YOUR HOST: DISCLOSURE

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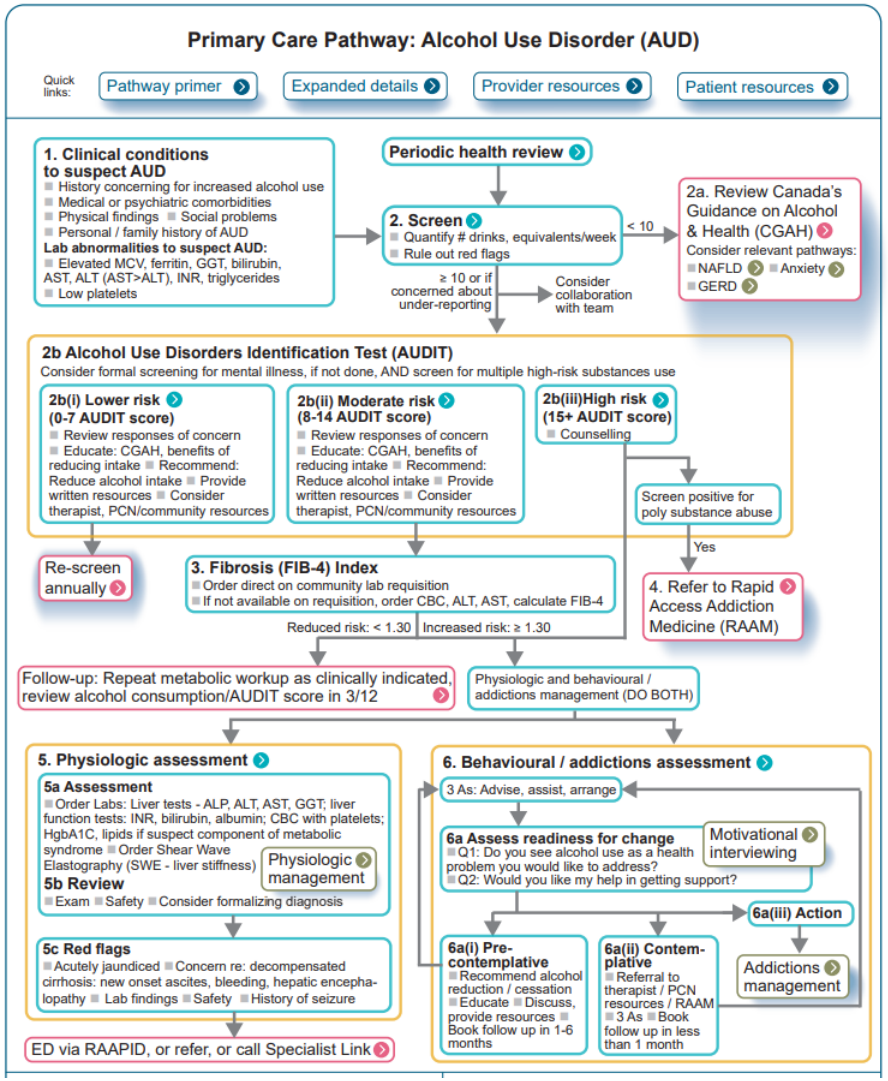
Disclosures

- Co-Medical Lead, AHS Rapid Access Addiction Medicine Program

AUD: PHARMACOTHERAPY

Alcohol use disorder pathway



Drug	Dose	Cautions and contraindications	Common side effects	Other notes
Naltrexone	50mg daily	Liver impairment (caution) Acute hepatitis, liver failure, concomitant opioid use (contraindications)	Drowsiness, nausea, insomnia, dizziness	Liver function testing required
Acamprosate	666mg tid	Renal impairment (dose reduction CrCl 30-50ml/min; contraindicated at CrCL<30ml/min)	Diarrhea (wanes over time), nausea	Requires special authorization in Alberta Drug Special Authorization Request
Disulfiram	125-500mg qd	Caution with concurrent diabetes, hypothyroidism, seizure disorders, nephritis, hepatic insufficiency or cirrhosis. Contraindications: concurrent alcohol or metronidazole intake, severe myocardial disease, coronary occlusion, active psychosis	Drowsiness, fatigue, metallic after taste, dermatitis. Rare hepatotoxicity.	Not currently available in Canada except through specialty compounding. Pt must abstain from alcohol at least 12 hours prior to the first dose. Disulfiram reaction can occur with alcohol intake up to 2 weeks after the last dose Liver function testing and CBC need to be monitored
Gabapentin	300-600mg tid	Renal impairment requires dose adjustment.	Dizziness, drowsiness, ataxia, peripheral edema, cognitive changes (especially in the elderly)	Diversion or misuse has been rarely reported
Topiramate	25-150mg bid (start at 25-50mg daily with	Renal disease (caution), history of kidney stones (contraindication), metabolic acidosis (contraindication)	Cognitive dysfunction, taste disturbance, anorexia, paresthesia, dizziness, renal stones	

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Original Investigation

Pharmacotherapy for Adults With Alcohol Use Disorders in Outpatient Settings

A Systematic Review and Meta-analysis

Daniel E. Jonas, MD, MPH; Halle R. Amick, MSPH; Cynthia Feltner, MD, MPH; Georgiy Bobashev, PhD; Kathleen Thomas, PhD; Roberta Wines, MPH; Mimi M. Kim, PhD; Ellen Shanahan, MA; C. Elizabeth Gass, MPH; Cassandra J. Rowe, BA; James C. Garbutt, MD

CONCLUSIONS AND RELEVANCE Both acamprosate and oral naltrexone were associated with reduction in return to drinking. When directly compared with one another, no significant differences were found between acamprosate and naltrexone for controlling alcohol consumption. Factors such as dosing frequency, potential adverse events, and availability of treatments may guide medication choice.

JAMA. 2014;311(18):1889-1900. doi:10.1001/jama.2014.3628

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Medications

- Anti craving medication is considered by some as the new standard of care. Consider for all patients with alcohol use disorder immediately post detox. Efficacy requires counseling and/or frequent physician monitoring.
- Underutilized
  - <1/3 of those with AUD receive treatment[1] and <10% with AUD receive pharmacotherapy[2]
  - Should be considered for all patients with moderate or severe alcohol use disorder[2,3,4,5,6] who:
    - Have current, heavy use and ongoing risk for consequences[4]
    - Motivated to reduce intake[4]
    - Prefer medication along with (ideally) or instead of psychological intervention[4]
    - Have no medical contraindications[4]
- Modeling study estimated that if 40% of all individuals with alcohol {use disorder mod-severe} received pharmacotherapy, there would be a 13% reduction in alcohol-attributable mortality in the European Union[1]

[1] Hasin D, Stinson F, Ogburn E, Grant B. 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. ArchGen Psychiatry. 2007;64(7):830-842.
[2] Jonas D, Amick H, Feltner C, Bobashev G, Thomas K, Wines R et al. Pharmacology for adults with alcohol use disorder in outpatient settings: a systematic review and meta-analysis. JAMA. 2014; 311(18):1889-1900.
[3] Spithoff S, Kahan M. Primary care management of alcohol use disorder and at-risk drinking. Can Fam Physician. 2015;61:515-521.
[4] Uptodate. Pharmacotherapy for alcohol use disorder. 2015.
[5] Jorgensen C, Pedersen B, Tonnesen H. The efficacy of disulfiram for the treatment of alcohol use disorder. Alcohol Clin Exp Res. 2011;35(10):1749-1758.
[6] Substance Abuse and Mental Health Services Administration and National Institute on Alcohol Abuse and Alcoholism. Medication for the treatment of alcohol use disorder: a brief guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2015.

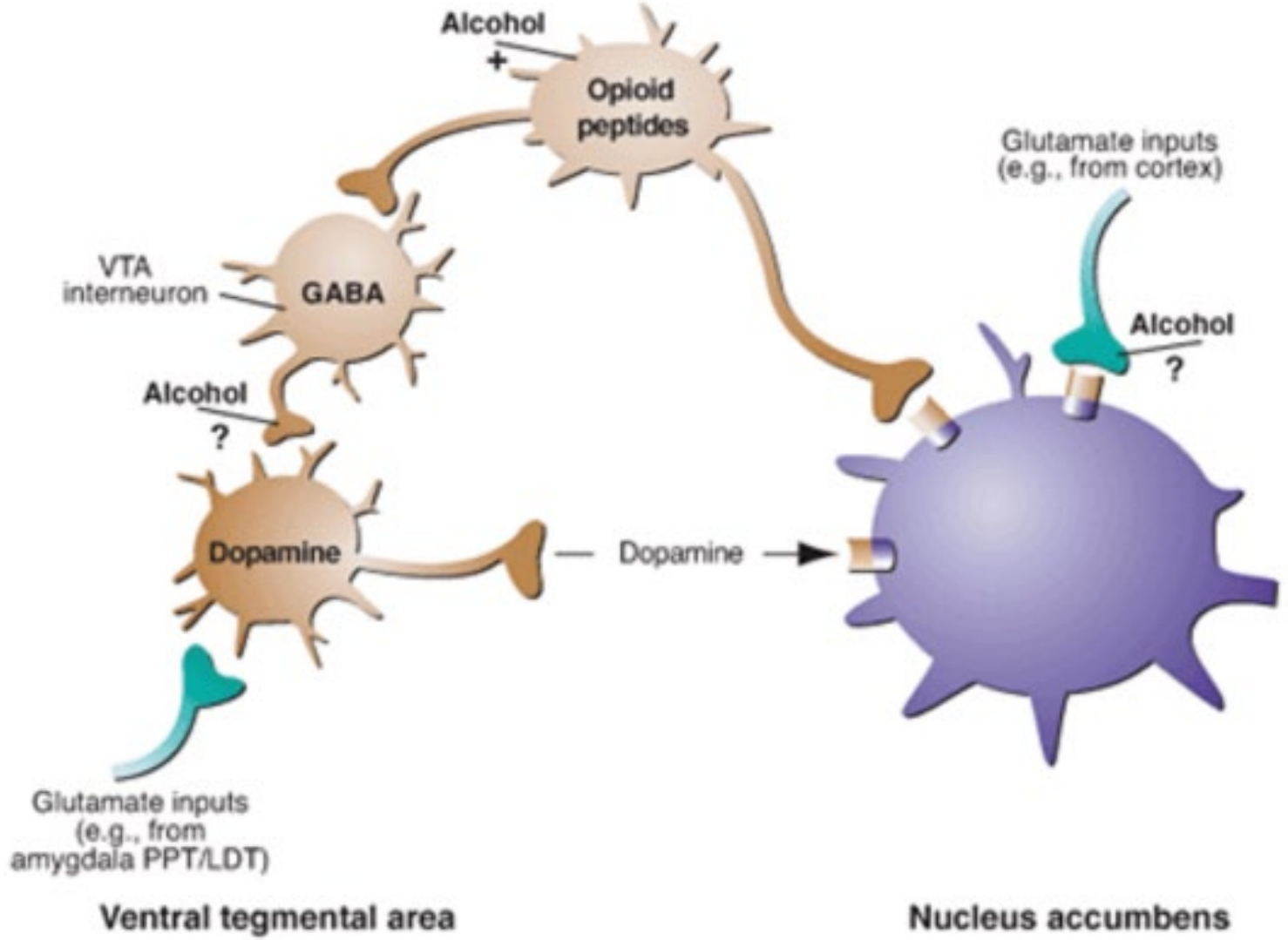
Relapse phase: When to consider pharmacotherapy

Treatment options:

1st Naltrexone
2nd Long Acting Naltrexone****
3rd Acamprosate
4th Disulfiram

- Barriers:
  - Cost?
  - Availability?
  - Prescriber awareness?
  - Education re: effectiveness?

Effects of alcohol on the brain



Nestler, E.J. Is there a common molecular pathway for addiction? *Nature Neuroscience* 8(11):1445–1449, 2005. PMID: 16251986

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Naltrexone

- Potent inhibitor at mu-receptor
- Modulates the mesolimbic dopamine system
- Patients do not experience the full euphorigenic/reinforcing effects of alcohol
- Meta-analysis evaluating 27 RTCs found a 36% reduction in rate of relapse
- Medication compliance maybe a limiting factor in oral treatment
- Dosed at 50mg /day
- S/E: GI – Abdominal pain, decreased appetite, nausea. Hepatotoxicity (1% of patients)
    - Sedation – Daytime sleepiness, fatigue, insomnia and headaches.

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Issues with Naltrexone

- Must be used in non-opioid users. If not sure, do a 0.4mg naloxone test dose to ensure this or get a urine screen
- Perioperative management with Naloxone: Stop 48-72 hours before OR
- Acute pain management:
  - Use Acetaminophen, NSAIDs, Local Blocks, Ketamine
  - IF ALL ELSE FAILS: Fentanyl

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Acamprosate

- Stabilizes glutamatergic neurotransmission during withdrawal
- Causes anti-craving and reduces protracted withdrawal
- Multiple good studies, and one meta-analysis which demonstrated improved 6-month abstinence rates 36.1% vs placebo at 23.4%
- Dosing: 666mg PO TID
- Recommended for patients with hepatic disease
- No drug-drug interactions

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Naltrexone PO and Acamprosate associated with improved consumption outcomes[1]

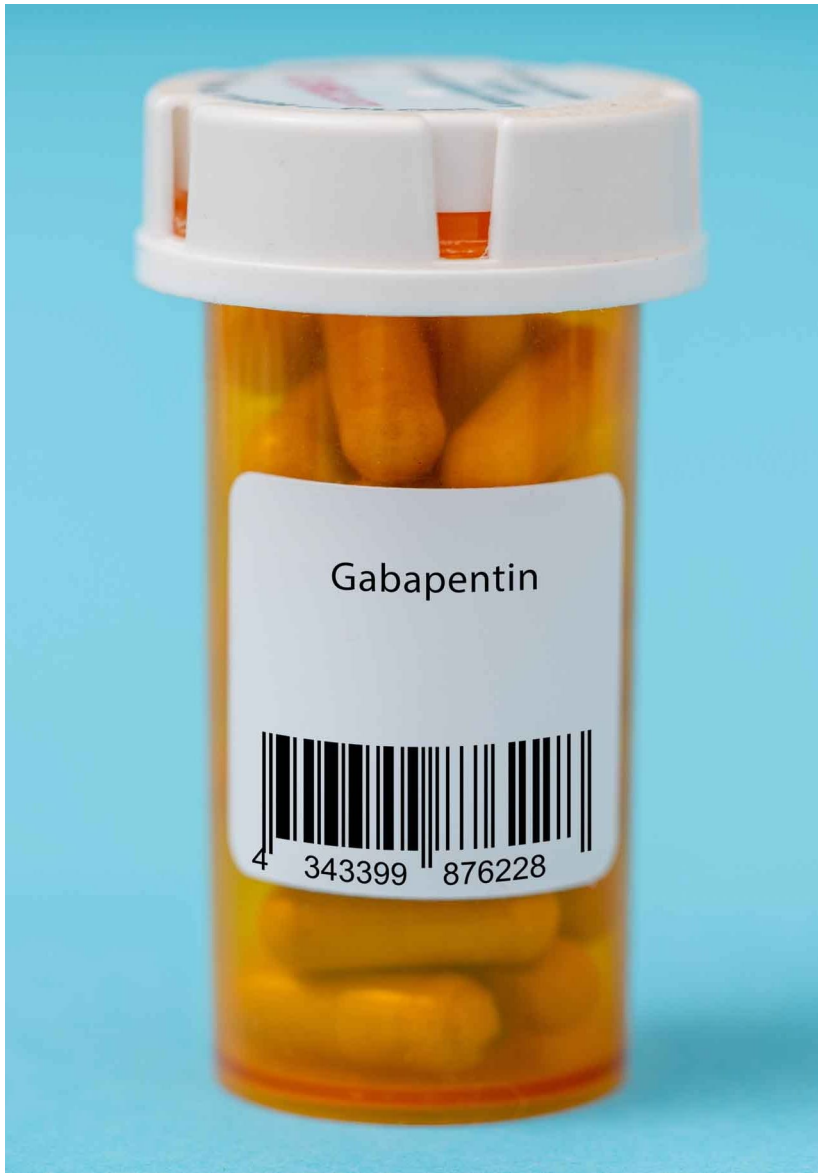
- Abstinence rates compared to placebo
  - Both Acamprosate and naltrexone po showed fewer returned to drinking (9% and 5% fewer respectively):
- NNT to prevent return to any drinking (abstinence)
  - Acamprosate:20
  - Naltrexone po: 12
- Return to heavy drinking compared to placebo
  - Acamprosate=no improvement
  - Naltrexone po=improvement with NNT: 12
    - 9% fewer returned to heavy drinking
  - Inadequate evidence in well-controlled trials or no benefit for other medication options, except weak evidence for valproic acid (see below)

[1] Jonas D, Amick H, Feltner C, Bobashev G, Thomas K, Wines R et al. Pharmacology for adults with alcohol use disorder in outpatient settings: a systematic review and meta-analysis. JAMA. 2014; 311(18):1889-1900.

AUD: PHARMACOTHERAPY

Gabapentin

- 600mg PO TID
- Found to be affective in treating alcohol dependence, relapse related symptoms of insomnia, dysphoria, and craving
- Abstinent rates of 17% were noted with this dosage.
- Useful for patients with concomitant anxiety, neuropathic pain, and sleep concerns
- Covered by Alberta Health
- Covered by many private drug plans; if 80% covered, cost to patient: $6/month, based on 300mg tid[2]
- Cost to patient if no coverage: $30/month[2]
- Some concern about abuse potential[3,4,5,6]



[1] Uptodate. Pharmacotherapy for alcohol use disorder. 2015
[2] Cost data provided by Pharmacist Rich Rego, Beacon Pharmacy, Calgary
[3] Markowitz J, Finkenbine R, Myrick H, et al. Gabapentin abuse in a cocaine user: implications for treatment? J Clin Psychopharmacology. 1997: 17:423.
[4] Reccoppa L, Malcolm R, Ware M. Gabapentin abuse in inmates with prior history of cocaine dependence. Am J Addict. 2004: 13:321.
[5] Victorri-Vigneau C, Guerlais M, Jolliet P. Abuse, dependency and withdrawal with gapapentin: a first case report. Pharmacopsychiatry. 2007:40:43.
6 Pittenger C, Desan P. Gabapentin abuse, and delirium tremens upon gabapentin withdrawal. J Clin Psychiatry. 2007: 68:483.

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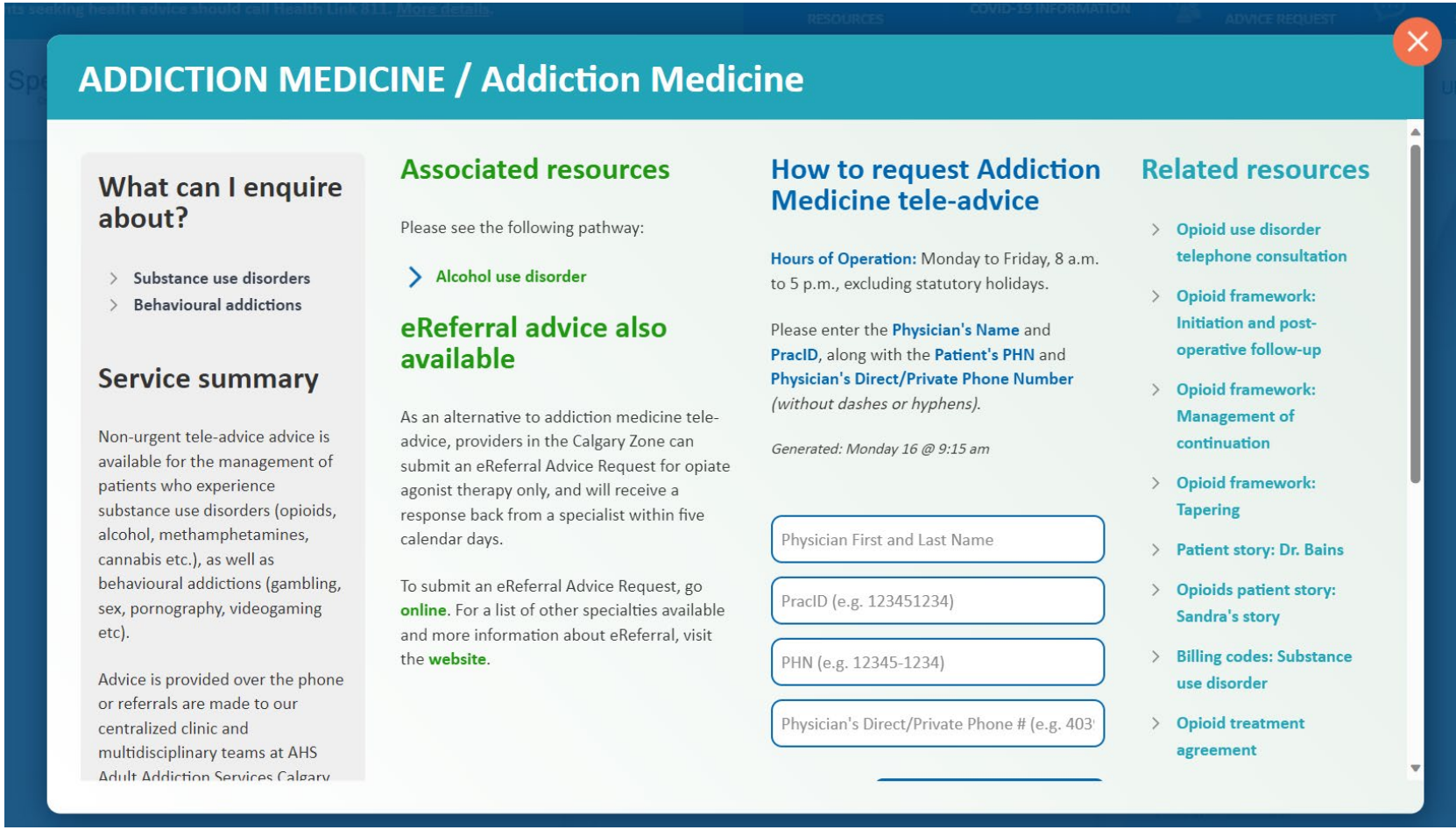
Resources:

- AHS Rapid Access Addiction Medicine Program (Raam)
  - Comprehensive physician and addiction counsellor-led program managing all substance and behavioral addiction concerns
  - 403-367-5000
- Specialist Link: Addiction medicine tele-advice
- AUD pathway



Q&A

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