Canadian Society of Internal Medicine

Annual Meeting 2017

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Update in Addiction Medicine

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CSIM Annual Meeting 2017

The following presentation represents the views of the speaker at the time of the presentation. This information is meant for educational purposes, and should not replace other sources of information or your medical judgment.

Learning Objectives:

1. Advise patients of the effectiveness and risks of buprenorphine and methadone in the treatment of opioid use disorder
2. Develop a process for providing safe transitions for patients on buprenorphine or methadone
3. Select an appropriate pharmacologic agent for treating alcohol use disorder

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Conflict Disclosures

I have no conflicts to declare

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Some of the drugs, devices, or treatment modalities Mentioned in this presentation are:

Buprenorphine/naloxone, methadone
Naltrexone, gabapentin, acamprosate
Baclofen, ondansetron, topiramate

I intend to make off-label therapeutic recommendations for medications

Scope of Hospital-based OAST

- Survey
- Development of the SMH addiction team

Case 1

30 yo woman with IV hydromorphone addiction presents with pneumonia requiring IV antibiotics and supplemental O2.

She uses hydromorphone 8 mg IV q3h, bought on the street. She complains of vague chest pain over the area of the pneumonia. She is requesting IV hydromorphone 8 mg q3h for the chest pain. She suggests she will have to get it somehow, to prevent withdrawal and ongoing pain, etc.

What do you recommend?

Case 2

50 yo man with opioid use disorder in remission x 3 years on methadone 75 mg daily. Admitted with ankle fracture requiring ORIF after sports injury.

What would you advise re pain control?

Case 2b

50 yo man with opioid use disorder in remission x 3 years on methadone 75 mg daily. Admitted with ankle fracture requiring ORIF after sports injury.

What would you advise re pain control?

What if the patient had not taken methadone x 4 days and was in withdrawal?

Case 3

Which OAST agent would you recommend for a 25 yo using po hydromorphone x 6 months and why?

Pharmacologic Treatment Options for Opioid Use Disorder in Canada

- Buprenorphine 2008
- Methadone 1963

Methadone

- Synthetic and full agonist
- Slow:
  - Absorption
  - Metabolism
  - Elimination
- T1/2 -24 h
- 1963

Methadone

Advantages

- Abstinence rates 70-80%
- Less OD death
- Blocks craving and euphoria
- Reduction in HIV HCV
- Crime violence
- Employment school
- Moms keep babies
- Psychological status

Disadvantages

- Access
- STIGMA
- Slow titration-weeks
- Take-home policy
- Severe WD decreases ability to wean
- OD risk
- Long-term effects

Methadone take-home policy

- No carries for first 2 months
- 1 per week for each month of abstinence thereafter

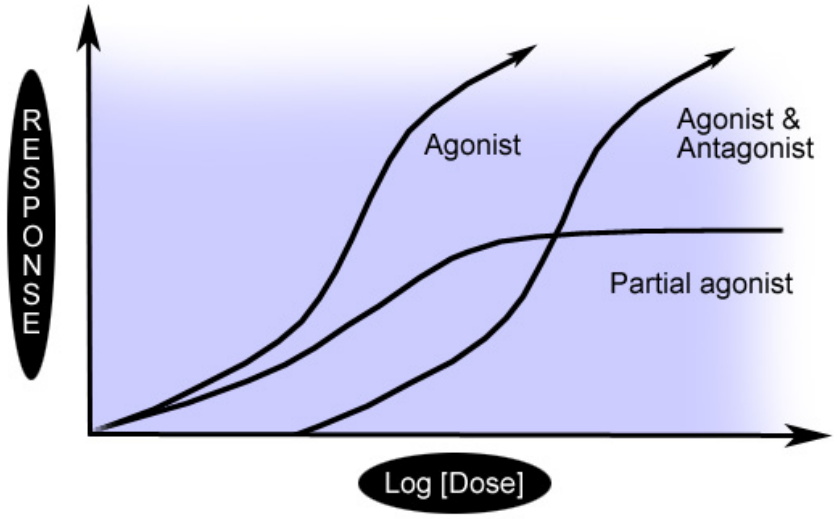
Methadone long-term

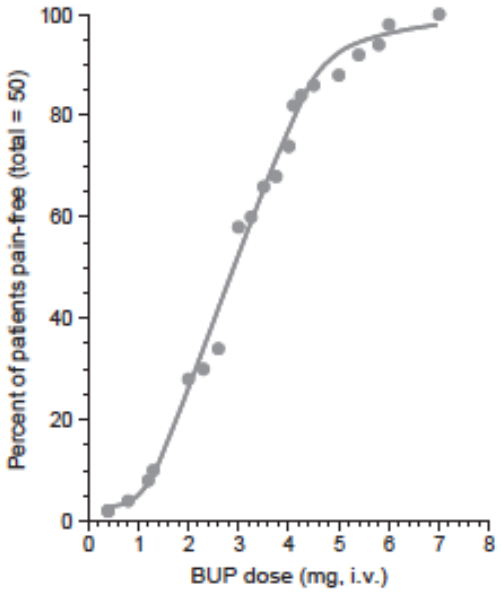
- Fracture risk and osteoporosis
- Oral health
- Weight gain?
- ED
- Sleep disturbance

Buprenorphine

- Buprenorphine AND naloxone 4:1
- Naloxone is active intravenously only
- Buprenorphine alone: restricted
- SL for addiction
- Partial mu agonist with slow rate of dissociation
- T1/2 -37h

Respiratory and Analgesic Effects





Buprenorphine

- Very high affinity for mu receptor
- Displaces other opioids from receptors
  - (8mg = 4mh hydromorphone)
- Less potent

= Precipitated withdrawal

Buprenorphine

Advantages

- Abstinence rates same*
- ACCESSIBLE
- Less stigma
- Safer: lower OD risk/benzo use
- Easier to taper/WD
- Rapid titration

Disadvantages

- Precipitated withdrawal
  - (may not be required with patch protocol)
- Efficacy in some high dose IV heroin users?

***Cochrane Database of Systematic Reviews**
9 MAY 2016 DOI: 10.1002/14651858.CD011117.pub2
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011117.pub2/full#CD011117-fig-00101

Buprenorphine

- Minimum moderate opiate withdrawal to begin induction
  - Use objective scale (e.g. COWS > 13)
- Initial dose of 2-4mg sl
- Reassess patient in 1 hour for precipitated withdrawal
- Prescribe take home dose as carry 4mg

Buprenorphine

- Titrate dose upwards to maintenance dose
  - Optimal maintenance dose:
    - No withdrawal symptoms for 24 hrs
    - No intoxication, sedation
    - Minimal side-effects
    - Significant improvement in cravings.
    - Cessation of opiate use (negative UDS)
    - No euphoria from opiate use

- Average maintenance dose is 8-12 mg, max is 24mg.

Maintenance dose can often be reached in 2-4 days

Take home doses

Health Canada recommends no more than weekend and holiday carries in the first two months of buprenorphine use

But there is no evidence to support this

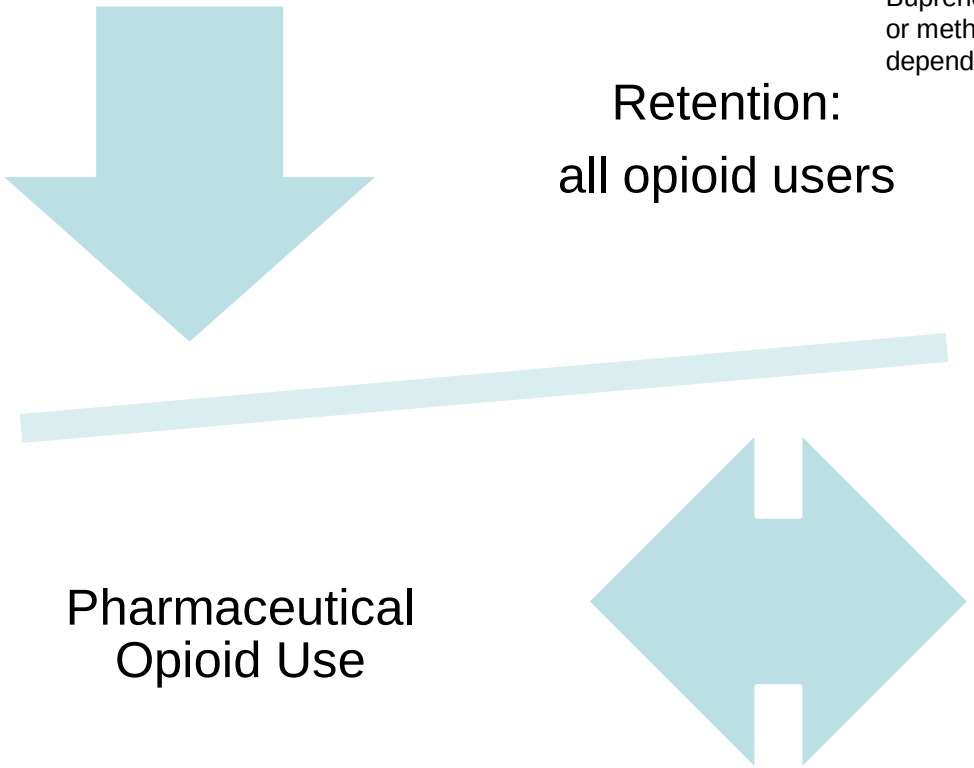
Take home doses

Individual Risk Assessment:

1. Unstable patients (SI, psychosis, cognitive symptoms, ongoing drug use, comorbid substance use, unstable housing) not to receive early take home doses
2. Clinically stable (absence of unstable features above) – could receive weekend and holiday take home in the first 2 months
3. More clinically stable (working, particularly stable social situation, no psychiatric symptoms) can get more carries than just weekends and holidays in the first 2 months, but carries still to be increased gradually.

Choice of Suboxone over Methadone

Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database 2014



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Choice of Suboxone over Methadone Patient Factors

1. High Risk For Methadone Toxicity:
   - Prolonged QTc
   - Elderly Patients
   - Medication that interfere with methadone metabolism
   - Sedative/Hypnotic or Alcohol Dependence
   - Respiratory Illness (e.g. COPD)
   - Milder Opiate Addiction (e.g. codeine, less than daily opioid use)
   - History of Methadone Abuse
2. Patients with good prognosis who may be able to taper off opioid agonist treatment after 6-12 months
   1. As buprenorphine may be easier to discontinue than methadone
3. Adolescents or Young Adult Patients
4. Patients who may need early carries

Buprenorphine is drug of choice especially if:

- High risk for methadone toxicity
- Young age
- Need early carries
- Good prognosis: short use and taper in <12 months

Additional Factors to Consider

- Pain control:

  Methadone: q8h

  – problematic for carries and titration

  Buprenorphine OD (for some q8h)

  – Based on complete or comparable pain relief, buprenorphine had full clinical analgesic efficacy in 25/26 of studies Raffa 2014

  – Less hyperalgesic effect

Goals of Methadone Treatment in Hospital

On Admission:

1. **Inform community pharmacist and MD of admission**
2. Obtain hx: dose, recent dose change, carries
3. Confirmation from pharmacy re last dose, compliance, prescriber
4. Recent substance use hx
5. Medications
6. Medical history
7. Safety –SI/HI/childcare/driving

Advocate for good pain control

Risk factors for methadone toxicity

- Loss of tolerance
- Organ failure
- Concurrent prescribing of benzodiazepines
- Changes in meds that inhibit or promote C-P450 system

Proactively adjust doses and measure response

Methadone if NPO

- Can give methadone in water
  - (clear OJ OK preop)
- NG methadone ok, can't be given IV
- Alternative - give small doses of short-acting opioid eg morphine 5-10 mg IV q3h PRN

Discharging In-patients on Methadone

- Contact community prescriber and pharmacist in advance to:
  - Avoid bridging or duplicate prescriptions
  - Discuss need to retrieve or alter carries
  - Advise of medical/psychiatric illnesses which may impact Rx
  - Discuss dose changes
  - Advise of and fax prescriptions for opioids

Peri-operative Buprenorphine

- Usually continue pre- and post-op
  - May need dose reduction
  - Rarely need to stop (re-induce, withdrawal?)
- Need higher doses of usual periop opioids
- May be able to titrate for chronic pain but not acute postop pain

Advocate Advocate Advocate

Case 1

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Case 3

Which OAST agent would you recommend for a 25 yo using po hydromorphone x 6 months and why?

Case 4

A 40 yo man presents with alcohol withdrawal. He drinks 26 oz of liquor per day. He has never been to a treatment centre and AA was “not for him”. He wants help to reduce his drinking.

What are your options?

Target Intervention to Stage of Change

Pre-contemplative	Contemplative	Action	Maintenance
SBIRT	Motivational Enhancement	Residential Treatment AA Medications Case management Day programs	Relapse prevention

The paradox

- >20000 patients studies
- High quality trials
- NNT and RRR comparable to other drugs
- Covered by ODB with EAP
- Work best with concomitant psychosocial interventions
- Treatment rate 10%
  - Hasin DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2007;64(7):830-842.

Seven medications you should know for treating alcohol use disorder:

- Naltrexone
- Gabapentin
- Acamprosate
- Topiramate
- Baclofen
- Ondansetron
- Disulfiram

Naltrexone:

- Opioid antagonist
- Anti-craving
- “Drug of choice”

Naltrexone:

- Indications
  - Commit to psychosocial program “weekly counseling”
  - Ok to be actively drinking
  - Reduces amount of alcohol consumed

Naltrexone:

- Contraindications:
  - Require opioids for pain or addiction etc
  - Liver disease
    - Cirrhosis
    - Transaminases (liver enzymes) > 3 times normal

Naltrexone:

- Start at 25 mg per day x 4 days then increase to 50 mg per day
- Covered by ODB with EAP approval (2 days-2 weeks delay)
- About $300/month if no coverage

naltrexone

Any drinking	Reduces heavy drinking and cravings	Cautions
NNT=20	NNT=12	Nausea, sleepiness, liver dysfunction and concomitant opioid use

Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, Kim MM, Shanahan E, Gass CE, Rowe CJ, Garbutt JC. Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient SettingsA Systematic Review and Meta-analysis. JAMA. 2014;311(18):1889–1900. doi:10.1001/jama.2014.3628

Naltrexone Depot

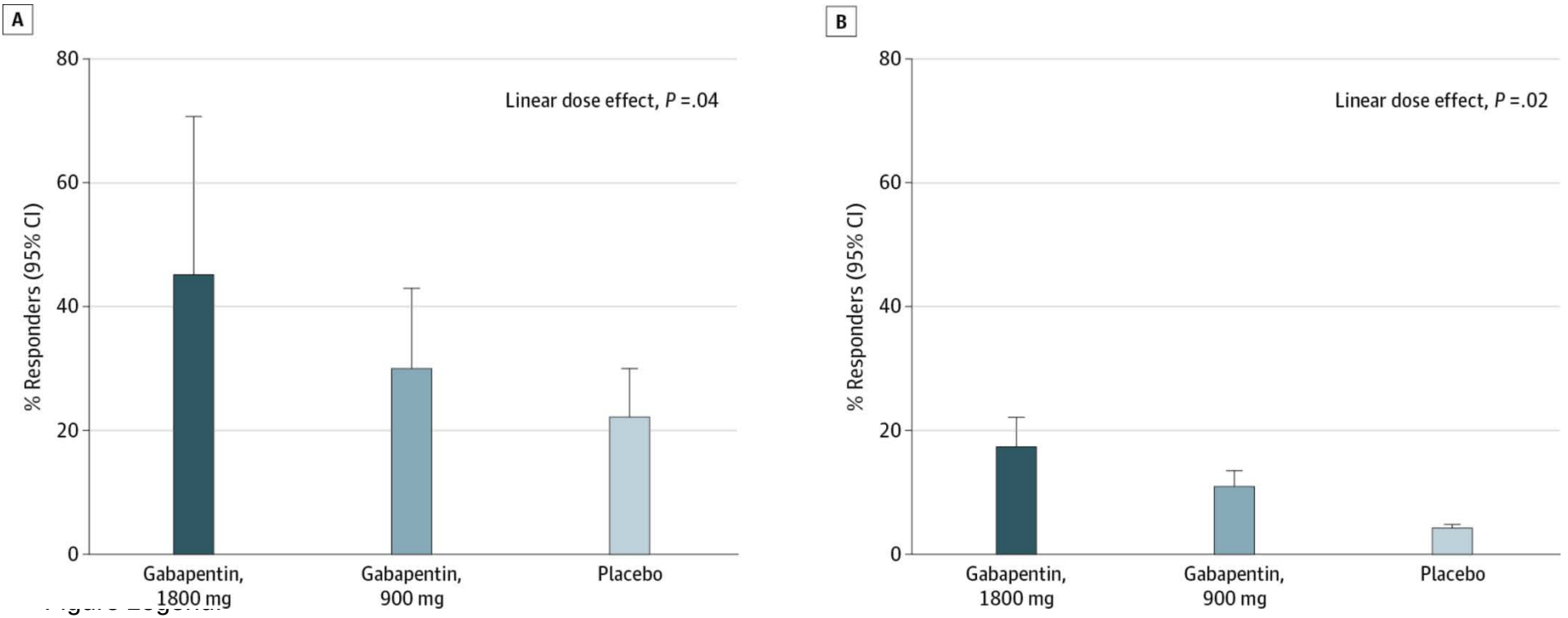
- Better outcomes

Gabapentin

- 300 mg hs start dose and increase by 300 mg per day, up to 900 mg (300 mg TID) or 1800 mg (600 mg poTID)
- 3 days abstinence
- 12 weeks data

From: **Gabapentin Treatment for Alcohol DependenceA Randomized Clinical Trial**

JAMA Intern Med. 2014;174(1):70-77. doi:10.1001/jamainternmed.2013.11950



Gabapentin Effects on Rates of No Heavy Drinking and Complete Abstinence During the 12-Week Study in the Intention-to-Treat Population A, No heavy drinking; B, complete abstinence. Error bars indicate 95% confidence intervals (N = 150).

Pharmacotherapy of Alcohol Use Disorders

Gabapentin		
S/E	Maintains abstinence	Reduces Heavy Drinking
Insomnia, drowsiness	NNT 8	NNT 5

Acamprosate:

- Mechanism: Increases GABA neurotransmission
- “Relapse prevention”, 4 days of abstinence prior to start
- Second line on ODB, naltrexone first or justify
- Discord in data

acamprosate

Maintains abstinence	Reduces heavy drinking	Cautions
NNT 12	No effect	Renal clearance and GI S/E

Jonas DE, Amick HR, Feltner C, Bobashev G, Thomas K, Wines R, Kim MM, Shanahan E, Gass CE, Rowe CJ, Garbutt JC. Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient SettingsA Systematic Review and Meta-analysis. JAMA. 2014;311(18):1889–1900. doi:10.1001/jama.2014.3628

COMBINE 2006*

Naltrexone effective

Acamprosate not effective

But European data: acamprosate effective**

*Anton RF, O'Malley SS, Ciraulo DA, et al; COMBINE Study Research Group. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA*. 2006;295(17):2003-2017.

**Donoghue, K., Elzerbi, C., Saunders, R., Whittington, C., Pilling, S., and Drummond, C. (2015), The efficacy of acamprosate and naltrexone in the treatment of alcohol dependence, Europe versus the rest of the world: a meta-analysis. Addiction, 110, 920–930. doi: 10.1111/add.12875.

Topiramate

- Glutamate antagonists & GABA agonists
- Doses up to 300 mg total
  - Start 25 mg PO BID (or qhs if concerned)
  - Titrate weekly by 25 mg PO BID as tolerated
- Limited by cognitive effects

Johnson BA, Rosenthal N, Capece JA, et al.; Topiramate for Alcoholism Advisory Board; Topiramate for Alcoholism Study Group. Topiramate for treating alcohol dependence: a randomized controlled trial. JAMA. 2007;298(14):1641–1651.

Likhitsathian S, Uttawichai K, Booncharoen H, Wittayanookulluk A, Angkurawaranon C, Srisurapanont M. Topiramate treatment for alcoholic outpatients recently receiving residential treatment programs: a 12-week, randomized, placebo-controlled trial. Drug Alcohol Depend. 2013;133(2):440–446.

Baclofen

- Mechanism of action: GABA-B receptor agonist
- Has psychoactive properties and hence street value, dependence etc
- Start 5 mg TID and titrate up by 5 mg TID – can use as high as 80 mg total daily dose

Baclofen

Conflicting and small RCTs

80% Renal clearance: patients with liver disease twice as likely to stop

Agabio R, Preti A, Gessa GL. Efficacy and tolerability of baclofen in substance use disorders: a systematic review. European Addiction Research 2013;19(6):325-45.

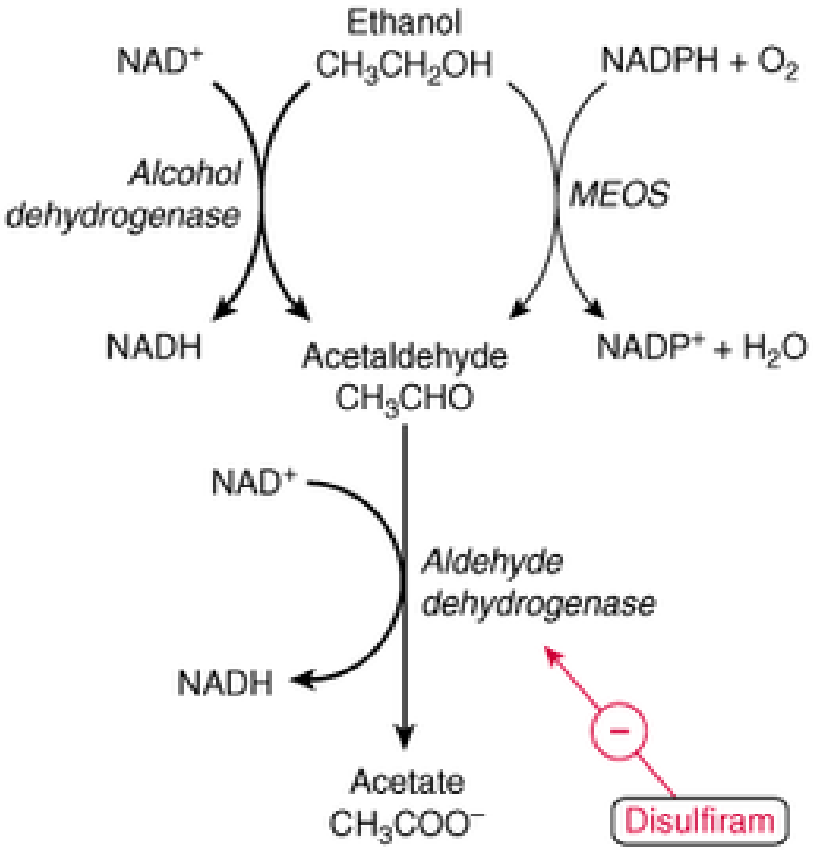
Ondansetron

Promising: small sample size, short-term data

Corrêa Filho JM, Baltieri DA. A pilot study of full-dose ondansetron to treat heavy-drinking men withdrawing from alcohol in Brazil. Addict Behav. 2013;38(4):2044–2051.

Disulfiram

- Prevents breakdown of ethanol into acetate
- Acetalaldehyde is toxic
- Leads to:
  - Flushing
  - Tachycardia
  - Tachypnea
  - Nausea and vomiting
  - Headache



Disulfiram

- Don’t use it
- Contraindicated in elderly/CAD
- Not manufactured in Canada but compounded
- “insurance policy” or buffer for those in recovery and are stable
  - Professionals eg pilots

Case 4

A 40 yo man presents with alcohol withdrawal. He drinks 26 oz of liquor per day. He has never been to a treatment centre and AA was “not for him”. He wants help to reduce his drinking.

What are your options?

Treat Addiction

Save Lives