Naltrexone: An Essential Option to Treat AUD

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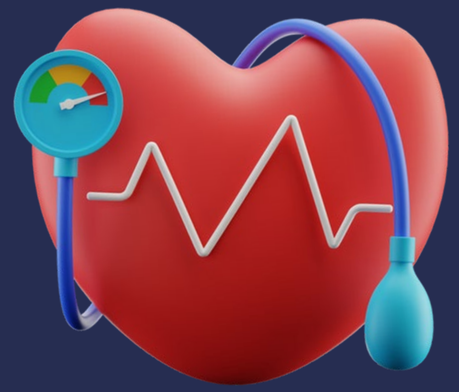

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Presenter: Dr. Jennifer Purdy

Relationships with financial sponsors:

- **Any direct financial relationships, including receipt of honoraria:**

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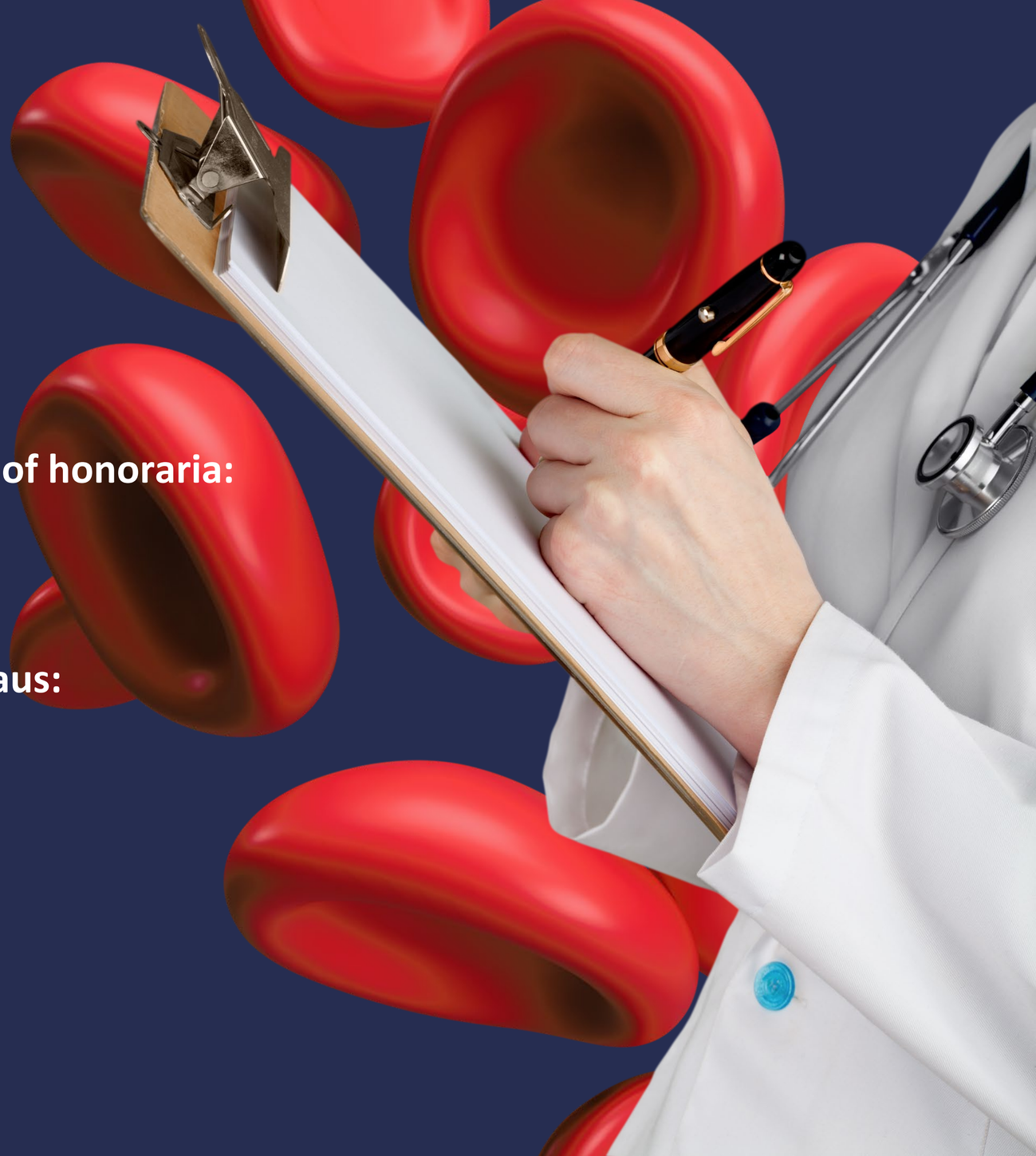


Objectives

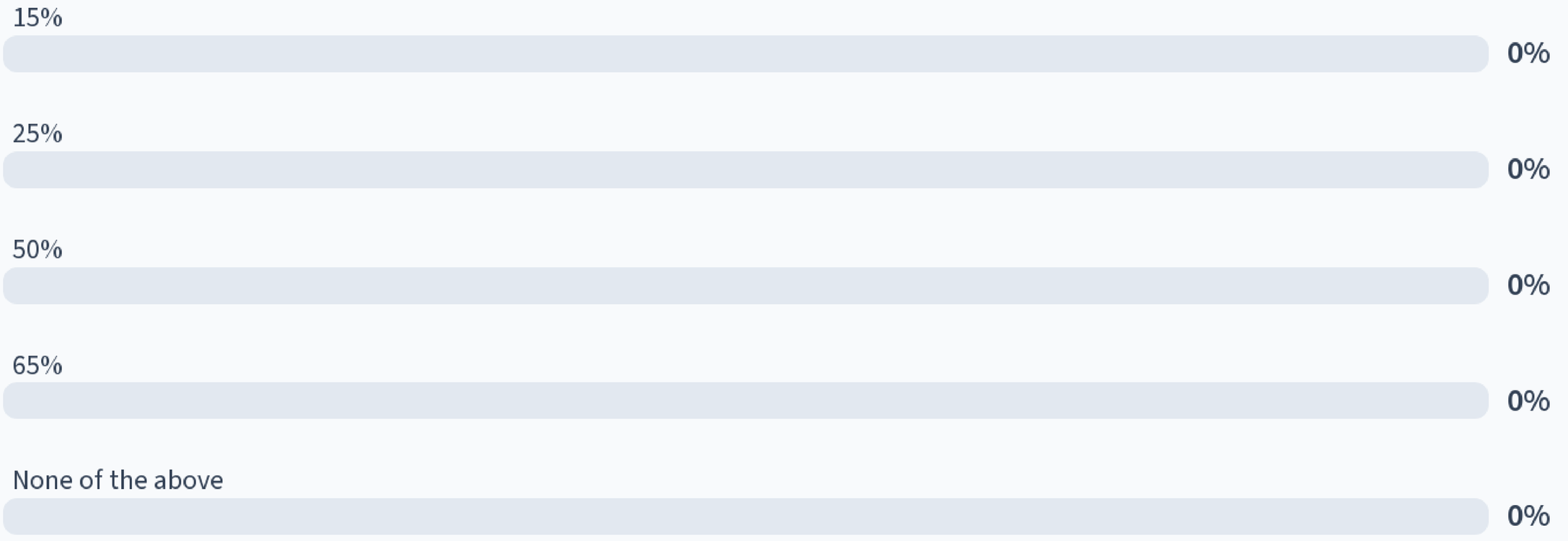
1. Recognize the importance of patient-directed Alcohol Use Disorder care.
2. Recognize how naltrexone can improve Alcohol Use Disorder.
3. Describe how to prescribe naltrexone using The Sinclair Method (TSM) for Alcohol Use Disorder.

PJ

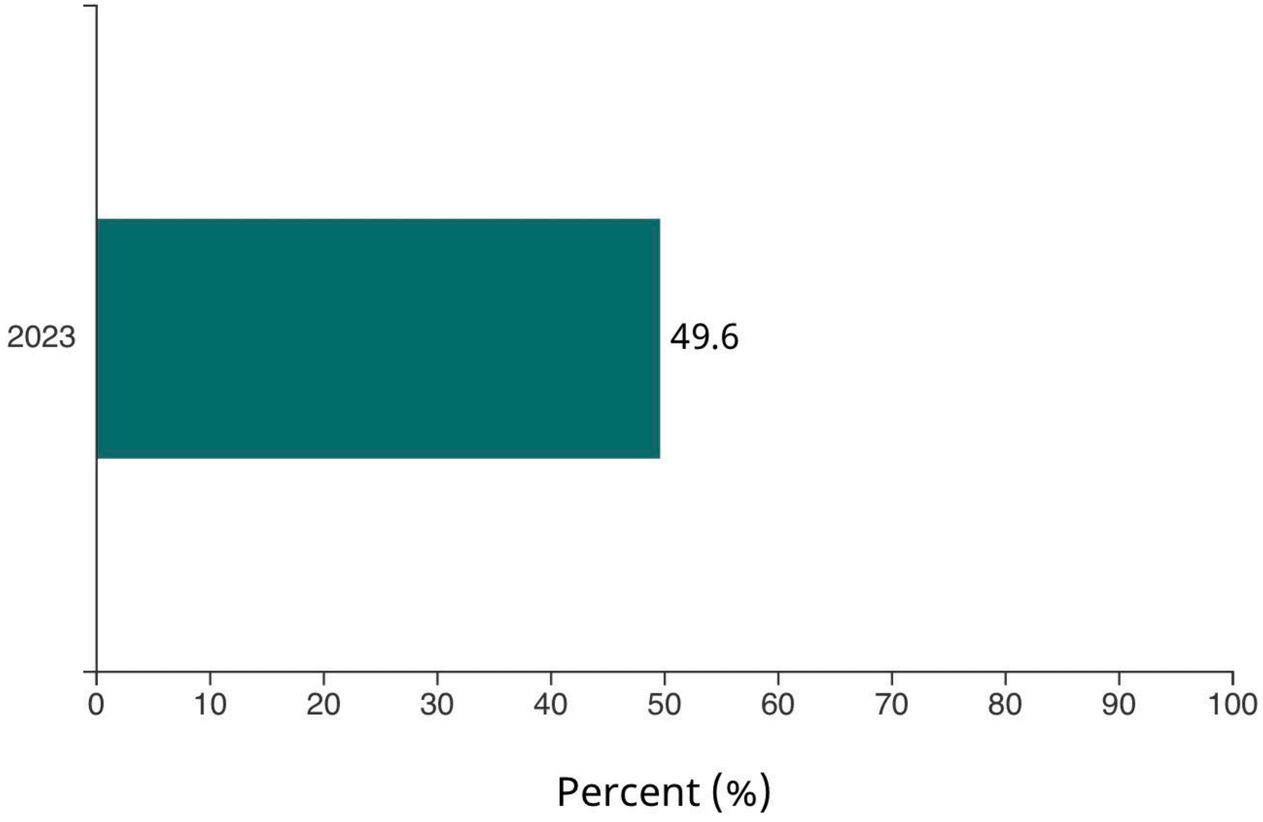
72 yo male, retired military: seen March 2019

- Has hypertension, GERD, hypercholesteremia.
- Is an infrequent drinker, but when drinking he drinks 13+ servings.
- Has tried: AA, ARC, out-patient hospital program, LESA program, cutting down.

Approximately what % of people in Canada 15 and older had a drink last week?

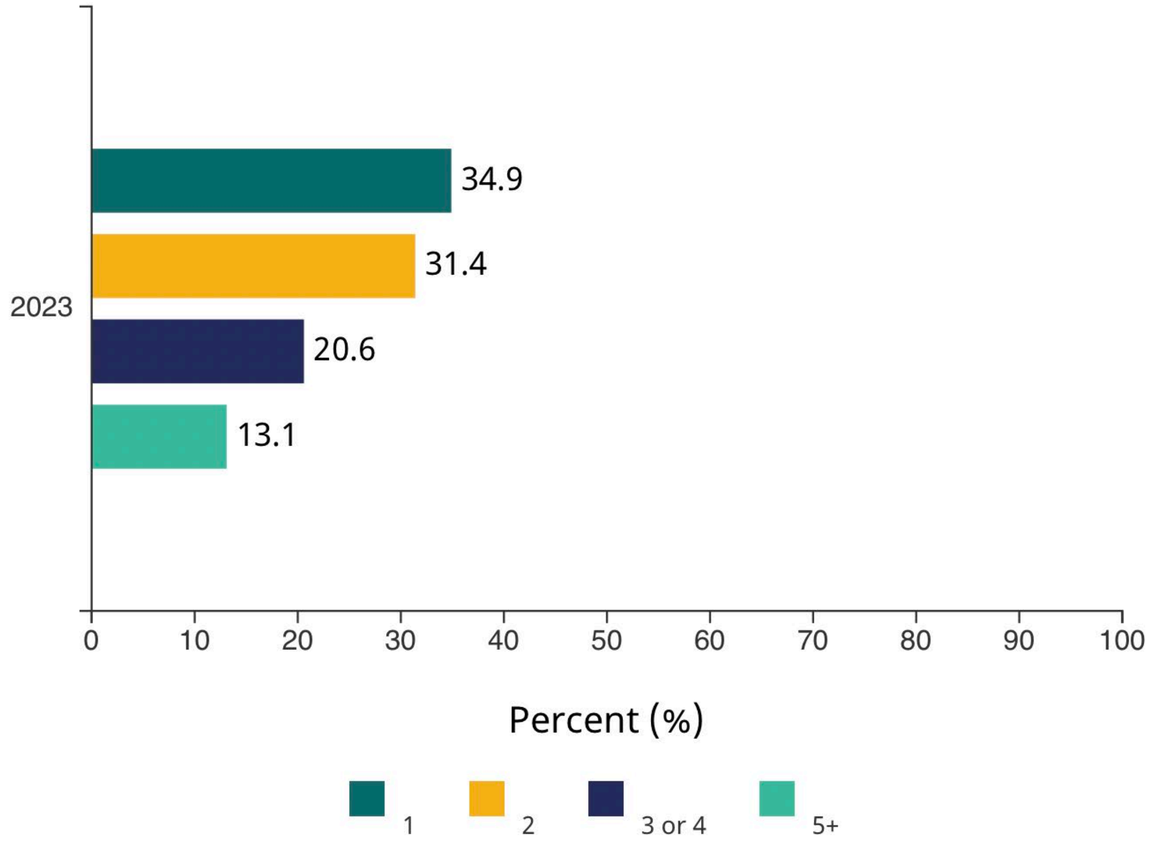


Percent of the population who has consumed 1 or more alcoholic drinks in the past 7 days



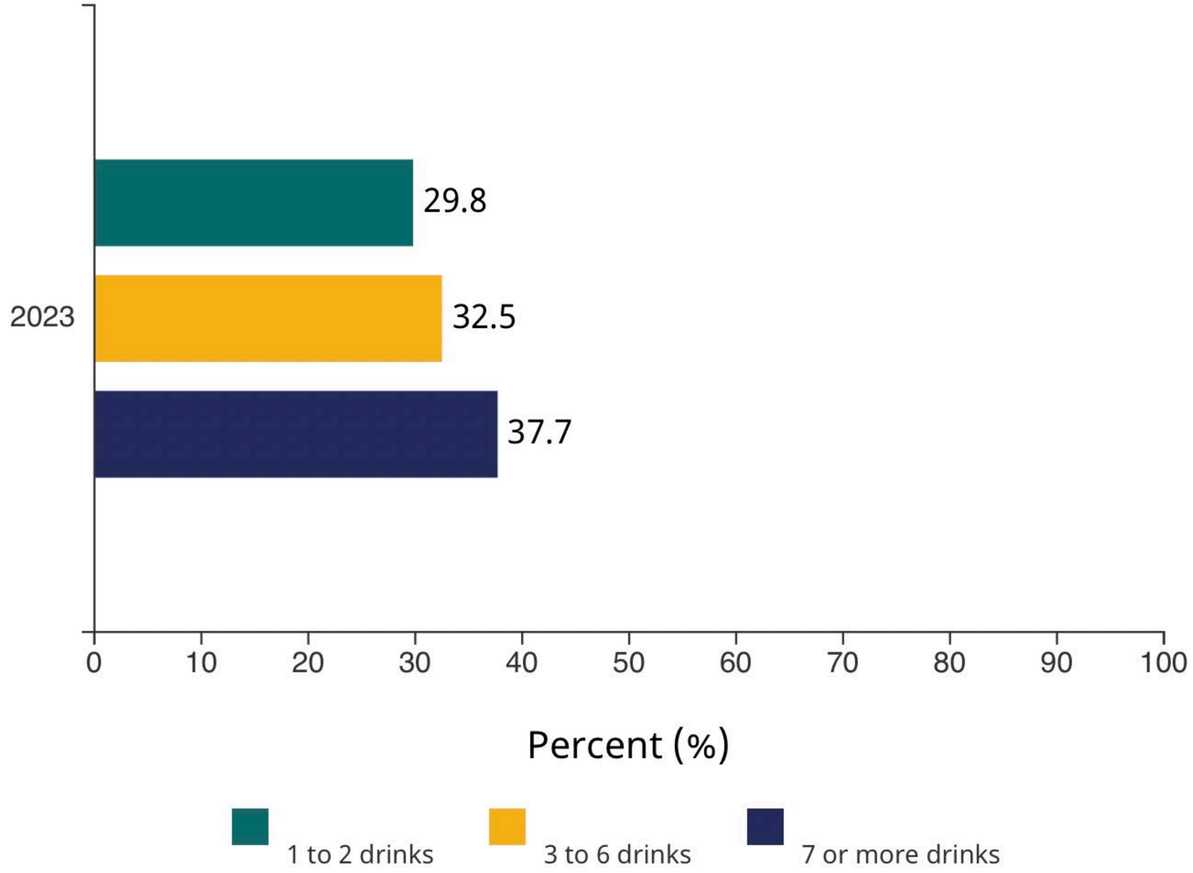
Data source: Canadian Substance Use Survey, 2023

Among those who have had an alcoholic drink in the past 30 days, percent who typically had 1, 2, 3 or 4, or 5 or more drinks on each occasion of drinking



Data source: Canadian Substance Use Survey, 2023

Among those who had a drink in the past 7 days, percent who had 1 or 2, 3 to 6, or 7 or more drinks in those 7 days



Data source: Canadian Substance Use Survey, 2023

Canada's Guidance on Alcohol and Health

To reduce the risk of harm from alcohol, it is recommended that people in Canada consider reducing their alcohol use.

The reasons to do so derive from the following facts:

a. There is a continuum of risk associated with weekly alcohol consumption where the risk of harm from alcohol is:
    - Low for individuals who consume 2 standard drinks or less per week;
    - Moderate for those who consume between 3 and 6 standard drinks per week; and
    - Increasingly high for those who consume 7 standard drinks or more per week.

b. Consuming more than 2 standard drinks per drinking occasion is associated with an increased risk of harms to self and others, including injuries and violence.

c. When pregnant or trying to get pregnant, there is no known safe amount of alcohol use.

d. When breastfeeding, not drinking alcohol is safest.

Sex and Gender

Above the upper limit of the moderate risk zone for alcohol consumption, the health risks increase more steeply for females than males.

Far more injuries, violence and deaths result from men's alcohol use, especially in the case of per occasion drinking.

Paradis, C., Butt, P., Shield, K., Poole, N., Wells, S., Naimi, T., Sherk, A., & the Low-Risk Alcohol Drinking Guidelines Scientific Expert Panels. (2023). Canada's Guidance on Alcohol and Health: Final Report. Ottawa, Ont.: Canadian Centre on Substance Use and Addiction.

When did you learn naltrexone existed?

20+ years ago 0%

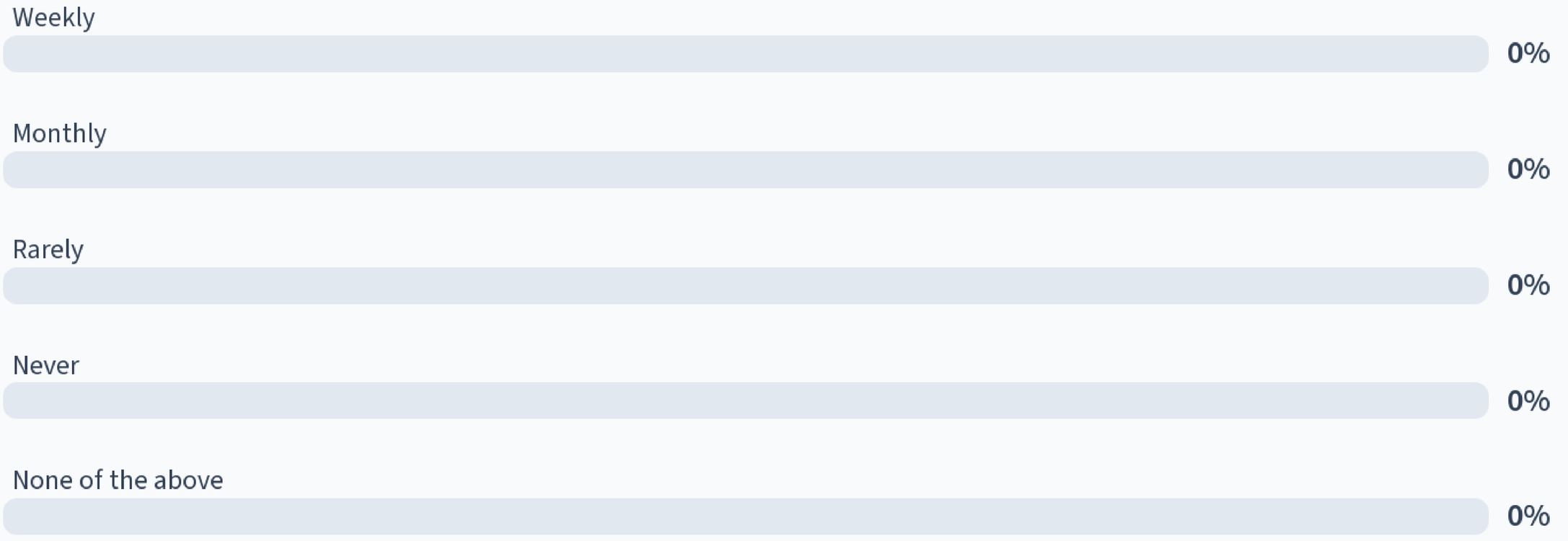
10+ years ago 0%

Past few years 0%

What's naltrexone? 0%

None of the above 0%

Have you prescribed naltrexone



Why this talk?

- Even though more MDs have heard of naltrexone in the past few years, many have not heard of The Sinclair Method.
- Many people think naltrexone is for short to medium term use only and should be prescribed to patients who agree to abstain and with abstinence as the goal.
- The known lag of research translating into clinical practice: 17 years!*
- The prevailing philosophy in the AUD world continues to be that abstinence is required.
- Should be two philosophies: abstinence or harm reduction are (case-dependent) acceptable end-states.
- Goal: increase clinician confidence in prescribing naltrexone using TSM.

*PMID: 22179294

Why is Abstinence so Hard?

Answer: Alcohol Deprivation Effect (ADE)

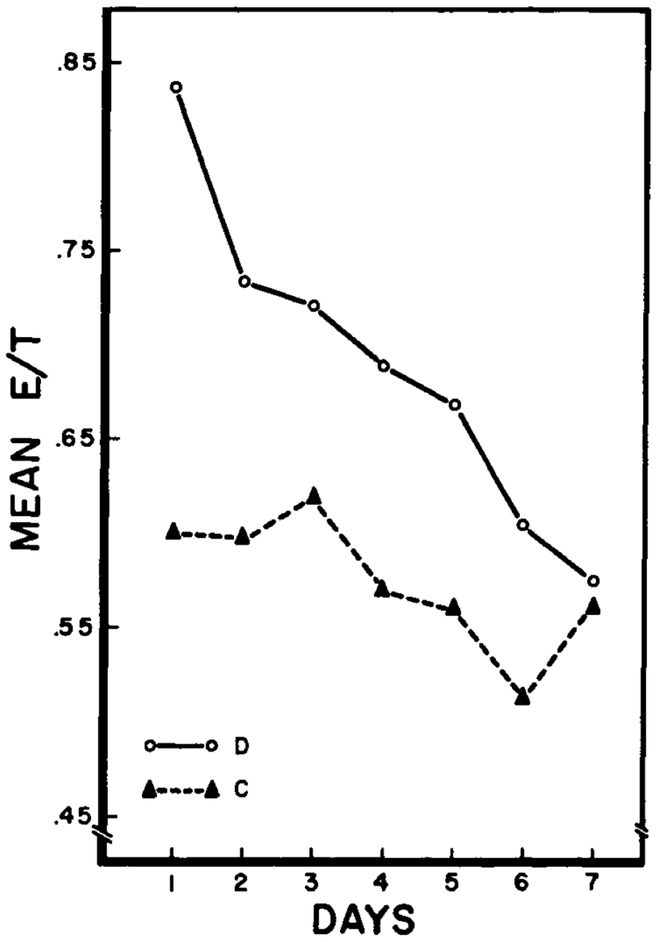


Fig. 1. Mean preference for EtOH for group D during periods following "alcohol deprivation" and for group C during the same time. For group D, "days" represent the number of days after the end of "alcohol deprivation."

Caption

Sinclair, J.D. and Senter, R.J. (1967). Increased preference for ethanol in rats following alcohol deprivation. *Psychon. Sci 8(*1), 11-12.

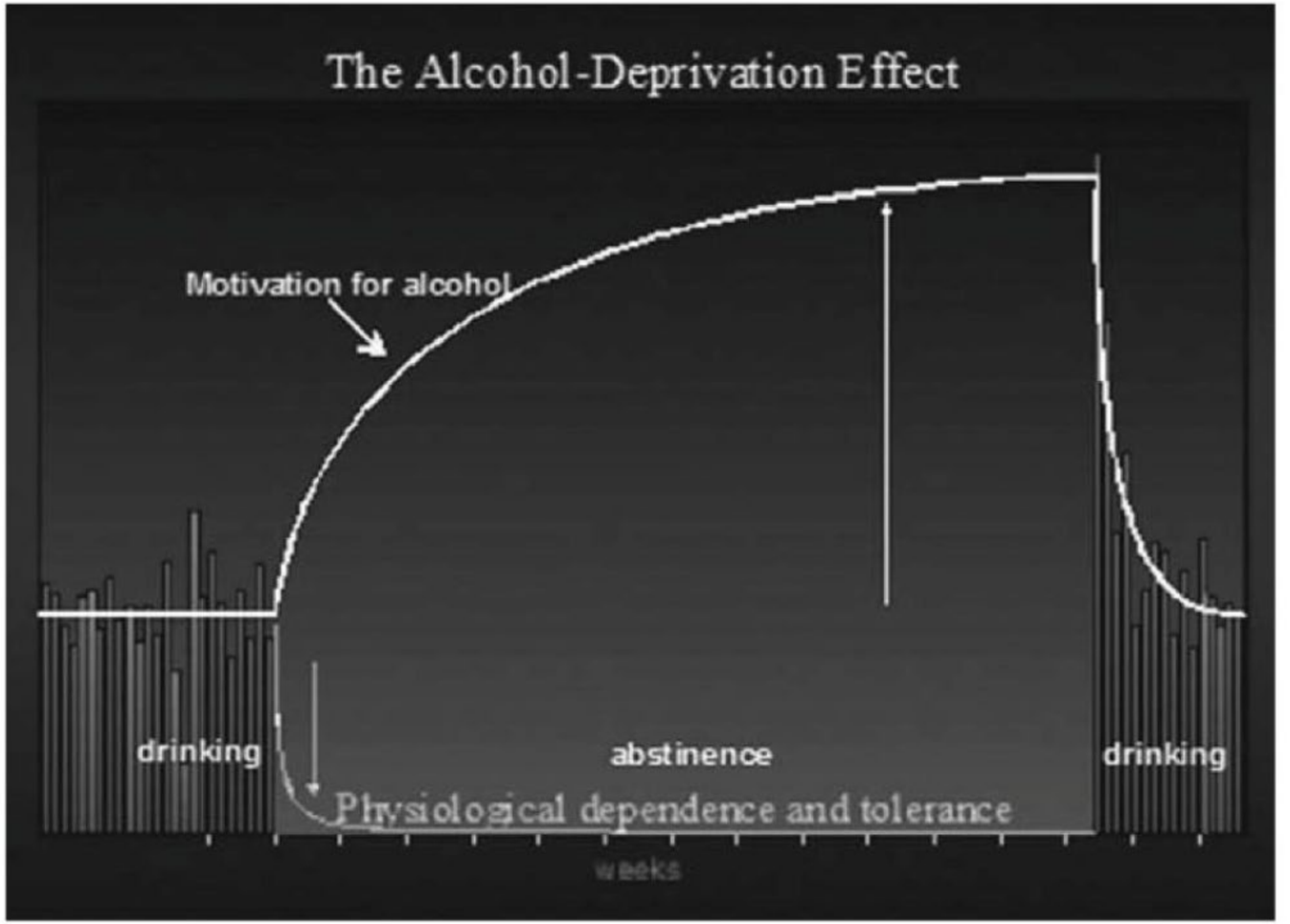


Figure 1. (Sinclair, JD. PowerPoint presentations, Finnish National Public Health Institute, 1997–2008). Original data are from published studies by Sinclair and Senter.[10, 11]

Eskapa, R. D. (2008). *The cure for alcoholism: the medically proven way to eliminate alcohol addiction*. BenBella.

Naltrexone

- Opioid antagonist. Exs of opioids: codeine, morphine, oxycocet, hydromorphone, etc.
- Peak concentration of 6-β-naltrexol (primary metabolite): 1 hour (has elimination half-life of 13 hours).
- Approved by FDA/ Health Canada in mid-1990s.
- Considered first-line treatment in Canada (British Columbia Centre on Substance Use) and the USA (2017 American Psychiatric Association Practice Guideline).
- Cannot be abused.
- Effects on liver: Black-box warning (but at a very high 300 mg dose), risk-benefit analysis, LFTs monitoring in patients with elevated LFTs.

BRITISH COLUMBIA CENTRE ON SUBSTANCE USE

Networking researchers, educators & care providers

Pharmacotherapy Options for Alcohol Use Disorder

	First Line Pharmacotherapy		*Second Line Pharmacotherapy*	
	Naltrexone	**Acamprosate**	**Topiramate**	**Gabapentin**
Concurrent Alcohol Use	No well-described safety risk Tx after WDM may be more effective	No well-described safety risk Tx after WDM may be more effective	No well-described safety risk	No well-described safety risk at therapeutic dose Abstinence recommended after tx Abstinence for ≥3 days may improve outcomes
Contra-indications	1. Naltrexone hypersensitivity 2. Any current opioid use (Rx or nonmedical) 3. Acute opioid withdrawal 4. Acute hepatitis or liver failure	1. Acamprosate hypersensitivity 2. Severe renal impairment 3. Breastfeeding	1. Topiramate hypersensitivity 2. Pregnant or planning pregnancy 3. Narrow angle glaucoma 4. Nephrolithiasis	Gabapentin hypersensitivity
Cautions	1. Renal impairment 2. Severe hepatic impairment 3. Concomitant use of other potentially hepatotoxic drugs 4. Pregnancy and breastfeeding* 5. Adolescent patients (<18 years)*	1. Moderate renal impairment 2. Adolescent and geriatric (>65 years) patients* 3. Pregnancy*	1. Concomitant use of valproic acid 2. Conditions/therapies that predispose to acidosis	1. Renal impairment 2. Pregnancy and breastfeeding* 3. Adolescent and geriatric (>65 years) patients* 4. Concomitant use of opioids and other CNS depressants 5. Compromised respiratory function 6. Neurological disease or cognitive impairment
Side Effects	Nausea, headache, and dizziness Starting at low dose and/or abstinence can reduce side effects	Diarrhea, vomiting, and abdominal pain	Psychomotor slowing, difficulty concentrating, speech/language problems, somnolence, fatigue, and mood disturbance Starting at low dose and titrating up can reduce side effects	Ataxia, slurred speech, and drowsiness

ritish Columbia Centre on Substance Use (2025, November). *AUD Pharmacotherapy Tables.* https://www.bccsu.ca/wp-content/uploads/2020/04/AUD-Pharmacotherapy-Tables.pdf

How naltrexone works

- Blocks opioid receptors in brain.
- Alcohol leads to production of endorphins.
- Endorphins cannot fill opioid receptors thus no reinforcement.

- No naltrexone:

drinks —> Endorphins produced —> Endorphins bind to opioid receptors (**reinforceme**

- With naltrexone:

drinks —> Endorphins produced —> Endorphins bind to opioid receptors (**no reinforce**

The Sinclair Method (TSM)

- Patient takes naltrexone only on days when they are drinking, one hour before their first drink.
- If drinking timespan lasts 4-8 hours+, may need to take 2nd dose.
- Check-ins while drinking, drinking as a habit.
- Track their alcohol intake (apps available).
- On no-alcohol days, patient does not take naltrexone and is encouraged to find other pleasurable activities.

TSM Advantages

- Patient-directed care
- Cost and accessibility
- Compassionate treatment (versus disulfiram)

TSM Disadvantages

- Cost (although will be lesser than taking naltrexone daily)
- Non-adherence

Pavlov: Extinction

- Extinction occurs when there is no reinforcement of a response repeatedly over time.
- With naltrexone, extinction normally takes 6-9 months (but most improvement seen over first 4 months).
- One must drink for it to work.
- Naltrexone DOES NOT reduce cravings.

Clinical Trial > J Clin Psychopharmacol. 2001 Jun;21(3):287-92.
doi: 10.1097/00004714-200106000-00006.

Targeted use of naltrexone without prior detoxification in the treatment of alcohol dependence: a factorial double-blind, placebo-controlled trial

P Heinälä [1], H Alho, K Kiianmaa, J Lönnqvist, K Kuoppasalmi, J D Sinclair

Affiliations + expand

PMID: 11386491 DOI: 10.1097/00004714-200106000-00006

- 121 non abstinent participants with alcohol dependence (DSM IV)
- Intervention: sessions of cognitive coping skills (N=67) supportive therapy (N=54) and either naltrexone 50 mg/d (N=63) or placebo (N=58) daily for 12 weeks and thereafter for 20 weeks only when craving alcohol (ie targeted medication) in a prospective one-centre, dual, double-blind, randomized clinical trial.
- After first 12 weeks, the coping/naltrexone had best outcome, coping/placebo the worst.
- After 20 weeks: naltrexone not better than placebo in supportive groups, but in coping groups a significant effect: 27% of coping/naltrexone had no relapses vs 3% of coping/placebo.

Barriers/ Potential Barriers

- Some may be important to maintain; clinician-dependent
- Stigma, self-stigma
- Social barriers: supporters may be abstinence-only; there may also be enablers.
- $$$: for in-patient treatment, for psychotherapy, for naltrexone…
- LFTs (if testing), requirement (?) for counselling/psychotherapy

Compassion

- AUD is an illness.
- No different than high blood pressure, cholesterol, depression, heart disease, etc.
- Most people with AUD are much harder on themselves than they would be if a loved one or friend had AUD. (Solution: Socratic questioning - distancing)
- Remembering the first appointment is probably **very** stressful for this person, especially if they are not known to you or have not disclosed AUD previously.

A Typical First Visit

- Medical history, including prescribed medications, family history.
- I ask specifically about taking any opioids, or if they have been told that they have liver disease, etc. I explain **why**.
- History of alcohol consumption, drink of choice, is it most days or rarely, etc.
- Have they tried to cut down and if so how?
- AUDIT (Alcohol Use Disorders Identification Test): establish a diagnosis.
- **Wash-out period of opioids = 7 days recommended.**
- Explain how naltrexone works, and that it is being prescribed off-label.
- Find out what the patient's goal is: abstinence or harm reduction?

Prescribing naltrexone: TSM

- “starting dose take 25 mg (half tab) one hour before event for 2-4 days PRN; then, take one 50 mg tab one hour before event PRN; may take a 2nd tab after 4-8 hours PRN”
- sometimes patients may need more (75 mg) or less (25 mg)!
- sometimes pharmacies don’t want to refill “early” in spite of prescription; conversations help, or spell it out on prescription.

Follow-Up

- one to two weeks after medication start
- “I’m here as a resource to help you succeed.”
- This can be a lonely journey for some.
- Once patient on stable dose, doing well, 6 months to yearly follow-up.

Specific Circumstances

- Bariatric surgery or semaglutide
- Binge drinking
- Daily drinking

PJ

- F/U: May 2019: has had max 3 ETOH since starting medications.
- Wife and family were hesitant at first but they have seen a difference and are hopeful.
- April 2021: Had 2 beers in month of February. Drinks rarely, takes naltrexone every time he drinks.
- Since then lost to follow-up.

Summary

- Naltrexone is a first-line treatment for AUD.
- It represents patient-directed treatment.
- Naltrexone offers compassionate treatment for patients whose goal is abstinence or harm reduction.
- Understanding how naltrexone works allows us to understand why using The Sinclair Method (TSM) may be more effective in reducing or eliminating alcohol consumption.

Resources

- British Columbia Centre on Substance Use, bccsu.ca
- *Cure for Alcoholism* by Dr Roy Eskapa, PhD
- *CBT: Mind Over Mood*, by Dr Greenberger, PhD and Dr Padesky, PhD
- *CBT-I: Say Good Night to Insomnia*, by Dr Gregg Jacobs, PhD
- "Practical Approach to Substance Use Disorders for the Family Physician" Addiction Medicine Member Interest Group The College of Family Physicians of Canada (https://www.cfpc.ca/CFPC/media/PDF/MIGS-2021-Addiction-Medicine-ENG-Final.pdf)
- TSM Options (https://tsmoptions.org) for research papers, apps, other resources for patients and MDs

Questions & Discussion

THANK YOU!

PLEASE FILL OUT YOU SESSION EVALUATION NOW:

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