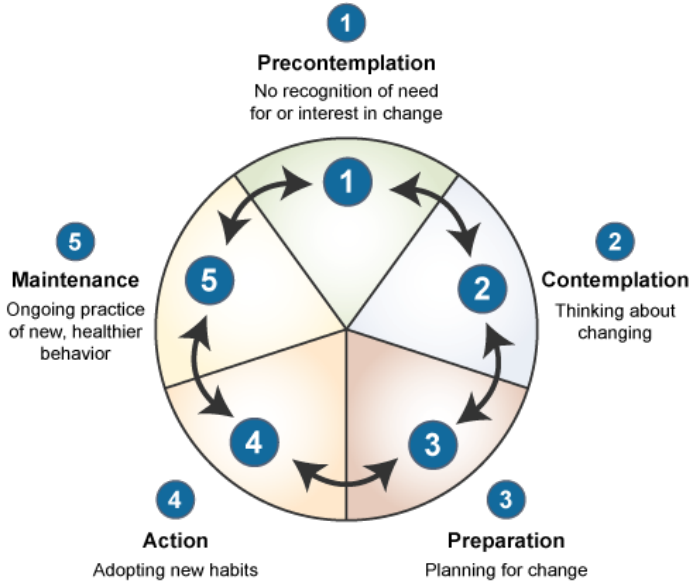
- Transtheoretical Model → determine stage of change → match therapy

Pre- and Contemplation

- Brief advice (aka BI)
- Supportive therapy
- Motivational interviewing

Preparation, Action, and **Maintenance**

- Same as above, plus
- CBT – relapse prevention
- Contingency Management
- 12-Step Facilitation (AA, NA)



Psychosocial Interventions

Brief Advice

- Direct advice about health problems, risk of use and suggestion to cut down/quit

Supportive Therapy

- Promote patient comfort and therapeutic alliance
- Identify key issues and problem solve
- Connect relationship problems with substance use

Motivational Interviewing

- Goal-oriented, patient-centered
- Explore and resolve ambivalence to elicit behaviour change
- Non-judgemental, non-confrontational

Spirit – **PACE**

Skills - **OARS**

O	***Open-ended*** questions that allow patients to give more information including their feelings, attitudes and understanding.
A	***Affirmations*** to help overcome self-sabotaging or negative thoughts.
R	***Reflections*** as a way to express ambivalence.
S	***Summarize*** to let your patient know that they are being heard.

Psychosocial Interventions

12-Step Facilitation/AA/NA

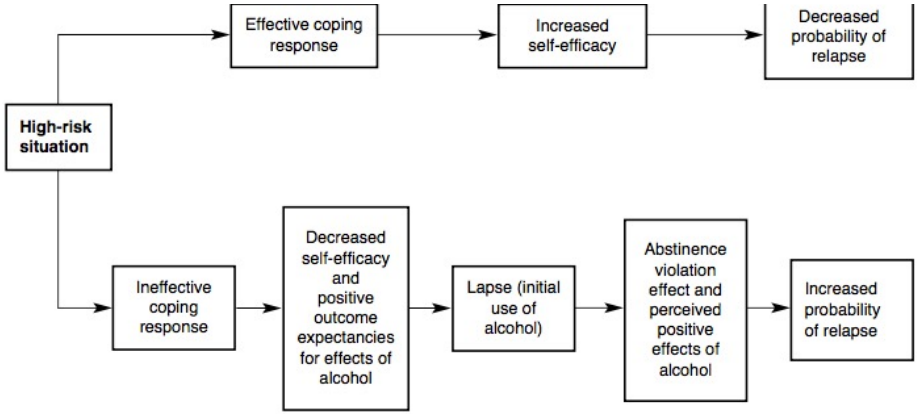
- Acceptance of addiction, lack of control, and need for abstinence
- Surrender control and have faith in higher power
- Themes of spirituality & pragmatism

Contingency Management

- ID target behaviour (measurable & meaningful – i.e. negative UDS)
- Provision of concrete reinforcement (e.g. $, goods, privileges) contingent upon producing the target behaviour

CBT-RP

- Identify learned/habitual patterns linking thoughts, feeling, behaviours & contexts to use
- Unlearning of above patterns by developing coping skills (i.e avoiding high-risk situations)



02

NICOTINE

Nicotine Use

- Nicotine binds to α4β2 nicotine receptors in the VTA → increase dopamine

- Smoking - decreasing prevalence with time
- Remains leading cause of death in Western nations

- Combination of **psychosocial + pharmacotherapy treatments** should be offered to every smoker interested in quitting
  - Psychosocial interventions:
    - Support every quit attempt
    - Strong dose-response relationship between session length and successful treatment, however short interventions (1-3min) are effective
    - Counseling by variety of formats (self-help, individual group, helpline, web-based)
  - Pharmacological treatment can increase quit success by 2-3x

Tobacco-Related Disorders (DSM-5)

- **Tobacco Use Disorder**

- **Tobacco Withdrawal**
  A. Daily tobacco use, for several weeks
  B. Abrupt cessation/reduction → withdrawal sx within 24 hours (4+ sx):
     1. Irritability, anger, frustration
     2. Depressed mood
     3. Anxiety
     4. Restlessness
     5. Concentration difficulties
     6. Insomnia
     7. Increased appetite
  C. Significant distress or impairment
  D. Not better explained by AMC, AMD, another substance

Nicotine Replacement Therapy

- Nicotine-containing products → reduce cravings and withdrawal symptoms
- Dose: 1 mg = 1 cigarette (approximate)
  - Titrate to effect
- Products:
  - Short-acting = gum, inhaler, lozenge, spray
  - Long-acting = patch (multiples of 7 mg)
- Side effects:
  - Vivid dreams
  - Local reaction
  - Cardiovascular effects

Bupropion SR (Zyban)

- Mechanism of action: Norepinephrine-Dopamine reuptake inhibitor
  - Stimulant effect → reduce cravings
  - Maintain DA and NE → reduce withdrawal symptoms
  - Antagonist effects at nicotinic receptors

- Dose: 150 mg OD x 3 days, 150 mg BID x 7-12 weeks
  - Start 1 week BEFORE quit date

- Side effects:
  - Anxiety, insomnia, dry mouth, dizziness
  - Cardiovascular effects (HTN)
- Contraindications: lowers seizure threshold
  - Avoid if seizure hx, eating disorder, ETOH/benzo withdrawal
  - Caution if bipolar disorder (risk of mania)

Varenicline (Champix)

- Mechanism of action: partial α4β2 nicotinic ACh receptor agonist
  - Release of dopamine → reduces cravings and withdrawal
  - Blocks reinforcing effects of nicotine from cigarettes
- Dose: 0.5 mg PO OD x 3d, 0.5mg BID x 4d, then 1mg BID for 12 weeks
  - Start 1 week BEFORE quit date

- Side effects:
  - Nausea, vivid dreams, insomnia
  - Cardiovascular effects (HTN)
- Neuropsychiatric risk:
  - 2008 – US FDA and Health Canada issued black box warning for varenicline regarding neuropsychiatric events (depression, suicidality)
  - Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) – 2016
    - No significant increase in serious neuropsychiatric events attributable to bupropion or varenicline compared with placebo for both groups
    - **Black box warning removed in 2016**

Comparison of pharmacotherapies

Pharmacological interventions for smoking cessation: an overview and network meta-analysis (Review)

Cahill K, Stevens S, Perera R, Lancaster T

THE COCHRANE COLLABORATION®

Figure. Odds Ratios for Smoking Abstinence of 6 Months or More

Comparison (Intervention vs Control)	No. of Studies	Total No. of Individuals	Absolute Quit Rates: Intervention n/N (%)	Absolute Quit Rates: Control n/N (%)	Odds Ratio (95% Credible Interval)
NRT vs placebo	119	51 225	4704/27 258 (17.3)	2464/23 967 (10.3)	1.84 (1.71-1.99)
Bupropion vs placebo	36	11 440	1214/6409 (18.9)	535/5031 (10.6)	1.82 (1.60-2.06)
Varenicline vs placebo	15	6293	964/3496 (27.6)	332/2797 (11.9)	2.88 (2.40-3.47)
Bupropion vs NRT	8	2581	191/954 (20.0)	375/1627 (23.0)	0.99 (0.86-1.13)
Varenicline vs NRT	0	0	NA	NA	1.57 (1.29-1.91)
Varenicline vs bupropion	3	1622	174/823 (21.1)	111/799 (13.9)	1.59 (1.29-1.96)

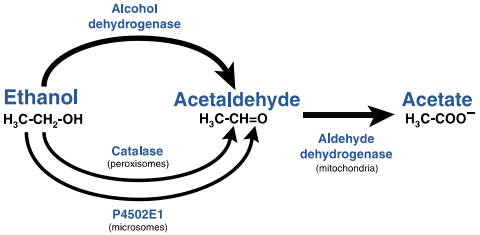
- NRT, bupropion, varenicline all superior to placebo
- Bupropion and NRT equal efficacy
- Varenicline superior to bupropion and NRT

03

ALCOHOL

Alcohol

- Precise mechanism not fully understood
  - No specific binding sites
  - Impacts ligand-gated ion channels to mediate CNS effects
- Functionally:
  - Enhances GABA-A receptor
  - Inhibits NMDA receptor
  - Interacts with serotonin, dopamine and opioid receptors
- Low-risk drinking guidelines
  - Women: ≤ 2/day and ≤ 10/week; Men ≤ 3/day and ≤ 15/week; +1 for special occasions



- Metabolism: zero-order
  - Approximately 3.3 mmol/L/hour or 15 mg/100mL/hour
  - Women have higher BAC (vs. men) due to less body water and lower ALDH in stomach
- Biomarkers: CDT (most sp/sn but less available), GGT (most sn and available)
  - AST/ALT (>2), MCV (macrocytic)
  - EtG (direct, detectable in urine x 72 hrs)

Alcohol-Related Disorders (DSM-5)

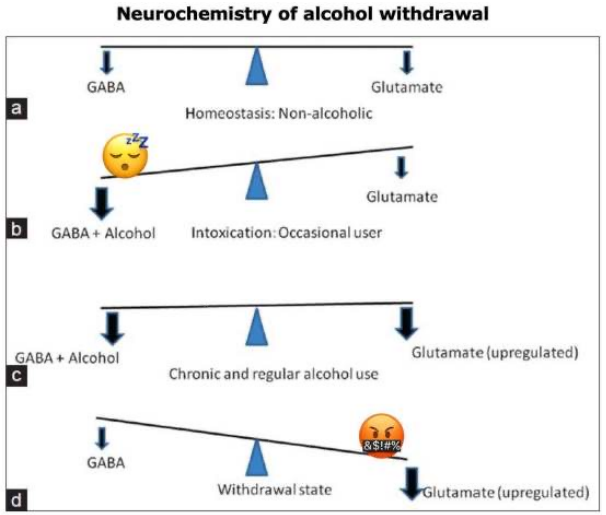
- **Alcohol Use Disorder**

- **Alcohol intoxication**
  - A. Recent alcohol ingestion
  - B. Problematic behavioural or psychological changes that develop during/shortly after ingestion
  - C. Signs or symptoms (1+):
    1. Slurred speech
    2. Incoordination
    3. Unsteady gait
    4. Nystagmus
    5. Attention/memory impairment
    6. Stupor/coma
  - D. Not better explained by AMC, AMD, another substance

- **Alcohol withdrawal**
  - A. Cessation/reduction in heavy and prolonged ETOH use
  - B. Withdrawal sx hours-days after reduction (2+ sx):
    1. Autonomic hyperactivity
    2. Incr hand tremor
    3. Insomnia
    4. Nausea/vomiting
    5. Transient hallucinations/illusions (visual, auditory, tactile)
    6. Psychomotor agitation
    7. Anxiety
    8. Generalized tonic-clonic seizures
  - C. Significant distress or impairment
  - D. Not better explained by AMC, AMD, another substance
  - ○ Specify if: with perceptual disturbances

Alcohol Withdrawal - Physiology

- Chronic use → **GABA** > Glutamate
  - GABA-r downregulated
  - NMDA-r upregulated
- Discontinue/decrease use
  - Relative activity **Glutamate** > GABA
  - Excess excitation
- Kindling phenomenon
  - Increasing severity of withdrawal symptoms (i.e. seizure threshold decreases with successive seizures)
  - Development of benzodiazepine-resistant alcohol withdrawal
  - Due to permanent dysregulation of GABA

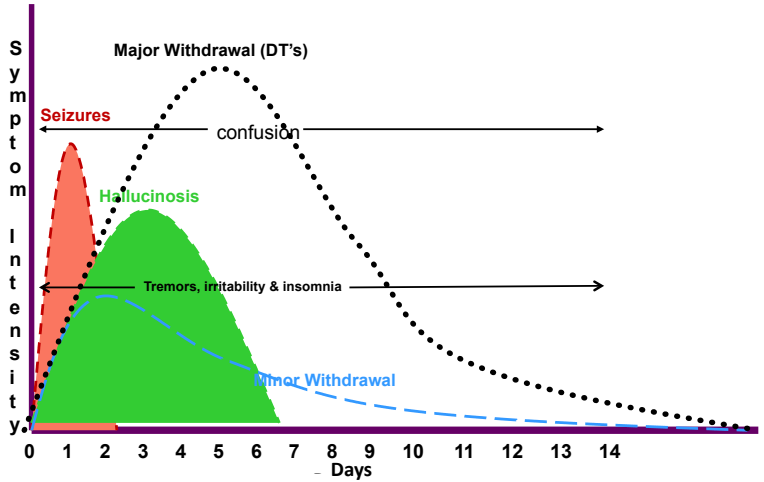


Alcohol withdrawal involves *deficient* GABA activity and *excessive* glutamate activity. Benzodiazepines augment GABA activity, but this is only part of the problem. Phenobarbital augments GABA activity and *also* inhibits glutamate signaling (via the AMPA-type glutamate receptor).

Kattimani S 2013 PMID 25013309

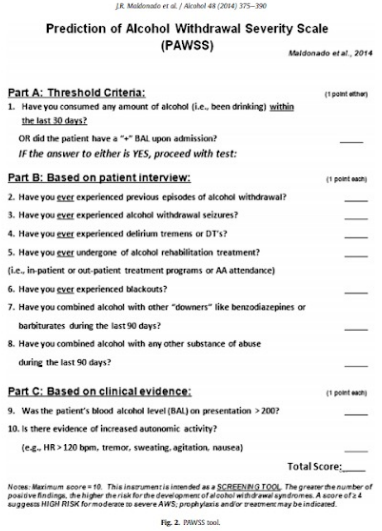
Alcohol Withdrawal - Presentation

- Typically peaks at 24-48 hours
- Resolves within 7-10 days
- Early/minor withdrawal
  - Usually within 6-48 hrs
  - Tremor, anxiety, GI upset, headache
- Withdrawal seizures
  - Usually within 12-24 hrs
  - Tonic-clonic, progresses to DTs in 1/3 of cases
  - Affects 10% of patients in ETOH withdrawal
- Alcoholic hallucinosis
  - Usually within 12-48 hrs
  - Transient, benign, intact sensorium, typically visual or tactile
  - Affects 25% of patients in ETOH withdrawal
- Delirium tremens
  - Up to 10-14 days, usually within 2-3 days
  - Autonomic hyperactivity (hyperthermia, tachycardia, HTN, diaphoresis)
  - Impaired LOC, psychotic symptoms
  - Affects 5% of patients in ETOH withdrawal → mortality 5%



Alcohol Withdrawal - Management

- Detection and risk stratification
  - Prediction of Alcohol Withdrawal Severity Scale (**PAWSS**)
    - 10 item scale to help determine risk of complicated withdrawal
    - **3 or less** - low risk, outpatient management
    - **4 or more -** higher risk, consider inpatient setting
  - Clinical Institute Withdrawal Assessment-Alcohol Revised (**CIWA-Ar**)
    - < 10 = mild
    - 10-20 = moderate
    - > 20 = severe
    - Repeat q1h until score < 8



J.R. Maldonado et al. / Alcohol 48 (2014) 375–390

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al., 2014

Part A: Threshold Criteria: (1 point either)

1. Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? ____
   OR did the patient have a "+" BAL upon admission? ____
   IF the answer to either is YES, proceed with test:

Part B: Based on patient interview: (1 point each)

2. Have you ever experienced previous episodes of alcohol withdrawal? ____
3. Have you ever experienced alcohol withdrawal seizures? ____
4. Have you ever experienced delirium tremens or DT's? ____
5. Have you ever undergone of alcohol rehabilitation treatment? (i.e., in-patient or out-patient treatment programs or AA attendance) ____
6. Have you ever experienced blackouts? ____
7. Have you combined alcohol with other "downers" like benzodiazepines or barbiturates during the last 90 days? ____
8. Have you combined alcohol with any other substance of abuse during the last 90 days? ____

Part C: Based on clinical evidence: (1 point each)

9. Was the patient's blood alcohol level (BAL) on presentation > 200? ____
10. Is there evidence of increased autonomic activity? (e.g., HR > 120 bpm, tremor, sweating, agitation, nausea) ____

Total Score: ____

Notes: Maximum score = 10. This instrument is intended as a SCREENING TOOL. The greater the number of positive findings, the higher the risk for the development of alcohol withdrawal syndromes. A score of ≥ 4 suggests HIGH RISK for moderate to severe AWS; prophylaxis and/or treatment may be indicated.

Fig. 2. PAWSS tool.

Table 2 Clinical Institute Withdrawal Assessment for Alcohol—revised (CIWA-Ar) scale

Clinical Institute Withdrawal Assessment for Alcohol revised	
Symptoms	**Range of scores**
Nausea or vomiting	0 (no nausea, no vomiting): 7 (constant nausea and/or vomiting)
Tremor	0 (no tremor): 7 (severe tremors, even with arms not extended)
Paroxysmal sweats	0 (no sweat visible): 7 (drenching sweats)
Anxiety	0 (no anxiety, at ease): 7 (acute panic states)
Agitation	0 (normal activity): 7 (constantly thrashes about)
Tactile disturbances	0 (none): 7 (continuous hallucinations)
Auditory disturbances	0 (not present): 7 (continuous hallucinations)
Visual disturbances	0 (not present): 7 (continuous hallucinations)
Headache	0 (not present): 7 (extremely severe)
Orientation/clouding of sensorium	0 (orientated, can do serial additions): 4 (disorientated for place and/or person)

Modified from Sullivan et al. [36]

Alcohol Withdrawal - Management

- Benzodiazepines
  - Consider loading dose(s) if history of complicated withdrawal
  - Symptom-triggered, based on CIWA score
  - Diazepam 10-20mg or Lorazepam 2-4 mg PO/SL/IM Q1H PRN (until score < 10)
    - Lorazepam if liver impairment, elderly, respiratory depression
    - Consider chlordiazepoxide if long-acting benzodiazepine needed
  - Barbiturates/propofol used in critical care in cases of Delirium Tremens

- Supportive measures and adjunctive medications
  - IV fluids, electrolyte replacement, multivitamin
  - Thiamine 300-500 mg PO/IM/IV daily x 3-5 days if lower risk, medically well
  - Thiamine 500mg IM/IV TID x 3-5 d → 250mg daily x 3-5 d → 100 mg od
    - If high risk of Wernicke's encephalopathy
  - Gabapentin 300-600 mg PO TID
    - Benzo-sparing, for mild withdrawal, and to transition to relapse prevention
  - Clonidine 0.1 – 0.2 mg PO BID to QID
    - Symptomatic relief for noradrenergic symptoms

Relapse Prevention Medications

Health Canada approved:

- Naltrexone
- Acamprosate
- Disulfiram

*note: APA guidelines(2018) recommend:

- Naltrexone (1B)
- Acamprosate (1B)
- Disulfiram (2C)
- Topiramate (2C)
- Gabapentin (2C)

Off-label:

- Topiramate
- Gabapentin
- Pregabalin
- Baclofen

Naltrexone

- Mechanism of action: Opioid receptor antagonist
  - Attenuates euphoric effects of alcohol
- NNT 12 (heavy drinking), NNT 20 (abstinence)
- Dose: 25 mg po daily x 3-4 days, then 50 mg po daily
  - Vivitrol - IM formulation (q4 weeks) available in the US
- Side effects:
  - GI upset (nausea/vomiting), sedation, headache, sleep disruption
- Contraindications:
  - Opioid agonist therapy
  - Liver impairment – avoid if liver enzymes > 3x upper limit of normal

Acamprosate

- Mechanism of action: Not well-understood
  - Modulates glutamate transmission and decreases NMDA-receptor binding
- NNT 12 (abstinence)
- Dose: 666 mg po TID (333 mg po TID if renal disease or wt < 60kg)
  - Best to start after ETOH discontinued for a few days
- Side effects:
  - GI upset (diarrhea - quite common), sleep disturbance
- Contraindications:
  - Severe renal disease

Disulfiram

- Indicated for **abstinence** only – ideally administration is supervised
- Mechanism of action: Aldehyde dehydrogenase INHIBITOR
  - Results in Acetaldehyde accumulation → flushing, palpitations, tachycardia, hypotension
  - Can be fatal in cases of cardiac collapse
- Dose: 125 – 500 mg po daily
  - Start > 48 hours after last ETOH ingestion
  - Resume ETOH > 14 days after medication stopped
- Side effects:
  - Sedation, neuropathy, hepatotoxicity
- Contraindications:
  - Cardiovascular disease, liver disease

Gabapentin and Pregabalin

- Mechanism of action: α2δ ligand (of calcium channel)
  - → inhibit calcium release → less CNS excitation and increased GABA transmission
  - Reduces withdrawal symptoms and cravings
  - Also used in seizure disorders and neuropathic pain

- Gabapentin - NNT 5 (heavy drinking) and NNT 8 (abstinence)
  - Dose: 100 mg TID or 30 mg QHS PO → increase by 300 mg every few days to 300-600 mg TID
  - Side effects: sedation, dizziness, GI upset, peripheral edema
  - Caution: Renal impairment

- Pregabalin
  - Dose: 75 – 150 mg po BID
  - Side effects: sedation, dizziness, dry mouth, peripheral edema
  - Contraindications: Severe renal impairment

Topiramate

- Anticonvulsant
- May reduce heavy drinking

- Mechanism of action: glutamate antagonist, GABA agonist

- Dose:
  - 25 mg po BID → increase by 25 mg daily → target 100 – 150 mg po daily
- Side effects:
  - Paresthesia, cognitive dulling
  - Weight loss
  - Risk of kidney stones
- Contraindications:
  - Pregnancy

Baclofen

- Muscle relaxant

- Mechanism of action: GABA-B receptor agonist

- Dose:
  - 5 – 15 mg po TID-QID
- Side effects:
  - Sedation
- Contraindications:
  - Pregnancy

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- Pregabalin
  - Dose: 75 – 150 mg po BID
  - Side effects: sedation, dizziness, dry mouth, peripheral edema
  - Contraindications: Severe renal impairment

04

OPIOIDS

Opioid-Related Disorders (DSM-5)

- **Opioid Use Disorder**

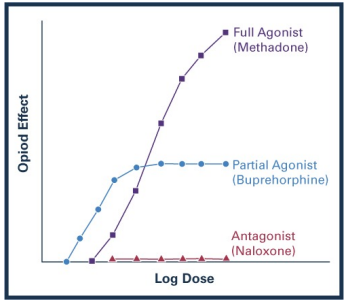
- **Opioid intoxication**
  - A. Recent opioid use
  - B. Problematic behavioural or psychological changes that develop during/shortly after ingestion
    - Euphoria/dysphoria, agitation/retardation, impaired judgement
  - C. Pupillary constriction and 1+ of the following:
    1. Drowsiness or coma
    2. Slurred speech
    3. Impaired attention/memory
  - D. Not better explained by AMC, AMD, another substance
  - Specify if: with perceptual disturbances

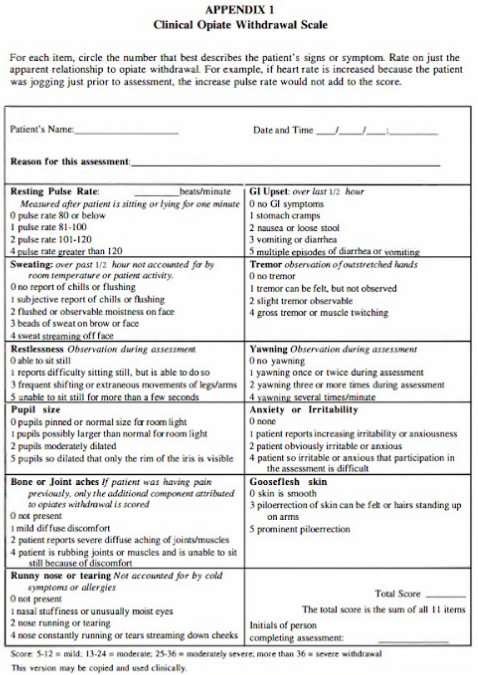
- **Opioid withdrawal**
  - A. Either cessation/reduction in heavy and prolonged use OR administration of opioid antagonist
  - B. Withdrawal sns/sx (3+):
    1. Dysphoric mood
    2. Insomnia
    3. Yawning
    4. Nausea/vomiting
    5. Diarrhea
    6. Lacrimation, rhinorrhea
    7. Pupil dilation, piloerection, sweating
    8. Fever
    9. Muscle aches
  - C. Significant distress or impairment
  - D. Not better explained by AMC, AMD, another substance

Opioid Use Disorder - Management

- Withdrawal management
  - Clinical Opioids Withdrawal Scale (**COWS**) – quantify severity
  - Opioid agonist
  - Clonidine 0.1 – 0.2 mg po Q4h for symptomatic treatment of hyperadrenergic symptoms
  - HIGH relapse rate and overdose risk if not transitioned to OAT after detox

- Opioid Agonist Therapy (OAT)
  - Methadone
  - Buprenorphine/naloxone
  - *SROM (sustained release oral morphine)*
  - *Injectable OAT*
- Abstinence
  - Naltrexone





APPENDIX 1
Clinical Opiate Withdrawal Scale

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.

Patient's Name:_____ Date and Time ___/___/___:_____

Reason for this assessment:_____

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 1/2 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 1/2 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 or 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 piloerrection of skin can be felt or hairs standing up on arms 5 prominent piloerrection
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 Initials of person completing assessment: _____

Score: 5-12 = mild; 13-24 = moderate; 25-36 = moderately severe; more than 36 = severe withdrawal

This version may be copied and used clinically.

Buprenorphine/Naloxone

- Mechanism of action: Partial mu-opioid receptor agonist
  - Long half-life – 24-48 hrs
  - Has a ceiling effect → <u>safer</u>
  - Naloxone only activates with IV use
- Dose: Classic (based on COWS score) vs. micro-dosing (off-label)

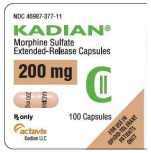
D/C opioids for 24+ hours **Day 1:** Check that COWS >12 Give 4 mg → Reassess 30-60 min later • If no withdrawal - done day 1 • If withdrawal sx - give 2 mg q1-2h until withdrawal sx better • Max 12 mg on day 1 **Day 2:** Start at day 1 dose • If withdrawal sx give 2-4mg q2-3h for max of 16 mg Up-titrate by 2-4 mg daily to target of 16-24 mg daily	Day 1: 0.25 mg SL daily Day 2: 0.25 mg SL BID Day 3: 0.5 mg SL BID Day 4: 1 mg SL BID Day 5: 2 mg SL BID Day 6: 4 mg SL BID Day 7: 12 mg SL daily

- Side effects: Sedation, cognitive dulling, constipation, sexual dysfunction
- Caution: Precipitated withdrawal; difficult to manage acute pain

Methadone

- Mechanism of action: Full mu-opioid receptor agonist
  - Long half-life – 15-55 hrs (variable)
  - Dose peaks at 3 hrs; steady state at 3-5 days
- Dose: 30 mg po daily → increase by 10-15 mg po q3-5 days (at most)
  - Target dose 80-120 mg daily (some patients need higher doses)
  - Missed doses require adjustment due to loss of tolerance
    - 1-2 days – no change to dose
    - 3-4 days – restart at 50% or 30 mg (whichever is highest)
    - 5+ days – back to starting dose (30mg)
  - Doses are much LOWER for chronic pain
- Side effects: Sedation, cognitive dulling, constipation, sexual dysfunction
- Caution:
  - QTc prolongation – risk of torsades-de-pointes
  - Extensive metabolism by CYP3A4 – careful with drug interactions
  - Risk of overdose and diversion – often requires daily witnessed doses

SROM



- 3rd line (BCCSU guidelines)
- 24 hr formulation
- Inadequate withdrawal suppression or intolerance to methadone/suboxone
- Dose: 30-60 mg on day 1
  - Increase q48 hrs depending in withdrawal sx Use 1:4 conversion if switching from MMT
- Limitations:
  - Chewing or crushing pellets can release entire content as bolus dose
  - Diversion risk (must be DWI)
  - Short half-life, missed doses can lead to quick loss of tolerance

iOAT

- Diacetylmorphine, hydromorphone
- Severe and/or refractory OUD
- Have not benefitted from PO OAT or are severe risk of overdose death
- *Refer to BCCSU guidelines for details*

05
Other substances

Cannabis
Stimulants
Hallucinogens

Cannabis

- Cannabinoids → diverse chemical compounds acting on cannabinoid receptors
  - CB1 receptors – primarily located in CNS (especially hippocampus, cerebellum)
  - CB2 receptors – primarily in the immune system
- 2 major compounds
  - Delta-9-tetrahydrocannabinol (THC) – psychoactive → psychosis, euphoria, addiction
  - Cannabidiol (CBD) – therapeutic effects
- Preparations
  - Marijuana, hashish, hash oil, joint, water pipe, vaporizers
- Onset of action
  - Inhalation: peak 10-30 mins, decreases 2-4h
  - Edibles: delayed onset, longer duration

Cannabis-Related Disorders (DSM-5)

- **Cannabis Use Disorder**

- **Cannabis intoxication**
  - A. Recent cannabis use
  - B. Problematic behavioural or psychological changes that develop during/shortly after ingestion
    - Motor incoordination, euphoria, anxiety, impaired judgement, social withdrawal
  - C. 2+ of the following:
    1. Conjunctival injection
    2. Increased appetite
    3. Dry mouth
    4. Tachycardia
  - D. Not better explained by AMC, AMD, another substance
  - Specify if: with perceptual disturbances

- **Cannabis withdrawal**
  - A. Either cessation/reduction in heavy and prolonged use
  - B. Withdrawal sns/sx within 1 week(3+):
    1. Irritability, anger, aggression
    2. Anxiety
    3. Restlessness
    4. Depressed mood
    5. Sleep difficulty
    6. Decreased appetite/weight loss
    7. Physical sx – i.e. abdo pain, tremor, sweating fever, chills, headache
  - C. Significant distress or impairment
  - D. Not better explained by AMC, AMD, another substance

Cannabis Use Disorder - Treatment

- Psychosocial interventions
  - CBT
  - Motivational interviewing
  - Contingency management

- Pharmacotherapy – off label
  - Cannabinoid agonists – i.e. nabilone → decrease withdrawal
  - Gabapentin
  - N-acetylcysteine (adolescents only) → increased abstinence

Cannabis – Patient Counselling Points

Canada's Lower-Risk Cannabis Use Guidelines (LRCUG)

Recommendations

- Cannabis use has health risks best avoided by abstaining
- Delay taking up cannabis use until later in life
- Identify and choose lower-risk cannabis products
- Don't use synthetic cannabinoids
- Avoid smoking burnt cannabis—choose safer ways of using
- If you smoke cannabis, avoid harmful smoking practices
- Limit and reduce how often you use cannabis
- Don't use and drive, or operate other machinery
- Avoid cannabis use altogether if you are at risk for mental health problems or are pregnant
- Avoid combining these risks

- *Therapeutic benefit* in MS, pediatric epilepsy, chronic neuropathic pain, chemo-induced n/v and HIV-associated weight loss
- Cannabis use disorder develops in 1/6 adolescents and 1/10 adults who *ever use*
- Can **destabilize** schizophrenia and bipolar disorder
- Regular use → may develop psychosis 2.7 years earlier
  - Associated with impaired memory, learning, and IQ

Stimulants

- Cocaine (DA, NE, 5HT reuptake inhibition)
  - Coca leaves → heated in solvent
    - Base (“crack”, smoked) and salt (“powder”, IN, IV)
  - Duration of action 20-30 minutes
  - Primary urinary metabolite us **benzoylecgonine** (BEG) → detectable up to ~48h
  - Cocaine + alcohol → *cocaethylene* (liver) → has independent stimulant and euphoric effects

- Amphetamines (DA, NE, 5HT reuptake inhibition; direct DA release via VMAT)
  - Synthetic, crystallized methamphetamine
  - Duration of action 8-24 hours

- Others
  - Khat (Catha edulis)
  - Bath salts (synthetic cathinones)

Stimulant-Related Disorders (DSM-5)

- **Stimulant Use Disorder**

- **Stimulant intoxication**
  - A. Recent stimulant use
  - B. Problematic behavioural or psychological changes
    - ■ Euphoria, affect blunting, sociability, hypervigilance, anxiety, stereotypies
  - C. 2+ of the following:
    1. HR changes
    2. BP changes
    3. Pupil dilation
    4. Sweats or chills
    5. Nausea or vomiting
    6. Weight loss
    7. Psychomotor agitation/retardation
    8. Muscle weak, resp depression, CP, arrhythmias
    9. Confusion, seizures, dyskinesias, dystonia
  - D. Not better explained by AMC, AMD, another substance
  - ○ Specify the stimulant, and if with perceptual disturbances

- **Stimulant withdrawal**
  - A. Cessation/reduction in heavy and prolonged use
  - B. Dysphoric mood and 2+:
    1. Fatigue
    2. Vivid unpleasant dreams
    3. In/hypersomnia
    4. Increased appetite
    5. Psychomotor agitation/retardation
  - C. Significant distress or impairment
  - D. Not better explained by AMC, AMD, another substance
  - ○ Specify the stimulant

Stimulant-Related Disorders - Treatment

- Intoxication
  - Supportive – reassurance, quiet environment, consider benzodiazepines PRN
  - If HTN → alpha-adrenergic blocker (avoid beta-blockers due to unopposed alpha stimulation)
- Withdrawal
  - Supportive
- Use disorder
  - Psychosocial interventions – contingency management, CBT
  - Pharmacological – off label
    - Cocaine
      - Bupropion 300 mg daily
      - Topiramate 200-300 mg daily
      - Prescription stimulants, i.e. Methylphenidate
    - Amphetamine
      - Bupropion 300 mg daily
      - Mirtazapine 30 mg daily
      - Naltrexone

Other Substances

- Caffeine (intoxication and withdrawal)
- Hallucinogens (no withdrawal disorder)
  - PCP – “angel dust”
    - Dissociative; associated with nystagmus, hypertension, and violent behaviour
  - Ketamine – emerging evidence in treatment-resistant depression
  - MDMA – evidence of withdrawal (due to serotonin depletion)
  - LSD, psilocybin
- Inhalants
  - Includes volatile hydrocarbons, nitrous oxide, amyl nitrites
  - ”Huffing,” “poppers”
  - Seen most commonly in adolescents, aboriginal communities
  - Widespread CNS effects, including dementia
- Sedative, hypnotic or anxiolytic
  - Includes benzodiazepines, z-drugs, barbiturates, **GHB**
  - Similar intoxication and withdrawal to alcohol

Resources

Smoking

- www.quitnow.ca
- www.smokershelpline.ca
- VGH Smoking Cessation Clinic

Harm Reduction

- Safe injection/consumption sites
  - Insite (Vancouver)
  - SafePoint, Quibble Creek (Surrey)
- Overdose prevention sites
- Take-home naloxone kits

- Alcohol and Drug info/referral service
  - 1 800 663 1441
- HealthLinkBC (811)

References:

DSM 5
BCCSU guidelines
APA substance use disorder guidelines

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