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SHM Rapid Clinical Updates

Alcohol Use Disorder: Inpatient Management

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Disclosures

Jagriti Chadha has no relevant financial or advisory relationships with corporate organizations related to this activity.

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Medical director, Addiction Consult Team

Hospitalist, Hospital Medicine Unit

Massachusetts General Hospital

Gene is an Instructor in Medicine at Harvard Medical School. He is board certified in internal medicine and addiction medicine. He has practiced hospital medicine at Massachusetts General Hospital for the past twenty years, served as director of hospital medicine. He completed a fellowship in Addiction medicine at Massachusetts General Hospital in 2019. He is the medical director and director of clinical operations for the Addiction Consult Team, part of the Substance Use Disorders Initiative at Massachusetts General Hospital.

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Pre-test questions

A 50-year-old male presents to the ER with cough and dyspnea and was found to have a pulmonary embolism. On further questioning he says that he consumes 2-3 beers at least 5 days a week. His alcohol use has led to significant relationship issues with his partner and difficulties performing his job. He would like to cut down but has difficulty doing so due to ongoing cravings.

What is his diagnosis with respect to his alcohol use?

A. No alcohol use disorder

B. Mild Alcohol use disorder

C. Moderate alcohol use disorder

D. Severe alcohol use disorder

Which of the following tools can be used to assess his risk for developing severe alcohol withdrawal syndrome?

A. Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

B. Clinical Institute Withdrawal Assessment of Alcohol, revised (CIWA-Ar)

C. Cut, Annoyed, Guilty, and Eye (CAGE) questionnaire

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Outline

- ❑ Diagnose alcohol use disorder (AUD)
- ❑ Review management of severe alcohol withdrawal syndrome
- ❑ Initiate evidence-based medications for AUD

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Objectives

- ❑ Diagnosing AUD
- ❑ AUD epidemiology
- ❑ Managing severe alcohol withdrawal syndrome
- ❑ Treating AUD

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Objectives

- ❑ **Diagnosing AUD**
- ❑ AUD epidemiology
- ❑ Managing severe alcohol withdrawal syndrome
- ❑ Treating AUD

Overview

Alcohol use disorder (AUD) defined by *DSM-5* criteria is a highly prevalent, highly co-morbid, disabling disorder that often goes untreated in the United States.

- Bridget F. Grant et al., NIAAA

AUD is a complex, multifactorial chronic brain disorder with early age of onset characterized by compulsive use despite *harmful consequences*, and a return to unhealthy behavior rate comparable to other chronic diseases; with a minority contributing to overall total economic and societal costs.

Certain demographics struggle severely with alcohol use disorders; often reflecting the intergenerational nature of AUD and its complex interaction with the aging physiology.

Individuals with AUD require a multidisciplinary care approach with an emphasis on longitudinal primary, mental/behavioral and psychosocial care.

Pharmacotherapy (MAUD) is effective and patient-centered if engaged in care but is underutilized.

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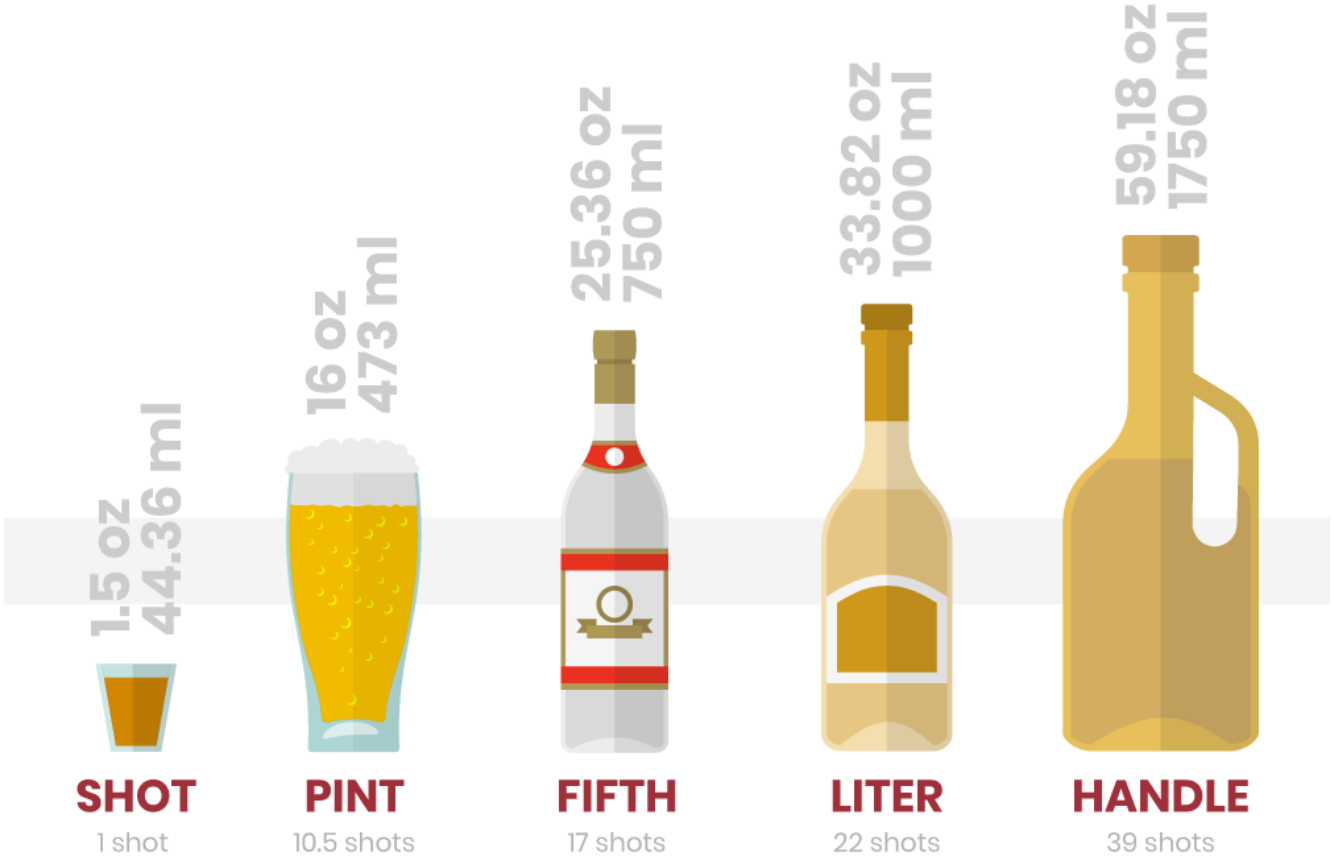
Grant, Bridget F et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III." *JAMA Psychiatry*. 2015. McLellan et al. Drug Dependence, a Chronic Medical Illness: Implications for Treatment, Insurance, and Outcomes Evaluation. *JAMA.* 2000

Clinical scenario

60-year-old male history of tobacco use disorder c/b COPD, alcohol use presenting to the ED with cough, dyspnea and chest pain found to have pulmonary embolus.

On substance use history, patient states he drinks a half a handle of vodka daily and can't recall the last time he did not drink.

How would you quantify his alcohol use?



https://home.binwise.com/blog/liquor-bottle-sizes#toc-common-liquor-bottles-sizes-chart

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Alcohol use patterns: a common understanding

National Institute on Alcohol Abuse and Alcoholism (NIAAA) and Substance Abuse and Mental Health Services Administration (SAMHSA) definitions (CONSUMPTION CRITERIA)

Binge drinking/Heavy episodic drinking (HED)

- pattern of drinking alcohol that brings the blood alcohol concentration (BAC) to ≥ 80mg mg/dL, ≥5 for ♂ or ≥4 ♀ drinks, in about 2 hours.

NIAAA defines heavy alcohol use

- ♂ ≥4 drinks on any day or ≥14 drinks/week
- ♀ ≥3 drinks on any day or ≥7 drinks/week (applies to older adults ≥60 years of age)

Binge drinking ≥5 days in the past month (SAMHSA)

High Intensity Drinking (HID) = ≥2x HED threshold

- mild = 1-2x HED (4-7 ♀/ 5-9 ♂)
- moderate = 2-3x HED (8-11 ♀/ 10-14 ♂)
- severe = >3x HED (≥ 12♀/ ≥ ♂)

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Hingson RW, Zha W, White AM. Drinking Beyond the Binge Threshold: Predictors, Consequences, and Changes in the U.S. *Am J Prev Med*. 2017;52(6):717-727.
Https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/moderate-binge-drinking

Clinical scenario (continued)

On substance use history, patient states he drinks half a handle of vodka daily and can’t recall the last time he did not drink.

He meets consumption criteria for heavy alcohol use, binge pattern.

Can we further characterize his binge drinking, and its consequences?

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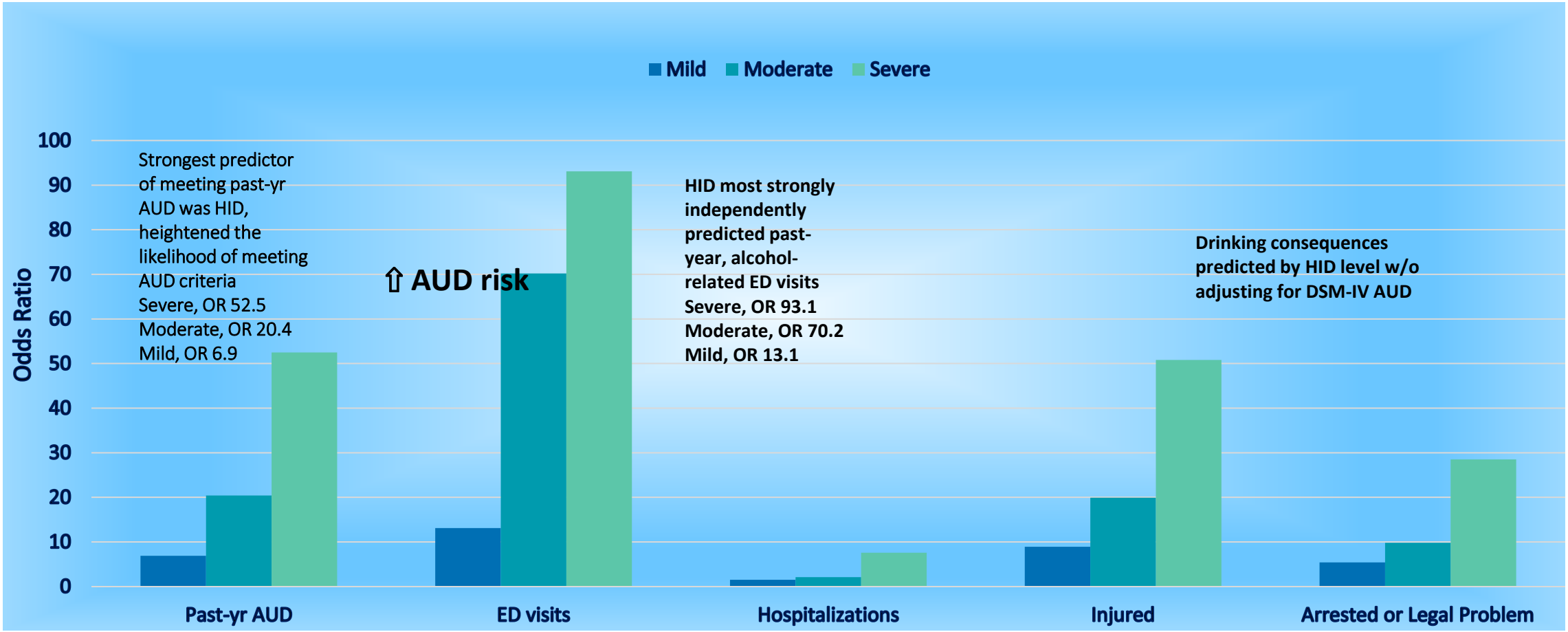
An emerging public health threat…
High-Intensity Drinking (HID)



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Hingson RW, Zha W, White AM. Drinking Beyond the Binge Threshold: Predictors, Consequences, and Changes in the U.S. *Am J Prev Med*. 2017;52(6):717-727.

Clinical scenario (continued)

60-year-old male history of tobacco use disorder c/b COPD, alcohol use presenting to the ED with cough, dyspnea and chest pain found to have a pulmonary embolus.

On substance use history, patient states he drinks half a handle of vodka daily and can't recall the last time he did not drink.

We now know he has a history of heavy alcohol use, high intensity drinking pattern.

IS HIS DRINKING CAUSING HIM HARM?

IS IT UNHEALTHY?

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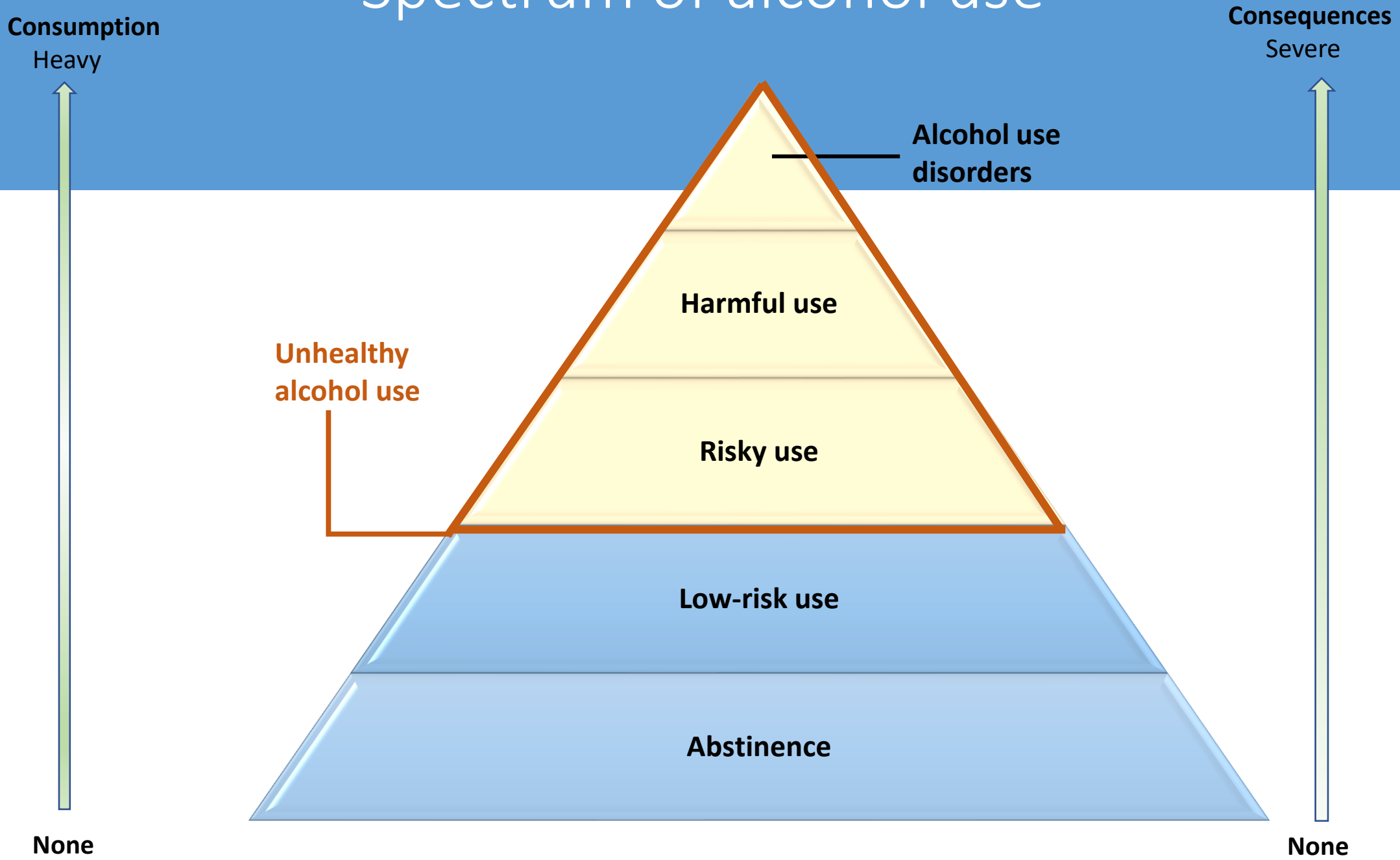
Spectrum of alcohol use



Clinical scenario (continued)

On substance use history, patient states he drinks half a handle of vodka daily and can't recall the last time he did not drink.

We now know he has a history of unhealthy alcohol use, high intensity drinking pattern.

He now states over the last 6 months his drinking spans the entire day. In the morning he experiences "some shakes" and nausea which goes away after his first drink. He has "undeniable urges" to drink and has been unable to cut down. He lost his job because of missed/late assignment. His wife left because she was "tired of his drinking". He was arrested 3 months ago for a DUI. And he reports, worsening anxiety and depression over the last two months.

DOES HE HAVE AN ALCOHOL USE DISORDER?

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Diagnostic and Statistical Manual of Mental Disorders– 5th edition (DSM-5)® criteria for alcohol use disorder

Domain		Criteria	Criteria (past 12-months)	Description
Impaired Control	**C**ontrol (loss of) Can't **C**ut down **C**ompulsive use **C**raving	1	Drank larger amounts/longer time	Alcohol consumed in larger amounts or over a longer period than intended
		2	Repeated attempts to quit/control drinking	Persistent desire or unsuccessful efforts to cut down or control alcohol use
		3	Significant time spent drinking	Significant time obtaining and drinking alcohol, or recovering from its effects
		4	Cravings	Craving, or a strong desire or urge to drinking alcohol
Social Impairment **5 Cs and 3 Rs of addiction**	**R**ole failure (s) **R**elationship issues	5	Neglected major roles to drink	Recurrent alcohol use resulting in a failure to fulfill major role obligations at work at work, school or home
		6	Social/interpersonal problems	Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol
		7	Activities given up because of drinking	Important social, occupational, or recreational activities are given up or reduced because of alcohol use
Risky use	**R**isk of bodily harm **C**onsequences	8	Hazardous use	Recurrent alcohol use in situations in which it is physically hazardous
		9	Physical/psychological problems	Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol
Pharmacological dependence		10	Tolerance	Tolerance, as defined by either of the following: (a) A need for markedly increased amount of alcohol to achieve desired effect
		11	Withdrawal	(b) A markedly diminished effect with continued use of the same amount Withdrawal, as manifested by either of the following: (a) The characteristic withdrawal syndrome for alcohol Alcohol (or a closely related substance) is taken to relieve or avoid withdrawal symptoms

Raffo et al. A data-driven method for identifying shorter symptom criteria sets: the case for DSM-5 alcohol use disorder. *Psychological Medicine*. 2019;49(6):931-939. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American. Psychiatric Association, 2013.

DOES HE HAVE A DSM-5 AUD?

He now states over the last 6 months his drinking spans the entire day. In the morning he experiences "some shakes" and nausea which goes away after his first drink. He has "undeniable urges" to drink and has been unable to stop of reduce his drinking. He lost his job because of missed/late assignment. His wife left because she was "tired of his drinking". He was arrested 3 months ago for a DUI. And he reports, worsening anxiety and depression over the last two months.

Control
Can't **C**ut down
Compulsion
Craving
Role failure(s)
Relationship issues
Meaningful activities ignored
Risk of bodily harm
Physical/physiological **C**onsequence
Tolerance
Withdrawal

9 criteria met = SEVERE AUD

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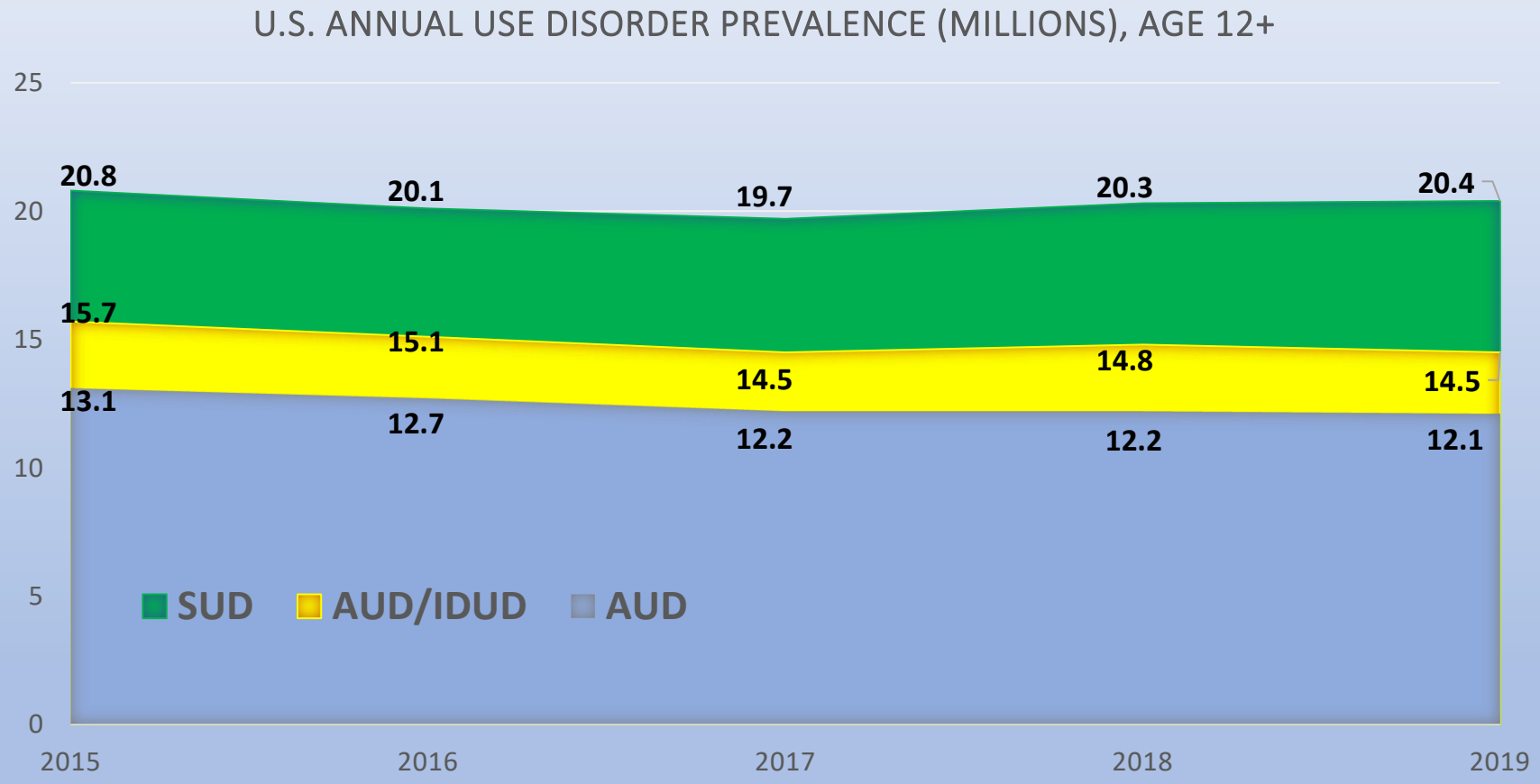
Objectives

- ❑ Diagnosing AUD
- ❑ **AUD epidemiology**
- ❑ Managing severe alcohol withdrawal syndrome
- ❑ Treating AUD

AUD is the most prevalent substance use disorder in the U.S.



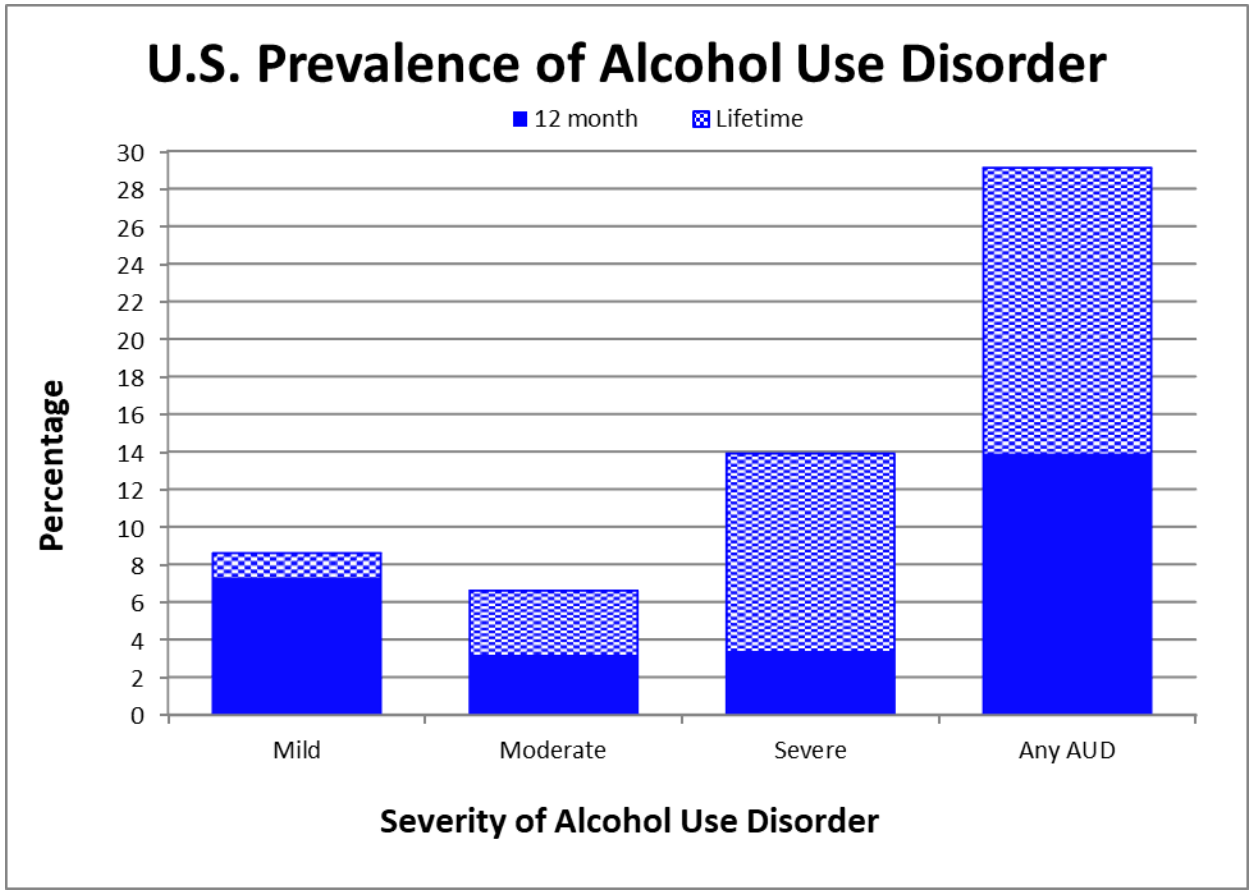
In 2019 Americans aged 18+

- 1 in 20 individuals had an AUD
- 3 in 4 individuals with a SUD had an AUD
- 1 in 9 individuals had an AUD and SUD

National Survey of Drug Use and Health, 2019; Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, National Survey of Substance Abuse Treatment Services (N-SSATS), 2009-2019; https://www.statista.com/statistics/

Epidemiology of *DSM-5* Alcohol Use Disorder

National Epidemiologic Survey on Alcohol and Related Conditions III



Alcohol use disorders	
12-month prevalence	13.9%
Lifetime AUD prevalence	29.1%
♂	17.6/36%
♀	10.4/22.7%
Any treatment	19.8%

Grant et al. Epidemiology of DSM-5 Alcohol Use Disorder. Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry.* 2015.

Grant et al. Prevalence of 12-Month Alcohol Use, High-Risk Drinking, and DSM-IV Alcohol Use Disorder in the United States, 2001 2002 to 2012-2013. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *JAMA Psychiatry*. 2017;4(9): 911-923

Prevalence of past 12-month healthcare utilization by severity of alcohol use disorder from 2015-2019 National Survey of Drug Use and Health (NSDUH)

	No AUD (*n* = 193,235)	Any AUD (*n* = 21,270)	Mild AUD (*n* = 14,134)	Moderate AUD (*n* = 4178)	Severe AUD (*n* = 2958)
	Weighted % (95% CI)	Weighted % (95% CI)	Weighted % (95% CI)	Weighted % (95% CI)	Weighted % (95% CI)
Any healthcare utilization	84.1 (83.9–84.3)	81.4 (80.7–82.1)***	81.3 (80.5–82.1)***	80.9 (79.2–82.7)***	82.7 (80.5–84.9)
Ambulatory care visit	82.6 (82.3–82.8)	78.8 (78.0–79.5)***	79.0 (78.1–79.8)***	77.8 (76.1–79.6)***	79.1 (76.8–81.5)**
Emergency room visit	25.7 (25.3–26.0)	30.0 (29.2–30.9)***	27.8 (26.7–28.9)***	30.4 (28.3–32.5)***	40.4 (37.4–43.4)***
Overnight hospitalization	10.0 (9.8–10.3)	9.7 (9.0–10.3)	8.3 (7.6–9.1)*	9.8 (8.4–11.1)	16.0 (14.0–17.9)***

Abbreviations: AUD, alcohol use disorder; CI, Confidence Interval.

[a]AUD definition derived from *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* diagnostic criteria.

*$p < 0.05$; ***$p < 0.001$. Reference group for each comparison was "No AUD" group.

Individuals with severe AUD 60% more likely to have utilized ED resources and to have been admitted in the past year.

Mintz et al. A Cascade of Care for Alcohol Use Disorder: Using 2015–2019 National Survey on Drug Use and Health Data to Identify Gaps in Past 12-month Care. Alcoholism, Clinical and Experimental Research. 2021;45(6*):* 1276–86

National Institute on Alcohol Abuse and Alcoholism

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Contact info:
NIAAA Press Office
301-443-2857
NIAAAPressOffice@mail.nih.gov

National Institute on Alcohol Abuse
and Alcoholism (NIAAA)
https://www.niaaa.nih.gov

NEWS RELEASE

FOR IMMEDIATE RELEASE
Wednesday, January 8, 2020

Alcohol-related deaths increasing in the United States

An analysis of U.S. death certificate data by researchers at the National Institute on Alcohol Abuse and Alcoholism (NIAAA), part of the National Institutes of Health, found that nearly 1 million people died from alcohol-related causes between 1999 and 2017. The number of death certificates mentioning alcohol more than doubled from 35,914 in 1999 to 72,558 in 2017, the year in which alcohol played a role in 2.6% of all deaths in the United States. The increase in alcohol-related deaths is consistent with reports of increases in alcohol consumption and alcohol-involved emergency department visits and hospitalizations during the same period. The new findings are reported online in the journal *Alcoholism: Clinical and Experimental Research*.

"Alcohol is not a benign substance and there are many ways it can contribute to mortality," said NIAAA Director Dr. George F. Koob. "The current findings suggest that alcohol-related deaths involving injuries, overdoses, and chronic diseases are increasing across a wide swath of the population. The report is a wakeup call to the growing threat alcohol poses to public health."

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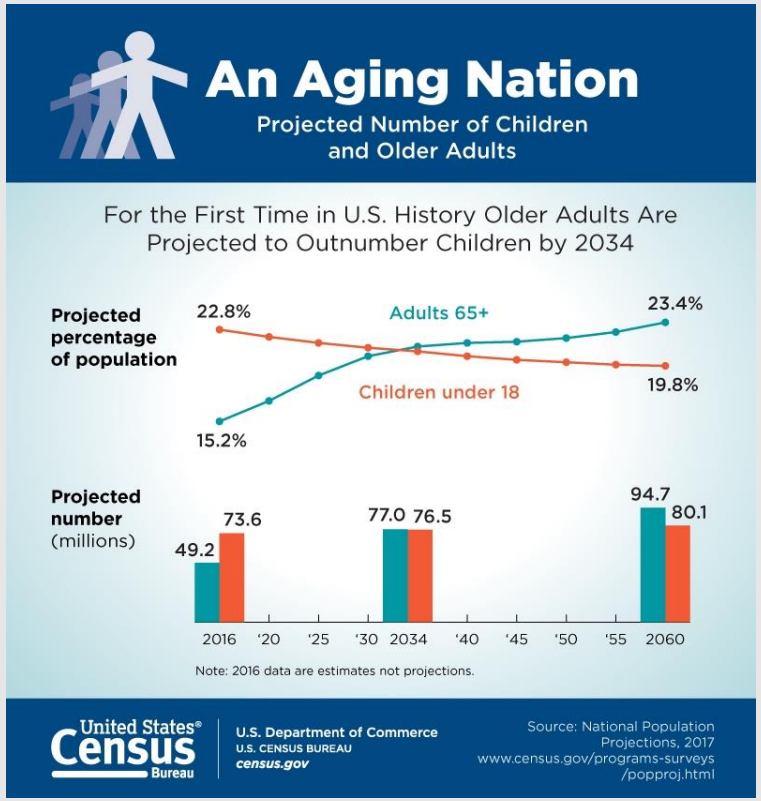
BABY BOOMER GENERATION
Years Born: 1944 to 1964
Current Ages: 54 to 74, first turned age 70 in 2017

A generational review

Han et al. Binge Drinking Among Older Adults in the United States, 2015-2017. J Am Geriatrics Society 2019. 2015-17 U.S. National Survey on Drug Use and Health, n= 10,927 adults

10.6% past month prevalence of excessive alcohol consumption (binge/heavy episodic drinking)



The New York Times

One in 10 Older Adults Binge Drinks, Study Says

A new study looked at the prevalence of heavy drinking among adults 65 and older, who are especially vulnerable to its effects.

AUD direct medical costs account for 58% of all hospital-based substance use disorder care

U.S. direct hospital costs for SUD care, 2017

Encounter type and SUD diagnosis type	Total	Substance							
		Alcohol	Cannabis	Hallucinogen	Inhalant	Opioid	Sedative	Stimulant	Other
ED									
Principal	1985 (1893 to 2077)	2082 (1982 to 2183)	1781 (1675 to 1886)	1677 (1493 to 1862)	1317 (1187 to 1446)	1736 (1642 to 1830)	1815 (1704 to 1926)	2058 (1944 to 2171)	1860 (1746 to 1975)
Secondary	740 (632 to 848)	773 (628 to 918)	491 (375 to 606)	419 (36 to 803)	NS	509 (328 to 690)	620 (316 to 923)	385 (276 to 494)	483 (330 to 637)
Inpatient									
Principal	9693 (9361 to 10 025)	9806 (9353 to 10 259)	8014 (7484 to 8545)	9204 (8709 to 9699)	NC	9068 (8678 to 9458)	8381 (8111 to 8652)	9690 (9336 to 10 045)	5704 (5476 to 5931)
Secondary	NS	NS	165 (36 to 294)	NS	NS	NS	374 (46 to 703)	504 (294 to 713)	NS
Total SUD cost, millions (2017), $*	13 170	7593	740	53	4	2212	371	1447	750

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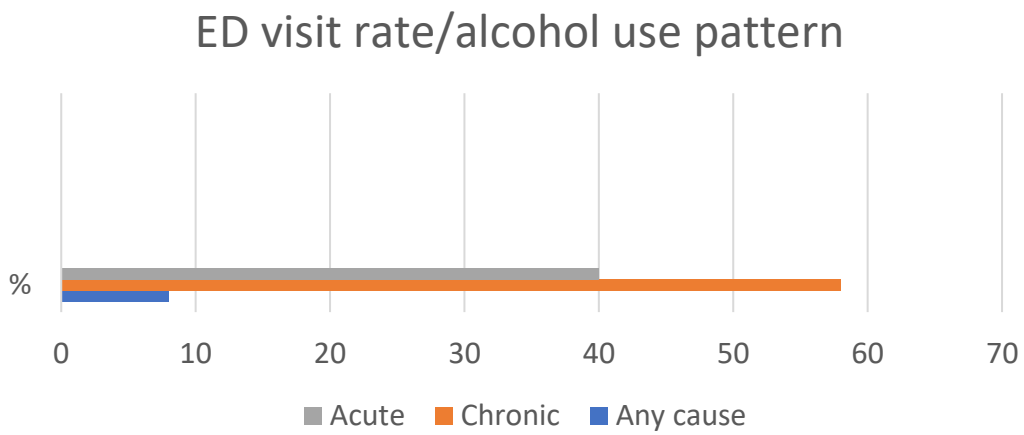
Peterson C, Li M, Xu L, Mikosz CA, Luo F. Assessment of annual cost of substance use disorder in US hospitals. JAMA Netw Open. 2021;4(3):e210242. doi:10.1001/jamanetworkopen.2021.0242JAMA

Healthcare utilization

National Institute on Alcohol Abuse and Alcoholism (NIAAA) study

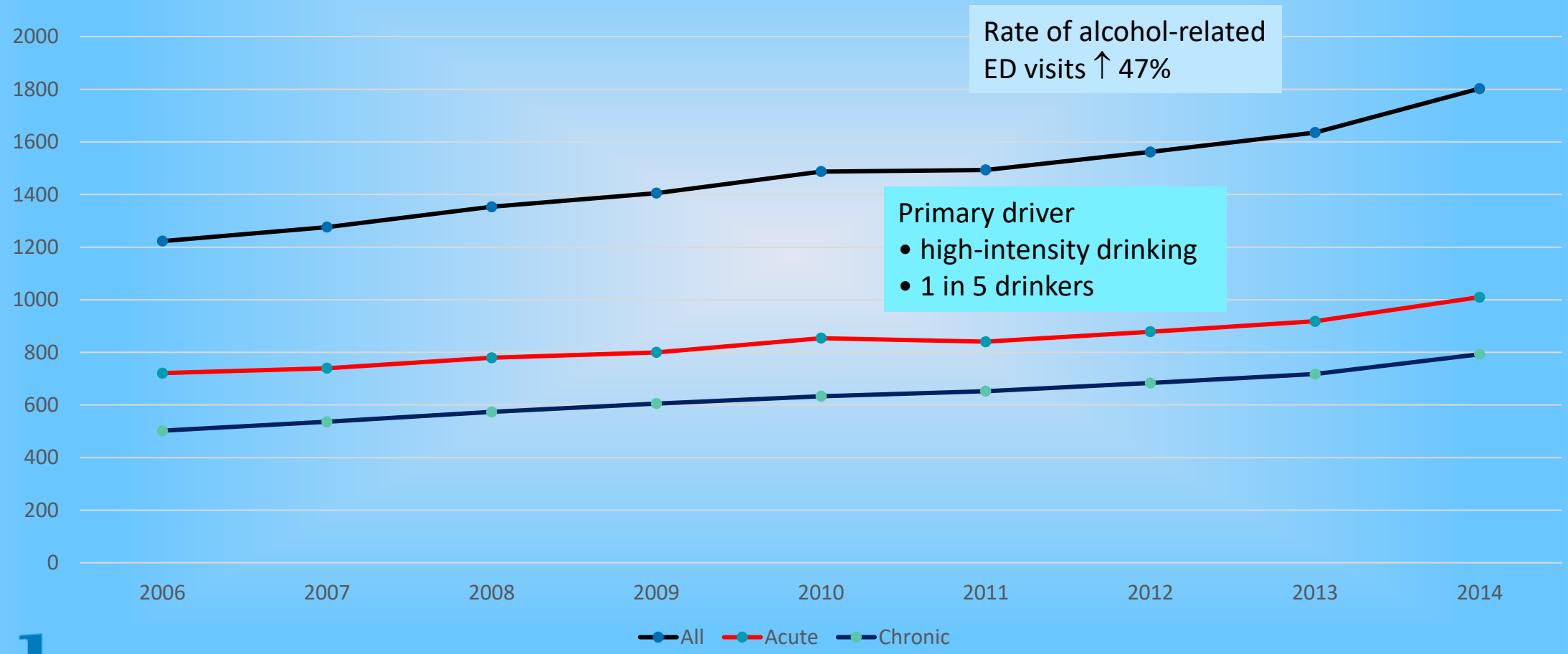
Alcohol-related ED visits

- 47% ⇧
- 210k ⇧ (average annual increase)
- annual ED medical emergencies ⇧ 3 to 5 million
- total annual costs ⇧ 4.1 billion to 15.3 billion



Aaron White, et al. Trends in Alcohol-Related Emergency Department Visits in the United States: Results from the Nationwide Emergency Department Sample, 2006 to 2014. Alcohol Clin Exp Res. 2018 Jan 2. 10.1111/acer.13559

Rates of All, Acute, and Chronic Alcohol-related ED visits and High-Intensity Drinking



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White et al. Trends in Alcohol-Related Emergency Department Visits in the United States: Results from the Nationwide Emergency Department Sample, 2006 to 2014. *Alcohol Clin Exp Res*. 2018. Linden-Carmichael et al. Contemporary alcohol use patterns among a national sample of U.S. adult drinkers. *J Addict Dis*. 2017.

Healthcare utilization

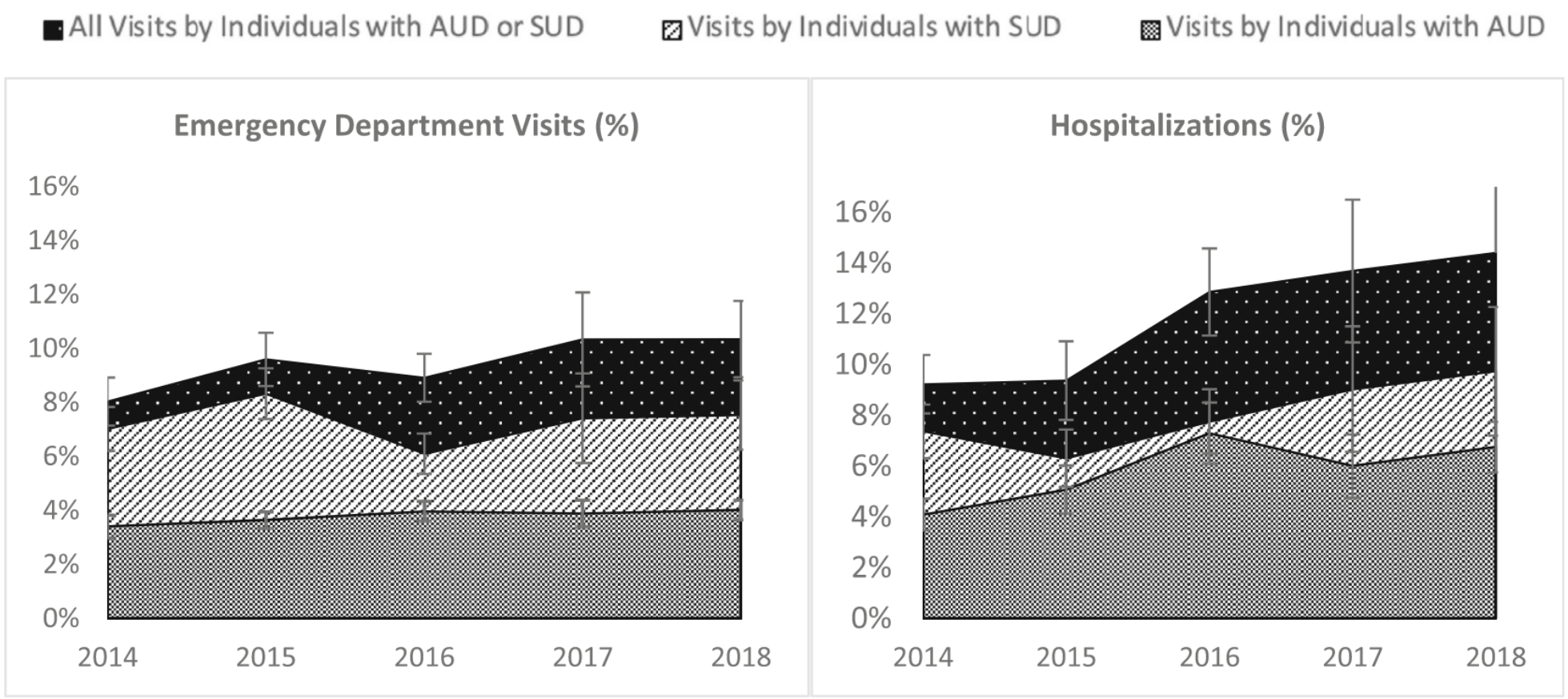
National Institute on Alcohol Abuse and Alcoholism (NIAAA) study

Department Sample (NEDS), a database that contains records from 945 hospitals across the country

- Total alcohol-related ER visits:
  - Overall increase: 61.4%
  - Increase for women: 69.1%
  - Increase for men: 57.9%
- Alcohol-related ER visits for individuals age 25-34:
  - Overall increase: 50.4%
  - Increase for women: 65.7%
  - Increase for men: 43.2%
- Alcohol-related ER visits for individuals age 55-64:
  - Overall increase: 68.3%
  - Increase for women: 80.1%
  - Increase for men: 65.7%

Aaron White, et al. Trends in Alcohol-Related Emergency Department Visits in the United States: Results from the Nationwide Emergency Department Sample, 2006 to 2014. Alcohol Clin Exp Res. 2018 Jan 2. 10.1111/acer.13559

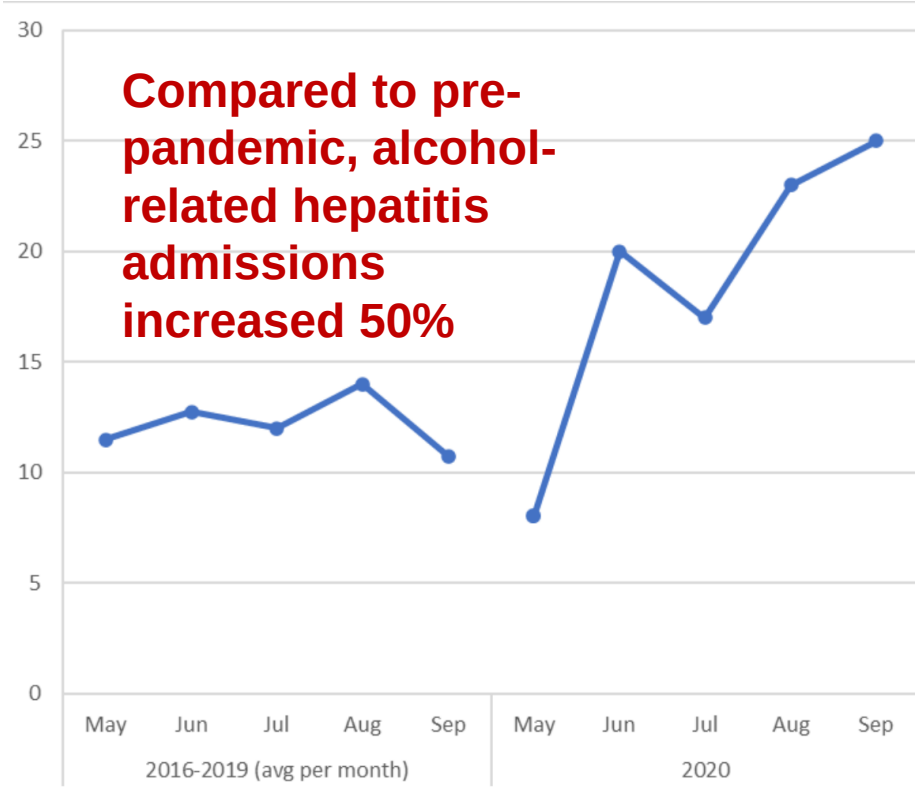
National Prevalence of Alcohol and Other Substance Use Disorders Among Emergency Department Visits and Hospitalizations: National Hospital Ambulatory Medical Care Survey (NHAMCS 2014–2018)



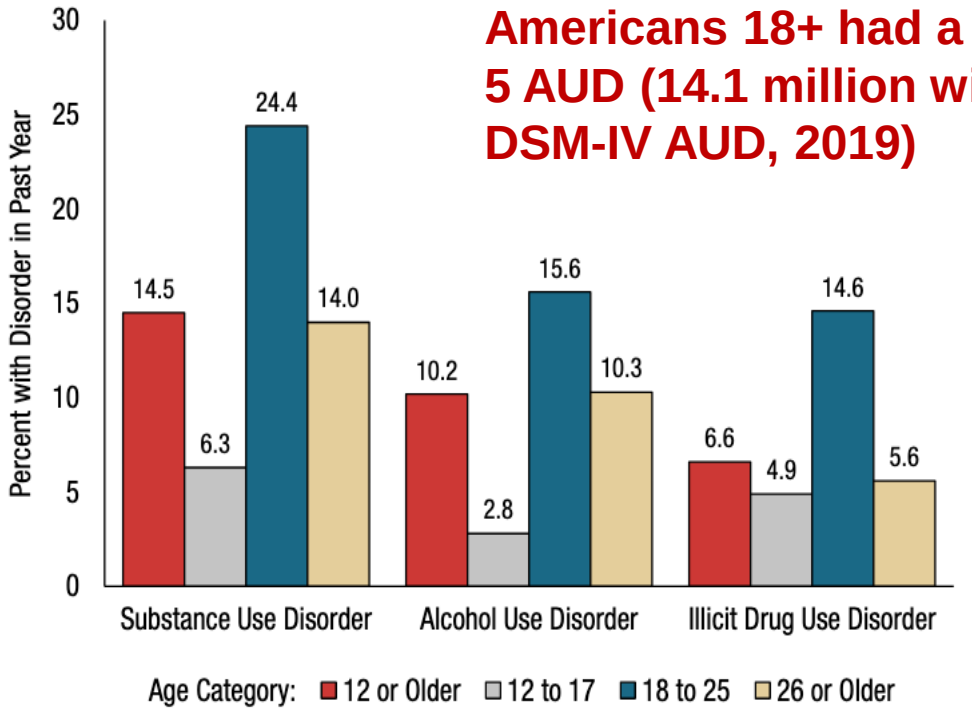
In this nationally representative study, AUD/SUD was present in 1/11 ED visits and 1/9 hospitalizations during this period, a 30% and 57% relative increase.

Alcohol related complications amidst COVID

Alcohol-related liver disease admissions to Henry Ford Health System hospitals for May through September for 2016–2019 (monthly average) compared to 2020.



In 2020, 27.6 million Americans 18+ had a DSM-5 AUD (14.1 million with a DSM-IV AUD, 2019)



Gonzalez HC, Zhou Y, Nimri FM, Rupp LB, Trudeau S, Gordon SC. Alcohol-related hepatitis admissions increased 50% in the first months of the CoViD-19 pandemic in the US [published online ahead of print, 2022 Jan 29]. *Liver Int*. 2022;10.1111/liv.15172. doi:10.1111/liv.15172.

Substance Abuse and Mental Health Services Administration. (2021). Key substance use and mental health indicators in the United States: Results from the 2020 National Survey on Drug Use and Health (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data/

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Objectives

- ❑ Diagnosing AUD
- ❑ AUD epidemiology
- ❑ **Managing severe alcohol withdrawal syndrome**
- ❑ Treating AUD

Alcohol Withdrawal Syndrome (AWS)

DSM-V Diagnostic Criteria

A. Cessation of (or reduction in) alcohol use that has been heavy and prolonged.

B. Two or more of the following developing within hours to days:

- Autonomic hyperactivity
- Increased hand tremor
- Insomnia
- N/v
- Transient visual, tactile, or auditory hallucinations or illusions
- Psychomotor agitation
- Anxiety
- GTCs

C. The s/s cause clinically sig distress or impairment in social, occupational functioning

D. The s/s are not attributable to another medical or psychiatric condition

Alcohol withdrawal is due to a *relative* decrease in serum alcohol level, not a complete absence of alcohol

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American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington, VA 2013.

Clinical scenario (continued)

60-year-old male history of tobacco use disorder c/b COPD, alcohol use presenting to the ED with cough, dyspnea and chest pain found to have pulmonary embolus.

We identified his alcohol consumption pattern as high intensity drinking (1/2 handle vodka daily, ~20 standard drinks).

We diagnosed him with a severe alcohol use disorder.

He states his last drink was two days ago.

He is afebrile, 103/74, 100. Alert, oriented x3, noted tremors and tongue fasciculations.

No BAL obtained on ED presentation.

WHAT IS THE LIKELIHOOD HE WILL DEVELOP A SEVERE ALCOHOL WITHDRAWAL SYNDROME?

Identifying Patients at Risk for AWS

- **PMHx/collaterals/labs**
- **Predictive tools**
  - AUDIT
    - Score ≥8; 100% sensitivity and 90.5% specificity in identifying pts who develop AWS
    - No pts with score <8 developed AWS
  - AUDIT-PC
    - Score ≥4; 91% sensitivity and 90% specificity in identifying pts who develop AWS
  - PAWSS

Alcohol screening questionnaire (AUDIT)

One drink equals:  12 oz. beer  5 oz. wine  1.5 oz. liquor (one shot)

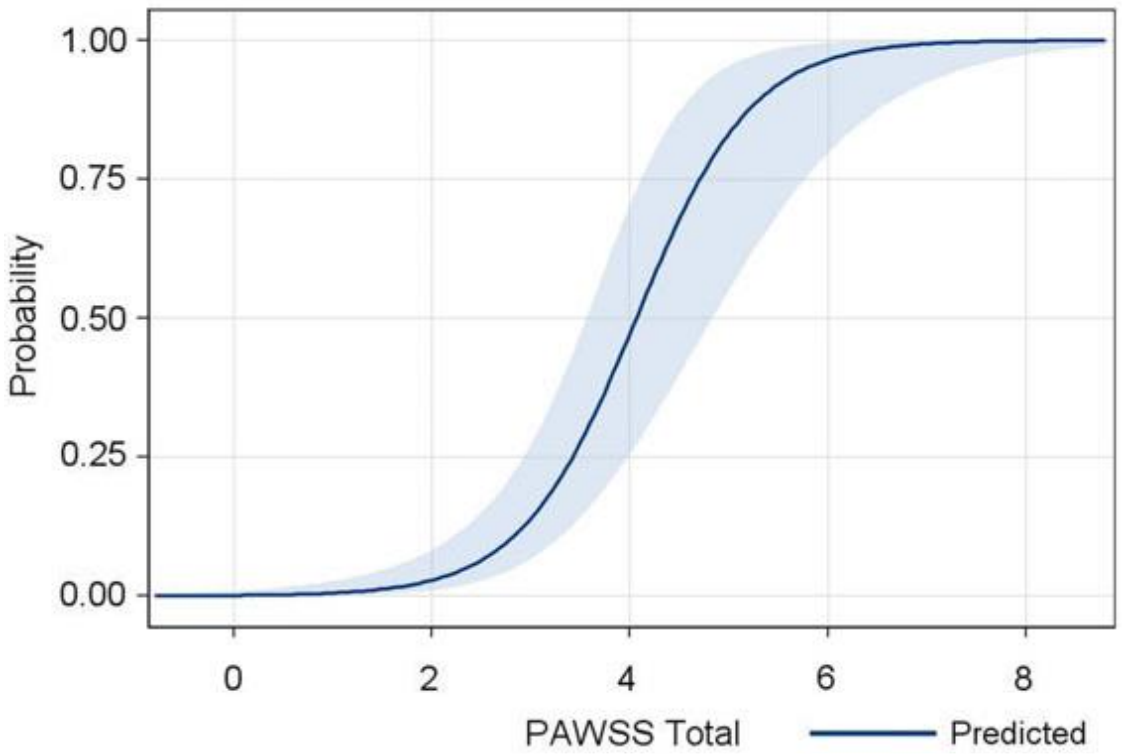
Scoring:	0 points per question	1 point per question	2 points per question	3 points per question	4 points per question
1. How often do you have a drink containing alcohol?	Never	Monthly or less	2 - 4 times a month	2 - 3 times a week	4 or more times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking?	0 - 2	3 or 4	5 or 6	7 - 9	10 or more
3. How often do you have four or more drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
5. How often during the last year have you failed to do what was normally expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because of your drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
9. Have you or someone else been injured because of your drinking?	No		Yes, but not in the last year		Yes, in the last year
10. Has a relative, friend, doctor, or other health care worker been concerned about your drinking or suggested you cut down?	No		Yes, but not in the last year		Yes, in the last year
Add the score for each column:		+	+	+	+
Total Score (add column scores) =					

Society of Hospital Medicine

Dolman JM, Hawkes ND. Combining the AUDIT Questionnaire and Biochemical Markers to Assess Alcohol Use and Risk of Alcohol Withdrawal in Medical Inpatients. Alcohol Alcohol. 2005;40(6):515–519. doi:10.1093/alcalc/agh189.
Pecoraro A, Ewen E, Horton T, et al. Using the AUDIT-PC to Predict Alcohol Withdrawal in Hospitalized Patients. J Gen Intern Med. 2014;29(1):34–40.doi:10.1007/s11606-013-2551-9.https://www.omao.noaa.gov/find/media/images/alcohol-screening-questionnaire-audit

Identifying Patients at Risk for severe AWS

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)



Score ≥ 4 LR 174
Score ≤ 3 LR 0.07

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

Maldonado et al, 2015

Part A: Threshold Criteria: ("Y" or "N", no point)

Have you consumed any amount of alcohol (i.e., been drinking) within the last 30 days? OR did the patient have a "+" BAL on admission? _____

IF the answer to either is YES, proceed with test:

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

1. Have you been recently intoxicated/drunk, within the last 30 days? _____
2. Have you ever undergone alcohol use disorder rehabilitation treatment or treatment for alcoholism? (i.e., in-patient or out-patient treatment programs or AA attendance) _____
3. Have you ever experienced any previous episodes of alcohol withdrawal, regardless of severity? _____
4. Have you ever experienced blackouts? _____
5. Have you ever experienced alcohol withdrawal seizures? _____
6. Have you ever experienced delirium tremens or DT's? _____
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 AWS.
A score of ≥ 4 suggests HIGH RISK for moderate to severe (complicated) AWS; prophylaxis and/or treatment may be indicated.

Society of Hospital Medicine

Maldonado J et al. Prospective Validation of the Prediction of Alcohol Withdrawal Severity Scale (PAWSS) in medically ill inpatients: a new scale for the prediction of complicated alcohol withdrawal syndrome. *Alcohol Alcoholism*. 2015. Wood et al. Will This Hospitalized Patient Develop Severe Alcohol Withdrawal Syndrome? The Rational Clinical Examination Systematic Review. *JAMA.* 2018;*320*(8), 825–833.

Clinical scenario (continued)

60-year-old male history of tobacco use disorder c/b COPD, alcohol use presenting to the ED with cough, dyspnea and chest pain found to have pulmonary embolus.

We identified his alcohol consumption pattern as high intensity drinking (1/2 handle vodka daily, ~20 standard drinks).

We diagnosed him with a severe alcohol use disorder.

He states his last drink was two days ago.

He is afebrile, 103/74, 100. Alert, oriented x3, noted tremors and tongue fasciculations.

No BAL obtained on ED presentation.

PAWSS score = 6

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Clinical scenario (continued)

Patient received 2mg IV lorazepam

Four hours later, vitals 122/82, 92

CIWA score 9 (tremors, anxiety, headaches)

Patient received 4mg IV lorazepam

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Clinical scenario (continued)

One hour later, now confused and attempting to get out of stretcher

Over the course of 20 minutes received 8mg IV lorazepam (total 16mg in past 2 hours)

Vitals 150/100, 102

CIWA 47!

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Alcohol withdrawal severity

Revised Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale

Tool to assess AWS symptoms, 10 items, easy to implement

Assessment of treatment effectiveness

Scoring

<8 mild, 8-15 moderate, >15 severe

Sullivan, 1991

- Less benzodiazepine use (50mg versus 75mg)

- No effect on rates of complications, LOS

Table 1. *Correlations (r values) of Individual Items With Total CIWA-A Score*

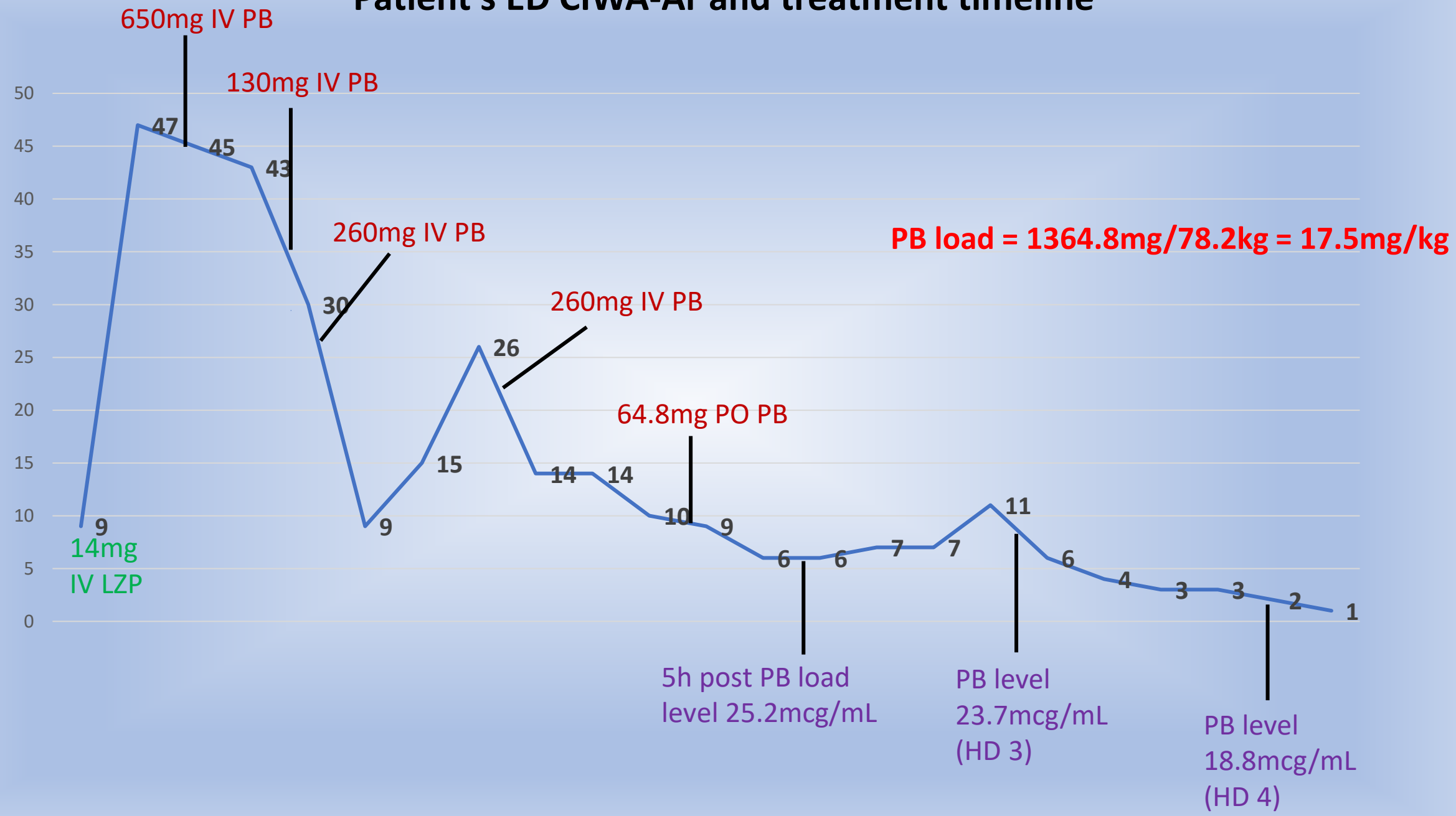
Sweating	0.58
Anxiety	0.55
Tremor	0.49
Auditory disturbances	0.48
Visual disturbances	0.48
Agitation	0.41
Nausea	0.40
Tactile disturbances	0.39
Headache	0.30
Orientation and clouding of sensorium	0.12

Pulse (r=0.27, p<0.005), SBP (r=0.14, NS), DBP (-0.14, NS) did not correlate with severity of withdrawal

Society of Hospital Medicine

Sullivan et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989. Sullivan et al. Benzodiazepine Requirements During Alcohol Withdrawal Syndrome. *J Clinical Psychopharmacology* 1991.

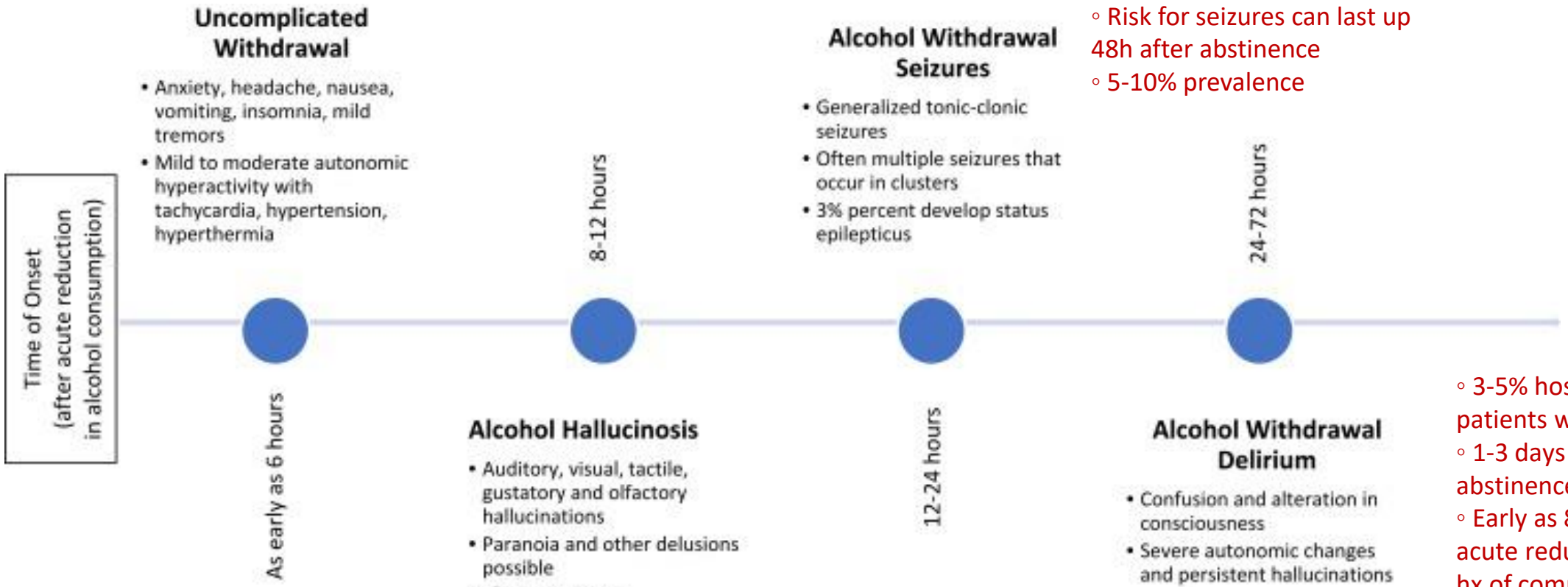
Patient's ED CIWA-Ar and treatment timeline



MGH Emergency D... | M | MGH Emergency Dept | MGH Emergency Dept

07/16 | 07/17

Stages of Alcohol Withdrawal Syndrome



Uncomplicated Withdrawal

- Anxiety, headache, nausea, vomiting, insomnia, mild tremors
- Mild to moderate autonomic hyperactivity with tachycardia, hypertension, hyperthermia

Alcohol Hallucinosis

- Auditory, visual, tactile, gustatory and olfactory hallucinations
- Paranoia and other delusions possible
- Clear sensorium

◦ 2-8% w/ chronic, heavy alcohol use, drinking at age 17 or earlier
◦ Antipsychotics can mask sxs of progressive w/d, delay tx

Alcohol Withdrawal Seizures

- Generalized tonic-clonic seizures
- Often multiple seizures that occur in clusters
- 3% percent develop status epilepticus

◦ Risk for seizures can last up 48h after abstinence
◦ 5-10% prevalence

Alcohol Withdrawal Delirium

- Confusion and alteration in consciousness
- Severe autonomic changes and persistent hallucinations

◦ 3-5% hospitalized patients w/ AWS
◦ 1-3 days after abstinence
◦ Early as 8 hours after acute reduction in use w/ hx of complicated W/D
◦ 20% mortality rate, infection, cardiac arrhythmias, respiratory failure

Society of Hospital Medicine

Wolf. Management of Alcohol Withdrawal in the Emergency Department: Current Perspectives. Open Access Emergency Medicine. 2020.

Clinical Institute Withdrawal Assessment of Alcohol, revised

CIWA-Ar

Compared to fixed-dose regimens:

- **Individualized dosing help reduce over- or under-dosing**
- **Reduced total benzodiazepine dose**
- **Shorter duration of treatment**
- **Reduced length of stay?**

Table 1. *Correlations (r values) of Individual Items With Total CIWA-A Score*

Sweating	0.58
Anxiety	0.55
Tremor	0.49
Auditory disturbances	0.48
Visual disturbances	0.48
Agitation	0.41
Nausea	0.40
Tactile disturbances	0.39
Headache	0.30
Orientation and clouding of sensorium	0.12

Society of Hospital Medicine

- Sullivan et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989.
- Sullivan et al. Benzodiazepine Requirements During Alcohol Withdrawal Syndrome. *J Clinical Psychopharmacology* 1991.
- ASAM Clinical Practice Guideline on Alcohol Withdrawal Management 2020

CIWA-Ar Disadvantages

- Patient cognitive and communicative abilities must be intact for questions to be answered appropriately
- Not validated in ED or or use in the ED or hospitalized patients
- Symptom-triggered protocols can be complicated by co-morbid psychiatric or medical illness given that there may be significant overlap between symptoms of alcohol withdrawal and a primary psychotic or mood disorder (anxiety, agitation, hallucinations).
- AWS symptoms may be seen independently in medically ill patients (N/V, headache, diaphoresis), delirium due to a separate etiology (clouded sensorium, perceptual disturbances).
- Patients may exaggerate the subjective symptoms of alcohol withdrawal in order to receive more benzodiazepines.

Society of Hospital Medicine

Sullivan et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989. Sullivan et al. Benzodiazepine Requirements During Alcohol Withdrawal Syndrome. *J Clinical Psychopharmacology* 1991.

Treatment of AWS

Overview

- **Outpatient management**
- **Inpatient management**
  - Supportive
  - Symptom-triggered benzodiazepines
  - Fixed-schedule benzodiazepines
  - Phenobarbital

Individualized Treatment for Alcohol Withdrawal

A Randomized Double-blind Controlled Trial

Richard Saitz, MD, MPH; Michael F. Mayo-Smith, MD, MPH; Mark S. Roberts, MD, MPP; Harriet A. Redmond, MS, ARNP, CARN; Donald R. Bernard, MD; David R. Calkins, MD, MPP

Objective.—To assess the effect of an individualized treatment regimen on the intensity and duration of medication treatment for alcohol withdrawal.

Design.—A randomized double-blind, controlled trial.

Setting.—An inpatient detoxification unit in a Veterans Affairs medical center.

Patients.—One hundred one patients admitted for the treatment of alcohol withdrawal who could give informed consent and had no history of seizures or medication use that might alter the clinical course of withdrawal.

Intervention.—Patients were randomized to either a standard course of chlordiazepoxide four times daily with additional medication as needed (fixed-schedule therapy) or to a treatment regimen that provided chlordiazepoxide only in response to the development of the signs and symptoms of alcohol withdrawal (symptom-triggered therapy). The need for administration of "as-needed" medication was determined using a validated measure of the severity of alcohol withdrawal.

Main Outcome Measures.—Duration of medication treatment and total chlordiazepoxide administered.

Results.—The median duration of treatment in the symptom-triggered group was 9 hours compared with 68 hours in the fixed-schedule group ($P<.001$). The symptom-triggered group received 100 mg of chlordiazepoxide, and the fixed-schedule group received 425 mg ($P<.001$). There were no significant differences in the severity of withdrawal during treatment or in the incidence of seizures or delirium tremens.

Conclusions.—Symptom-triggered therapy individualizes treatment, decreases both treatment duration and the amount of benzodiazepine used, and is as efficacious as standard fixed-schedule therapy for alcohol withdrawal.

(*JAMA*. 1994;272:519-523)

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Symptom-triggered vs fixed BZD regimen

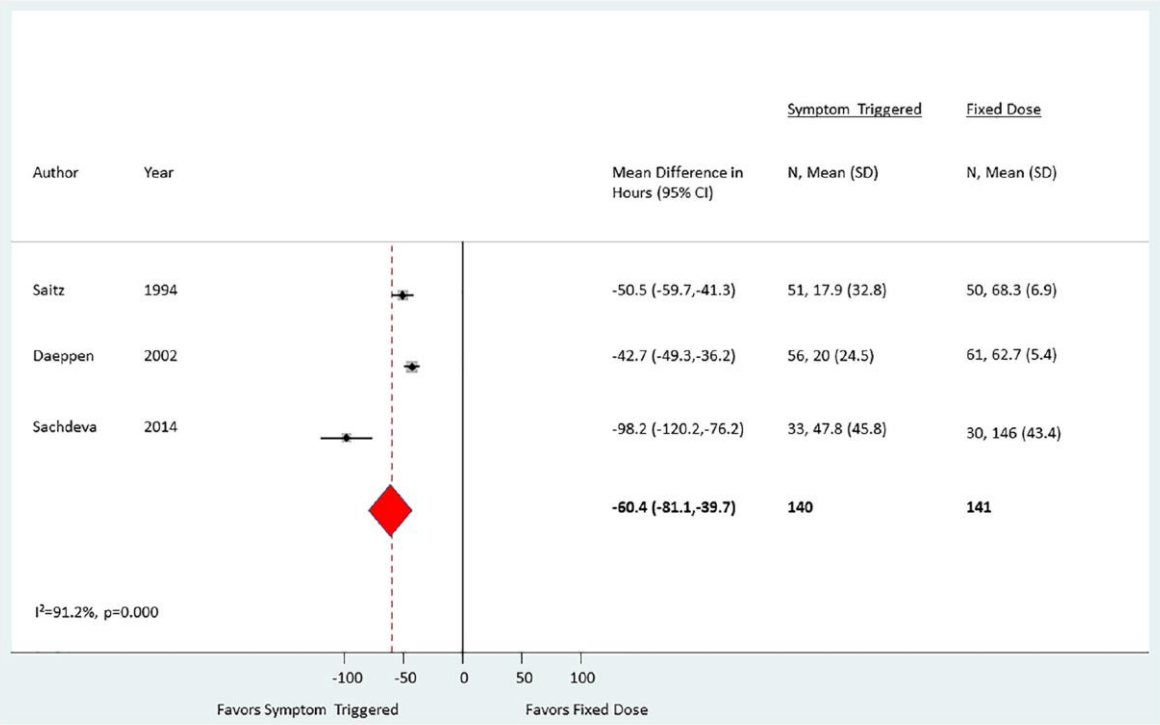


Figure 2 Difference in duration of treatment in hours.

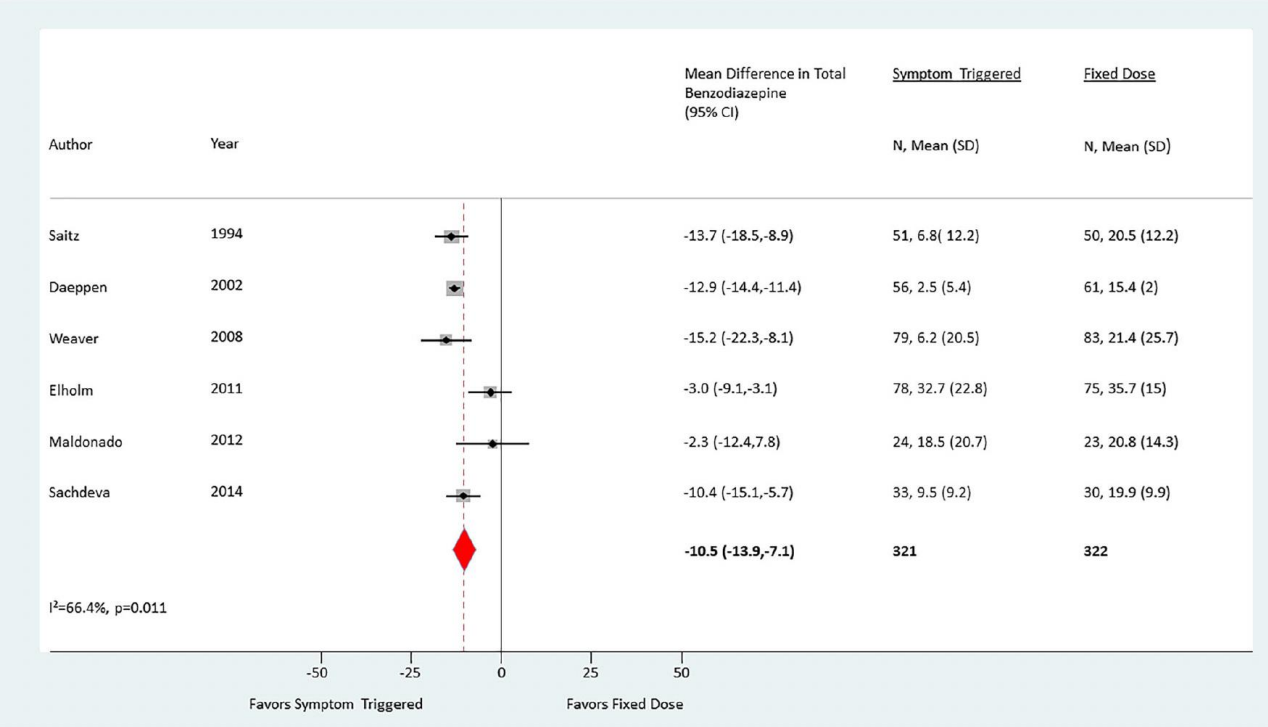


Figure 3 Difference in mean total benzodiazepine dose (mg lorazepam): symptom-triggered therapy (STT) vs fixed dose therapy (FDT).

Too few mortality, seizures, delirium to allow comparison

Shorter duration of treatment ≠ shorter LoS

Society of Hospital Medicine

Holleck et al. Symptom-triggered therapy for alcohol withdrawal syndrome: A systematic review and meta-analysis of randomized controlled trials. *Journal of General Internal Medicine.* 2019;*34*(6):1018–1024

ASAM 2020 Clinical Practice Guideline on Alcohol Withdrawal Management

Medication	Regimen	Description, Examples
Benzodiazepines *(doses in Chlordiazepoxide)*	Typical single dose	Mild withdrawal (CIWA-Ar < 10): 25–50 mg PO Moderate withdrawal (CIWA-Ar 10–18): 50–100 mg PO Severe withdrawal (CIWA-Ar ≥19): 75–100 mg PO
	Symptom-triggered	25–100 mg PO q4–6h when CIWA-Ar ≥10. Additional doses PRN.
	Fixed-dose	Taper daily total dose by 25–50% per day over 3–5 days by reducing the dose amount and/or dose frequency. Additional doses PRN. Day 1: 25–100 mg PO q4–6h Day 2: 25–100 mg PO q6–8h Day 3: 25–100 mg PO q8–12h Day 4: 25–100 mg PO at bedtime (Optional) Day 5: 25 to 100 mg PO at bedtime
	Front loading	*Symptom-triggered:* 50–100 mg PO q1–2h until CIWA-Ar < 10. *Fixed-dose:* 50–100 mg PO q1-2h for 3 doses.
Phenobarbital	Typical single dose	10 mg/kg IV infused over 30 minutes or 60-260 mg PO/IM.
	Monotherapy	*Symptom-triggered in the ICU:* 130 mg IV q30m to target a RASS score of 0 to -1. *Fixed dose in the ED:* Loading dose 260 mg IV, then 130 mg IV q30m at physician's discretion. *Fixed dose in ambulatory management:* Loading dose 60–120 mg PO. Then 60 mg PO q4h until patient is stabilized. Then 30–60 mg PO q6h tapered over 3–7 days. Additional doses PRN.
	Adjunct therapy	*Single dose in the ED:* 10 mg/kg IV infused over 30 minutes. *Escalating dose in the ICU:* After maximum diazepam dose (120 mg), if RASS ≥1, escalating dose of 60 mg → 120 mg → 240 mg IV q30m to target RASS score of 0 to -2.
Carbamazepine (Tegretol)	Monotherapy	600–800 mg total per day tapered to 200–400 mg/d over 4–9 days.
	Adjunct therapy	200 mg q8h or 400 mg q12h.
Gabapentin (Neurontin)	Monotherapy	Loading dose 1200 mg, then 600 mg q6h on Day 1 or 1200 mg/d for 1–3 days, tapered to 300–600 mg/d up to 4–7 days. Additional doses PRN.
	Adjunct therapy	400 mg q6–8h.
Valproic acid (Depakene)	Monotherapy	1200 mg/d tapered to 600 mg/d over 4–7 days or 20 mg/kg/d.
	Adjunct therapy	300–500 mg q6–8h.

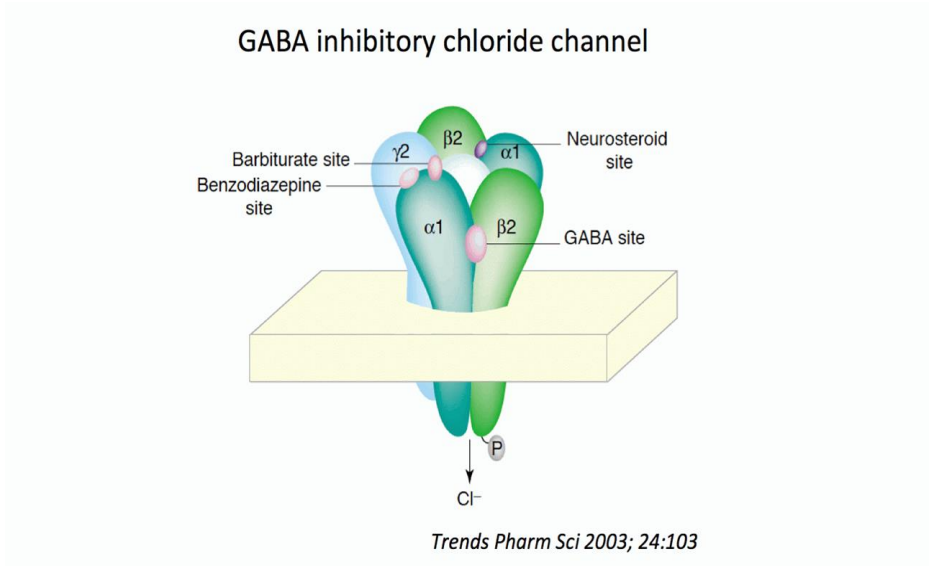
CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol, Revised; ED, Emergency Department; h, hour(s); ICU, Intensive Care Unit; IM, intramuscularly; IV, intravenously; m, minute(s); mg, milligrams; PO, by mouth; PRN, as needed; q, every; RASS, Richmond Agitation Sedation Scale.

Phenobarbital

Rationale

- **Some pts may not response to BZDs due to GABA subunit changes leading to BZD cross-tolerance**
  - PHB both decrease glutamate activity and increase duration of GABA-A Cl channel opening – unique binding site
- **Iatrogenic BZD-induced delirium**
- **Wide margin of safety**
- **Targeted dosing to therapeutic serum conc**
- **Rapid onset and long duration**

Dosage Form	Bioavailability	Comments
IM	100% (F = 1)	Onset of action within 30 min; time to peak concentrations ≤3 hr
IV	100% (F = 1)	Immediate onset of action
Rectal	90% (F = 0.9)	Faster rate of absorption than oral or IM routes
Oral (capsules, tablets, elixir)	90% to 100% (F = 0.90–1)	Time to peak variable (~2 hr)



Trends Pharm Sci 2003; 24:103

Society of Hospital Medicine

Nisavic et al. (2019). Use of phenobarbital in alcohol withdrawal management - A retrospective comparison study of phenobarbital and benzodiazepines for acute alcohol withdrawal management in general medical patients. 2019. *Psychosomatics. 2019*;*60*(5):458–467. Young et al. Intravenous Phenobarbital for Alcohol Withdrawal and Convulsions. 1987. Annals of Emergency Medicine.

Phenobarbital vs. benzodiazepines

TABLE 3. Medical Outcomes of Patients Treated With Benzodiazepines or Phenobarbital for Alcohol Withdrawal Symptoms

	Benzodiazepines ($N = 419$)	Phenobarbital ($N = 143$)	Test statistics, p value
Primary outcomes	N (%)	N (%)	
Seizures	4 (1%)	1 (1%)	NS
Hallucinations	10 (2%)	3 (2%)	NS
Delirium	28 (7%)	6 (4%)	$\chi^2 = 1.16, p = 0.28$
ICU admissions	48 (12%)	17 (12%)	$\chi^2 = 0.01, p = 0.89$
Secondary outcomes			
Left against medical advice	50 (12%)	9 (6%)	$\chi^2 = 3.61, p = 0.06$
Mortality	1 (0%)	0 (0%)	NS
	Mean ± SD	**Mean ± SD**	
Length of stay (days)	5.14 ± 5.54	5.31 ± 2.91	$t = 0.34, p = 0.73$
ICU length of stay (days)	3.56 ± 3.19	3 ± 2.89	$t = -0.64, p = 0.53$
Medication adverse events	***N* (%)**	***N* (%)**	
Pancytopenia	0 (0%)	1 (1%)	NS
Sedation	6 (1%)	0 (0%)	NS

The abbreviation "NS" denotes instances where insufficient data were available for statistical analysis.

Note: Benzodiazepine group includes those initially treated with benzodiazepines and then transitioned to phenobarbital and phenobarbital group includes one patient initially treated with phenobarbital and transitioned to benzodiazepines mid-taper.

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Nisavic et al. Use of phenobarbital in alcohol withdrawal management - A retrospective comparison study of phenobarbital and benzodiazepines for acute alcohol withdrawal management in general medical patients. *Psychosomatics*, *60*(5), 458–467. doi:10.1016/j.psym.2019.02.002

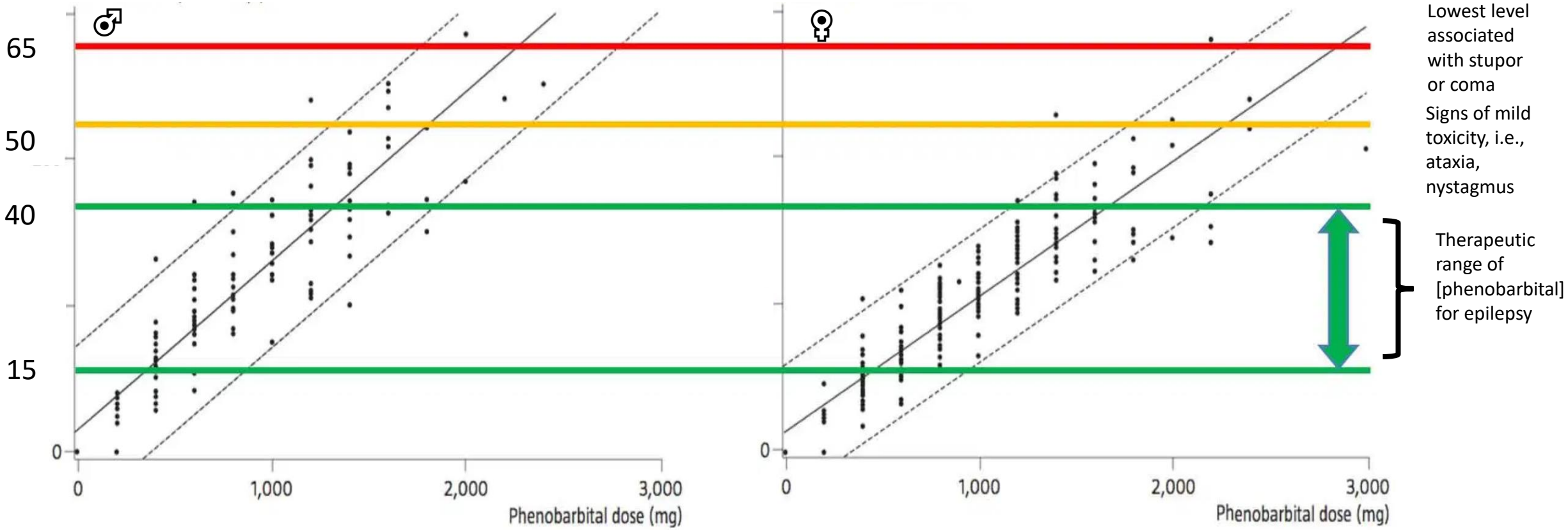
Phenobarbital (doses used for AWS) has a wide margin of safety; targeted dosing to therapeutic serum concentration

Ideal [phenobarbital] for treatment of alcohol withdrawal is unclear

If a patient's weight is considered, these relationships would be even more tightly linear

Based on this data, 1 gram of phenobarbital would achieve a reasonable phenobarbital level in nearly all patients

Relationship between cumulative dose (mg) and plasma phenobarbital concentration (µg/mL) among patients treated for alcohol withdrawal



Tangmose et al. Linear Correlation Between Phenobarbital Dose and Concentration in Alcohol Withdrawal Patients. *Danish Medical Bulletin.* 2010;57(8)

MGH experience: Phenobarbital IM Protocol

Order Sets

- Cirrhosis:
  - 8 mg/kg if with acute withdrawal symptoms
  - 6 mg/kg if no active symptoms
- Risk of respiratory compromise (pneumonia, chest tube, rib fracture, pulmonary contusion, COPD, asthma):
  - 8 mg/kg if with acute withdrawal symptoms
  - 6 mg/kg if no active symptoms
- Risk of sedation: If 2 or more of the following, consider 6-8 mg/kg
  - Age >65 years old
  - Non-cirrhotic hepatic dysfunction
  - Active medication order for opioids
  - Recent head injury
  - Active medication order for sedatives
- If the patient has received benzodiazepines in the last 8-12 hours:
  - If between 8 mg and 30 mg lorazepam (or equivalent dosing of another benzodiazepine), decrease phenobarphital load by 2 mg/kg
  - If >30 mg lorazepam (or equivalent dosing of another benzodiazepine) with ongoing active symptoms of alcohol withdrawal, 6-8 mg/kg loading dose

DO NOT give benzodiazepines once phenobarbital is initiated.

○ PHENobarbital-based Alcohol Detox 6 mg/kg load

○ PHENobarbital-based Alcohol Detox 8 mg/kg load

○ PHENobarbital-based Alcohol Detox 10 mg/kg load

◉ PHENobarbital-based Alcohol Detox 12 mg/kg load

○ PHENobarbital-based Alcohol Detox Intravenous Load

◉ PHENobarbital-based Alcohol Detox Intramuscular Load: 4 mg/kg, Intramuscular, Every 3 hours, for 3 doses (equivalent of 12 mg/kg target dose)

☑ PHENobarbital (LUMINAL) 130 mg/mL injection 234 mg ($$$)
234 mg (rounded from 237.2 mg = 4 mg/kg × 59.3 kg Ideal weight), Intramuscular, Every 3 hours, Next dose today at 1345, For 3 doses
Do NOT administer benzodiazepines to patient while on phenobarbital.

ⓘ **PHENobarbital**
↑ Single dose of **234 mg (4 mg/kg) exceeds** recommended maximum of **88.95 mg (1.5 mg/kg)**, over by **164%**
↑ Daily dose of **702 mg (4 mg/kg Every 3 hours) exceeds** recommended maximum of **177.9 mg (3 mg/kg)**, over by **295%**

☑ PHENobarbital PO Taper - starting Day 2

PHENobarbitaL (LUMINAL) tablet 64.8 mg ($$) ⓘ
64.8 mg, Oral, 2 times daily, Next dose tomorrow at 0900, For 2 days
This order is for Phenobarbital Oral Taper, Days 2 and 3 Dosing (of 5 total days on the Alcohol Withdrawal Treatment Protocol - note that this oral taper begins on the day after the Phenobarbital Load is completed).

Followed By

PHENobarbitaL (LUMINAL) tablet 32.4 mg ($$)
32.4 mg, Oral, 2 times daily, Next dose on Sun 8/22/21 at 0900, For 2 days
This order is for Phenobarbital Oral Taper, Days 4 and 5 Dosing (of 5 total days on the Alcohol Withdrawal Treatment Protocol).

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Objectives

- ❑ Diagnosing AUD
- ❑ AUD epidemiology
- ❑ Managing severe alcohol withdrawal syndrome
- ❑ **Treating AUD**

FDA approved pharmacotherapy for alcohol use disorders

Medication	Mechanism of Action	Route	Dosage	Indication	Contraindication	Clinical Pearls
Naltrexone (Revia®)	Opioid antagonist/decreases reinforcing effect of EtOH	PO	50 mg/d	Reduction in EtOH or Abstinence	Opioid dependence or active use disorder/agonist Rx	Can start if actively drinking or abstinent
Naltrexone (Vivitrol®)	Opioid antagonist/decreases reinforcing effect of EtOH	IM	380 mg gluteal/month	Reduction in EtOH or Abstinence	Opioid dependence or active use disorder/agonist Rx	If rapid start, observe tolerance of oral dose first at least 60 mins prior to injection
Acamprosate (Campral®)	Unclear: GABA receptor agonist/NMDA modulator/glutamate inhibitor	PO	666mg TID	Abstinence	Severe renal dysfunction	Consider 999mg bid if cannot tolerate TID dosing. Best outcomes if start at least a few days after EtOH cessation
Disulfiram (Antabuse ®)	Aversive, aldehyde dehydrogenase inhibitor causes accumulation of aldehyde	PO	250-500 mg/d	Abstinence	Pregnancy, Elderly, Esophageal Varices, CAD, Nickel Allergy, Active EtOH	Reserved for those patients with clear desire and ability to abstain. Not recommended as first line agent. Can be helpful in risky situations, “prn” Caution with hand sanitizer/mouthwash/other alcohol containing products

Efficacy and Tolerability of Long-Acting Injectable Naltrexone (ER-NTX) for Alcohol Dependence: A Randomized Controlled Trial

Table 3. Analyses of Primary and Secondary Efficacy Outcomes*

	Population	Naltrexone 380 mg vs Placebo		Naltrexone 190 mg vs Placebo	
		Hazard Ratio (95% CI)	*P* Value	Hazard Ratio‡ (95% CI)	*P* Value
Primary outcome					
Heavy drinking	624	0.75 (0.60-0.94)	.02	0.83 (0.68-1.02)	.07
Sex					
Men	423	0.56 (0.41-0.77)	<.001	0.83 (0.64-1.07)	.16
Women	201	1.23 (0.85-1.78)	.28	1.07 (0.73-1.58)	.72
Goal of total abstinence					
Yes	270	0.72 (0.48-1.06)	.11	0.88 (0.61-1.28)	.50
No	354	0.79 (0.59-1.05)	.10	0.91 (0.70-18)	.48
Lead-in drinking					
Yes	571	0.79 (0.62-1.00)	.05	0.83 (0.75-1.15)	.48
No	53	0.20 (0.07-0.62)	.005	0.05 (0.02-0.15)	<.001
Secondary outcomes					
Risky drinking†	624	0.90 (0.76-1.07)	.23	0.95 (0.81-1.13)	.58
Nonabstinent days	624	0.96 (0.83-1.11)	.58	0.98 (0.85-1.14)	.80

*For the primary end point (heavy drinking), the Hochberg method was used to adjust multiple comparisons. As specified a priori, the secondary outcomes (drinking more than the National Institute on Alcohol Abuse and Alcoholism–specified level of risky drinking and nonabstinent days) are included for informational purposes, and no adjustments were made.

†National Institute on Alcohol Abuse and Alcoholism–specified level of risky drinking is more than 2 drinks per day for men and more than 1 drink for women.

‡Treatment effect size is derived from the estimate of the hazard ratio (HR) for each individual treatment relative to placebo: HR = 1 indicates no treatment effect (ie, treatment effect size = 0); HR = 0.75 is a 25% reduction of heavy drinking relative to placebo (ie, treatment effect size relative to placebo = 0.25); HR = 1.25 is a 25% increase of heavy drinking relative to placebo (ie, treatment effect size relative to placebo = 1.25).

- ER-NTX 380mg: 25% greater reduction in rate of heavy drinking (p=0.02)
- ER-NTX 190mg: 17% greater reduction
- 15% reduction in γ-GT

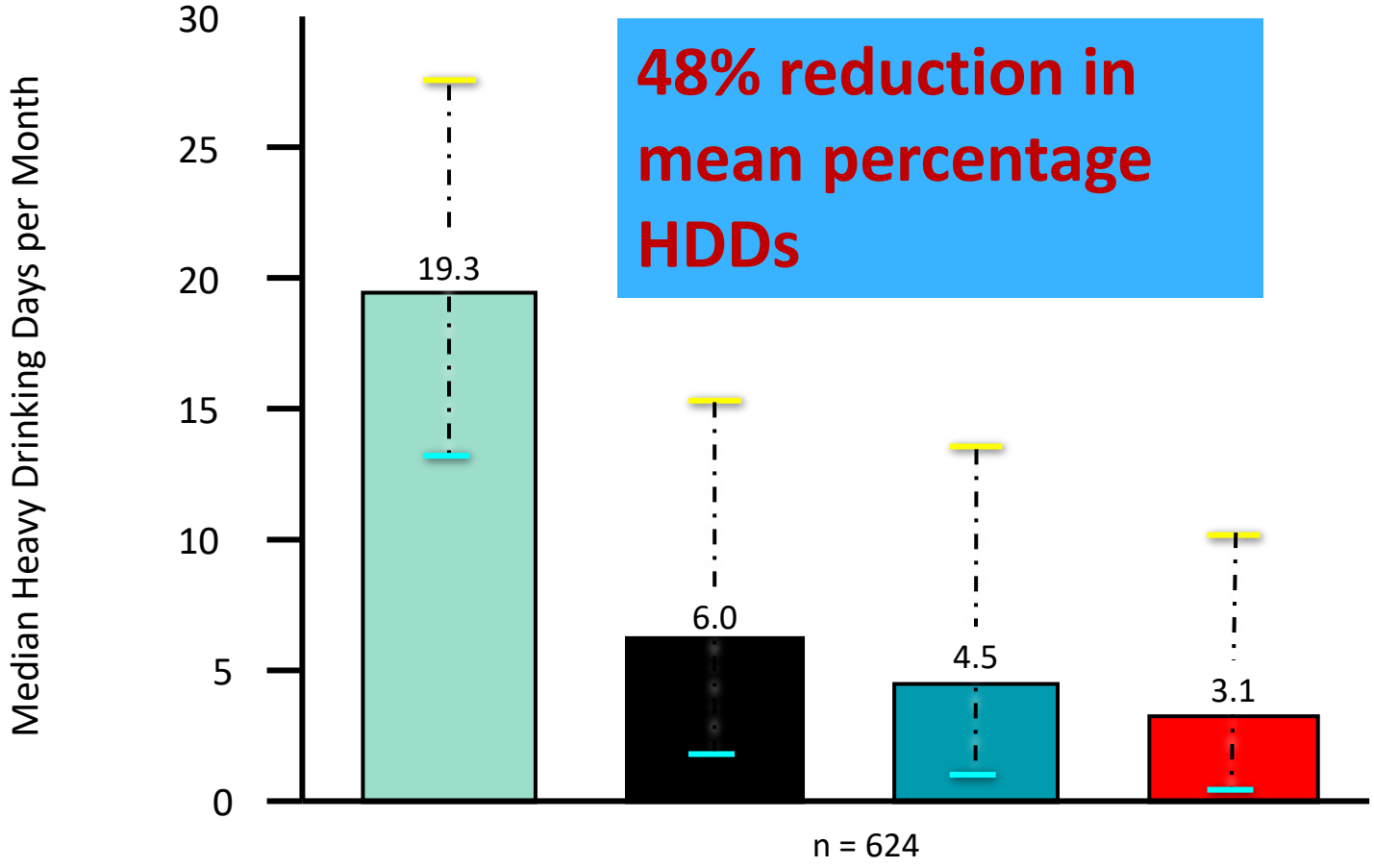
Subgroup analyses

- ♂: 44% greater reduction (p <0.01)
- ♀: factor analyses did not show explanations for lack of treatment responses
- Alcohol use (91.7%): 21% greater reduction (p=0.05)
- No alcohol use: ⇧ total abstinent rates (41%, ER-NTX 380mg, 35% 190mg, 17% placebo)

Society of Hospital Medicine

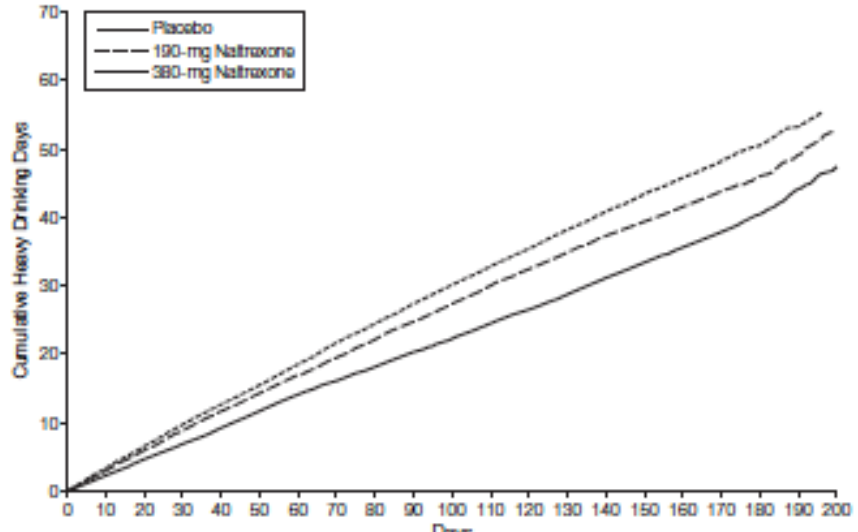
Garbutt JC, Kranzler HR, O'Malley SS, et al. Efficacy and tolerability of long-acting injectable naltrexone for alcohol dependence: a randomized controlled trial. JAMA. 2005;293(16):1617-1625.

Efficacy and Tolerability of Long-Acting Injectable Naltrexone for Alcohol Dependence: A Randomized Controlled Trial



48% reduction in mean percentage HDDs

Figure 2. Primary Efficacy Analysis: Mean Heavy Drinking Event Rate



Treatment Dose	1	2	3	4	5	6
No. of Patients						
Placebo	209	194	169	160	142	134
Naltrexone						
190 mg	210	187	169	156	144	137
380 mg	205	186	161	147	139	130

Intention-to-treat analysis shows the cumulative mean event rate of heavy drinking during the study by treatment group. The participant retention rates are shown at 4-week intervals through 24 weeks, which was the intended duration of the treatment.

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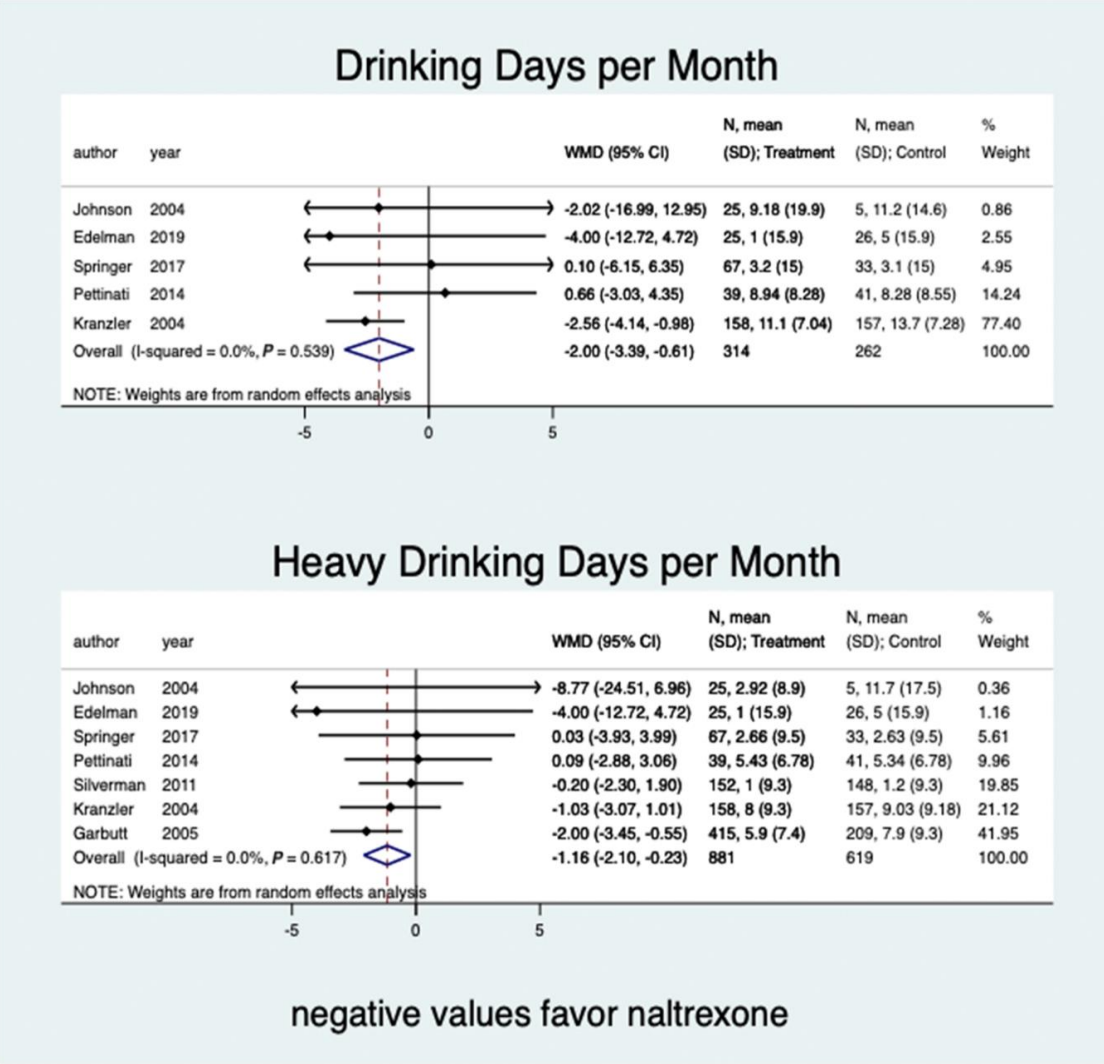
ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION
REVIEW
doi:10.1111/add.15572

Effect of extended-release naltrexone on alcohol consumption: a systematic review and meta-analysis



1° outcomes

- Monthly DDs – two fewer (5 studies, WMD -2.0, p = 0.03)
- Monthly HDDs – 1.2 fewer (7 studies, WMD -1.2, p = 0.02)
- Relapse to any drinking (abstinence for duration of trial) - pooled RD 2% (3 studies, p = 0.15, moderate heterogeneity)
- Relapse to heavy drinking (no HDD during trial) – pooled RD 1% (4 studies, p = 0.8)

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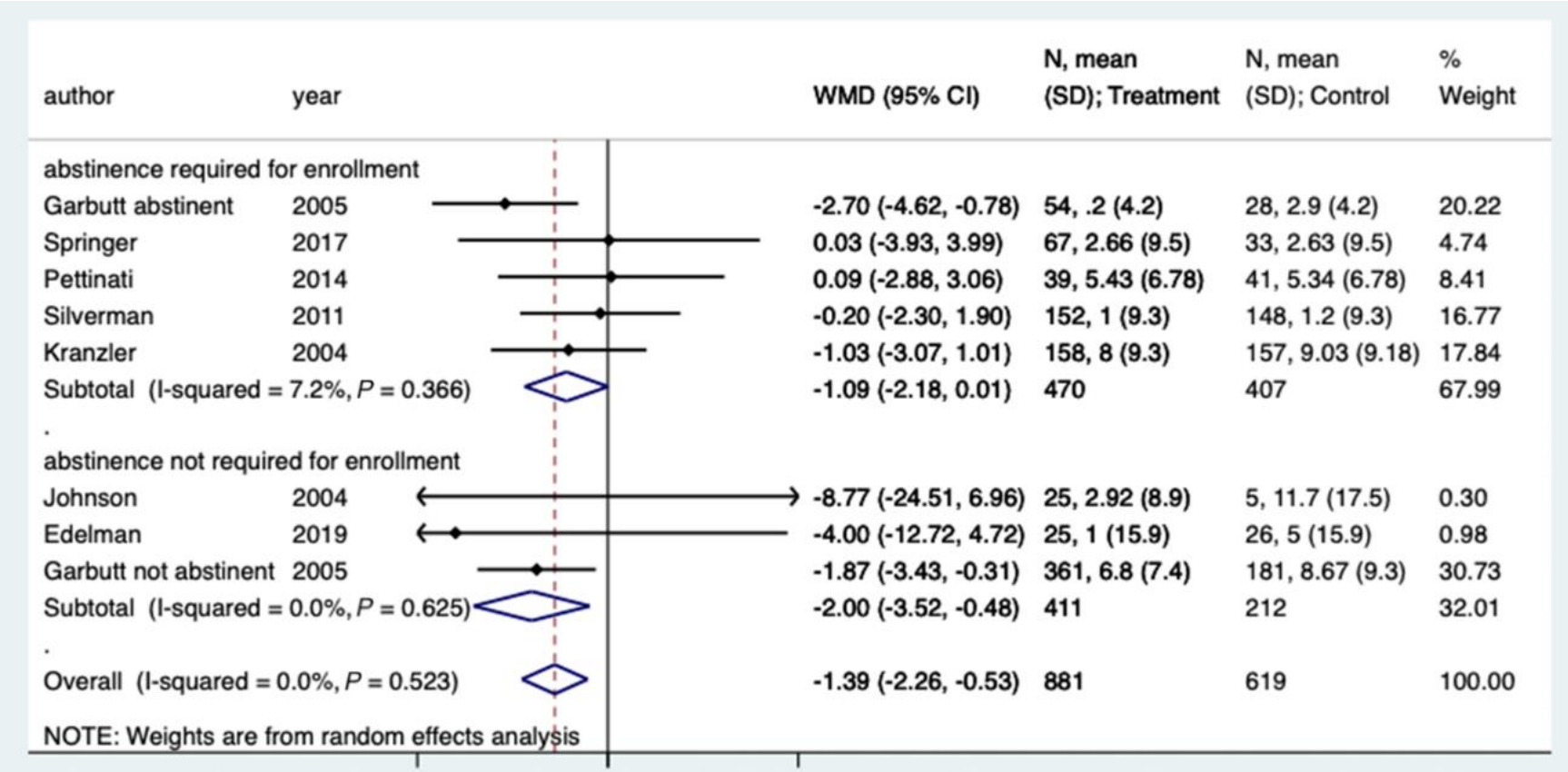

- No abstinence – WMD -2.0 (p = 0.01)
  - Driven by largest study (31% weight)
- Possible benefit of XR-NTX w/ active drinking

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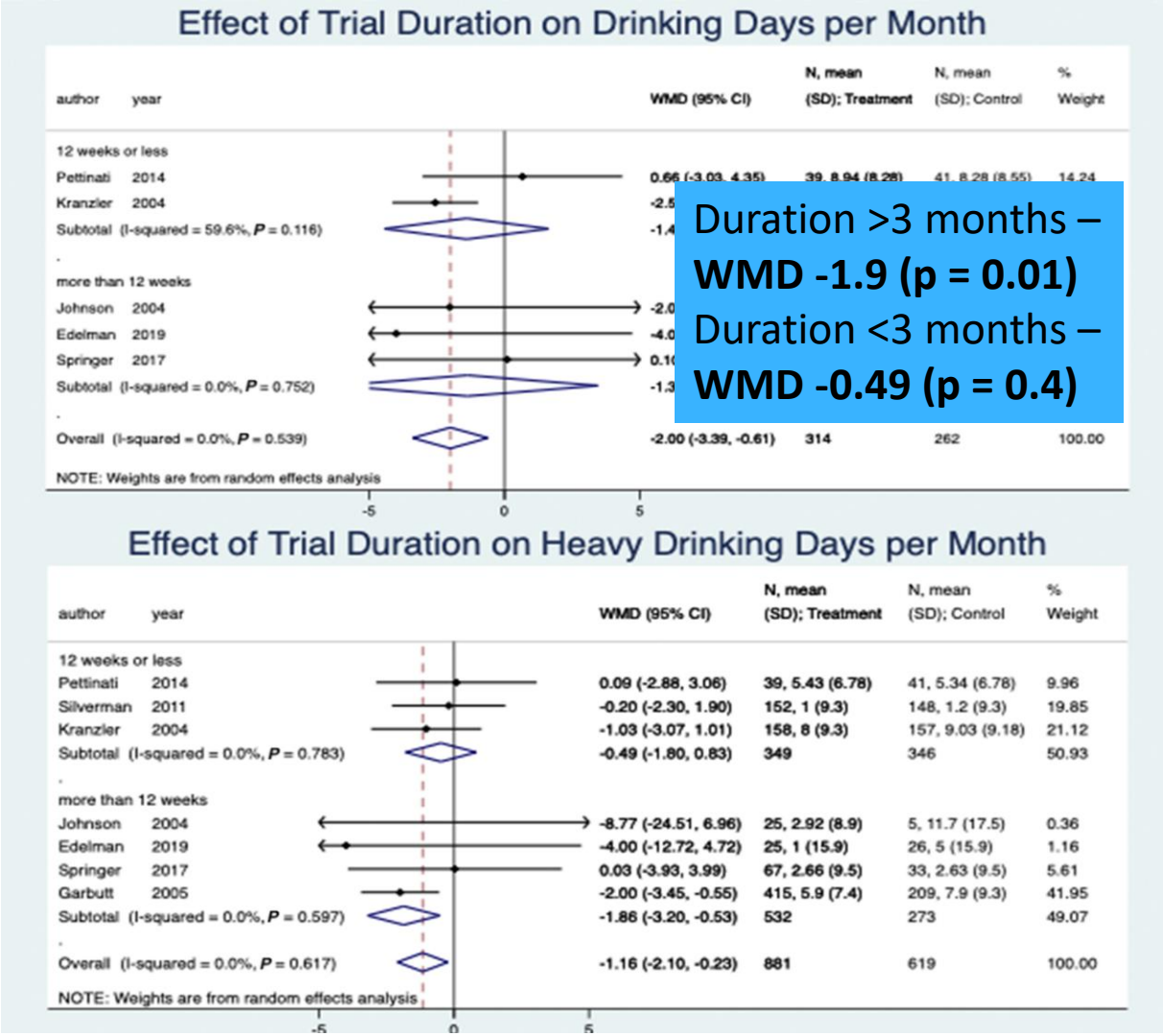


Duration >3 months – **WMD -1.9 (p = 0.01)**

Duration <3 months – **WMD -0.49 (p = 0.4)**

Overall,
XR-NTX + psychosocial interventions significantly reduced number of DD and HDD per month, modest but statistically significant effect sizes

Treatment duration (>3 months) significant reductions in monthly HDD (-1.9 days)

Results support the efficacy of XR-NTX for reducing heavy drinking, and in those who initiate treatment while abstinent, promoting abstinence (modest effect size)

Unclear effect on alcohol consumption outcomes given the absence of longer duration studies

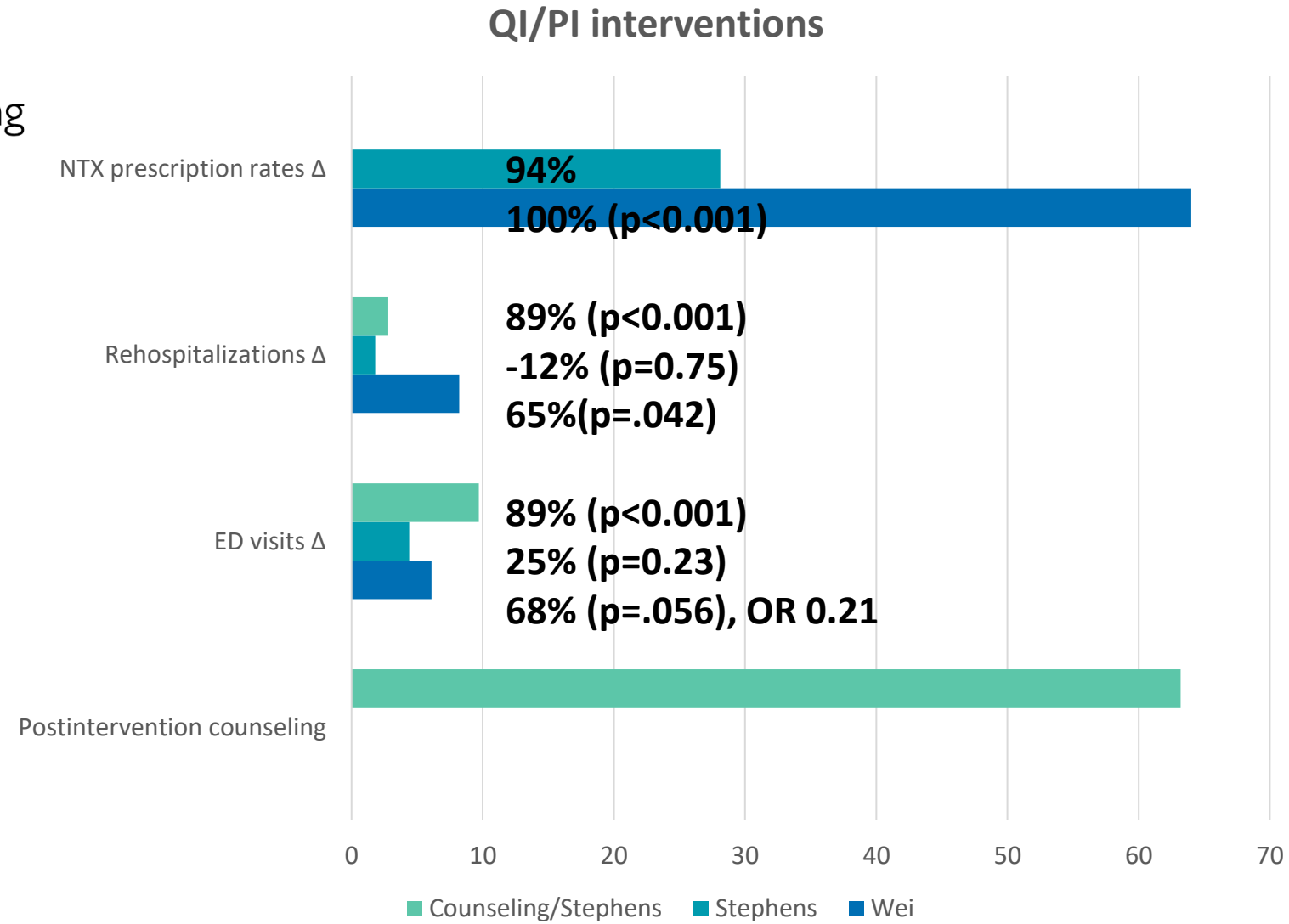
No clinical outcomes reported, unable to evaluate XR-NXT effects on alcohol associated morbidity and mortality

Naltrexone Initiation in the Inpatient Setting for Alcohol Use Disorder: A Systematic Review of Clinical Outcomes

2 small pre-post intervention trials[1,2]

USCF IM residency discharge planning protocol[1], UNC HM patient education/eligibility protocol[2]

Multidisciplinary teams (providers, SWs, CMs, addiction specialists, director of Alcohol and Substance Use program)



[1]Wei. An inpatient treatment and discharge planning protocol for alcohol dependence: efficacy in reducing 30-day readmissions and emergency department visits. J Gen Intern Med. 2015;30(3):365-370. [2]Stephens. Implementation of a process for initiating naltrexone in patients hospitalized for alcohol detoxification or withdrawal. J Hosp Med 2018;13(4):221-228. Kirchoff et al. Naltrexone Initiation in the Inpatient Setting for Alcohol Use Disorder: A Systematic Review of Clinical Outcomes. Mayo Clin Proc Innov Qual Outcomes. 2021;5(2):495-501.

ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION
RESEARCH REPORT
doi:10.1111/add.15384

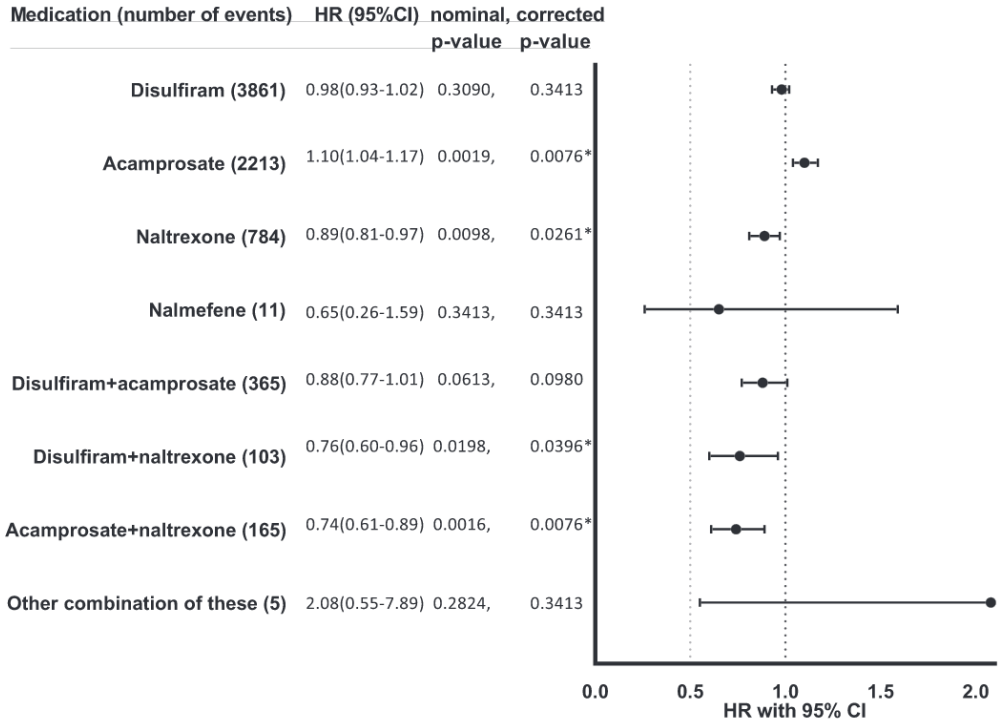
Real-world effectiveness of pharmacological treatments of alcohol use disorders in a Swedish nation-wide cohort of 125 556 patients

Design nation-wide, register-based prospective cohort study

Setting Sweden (state-funded health care system)

Cohort residents aged 16-64 w/ registered first-time treatment contact due to AUD (7/2006- 12/2016, N= 125,556, 62.5% ♂, median age 38.1 years, median f/u 4.6 years)

Outcomes *AUD related hospitalizations*, all-cause hospitalizations, all-cause mortality



Pharmacotherapy: effects on alcohol associated morbidity and mortality

Longer duration NTX use associated with lower risk of AUD hospitalization

Duration of medication use (days)	HR (95%CI)	p-value	N of events
Disulfiram			
≤30	1.01 (0.97–1.06)	0.6453	2010
31 – 180	1.05 (0.99–1.10)	0.0927	1677
>180	1.08 (0.93–1.25)	0.318	174
Acamprosate			
≤30	1.23 (1.16–1.30)	<0.0001	1309
31 – 180	1.20 (1.12–1.29)	<0.0001	805
>180	1.05 (0.86–1.28)	0.6459	98
Naltrexone			
≤30	0.82 (0.76–0.89)	<0.0001	610
31 – 180	0.75 (0.65–0.87)	0.0002	168
>180	0.43 (0.19–0.96)	0.0389	6

AUD severity subgroup analysis (patients with acute alcohol intoxication or other alcohol-related diagnosis)
- NTX (HR 0.71) and NTX+acamprosate (HR 0.89) associated with lower risks for AUD related hospitalizations
- No medication effects on adjusted risk of all-cause mortality

Heikkinen et al. Real-world Effectiveness of Pharmacological Treatments of Alcohol Use Disorders in a Swedish Nation-wide Cohort of 125 556 Patients. *Addiction. 2021;116(8):* 1990–98

Inpatient Addiction Consultation for Hospitalized Patients Increases Post-Discharge Abstinence and Reduces Addiction Severity

Sarah E. Wakeman, MD[1,2], Joshua P. Metlay, MD, PhD[1,2], Yuchiao Chang, PhD[1,2], Grace E. Herman, BA[3], and Nancy A. Rigotti, MD[1,2]

[1]Division of General Internal Medicine, Massachusetts General Hospital, Boston, MA, USA; [2]Harvard Medical School, Boston, MA, USA; [3]Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA.

Intervention: Addiction consultation from a multidisciplinary specialty team offering pharmacotherapy initiation, motivational counseling, treatment planning, and direct linkage to ongoing addiction treatment.

Main measures: Addiction Severity Index (ASI) composite score for alcohol and drug use and self-reported abstinence at 30 days post-discharge. Secondary outcomes included 90-day substance use measures and self-reported hospital and ED utilization.

Key results: Among 265 participants with 30-day follow-up, a greater reduction in the ASI composite score for drug or alcohol use was seen in the intervention group than in the control group (mean ASI-alcohol decreased by 0.24 vs. 0.08, $p < 0.001$; mean ASI-drug decreased by 0.05 vs. 0.02, $p = 0.003$.) There was also a greater increase in the number of days of abstinence in the intervention group versus the control group (+12.7 days vs. +5.6, $p < 0.001$). The differences in ASI-alcohol, ASI-drug, and days abstinent all remained statistically significant after controlling for age, gender, employment status, smoking status, and baseline addiction severity ($p = 0.018$, 0.018, and 0.02, respectively). In a sensitivity analysis, assuming that patients who were lost to follow-up had no change from baseline severity, the differences remained statistically significant.

Conclusions: In a non-randomized cohort of medical inpatients, addiction consultation reduced addiction severity for alcohol and drug use and increased the number of days of abstinence in the first month after hospital discharge.

Clinical scenario (continued)

Patient's mental status continued to improve.

He was seen by the Addiction Consult Team (ACT) on hospital day 3. He agreed to mAUD.

He received 380mg intramuscular naltrexone.

He was discharged on hospital day 5.

Follow-up AUD care was arranged through the MGH Bridge clinic.

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Post-test questions

A 50-year-old male presents to the ER with cough and dyspnea and was found to have a pulmonary embolism. On further questioning he says that he consumes 2-3 beers at least 5 days a week. His alcohol use has led to significant relationship issues with his partner and difficulties performing his job. He would like to cut down but has difficulty doing so due to ongoing cravings.

What is his diagnosis with respect to his alcohol use?

A. No alcohol use disorder

B. Mild Alcohol use disorder

C. Moderate alcohol use disorder

D. Severe alcohol use disorder

Which of the following tools can be used to assess his risk for developing severe alcohol withdrawal syndrome?

A. Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

B. Clinical Institute Withdrawal Assessment of Alcohol, revised (CIWA-Ar)

C. Cut, Annoyed, Guilty, and Eye (CAGE) questionnaire

Final key points…

❑ Alcohol related morbidity and mortality has increased significantly in the U.S., treatment of AUD remains underutilized.

❑ Phenobarbital is effective, may be clinically superior, to benzodiazepines for the treatment of severe alcohol withdrawal syndrome.

❑ Inpatient initiation of ER-NTX for AUD is highly effective and reduces short-term heavy alcohol use (possibly greater effects in active drinkers, ♂ patients and patients interested in alcohol use reduction not abstinence)

❑ Longer durations of ER-NTX are associated with significant reductions in AUD related hospitalizations (emphasizes that patients with AUD are primary-care connected and have ongoing AUD education/counseling and behavioral interventions)

❑ Hospitalists can utilize QI/PI interventions to increase the number of hospitalized patients with AUD initiated on evidence-based, FDA-approved pharmacotherapy

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Thank you

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Drug	Mechanism of Action	Dose	Data	Contraindications	Monitoring
Naltrexone (first-line therapy)	Mu-opioid receptor blockade, to suppress the reward pathway and reduce craving	50-100 mg/day PO or 380 mg/monthly IM	Decreased risk or recurrence in first 3 months by 36%; 25% decrease in heavy drinking days as compared to placebo	• Current opioid use • Liver failure • Pregnancy category C	Consider LFTs Patients should carry a wallet card indicating use of naltrexone
Acamprosate (first-line therapy)	Modulation of glutamate neurotransmission to reduce craving	666 mg TID; 333 mg TID if CrCl 30-50 ml/min	Increased abstinence at 6 months by 36% as compared to placebo; no effect seen in other trials	• Severe renal impairment (CrCl < 30 ml/min) • Pregnancy category C	Renal function
Disulfiram	Causes unpleasant withdrawal-like reaction when alcohol is consumed	250 mg/day x 1-2 weeks, followed by maintenance dose 100-500 mg/day	Decreased alcohol consumption and heavy drinking days, increased time to first drink, and increased number of abstinence days - superior to effect of naltrexone and acamprosate - but effect only seen when taken under supervision	• Concurrent alcohol use or use of Flagyl • CAD • Severe myocardial disease • Rubber/thiuram hypersensitivity • Psychosis Pregnancy category C	LFTs
Topiramate (not FDA approved)	Enhances GABA activity to suppress dopamine release during a drinking episode to reduce pleasure from drinking and craving	Up-titrate from 50 mg/day to 150 mg BID	Decreased heavy drinking days (between 8-27%), decreased number of drinks per drinking day, and increased number of abstinent days by 25%. Not significantly different from effect of naltrexone	Known teratogenic effects in pregnancy	Bicarbonate
Gabapentin (not FDA approved)	Indirect GABA modulation via selective blockade at voltage-gated calcium-channel	1200 -1800 mg/day, usually in TID dosing	19% decrease in heavy drinking, 14% increase in abstinence; greatest effect in those with more alcohol withdrawal NNT for abstinence of 2.7 compared with placebo	Caution in patients with co-occurring opioid use disorder given higher rates of gabapentin misuse when used synergistically with opioids	Renal function