

Alcohol Use Disorder

Diagnosis, Pathophysiology, and Evidence-Based Treatment



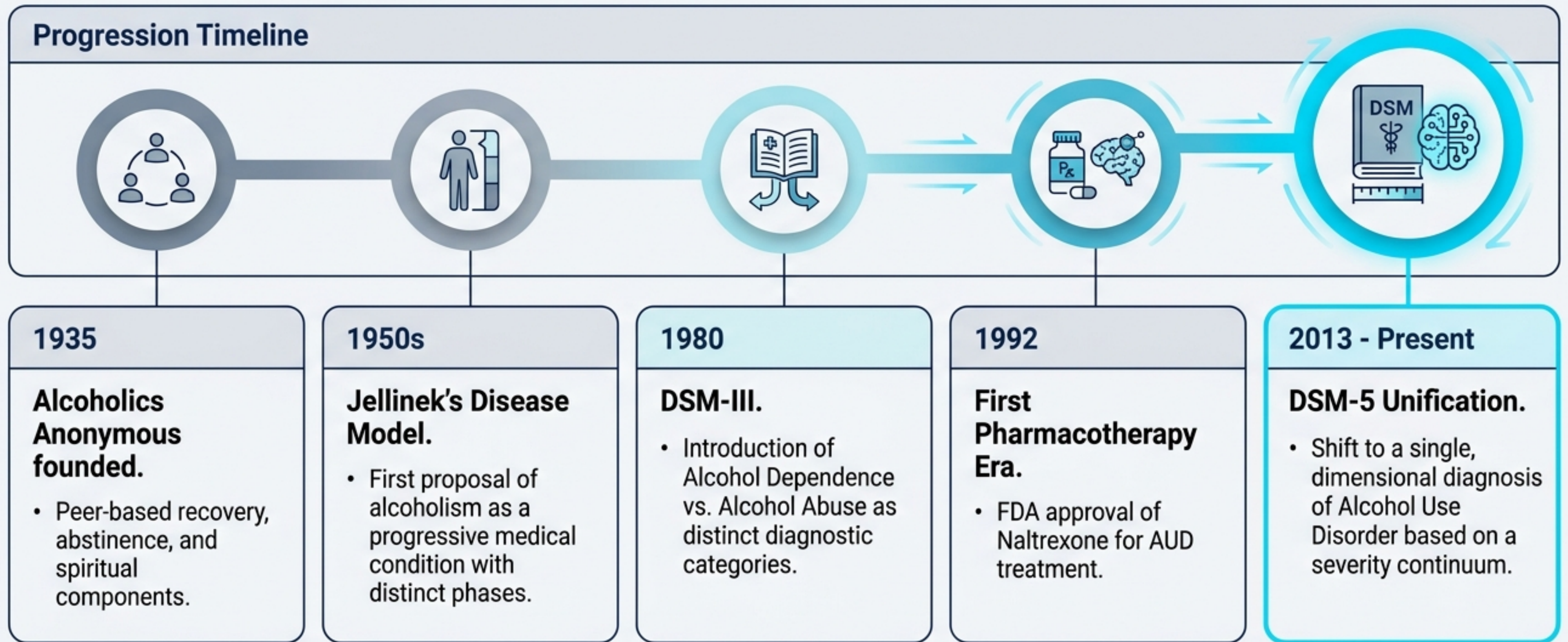
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👤 For Clinicians

📅 March 2026

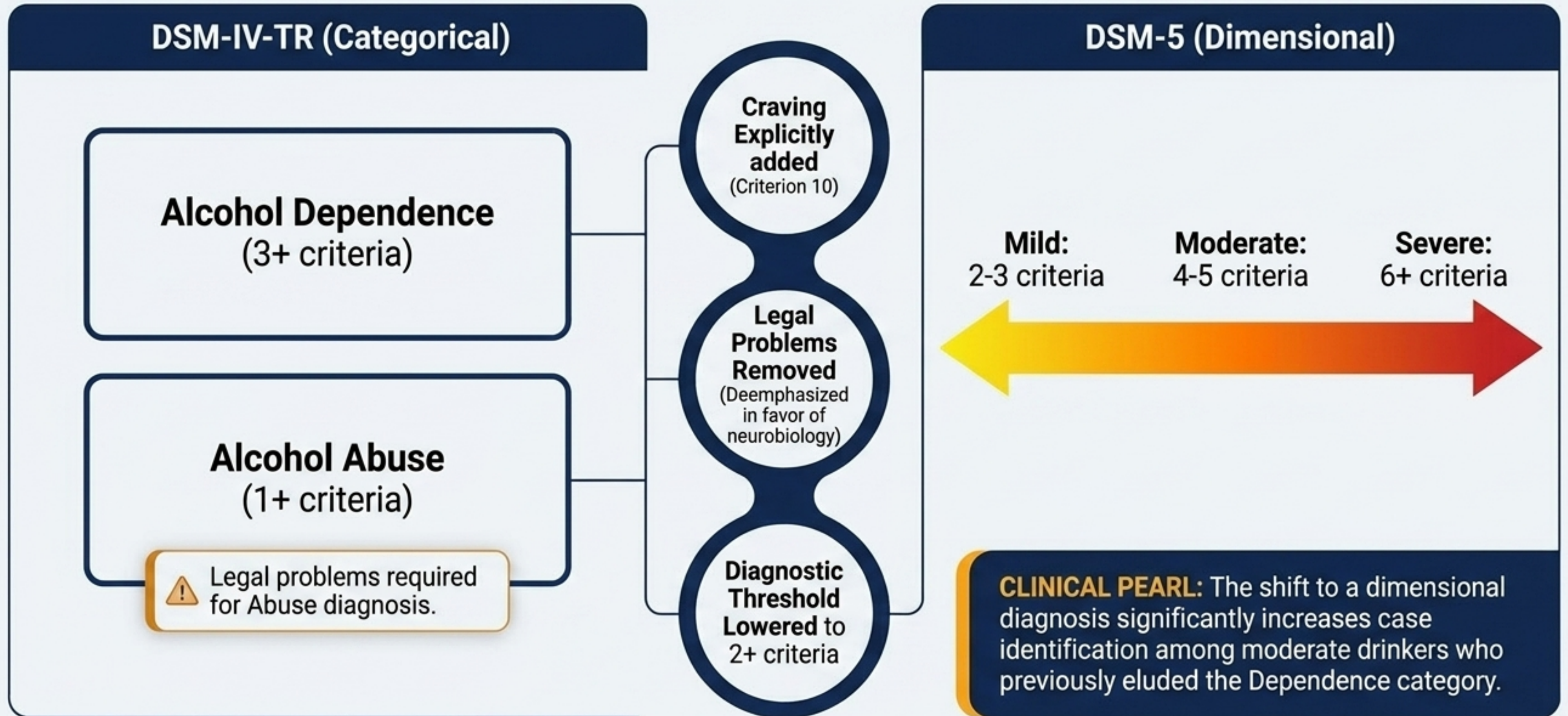
A Clinical Reference Blueprint | Synthesized from
PsychoPharmRef (Data current as of May 2026)

The Conceptual Evolution of Alcohol Use Disorder



CLINICAL PEARL: Contemporary understanding recognizes AUD as a chronic, relapsing brain disorder involving the dysregulation of reward circuitry, stress response systems, and executive function.

The Diagnostic Shift from Categorical to Dimensional



The 11 Diagnostic Criteria for AUD

Diagnosis requires meeting 2 or more criteria within a 12-month period.

Loss of Control

1. Larger amounts or longer periods than intended

2. Unsuccessful efforts to cut down/control

3. Great deal of time spent obtaining, using, recovering

4. Craving or strong desire to use

Social & Role Impairment

5. Failure to fulfill major role obligations

6. Continued use despite social/interpersonal problems

7. Important activities given up or reduced

Physical Risk & Physiology

8. Recurrent use in physically hazardous situations

9. Continued use despite knowledge of physical/psychological problems

10. Tolerance (need for increased amounts or diminished effect)

11. Withdrawal (symptoms or drinking to avoid them)

Heterogeneity in Presentation: Three Core Clinical Phenotypes

18M Adults with AUD
in the U.S. (2024)



Early-Onset

Onset:
< Age 25

Etiology:
High genetic loading, family history.

Traits:
Impulsivity, conduct disorder.

Course:
Generally more severe; rapid progression.



Late-Onset

Onset:
> Age 55

Etiology:
Psychosocial triggers (retirement, grief, medical illness).

Traits:
Lower genetic risk, higher environmental driver.

Course:
Often exhibits a better treatment response.



Chronic Relapsing

Onset:
Variable

Etiology:
Profound brain reward dysregulation.

Traits:
Repeated attempts to quit followed by return to use.

Course:
Characterized by cycles of withdrawal, abstinence, and relapse.

Pathophysiology of Tolerance and Withdrawal

Normal Brain



Chronic Alcohol Exposure & Withdrawal

Step 1: Alcohol drops heavy weight on GABA (enhancing inhibition).



Step 2: Brain upregulates Glutamate (pushes right side down) to adapt.



Step 3: Alcohol is suddenly removed.

Seesaw slams aggressively down on the Glutamate side, causing withdrawal.



Clinical Consequences

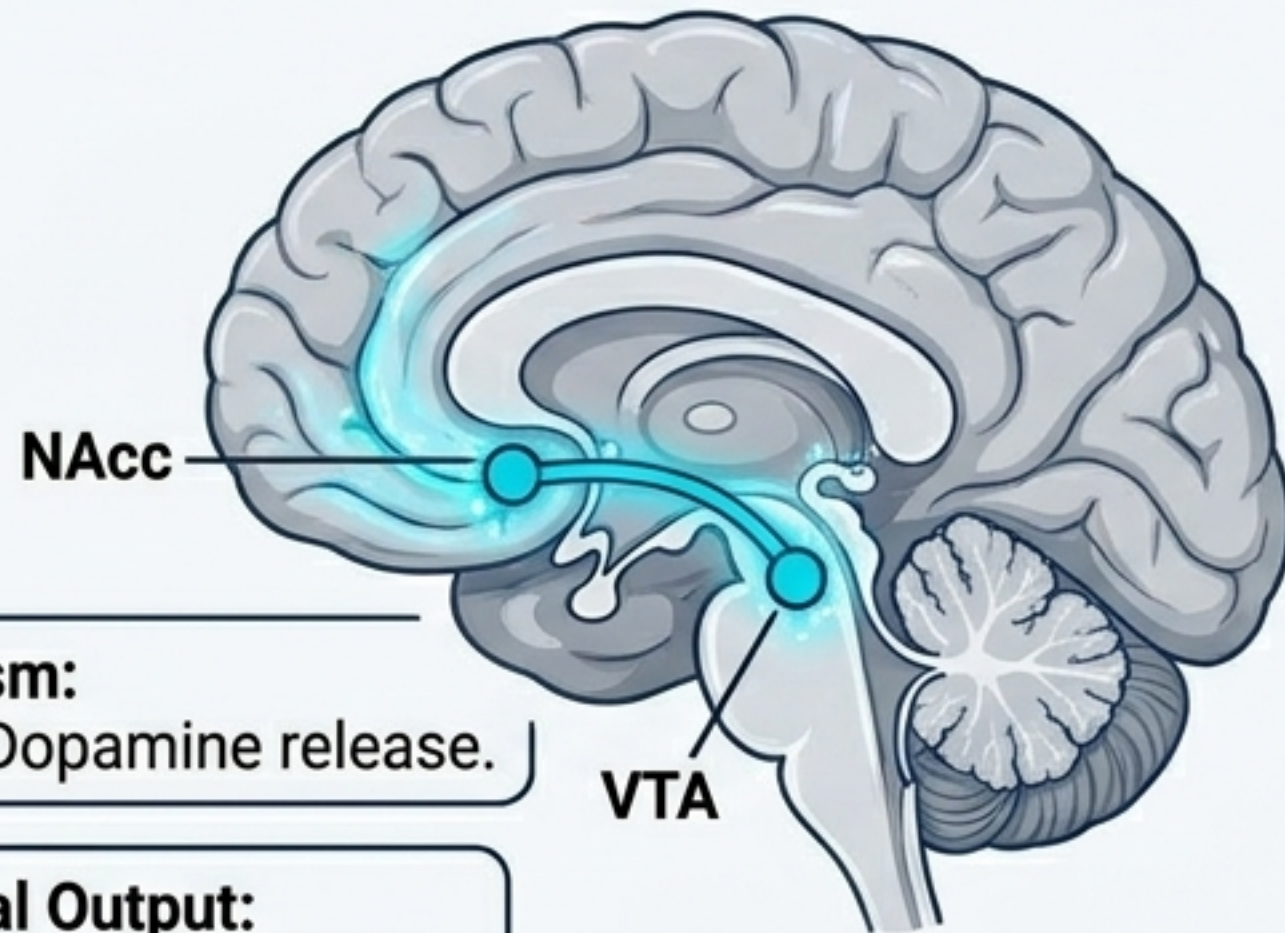
Acute: Anxiolysis, Sedation, Disinhibition.

Chronic (Adaptation): Tolerance, Dependence.

Withdrawal (Hyperexcitability): Tremor, Seizures, Hallucinations, Autonomic Dysregulation.

The Transition from Liking to Wanting

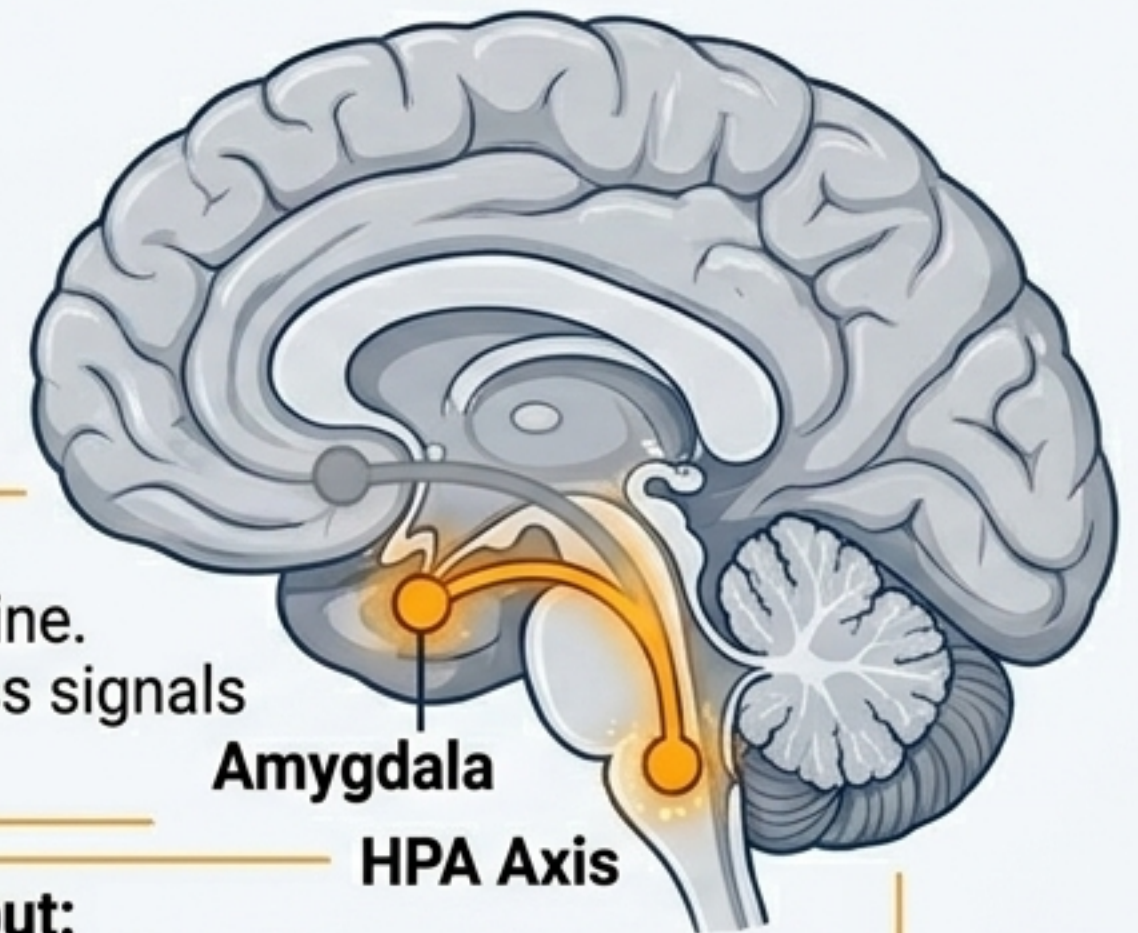
Acute Alcohol (Positive Reinforcement)



Mechanism:
Massive Dopamine release.

Behavioral Output:
Reward salience, euphoria, motivation (Liking).

Chronic Alcohol (Negative Reinforcement)

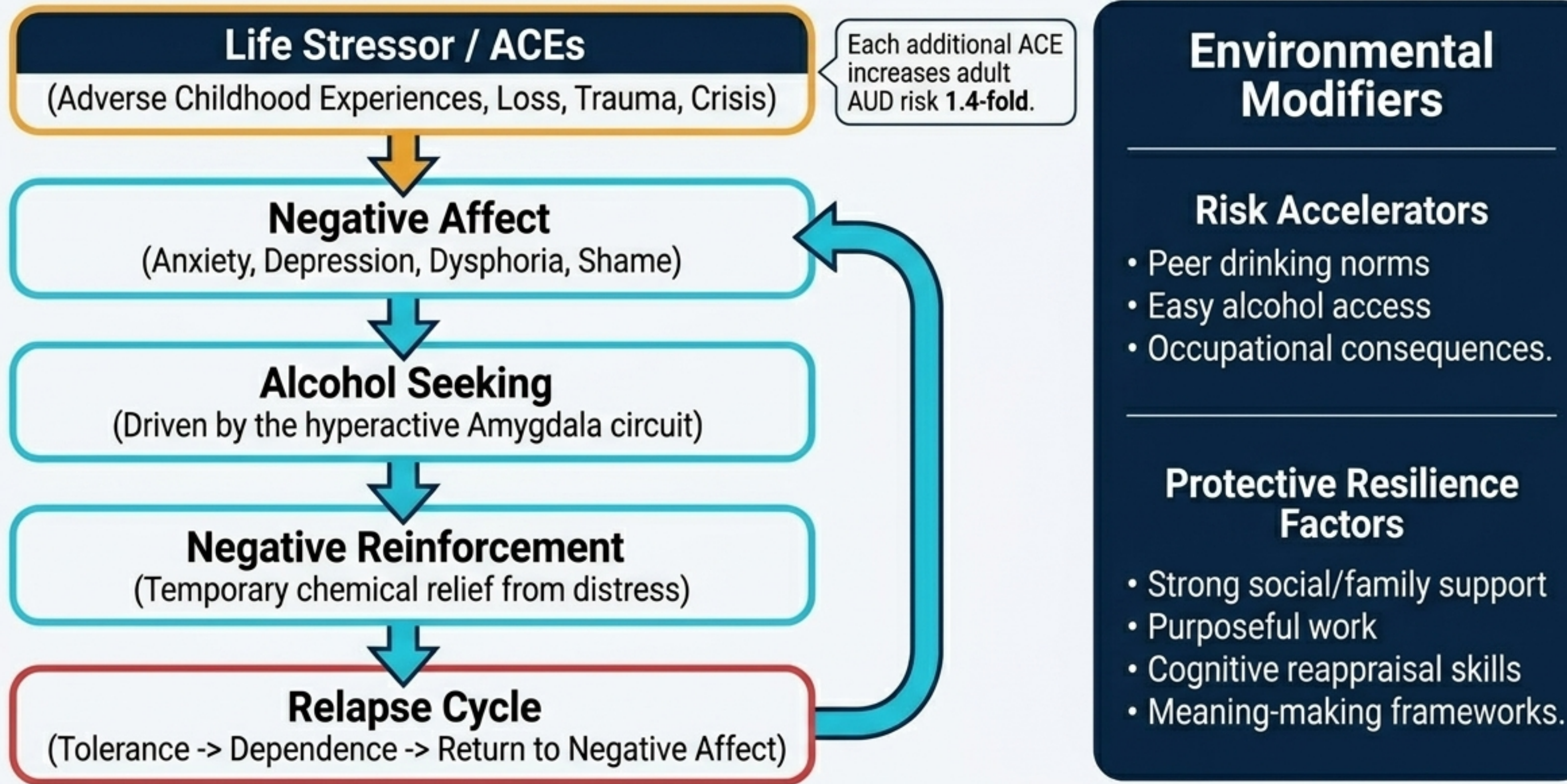


Mechanism:
Blunted Dopamine.
Sensitized stress signals (Cortisol/CRH).

Behavioral Output:
Heightened anxiety, dysphoria. Patient drinks to relieve stress, not to get high (Wanting).

CLINICAL PEARL: Repeated alcohol exposure downregulates the dopamine reward system while hyper-sensitizing the amygdala's stress response. Patients are no longer drinking for pleasure; they are drinking to achieve biochemical baseline.

Environmental Modifiers: The Stress-Induced Drinking Cascade



First-Line Pharmacotherapy Comparison

Medication	Primary Mechanism	Typical Dosing	Efficacy & Clinical Considerations
Naltrexone	Opioid antagonist (blocks VTA reward circuit activation).	50 mg PO daily or 380 mg IM monthly.	NNT=9-12 (abstinence). Reduces heavy drinking. Opioids contraindicated. Monitor LFTs. FDA warning for suicidal ideation. Excellent for craving reduction .
Acamprosate	Glutamate modulator (restores excitatory-excitatory-inhibitory balance on the seesaw).	1998 mg daily (666 mg TID).	NNT=8-11 (abstinence). Safe in liver disease. Renal excretion (avoid if CrCl <30). Ideal for highly anxious individuals. TID dosing impacts adherence.
Disulfiram	Aldehyde dehydrogenase inhibitor (aversive reaction).	250 mg daily.	NNT=10 (abstinence). Best with high monitoring. Hepatotoxicity risk. Severe alcohol reaction . Requires immense patient commitment .

Second-Line and Emerging Pharmacotherapies

Topiramate

Profile: Anticonvulsant (enhances GABA, inhibits Glutamate).

Dose: Titrate to 200-300 mg daily.

Highlights: Efficacy comparable to first-line agents. Excellent for comorbid bipolar or migraines.

Watch For: Cognitive impairment (word-finding), paresthesias, weight loss.

Gabapentin

Profile: GABA-analogue anticonvulsant.

Dose: 900-1800 mg daily (divided).

Highlights: Minimal drug interactions. Highly useful for comorbid anxiety or AUD-related insomnia.

Baclofen

Profile: GABA-B receptor agonist.

Dose: 15-20 mg TID.

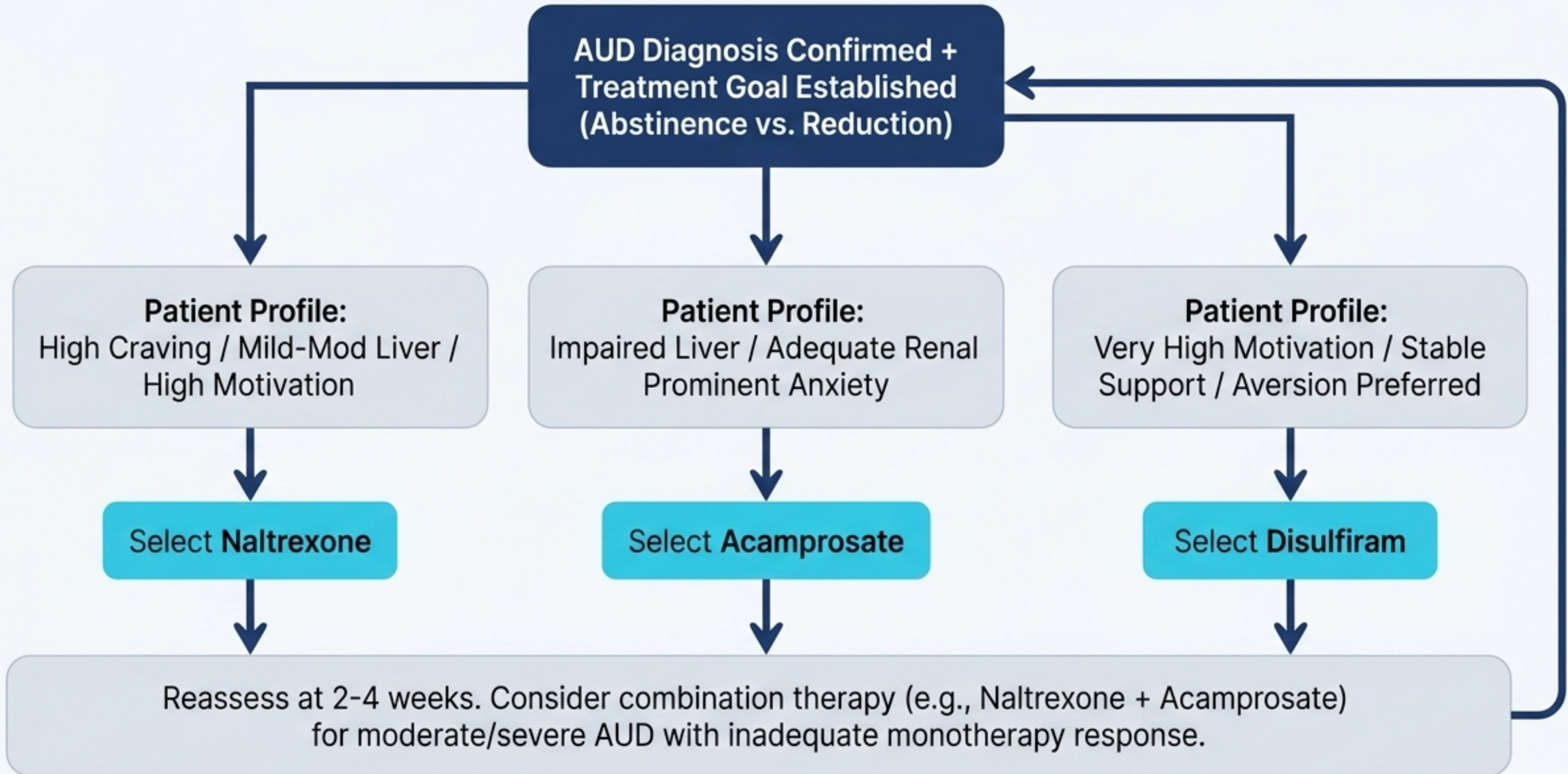
Highlights: Mixed evidence, but promising for anxiety-heavy presentations. Risk of withdrawal if stopped abruptly.

Nalmefene

Profile: Opioid antagonist (longer half-life than naltrexone).

Highlights: Approved in Europe (18mg daily). Not currently FDA-approved. Potential advantages in hepatic metabolism.

Medication Selection Algorithm



Core Psychosocial and Behavioral Interventions



Cognitive-Behavioral Therapy (CBT)

Identifies triggers, urges (Urge Surfing), and modifies maladaptive thoughts. Durable effects >12 months.



Motivational Interviewing (MI)

Client-centered approach to elicit intrinsic "change talk." Highly effective for early-stage engagement and resolving ambivalence.



Contingency Management (CM)

Operant conditioning using tangible reinforcers (vouchers) for verified abstinence. Highest short-term efficacy (NNT 3-5).



Community Reinforcement (CRA)

Restructures the patient's environment to make sober living more rewarding than drinking. Superior for patients lacking psychosocial stability.



Family & Couples Therapy

Addresses relationship dysfunction and explicit enabling behaviors. Essential for interpersonal recovery.

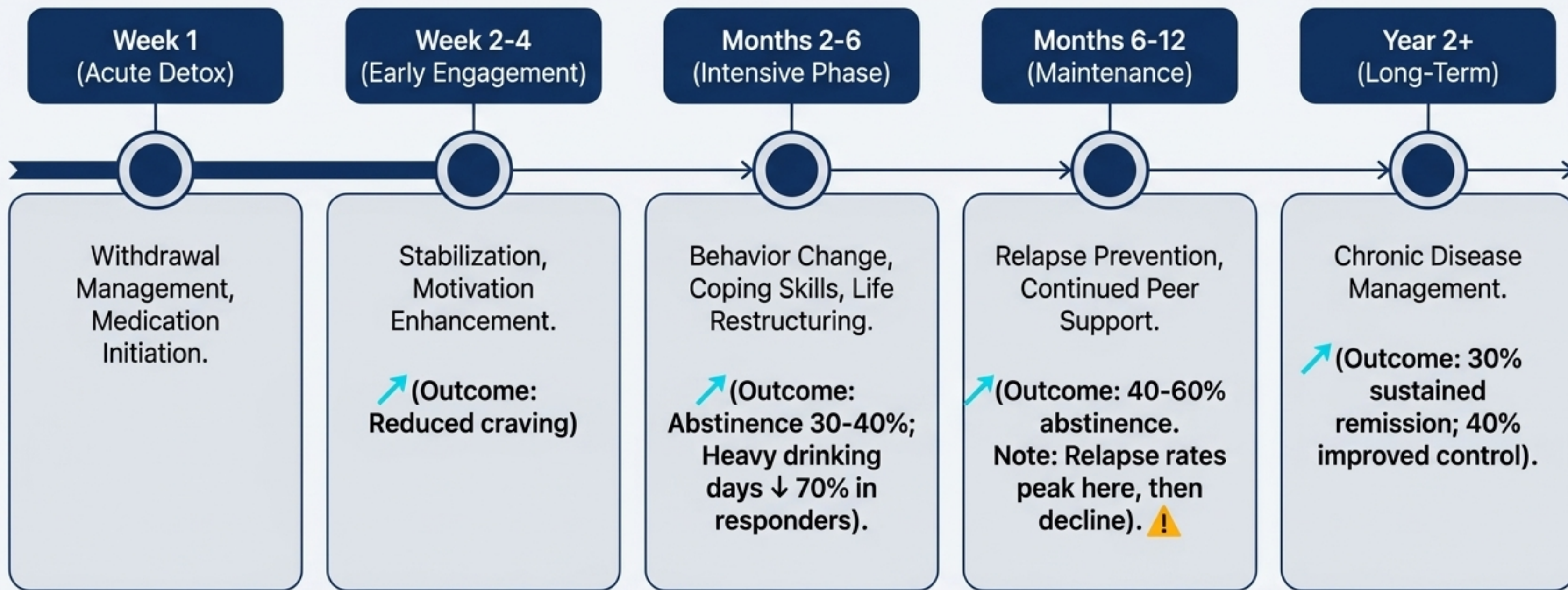


Peer Support / Mutual Aid

AA (12-step) and SMART Recovery. Provides community, accountability, and meaning-making. Predicts better long-term outcomes.

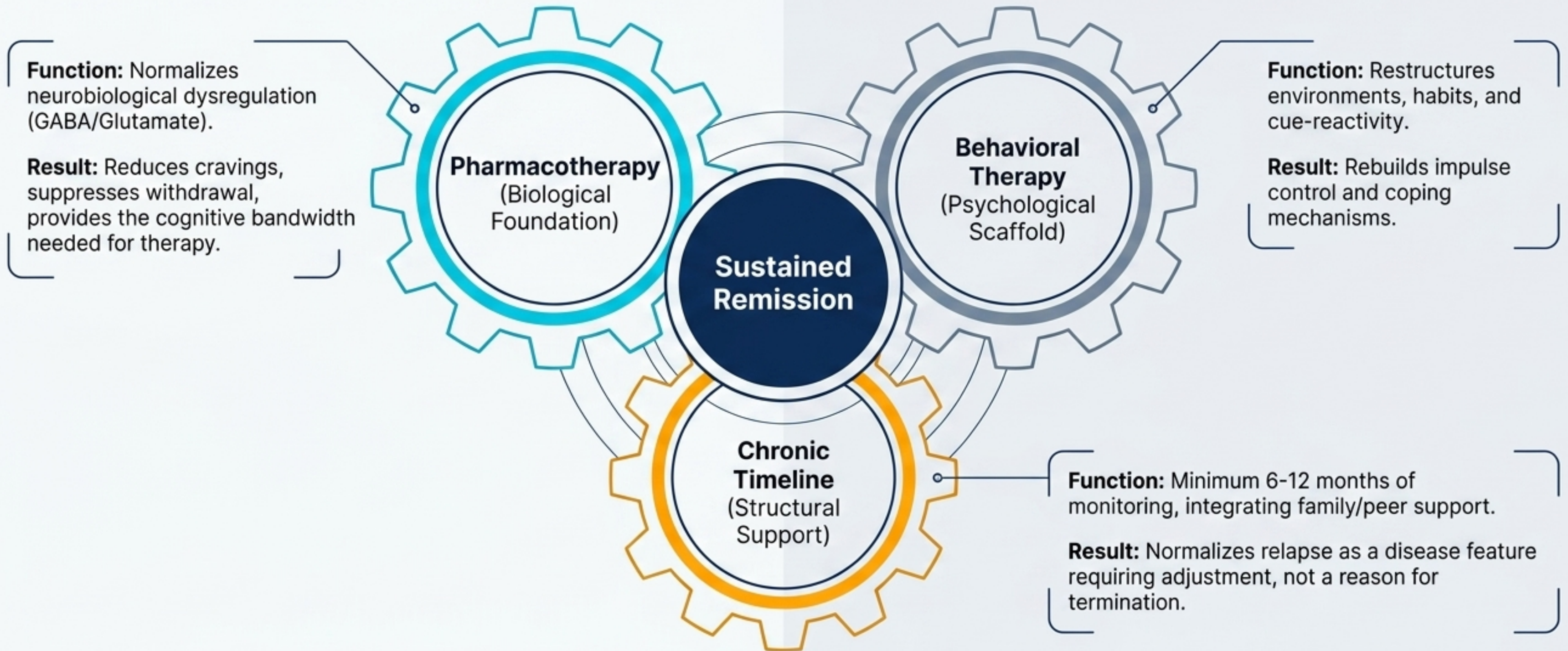
Treatment Response Timeline & Expected Outcomes

Clinical Gantt Chart



STATISTIC: Only 10% of patients with AUD receive any treatment. Sustained engagement is the strongest predictor of long-term remission.

The Integrated Chronic Disease Engine



Clinical Pearl

SYNTHESIS: AUD cannot be cured by a 28-day detox. Sustained remission requires pharmacotherapy to stabilize the brain's hardware, behavioral therapy to rewrite the software, and chronic care management to protect the system long-term.