Outpatient Alcohol Withdrawal Management

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Disclosures

I have NO financial disclosure or conflict of interests with the presented material in this presentation.

Off-label use of medications will be discussed.

Objectives

- Describe the pathophysiology of alcohol withdrawal.
- Identify red flag predictors of severe withdrawal.
- Stratify patients for outpatient vs inpatient withdrawal management.
- Describe medications used for the management of outpatient alcohol withdrawal.

Alcohol

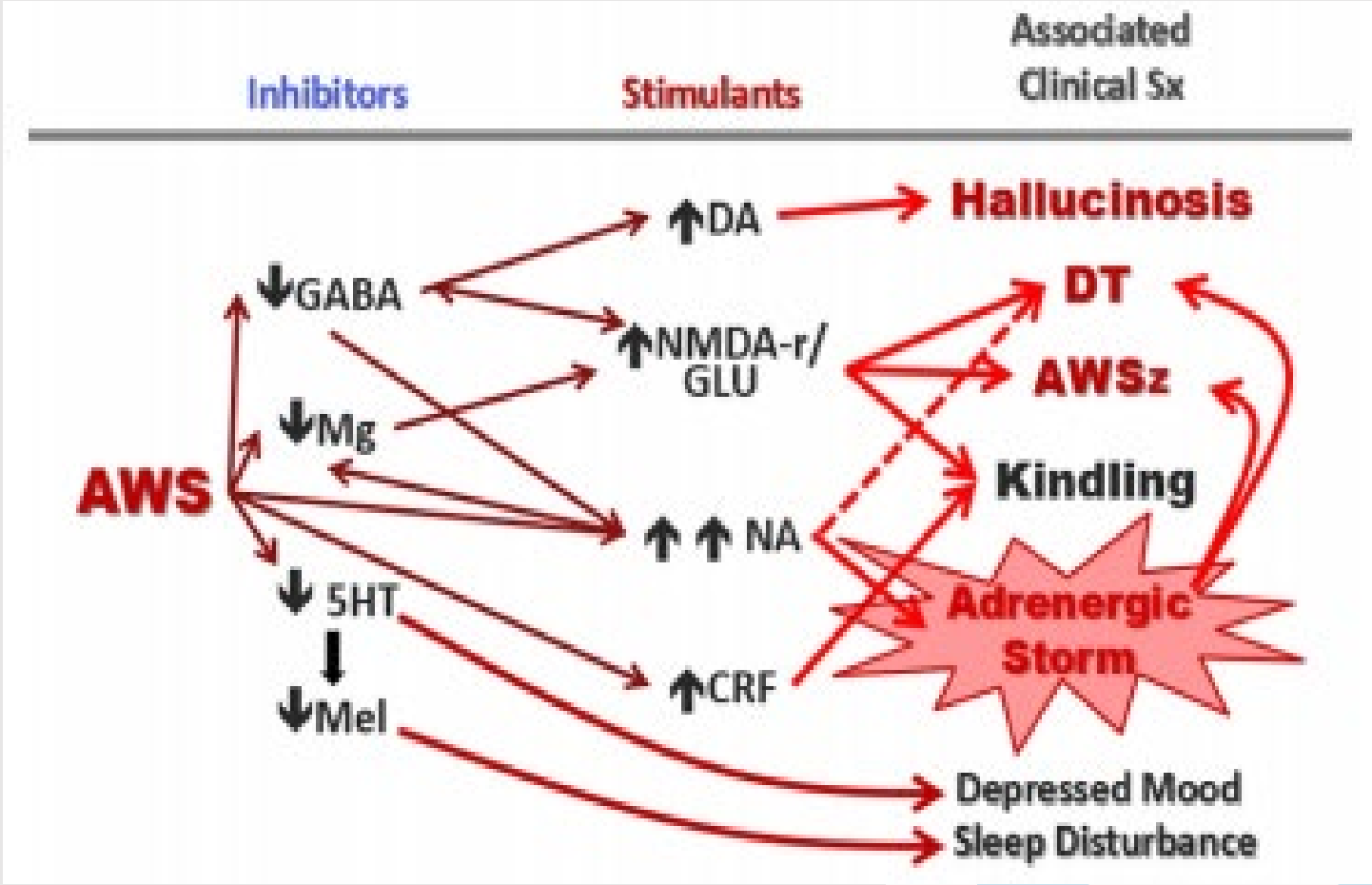
- MLDA is 21, 1984, regulated
- >200 diseases and injury-related health conditions, ~95K US and 3M worldwide annually deaths in 2019
- Addictive with high relapse rate, 29% lifetime prevalence, 28.3M US NSDUH 2020
- Few receive treatment, 6.7%, mild-moderate effect size
- Most common withdrawal syndrome, deadly

Alcohol Withdrawal

Alcohol Withdrawal

- 20% with alcohol use disorder will develop withdrawals, 5.7M
- 13-71% will develop significant symptoms
- Estimated mortality 1-7%, DTs
- Kindling process plays a factor, increases likelihood and worsens
- 10-20% of individuals require inpatient withdrawal treatment
- Outpatient withdrawal management is cost-effective, often patient preferred, has similar outcomes as inpatient, and SAFE; mild to moderate withdrawals

- ↓ in GABA activity
- ↑ in glutamate activity
- ↑ upregulation of calcium channel activity
- ↑ in noradrenergic activity

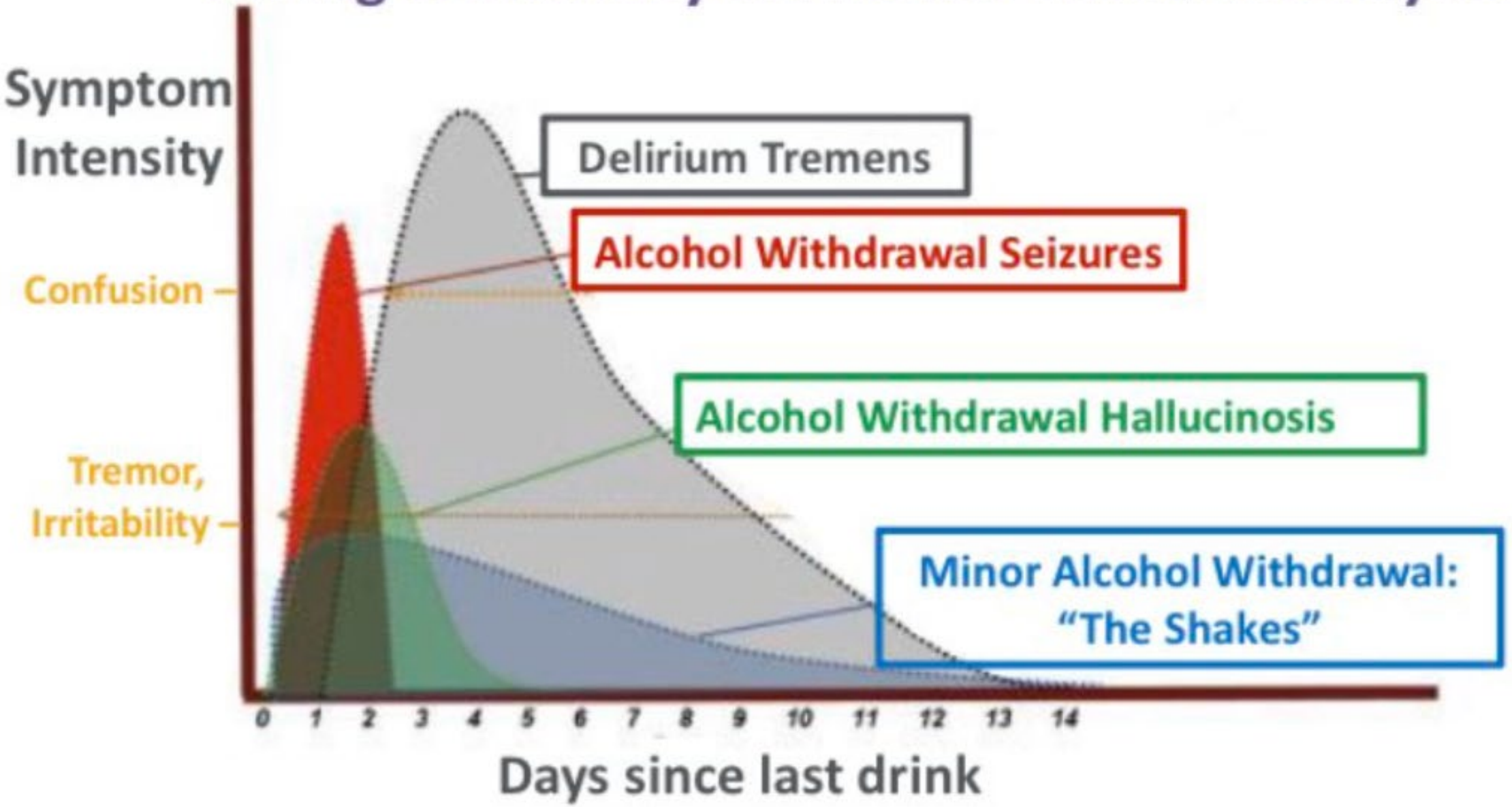


Alcohol Withdrawal DSM-5

- Cessation or reduction in alcohol use
- Two or more within hours or days
  - Autonomic hyperactivity (sweating; HR>100)
  - Increased hand tremors
  - Insomnia
  - Nausea or vomiting
  - Transient visual, auditory, tactile hallucinations
  - Psychomotor agitation
  - Anxiety
  - Generalized tonic-clonic seizures
- The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication with another substance

Syndrome	Clinical Findings	Onset and Duration	Additional
Minor*	Tremulousness, anxiety, irritability, headache, diaphoresis, palpitations, hypertension, orthostatic hypotension, tachycardia, anorexia, GI upset, vivid dreams, insomnia and normal mental status examination	6-36 hours, peak at 24 hours, may begin before BAL is 0	• Usually symptoms will subside without treatment within 5 to 7 days but can last up to 10 to 14 days
Alcohol withdrawal seizures	Generalized, tonic-clonic, status epilepticus is rare	8-48 hours, peaks after 24 hours after last drink	• Typically patients need to be drinking heavily for at least 2-3 months • 30-50% progress to DTs if untreated • 1/3 will only have one, 2/3 will have multiple • May not be preceded by early withdrawal symptoms
Alcoholic hallucinosis	Transient; visual, auditory and/or tactile with clear consortium	8-96 hours,	• Typically patients need to be drinking for more than 10 years • Can become frank hallucinations
Delirium Tremens	Confusion, disorientation, fluctuating or clouded consciousness, agitation, insomnia, fever, autonomic hyperactivity, terror, agitation, primarily visual hallucinations, sometimes tactile hallucinations	48-96 hours, seen up to two weeks after last drink	• Always preceded by early withdrawal symptoms • 80% of DTs resolve within 72 hours; those that don’t, mortality rate 1- 15% • DT-related death causes: infections, cardiac arrhythmias, fluid and electrolyte abnormalities, pyrexia, poor hydration, hypertension, or suicide in response to hallucinations or delusions

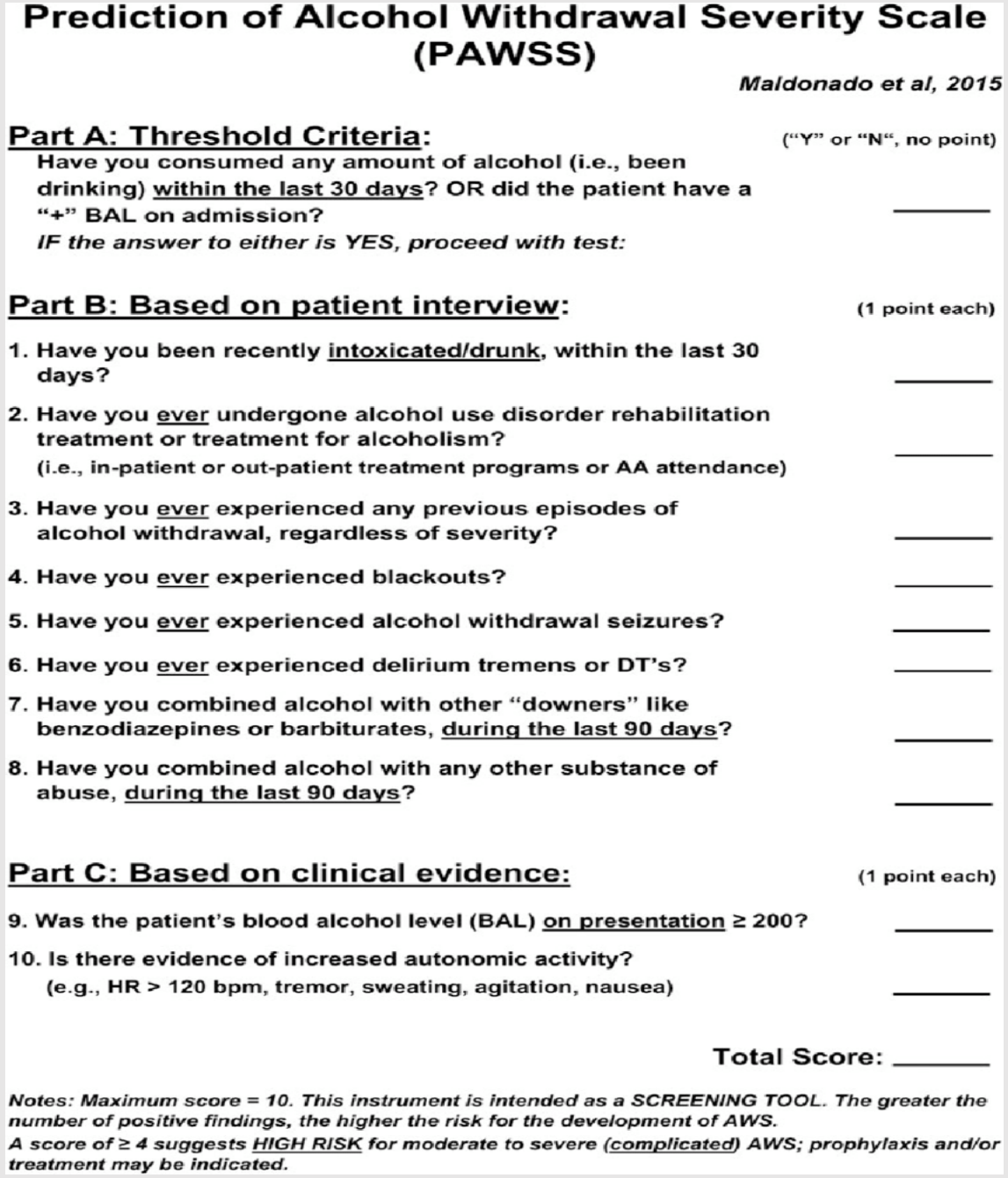
Timing & Intensity of Alcohol Withdrawal Syndromes



Assessment

Outpatient Withdrawal Treatment Tools

- Patient interview, not always helpful
- Collateral
- Patient chart, PDMP, ED visits, discharge summaries, labs, imaging, medications
- Physical and neurological exam, vitals, BAL, BrAC, labs, EKG
- DSM-5
- AUDIT-C, PAWSS, CIWA-Ar, OCDS
- Availability, support, setting; clinic hours, pharmacy access, social work, case management, peer support, home support; clinic, urgent care, ED, IOP, PHP, rehab; extended vs without extended onsite monitoring (level I, level II)



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.

PAWSS

- Excellent inter-reliability, $\varkappa = 0.75$
- Sensitivity = 93%, PAWS≥4
- Specificity = 99%, PAWS<4
- Practical in outpatient setting
- Alternatives:
  - Luebeck Alcohol Withdrawal Scale (LARS-10)
  - Alcohol Withdrawal Rating Scale

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

Nausea and Vomiting
0 – No nausea or vomiting
1
2
3
4 – Intermittent nausea with dry heaves
5
6
7 – Constant nausea, frequent dry heaves and vomiting

Paroxysmal Sweats
0 – No sweat visible
1 – Barely perceptible sweating, palms moist
2
3
4 – Beads of sweat obvious on forehead
5
6
7 – Drenching sweats

Agitation
0 – Normal activity
1 – Somewhat more than normal activity
2
3
4 – Moderate fidgety and restless
5
6
7 – Paces back and forth during most of the interview or constantly thrashes about

Visual Disturbances
0 – Not present
1 – Very mild photosensitivity
2 – Mild photosensitivity
3 – Moderate photosensitivity
4 – Moderately severe visual hallucinations
5 – Severe visual hallucinations
6 – Extreme severe visual hallucinations
7 – Continuous visual hallucinations

Tremor
0 – No tremor
1 – Not visible, but can be felt at finger tips
2
3
4 – Moderate when patient's hands extended
5
6
7 – Severe, even with arms not extended

Tactile Disturbances
0 - None
1 – Very mild paraesthesias
2 – Mild paraesthesias
3 – Moderate paraesthesias
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Headache
0 – Not present
1 – Very mild
2 - Mild
3 - Moderate
4 – Moderately severe
5 - Severe
6 – Very severe
7 – Extremely severe

Auditory Disturbances
0 – Not present
1 – Very mild harshness or ability to frighten
2 – Mild harshness or ability to frighten
3 – Moderate harshness or ability to frighten
4 – Moderately severe hallucinations
5 – Severe hallucinations
6 – Extremely severe hallucinations
7 – Continuous hallucinations

Orientation and Clouding of the Sensorium
0 – Oriented and can do serial additions
1 – Cannot do serial additions
2 – Disoriented for date but not more than 2 calendar days
3 - Disoriented for date by more than 2 calendar days
4 – Disoriented for place/person

Cumulative scoring

Cumulative score	Approach
0 – 8	No medication needed
9 – 14	Medication is optional
15 – 20	Definitely needs medication
>20	Increased risk of complications

CIWA-Ar

- Gold-standard, serially measured
- Excellent inter-reliability, $\varkappa = 0.93$
- Sensitivity = 47%, CIWA>8
- Specificity = 88%, CIWA<8
- Practical in outpatient setting
- Medical and mental status can alter scores
- Alternatives:
  - Richmond Agitation-Sedation Scale
  - Objective Alcohol Withdrawal Scale
  - Adult Michigan Withdrawal Severity Assessment Scale

Who should be admitted?

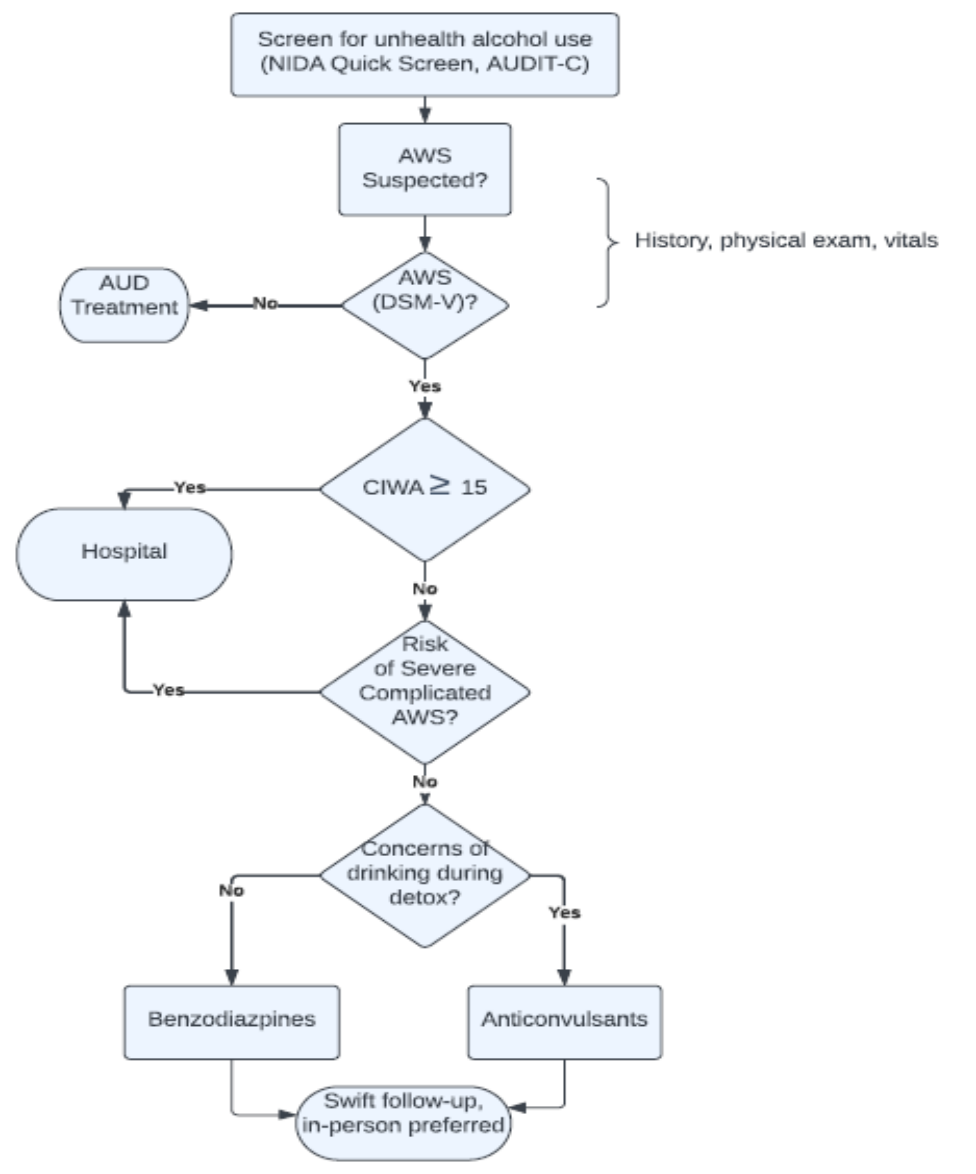
- CIWA ≥ 15
- History of severe withdrawals, DTs, withdrawal seizures and hallucinosis
- Predictors of severe withdrawals, PAWSS≥4, LARS-10>9
- Pregnant and Elderly, >65
- Housing and social insecurities, housing safety, homeless, cell phone access
- Co-substance use disorders, GABAergics
- Severe/decompensated medical and surgery co-morbidities, poor PO
- Decompensated psychiatrically, suicidal, psychotic
- Failed outpatient withdrawal treatment

Stratification Tips

- Lots of factors not helpful, daily intake, duration of heavy drinking, gender, race
- First 24-48 hours and CIWA<8, unlikely severe withdrawals
- BAL ≤ 200mg/dl and intoxicated, left lateral decubitus position
- High BAL without signs of intoxicationHigh BAL with withdrawal signs
- Acute medical problems, trauma and infection
- Lab abnormalities, Mg, K, Na, Cl, LFTs, homocysteine, thrombocytopenia, erythrocyte sedimentation rate

Outpatient Alcohol Withdrawal Management

Outpatient Withdrawal Management



- Appropriate patient selected
- Ideally patient should be seen in withdrawals, intoxicated patients cannot drive
- Pharmacotherapy interventions, benzodiazepines, anticonvulsants and adjuncts
- Prophylactic nutrition support, 1 mg of folic acid, 1 MVI and 100 mg daily B1
- Non-medication interventions, therapy, support group (sponsor, family), fluids, food, hygiene, sleep hygiene, maintenance of a non-alcohol/drug environment

Benzodiazepines

- Alleviates deficiency of GABA activity, GABA-A agonist, all ~ efficacy
- Misuse potential, deadly when combined with other central respiratory drive depressants, “prime”
- Side effects: anterograde amnesia, sedating, rebound withdrawals, falls, delirium, etc.
- Contraindications: allergy, active intoxication, history of paradoxical disinhibition, history of benzodiazepine-resistant alcohol withdrawal
- Caution: history of failed outpatient detoxifications due to continuous alcohol use, severe alcohol use disorder, high OCDS, opioids*

Benzodiazepines

- Scheduled-taper, divided dosing, single-daily dosing, dose equivalent, various “protocols”
- Loading dose, Sellers method
- Symptom-triggered not advised in outpatient setting
- Longer-acting benzodiazepines are preferred, smoother withdrawal course, reduction in breakthrough/rebound symptoms, reduced days dosing, less misuse or diversion potential

2 Std Drinks = 1mg of Ativan

Benzodiazepine	Equivalent to 5 mg diazepam (mg) *
Alprazolam (Xanax®)**	0.5
Bromazepam (Lectopam®)	3–6
Chlordiazepoxide (Librium®)	10–25
Clonazepam (Rivotril®)	0.5–1
Clorazepate (Tranxene®)	7.5
Flurazepam (Dalmane®)	15
Lorazepam (Ativan®)	0.5–1
Nitrazepam (Mogadon®)	5–10
Oxazepam (Serax®)	15
Temazepam (Restoril®)	10–15
Triazolam (Halcion®)**	0.25

Examples of Standard Tapers

- Chlordiazepoxide 50 mg QID x 4 doses → 25 mg QID x 4 doses → 10 mg QID x 4 doses THEN STOP
- Diazepam 10 mg QID x 4 doses → 5 mg QID x 4 doses → 2 mg QID x 4 doses THEN STOP
- Clorazepate 30 mg TID x 4 doses → 15 mg TID x 3 doses → 7.5 mg TID x 3 doses THEN STOP

Anticonvulsants

- Glutamate and Calcium-channel modulation
- Effective in managing mild to moderate alcohol withdrawals, prophylactic treatment for alcohol withdrawal seizures
- Insufficient evidence as monotherapy in severe withdrawals
- No addictive potential, do not cause respiratory depression
- Do not inhibit learning, reduce rebound withdrawals, PAWSS
- Taper lengths are longer, 5 days or more

Drug	T ½	Product Availability	Metabolism	Mechanism Action
Oxcarbazepine *	1-5 hours	Oral	Hepatic	Inhibits voltage-gated Ca+ channels decreasing cortisol release of Glutamate.
Carbamazepine *	25 hours	oral	Hepatic	Stabilizes neuronal membranes. Inhibits voltage-gated Na+ channels and/or Ca+ channels (decreasing cortisol release of Glutamate). Ca+ channel blockers. Excitatory amino acid antagonists.
Valproic acid *	9-16 hours	oral or intravenous	Hepatic	GABA transaminase inhibitor (increase GABA). Inhibits voltage-sensitive Na+ channels leading to decrease release of Glutamate from cortisol. Decrease release of the epileptogenic amino acid, GHB.
Gabapentin *	5-7 hours	Oral	None; renal excretion	Voltage-gated Ca+ channels blockade leads to decrease in Glutamate release from the cortisol. NMDA antagonism. Activation of spinal alpha-2 adrenergic receptors. Attenuation of Na+-dependent action potential.
Vigaberin	5-8 hours	Oral	None; renal excretion	Blocks the reuptake of GABA and inhibits the catabolism of GABA thus increasing GABA levels. Inhibition of voltage-sensitive Na+ channels.
Tigabine	7-9 hours	Oral	Hepatic	Blocks the reuptake of GABA leading to an increase in GABA levels. Inhibition of voltage-sensitive Na+ channels.

Examples of Standard Tapers

- Valproic acid 500mg TID x 3 doses → 500mg BID x 6 → 250mg BID BID x 7 doses THEN STOP
- Carbamazepine 200mg QID x 8 doses → 200mg TID x 6 doses → 200mg BID x 6 doses → 200mg Once THEN STOP
- Oxcarbazepine 300mg BID x 6 doses → 150mg BID x 8 doses THEN STOP
- Gabapentin 300mg QID x 12 doses → 300mg TID x 3 doses → 300mg BID x 2 doses → 300mg Once THEN STOP

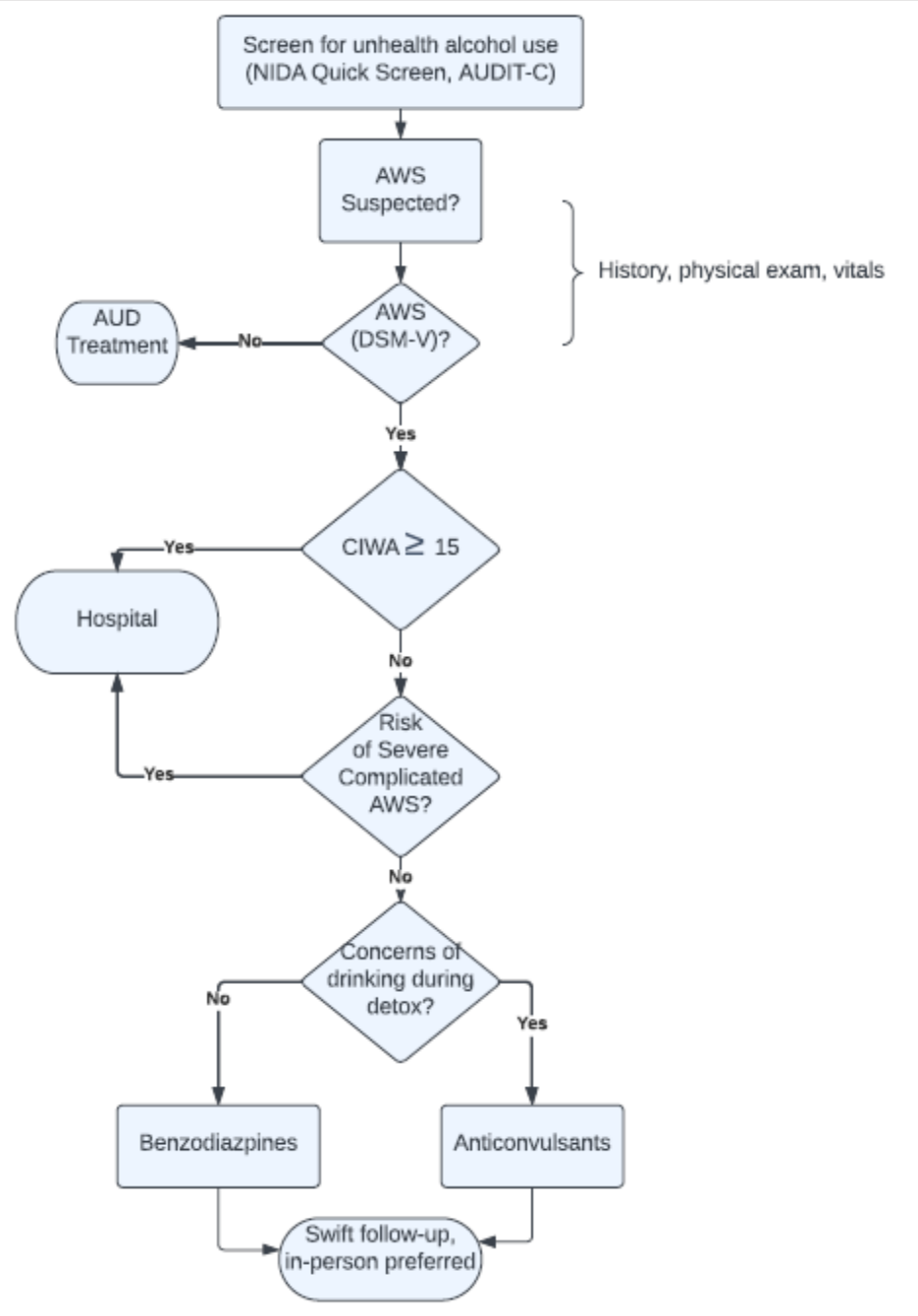
α-adrenergic agonists

- α-adrenergic agonists: clonidine and guanfacine
- Used in mild to moderate alcohol withdrawal management, no known anticonvulsant activity, as an adjunct in an outpatient setting
- Reduce the autonomic nervous system manifestations, may mask certain withdrawal symptoms
- α-adrenergic agonists are potentially neuroprotective

Drug	T ½	Product Availability	Metabolism	Mechanism Action
Guanfacine *	2.5 hours	Oral	Hepatic	Highly selective agonist of the α2A adrenergic receptor reduces peripheral sympathetic outflow and thus a reduction in peripheral sympathetic tone (SBP, DBP) by decreasing norepinephrine levels and indirectly reducing glutamate levels.
Clonidine *	11 mins	Oral, intravenous, or transdermal	Hepatic	Highly selective agonist of the α2A adrenergic receptor reduces peripheral sympathetic outflow and thus a reduction in peripheral sympathetic tone (SBP, DBP) by decreasing norepinephrine levels and indirectly reducing glutamate levels.

When should they go to the ED?

- Disorientation, confusion
- Falls
- Hallucinations
- Seizures
- HR ≥ 110, BP ≥ 170/110
- Worsening signs of objective and subjective withdrawals
- Caregiver confidence dwindling
- Patient's confidence dwindling
- Can't stop drinking



Bottom line

- Safety first
- Recommend in-person assessment
- Recommend fixed regimen in outpatient setting
- Utilize staff and all supports
- Seek mentorship
- Swift follow-up, suggest in-person

Summary

- Outpatient alcohol withdrawal management is a safe and effective treatment model for mild to moderate alcohol withdrawals for the appropriate patient
- Benzodiazepines are still the mainstay of treatment, however anticonvulsants are effective alternatives, and α-adrenergic agonists are effective adjunctive agents
- A thorough assessment and physical exam, strong staff support, and appropriate follow-up are invaluable in this treatment model

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