

A Review of Alcohol and Substance Use in the Life Insurance Setting

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Introduction



Substance Related and Addictive Disorders

- DSM 5
 - 10 separate classes of drugs
 - Alcohol
 - Caffeine
 - Cannabis
 - Hallucinogens
 - Phencyclidine
 - Other
 - Inhalants
 - Opioids
 - Sedatives, hypnotics and anxiolytics
 - Stimulants
 - Amphetamine-type
 - Cocaine
 - Tobacco
 - Other

Substance Related and Addictive Disorders

- DSM 5
 - Substance Use Disorders
 - Substance Induced Disorders
 - Intoxication
 - Withdrawal
 - Substance/medication induced mental disorders
 - Psychotic disorders
 - Bipolar disorder
 - Depressive disorders
 - Anxiety disorders
 - Obsessive-compulsive disorders
 - Sleep disorders
 - Sexual dysfunctions
 - Delirium
 - Neurocognitive disorders





COVID-19 Pandemic: Alcohol Use and Mortality



https://www.niaaa.nih.gov/news-events/research-update/alcohol-related-deaths-which-increased-during-first-year-covid-19-pandemic-continued-rise-2021



Alcohol: Terminology

- Unhealthy Alcohol Use Unhealthy alcohol use encompasses the spectrum of alcohol use that can result in health consequences, including:
 - Use of amounts that risk consequences
 - Use that has already resulted in consequences but not yet a diagnosable alcohol use disorder
 - Use accompanied by features meeting DSM-5 diagnostic criteria for alcohol use disorder (AUD)

Alcohol: Terminology

- Risky use Risky alcohol use refers to consumption of an amount of alcohol that puts an individual at risk for health consequences
- The National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the United States has estimated consumption amounts of alcohol that increase health risks:
- Males under age 65
 - More than 14 standard drinks per week on average
 - More than 4 drinks on any day
- Females (all ages) and Males 65 years and older
 - More than 7 standard drinks per week on average
 - More than 3 drinks on any day

Alcohol: Terminology – What counts as a drink?



Each drink shown above represents one U.S. standard drink and has an equivalent amount (0.6 fluid ounces) of "pure" ethanol.

Alcohol: Terminology

- Binge drinking (Too much, too fast) Binge drinking has been defined by the NIAAA as "drinking so much within about two hours that blood alcohol concentration levels reach 0.08g/dL".
 - In women, this typically occurs after approximately four standard drinks.
 - In men, after about five standard drinks.
 - Binge drinking is associated with acute injuries due to intoxication.
 - It increases the risk of falls, burns, car crashes, memory blackouts, medication interactions, assaults, drownings, and overdose deaths.
 - May be associated with an increased cardiovascular risk.

- Heavy drinking (Too much, too often) includes binge drinking and has been defined for women as 4 or more drinks on any day or 8 or more per week, and for men as 5 or more drinks on any day or 15 or more per week.
 - Raises the risk for both acute harms, such as falls and medication interactions, and for chronic consequences, such as AUD and dose-dependent increases in liver disease, heart disease, and cancers.

Alcohol Terminology: Alcohol Use Disorder

DSM-5 diagnostic criteria for alcohol use disorder

- A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least 2 of the following, occurring within a 12-month period:

 Alcohol is often taken in larger amounts or over a longer period than was intended.
 There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
 A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
 Craving, or a strong desire or urge to use alcohol.
 Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
 Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
 - 7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
 - 8. Recurrent alcohol use in situations in which it is physically hazardous.
 - 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.
 - 10. Tolerance, as defined by either of the following:
 - a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.
 - b. A markedly diminished effect with continued use of the same amount of alcohol.
 - 11. Withdrawal, as manifested by either of the following:

a. The characteristic withdrawal syndrome for alcohol (refer to Criteria A and B of the criteria set for alcohol withdrawal, pp. 499 to 500).

b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms.

Specify if:

In early remission: After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met for at least 3 months but for less than 12 months (with the exception that Criterion A4, "Craving, or a strong desire or urge to use alcohol," may be met).

In sustained remission: After full criteria for alcohol use disorder were previously met, none of the criteria for alcohol use disorder have been met at any time during a period of 12 months or longer (with the exception that Criterion A4, "Craving, or a strong desire or urge to use alcohol," may be met).

Specify if:

In a controlled environment: This additional specifier is used if the individual is in an environment where access to alcohol is restricted.

Code based on current severity: Note for ICD-10-CM codes: If an alcohol intoxication, alcohol withdrawal, or another alcohol-induced mental disorder is also present, do not use the codes below for alcohol use disorder. Instead, the comorbid alcohol use disorder is indicated in the fourth character of the alcohol-induced disorder code (see the coding note for alcohol intoxication, alcohol withdrawal, or a specific alcohol-induced mental disorder). For example, if there is comorbid alcohol intoxication and alcohol use disorder, only the alcohol intoxication code is given, with the fourth character indicate indicated in the comorbid alcohol use disorder. F10.129 for mild alcohol use disorder with alcohol intoxication or F10.229 for a moderate or severe alcohol use disorder with alcohol intoxication.

Specify current severity:

305 (F10.1) Mild: Presence of 2 to 3 symptoms.

303.9 (F10.2) Moderate: Presence of 4 to 5 symptoms.

303.9 (F10.2) Severe: Presence of 6 or more symptoms.

DSM-5: American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ICD-10-CM: International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Clinical Modification.

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Alcohol: Epidemiology

- 2019 US National Survey on Drug Use and Health
 - 24% admit to binge drinking episode in past 30 days
 - 6% admit to heavy drinking in past 30 days
- The National Institute on Alcohol Abuse and Alcoholism
 - 28% with risky use
 - 19% exceeding just the daily limit (binge drinkers not exceeding the weekly limit)
 - 9% exceeding both the daily and weekly limits

Unhealthy Alcohol Use: Medical Consequences

- Trauma or injury
- Anxiety, depression, suicidality
- Comorbid substance-use disorders
- Sleep disturbance
- Hypertension
- Cardiac symptoms
- Central or peripheral neurologic symptoms
- Gastrointestinal symptoms
- Increased liver enzymes, including elevated gamma-glutamyl transpeptidase
- Bone marrow suppression
- Macrocytosis
- Malignancies of various organ systems
 - Oropharynx
 - Gastrointestinal
 - Breast

Moderate Alcohol Use and Mortality

- Mixed data
 - Several studies with lower mortality in moderate drinkers compared with abstainers or heavy drinkers
 - ~10 to 30% lower compared to abstainers consistent across both sexes
 - Supports the concept of a "J Curve" for alcohol use and mortality
 - More evident when drink of choice was wine
 - Emerging data that the "safe limit" is lower than most recent guidelines suggest
 - 6 grams per day for males \rightarrow 3 drinks per week
 - 2 to 6 grams per day for females \rightarrow 1 to 3 drinks per week

Unhealthy Alcohol Use: Biomarkers

- None are sensitive for unhealthy alcohol use
 - Require heavy and repeated recent consumption to be elevated
- Liver Enzymes
 - ALT, AST, GGT
- Complete Blood Count (CBC)
 - Hemoglobin \rightarrow Anemia
 - Mean Corpuscular Volume (MCV) > 100 fL \rightarrow Macrocytosis
 - $-\downarrow$ RBC, WCC, Platelets \rightarrow Pancytopenia
- ↑ HDL Cholesterol

Biomarker	Sensitivity (%)	Specificity (%)
ALT	18 - 58	50 - 57
AST	15 - 69	47 - 68
GGT	34 - 85	11 - 95
MCV	34 - 89	26 - 95
CDT	39 - 94	82 - 100
CDT + GGT	90+	98

Adapted from 2018 AAIM Triennial Alcohol and Substance Misuse Workshop



Unhealthy Alcohol Use: Biomarkers

- Carbohydrate <u>deficient</u> transferrin (CDT)
 - Chronic heavy alcohol use reduces the number of carbohydrate moieties (distinct part of a large molecule) attached to transferrin → Increased CDT level
 - CDT normalizes within several weeks of abstinence of alcohol use
- CDT is not an especially good test
 - Sensitivity 50%
 - Specificity 90%
- Assuming:
 - Prevalence of heavy alcohol use in the population as 5%
 - PPV = (Sensitivity x Prevalence)/((Sensitivity x Prevalence) + ((1 Specificity) x (1 Prevalence)))
 - $PPV = (0.5 \times 0.05)/((0.5) \times 0.05) + ((1 0.90) \times ((1 0.05)) = (0.025)/((0.025) + (0.095)) = 0.21 = 21\%$

- Meaning of a positive CDT test interpretation depends heavily on the pretest probability
- Can use likelihood ratio approach to get the clinical posttest probability of alcohol abuse
- Requires that you know the sensitivity and specificity of various factors
 - HDL cholesterol
 - MCV
 - GERD/Gastritis
 - Anxiety/Depression
 - History of gout
 - Smoking
 - Others

Case 1

- Applicant A is a 35 year old female non-smoker
- She is an avid exerciser, runs marathons regularly, wears a Fitbit
- Her HDL value is 92 mg/dl,
- She admits to rare use of alcohol
- A reflex CDT is abnormal
- How would you assess the mortality risk? (Preferred, STD, mild sub-STD, moderate sub-STD, high sub-STD)

Case 2

- Applicant B is a 55 year old male smoker
- Upper GI endoscopy 2 years ago GERD/mild gastritis Esomeprazole prescribed
- · He admits to 2 drinks most days, CBC shows a mildly elevated MCV value
- His HDL is 72 mg/dl, borderline high normal LFTs
- His reflex CDT is normal
- How would you assess his mortality risk? (Preferred, STD, mild sub-STD, moderate sub-STD, high sub-STD)

- Likelihood ratio is the ratio of the likelihood of a positive or negative test in those with and without a given condition
 - LR (positive) = sensitivity/1-specificity or TP/FP
 - LR (negative) = 1-sensitivity/specificity or FN/TN
- You can chain multiple likelihood ratios to get a post test probability
 - However, must first convert from probability to odds and then back to probability
- Pretest odds = pretest probability/1-pretest probability (where pretest probability is the prevalence in the general population)
- Post test odds = pretest odds x LR
- Post test odds = pretest odds x LR1 x LR2 x LR3
 - When multiple factors are involved
- Post test probability = (post test odds)/(post test odds + 1)
- Advantage of this approach is that you can use the LR for multiple tests or clinical factors



Case 1: Alcohol Abuse Probability Calculation

- Likelihood Ratios of Clinical Markers for Alcohol Abuse
- Case 1:
 - ↑HDL (LR+ 2.17)
 - CDT abnormal (LR+ 5.00)
 - Non-smoker (LR- 0.34)

Test	LR+	LR-
Smoke 1	2.17	0.34
Gastritis	2.14	0.70
HDL	2.17	0.84
MCV	2.43	0.89
CDT/HAA	5.00	0.56

 Alcohol Abuse Pre-test Probability = general prevalence in population = 5% for this calculation

Case 1: Alcohol Abuse Probability Calculation

• Pre-test Odds = Pre-test probability/(1-pretest probability) = 0.05/(1-0.05) = 0.05/(0.95) = 0.053

•	Post-test Odds = Pre-test odds x Likelihood ratios of independent alcohol markers	Test	LR+	LR-
•	Post-test Odds = 0.053 x HDL +ve LR x smoker -ve LR = 0.053 x 2.17 x 0.34 = 0.039	Smoke 1 Gastritis	2.17 2.14	0.34 0.70
•	With +ve CDT: Post-test Odds = 0.039 x 5.00 = 0.195	HDL MCV CDT/HAA	2.17 2.43 5.00	0.84 0.89 0.56

- Post-test Alcohol Abuse Probability = (Post-test odds)/(post-test odds +1) = 0.195/(0.195 + 1) = 0.195/1.195 = 0.16 = 16%
- Assuming average rating +200 for Alcohol Abuse then rating for this applicant = +200 x post-test Alcohol Abuse probability = +200 x 0.16 = +32
- A positive CDT test does not automatically mean high risk

Case 2: Alcohol Abuse Probability Calculation

- Likelihood Ratios of Clinical Markers for AUD
- Case 2:
 - Smoker (LR 2.17)
 - Gastritis (LR 2.14)
 - **↑HDL** (LR 2.17)
 - ↑MCV (LR 2.43)
 - CDT-ve (LR 0.56)

Test	LR+	LR-
Smoke 1	2.17	0.34
Gastritis	2.14	0.70
HDL	2.17	0.84
MCV	2.43	0.89
CDT/HAA	5.00	0.56

 Alcohol Abuse Pre-test Probability = general prevalence in population = 15% for this calculation

Case 2: Alcohol Abuse Probability Calculation

• Pre-test Odds = Pre-test probability/(1-pretest probability) = 0.15/(1-0.15) = 0.15/0.85 = 0.176

Test	LR+	LR-
Smoke 1	2.17	0.34
Gastritis	2.14	0.70
HDL	2.17	0.84
MCV	2.43	0.89
CDT/HAA	5.00	0.56

Post-test Odds = Pre-test odds x Likelihood ratios of independent alcohol markers

- Post-test Odds = 0.176 x HDL +ve LR x smoker +ve LR x MCV +ve LR x Gastritis +ve LR = 0.176 x 2.17 x 2.17 x 2.43 x 2.14 = 4.3
- With -ve CDT: Post-test Odds = 4.3 x 0.56 = 2.42
- Post-test Alcohol Abuse Probability = (Post-test odds)/(post-test odds +1) = 2.42/(2.42 + 1) = 2.42/3.42 = 0.71 = 71%
- Assuming +200 for Alcohol Abuse then rating for this applicant = +200 x post-test Alcohol Abuse probability = +200 x $0.71 = 142 \approx +150$
- A negative CDT test <u>does not automatically mean no/low risk</u>

Alcohol Use Disorder (AUD) – Epidemiology

- Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. (2015)
 - 14% of American adults meet current AUD criteria
 - 29% of American adults meet criteria for AUD in their lifetime

- Risk factors for AUD
 - Male gender
 - Ages 18-29
 - Native American and white ethnicity
 - Other substance use disorder
 - Comorbid psychopathology (MDD, BPD)
 - Personality disorder \rightarrow cluster B

Alcohol Use Disorder – Relapse and Remission

- Based on 3 general population longitudinal studies:
 - Approximately 50% of alcoholics relapse within 6 years
 - Risk of relapse remained significant for at least 10 years post-treatment
 - Risk of relapse highest in first 5 years compared to years 6 to 10

Alcohol Use Disorder – Mortality

- Based on 4 general population longitudinal studies:
 - Some heterogeneity in reported mortality
 - Consensus→ Standardized Mortality Ratios of AUD is 2-3 times that of the general population





Opioid Therapy in the Context of the Opioid Epidemic

- 1997 new clinical guidelines for the management of chronic non-cancer pain (CNP)
 - Per capita retail purchases of methadone, hydrocodone and oxycodone increased 13-fold, 4-fold and 9-fold respectively over 10 years following the 1997 guidelines
 - Resulted in 3% of Americans receiving long-term treatment for CNP with opioids
 - Accompanied by increase in opioid dependence, overdoses and mortality
 - Opioid prescribing has decreased since 2012
 - New CDC Guideline for Prescribing Opioids for Chronic Pain in 2016
 - Updated in 2022: Critical addition on how to taper opioids

Chronic Pain in the US: New Data

- 2020 Survey -
 - 1 in 5 adults experienced chronic pain most used a mix of medication and non-pharmacologic therapies to manage their pain
 - OTC pain medication most commonly used
 - Exercise the most common non-pharmacologic therapy used.
 - 1 in 4 adults relied on medication alone
 - Opioid use for CNP decreased from 15.2% in 2019 to 13.5% in 2020
- 2019 Survey -
 - 55% of adults with CNP used only non-opioid pain management techniques
 - 11% used both opioids and non-opioid techniques
 - 4% used only opioids
- Both surveys More likely to only use opioids for CNP in:
 - Older ages 45 to 64y vs. 18 to 44y (19% vs 8%)
 - Women vs. men (17% vs. 13%)

Opioid Use: Morphine Milligram Equivalents (MME)

Medication	Approximate Equivalent Doses (Oral Form, Immediate Release)	Approximate Equianalgesic Dose Ratio (Morphine: Alternate Opioid)
Codeine	200 mg	1:7
Hydrocodone	30 mg	1:1
Morphine	30 mg	1:1 (reference standard)
Oxycodone	20 mg	1.5:1
Hydromorphone	7.5 mg	4.1

Opioid Use: Average Daily Dose and Overdose Risk

Morphine Equivalents (mg/d)	Hazard Ratio for Serious Overdose
None	1
< 20	5
20 - 49	6
50 – 99	16
100 up	50

Opioid Use: Risk Factors for Misuse and Overdose

- Male gender
- History of other substance misuse or overdose
- Mental health Diagnoses
 - Major Depressive Disorder
 - o Bipolar Mood Disordero PTSD
- Pulmonary Disease / OSA
- Family history of alcohol or substance abuse
- Prescription opioid misuse highest ≤ 45 years
- Prescription opioid overdose highest 25 54 years
- Recent abstinence

- Opioid Use Risks
 - Long-term opioid use (> 3 months)
 - Higher average daily dose
 - Long-acting formulations (methadone, transdermal fentanyl)
 - Combination of opioids with benzodiazepines or alcohol
 - Illicit opioid use
 - Early refill requests
 - Multiple prescribers

Sources:

Becker, William, et al, *Prescription Drug Misuse: Epidemiology, Prevention, Identification and Management*, UpToDate, July 2018 Gupta, Anita, et al, *Use of Opioids in the Management of Chronic Non-Cancer Pain*, UpToDate, September, 2017 Volkow, ND, *Opioid Abuse in Chronic Pain — Misconceptions and Mitigation Strategies*, New England Journal of Medicine, 2016; 374;13: 1253-1263 Centers for Disease Control and Prevention. Prescription Opioid Overdose Data. Retrieved August 12, 2018. https://www.cdc.gov/drugoverdose/data/overdose.html

From Long-Term Opioid Therapy to Opioid Use Disorder

- High risk of abuse, dependence and opioid use disorder (OUD)
 - 35% meet criteria for lifetime OUD
 - 25% meet criteria for current OUD
- Risk factors for developing OUD
 - Younger age (under age 40)
 - Severe pain
 - Psychiatric comorbidity
 - Depression
 - Current use of psychotropic medication
 - Past-history of Substance Use Disorder

Opioid/Opiate Use Disorder – Relapse, Recovery and Mortality

- Over 85% of all abstinence episodes following opioid addiction were followed by relapse within 5 years.
- Hser et al. (2015) found SMRs mostly in the range of <u>6 to 20 times</u> the rates of the general population.
- Based on the meta-analysis by Larney et al. (2020) the pooled all-cause SMR for opioid use disorder, <u>based</u> on 43 cohorts, was 10.03 (95%CI, 7.64-13.17), with <u>substantial heterogeneity</u>
- In a <u>meta-analysis of twenty-seven cohorts</u> reporting standardized mortality ratios (SMRs) the pooled SMR was 14.66





Cocaine Use

- Found in the leaves of the coca plant that grows in the Andes mountains in S. America
- National Survey on Drug Use and Health
 - 5.5 million community-dwelling current users
 - Mean age of first cocaine use is 22.6 years
- Patterns of Use
 - 73% low frequency, low quantity users
 - 8% moderate weekly users
 - 18% moderate daily users
 - 1% frequent, heavy users
- Risk Factors for Cocaine Use
 - Male sex
 - Single marital status
 - Tobacco or alcohol use
 - Cluster B personality disorders (Antisocial, borderline)

Cocaine Use

- Recreational cocaine is illicitly produced
 - Illicit cocaine typically comprises only 40-60% cocaine
 - Common adulterants
 - Caffeine
 - Lidocaine
 - Benzocaine
 - Phenacetin
 - Levamisole
- Cocaine use is highly associated with concurrent/simultaneous use of other substances
 - Alcohol in 95% of users \rightarrow cocaethylene (simultaneous cocaine and alcohol)
 - Cannabis in 64% of users
 - Other substances includes opioids and amphetamines

Cocaine Use

- · Complications associated with chronic use
 - Seizures
 - Stroke
 - Cognitive impairment
 - Movement disorders
 - Headache
 - Brain structure
 - Impaired myelin integrity
 - Decreased neuromelanin \rightarrow reduced dopamine activity
 - Suicidal ideation and attempts
 - Psychosis
 - Hypertension
 - Acute heart failure
 - Myocardial infarction
 - Lung damage (especially with crack cocaine smoking)

Cocaine Use Disorder

- 1 million community-dwelling individuals in the USA (~18% of current users)
- Associated with significant increased mortality and morbidity
- Leading causes of mortality
 - Accidental injury
 - Suicide
 - Homicide
 - HIV/AIDS-related

Cocaine Use Disorder – Mortality

- Studies evaluating regular cocaine use and mortality found relatively similar standardized mortality ratios (SMRs).
 - A French study estimated an SMR of 4.36 for males and 7.7 for females
 - Italian study showed a SMR of 4.6 for males
 - Canadian study estimated an SMR of 4.74
- A limitation of many of the studies is that the recruited participants were treatment-seeking dependent cocaine users and therefore at higher risk of premature death compared to recreational users.
 - Caution is advised when generalizing this mortality risk to all cocaine users. Degenhardt et al. found no studies that followed users who only snorted cocaine.
 - It is likely that intranasal cocaine users have much lower mortality and morbidity risks than those who smoke or inject the drug.

Amphetamine Use Disorders – Mortality

- Less data compared to alcohol and opioids abuse studies
- There is substantial heterogeneity in the mortality ratios reported in studies
- Stockings et al. identified 25 eligible cohorts, who were followed for more than 750 000 person-years.
 - Based on their meta-analysis they found that people with regular or dependent amphetamine use had a 6.3- fold elevated rate of mortality compared to their age peers.
- Singleton et al. noted only a single study that recorded the length of amphetamine use at baseline (data available for 1985–1992).
 - This study found an extremely high mortality rate in those who had used for 5 years or longer with a crude mortality rate of 7.34/100 person-years with a confidence interval of 3.89–11.16 (Van Haastrecht et al. 1996)





Substance Use Disorder – Recovery and Relapse

- Traditionally the treatment of SUD has centered upon an initial evaluation and acute treatment, followed by discharged all within a period of weeks or months.
- Some individuals can be treated successfully in this traditional framework, more than half require <u>multiple episodes of</u> treatment over several years to achieve and sustain recovery.
- Several longitudinal studies have shown that, on average, people reach sustained abstinence only after three to four episodes of different kinds of treatment over a number of years.
- Long-term recovery rates ranged from one fifth to over half, varying by:
 - Age of first use (< age 20 yrs vs. > age 20 yrs)
 - Years to first treatment (shorter is better)
 - Prior treatment history (2-3 treatment episodes)
 - Type of treatment (long-term approaches improve rates of success)
 - Pattern of substance use (type of drug; polydrug; route of use)
 - Extent of co-occurring psychiatric disorders (Relapse is common with dual diagnoses)

Substance Use Disorder – Mortality

• Even though all mental health disorders are associated with premature mortality, substance use disorders are associated with highest mortality rates.

• Pitkanen et al. (2020) found in a sample of men and women who had sought treatment for AUDs/SUDs between 1990 and 2009, the risk of death up to 15 years after seeking treatment was very high.



Polydrug Abuse – Mortality

- Polydrug use in general increases the risk of mortality.
- Polydrug Use Disorders doubled the risk of mortality compared to single use disorders

Underwriting Substance Use Disorders

- Red Flags
 - Comorbid Serious Mental Illness
 - More than 2 to 3 treatment episodes
 - Age of first drug use during adolescence
 - Alcohol Use Disorder \rightarrow alcohol withdrawal syndrome
 - Opioid Use Disorder \rightarrow Current opioid substitution therapy
 - Polydrug use
- "Favorable" findings
 - Age of first drug use after 21
 - Short duration from initial drug use to first treatment episode (< 5 years)
 - Treatment with the "Gold Standard" or other long-term approach (AA, NA)
 - No significant psychiatric comorbidity
 - Stable occupational and social environment
 - For Alcohol Use Disorder → evidence of compliance with anti-alcoholism medications (Naltrexone, Acamprosate, Disulfiram, Topiramate, Gabapentin)
 - Evidence of candor



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