Risky drinking and alcohol use disorder: Epidemiology, clinical features, adverse consequences, screening, and assessment

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INTRODUCTION

The degree to which individuals consume alcohol varies greatly, as does alcohol's impact on health and the risk of associated behavioral and medical problems [1]. An estimated 4 to 40 percent of medical and surgical patients experience problems related to alcohol [2]. More than 85,000 deaths a year in the United States are directly attributed to alcohol use [3]; the annual economic cost of alcohol use is estimated to be over $250 billion [4]. Approximately 1 in 10 deaths among working age adults results from excessive drinking [5].

Unhealthy alcohol use ranges from use that puts patients at risk of health consequences to use causing multiple medical and/or behavioral problems meeting the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) diagnostic criteria for alcohol use disorder.

The epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis of patients with unhealthy alcohol use, including alcohol use disorder, are reviewed here. Screening and brief intervention for unhealthy alcohol use are reviewed separately. Pharmacotherapy, psychosocial treatment, and medically supervised withdrawal for patients with alcohol use disorder are also reviewed separately.

- (See "Screening for unhealthy use of alcohol and other drugs in primary care".)
- (See "Brief intervention for unhealthy alcohol and other drug use: Efficacy, adverse effects, and administration".)
- (See "Alcohol use disorder: Pharmacologic management".)
- (See "Alcohol use disorder: Psychosocial management".)
- (See "Management of moderate and severe alcohol withdrawal syndromes".)
- (See "Alcohol withdrawal: Ambulatory management".)

TERMINOLOGY

Many terms have been used to describe alcohol use and alcohol-related problems and disorders; this terminology has continued to evolve over time. The most useful, consistently defined terms are discussed below:

Unhealthy alcohol use — Unhealthy alcohol use encompasses the spectrum of alcohol use that can result in health consequences [6], including:

- Use of amounts that risk consequences (see 'Risky use' below)
- 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 (see 'Alcohol use disorder' below)

Risky use — Risky alcohol use refers to consumption of an amount of alcohol that puts an individual at risk for health consequences. By definition, the condition of people with risky alcohol use is not so severe as to meet diagnostic criteria for an alcohol use disorder. Individuals with risky alcohol use may go on to develop an alcohol use disorder [7].

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) in the United States has estimated consumption amounts of alcohol that increase health risks [7]:

- 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

Specifying these thresholds is an inexact science based on epidemiological evidence. Amounts are based on a “standard drink,” which is defined as 14 grams of ethanol, as found in 5 ounces of wine, 12 ounces of beer, or 1.5 ounces of 80 proof spirits. The number and size of drinks that define risky amounts varies internationally.

Smaller amounts of regular alcohol use can constitute risky use in specific groups (eg, pregnant women, or people who experience alcohol-associated injuries or infection with a sexually transmitted diseases).

Synonyms for risky use include hazardous use and at-risk use. Heavy alcohol use, a related term without a well-specified, widely accepted definition, can refer to a pattern over time or to a single episode of heavy drinking.

Binge drinking — 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" [7]. In women, this typically occurs after approximately four standard drinks, and, in men, after about five standard drinks. Binge drinking is associated with acute injuries due to intoxication and may be associated with an increased cardiovascular risk [8].

Alcohol use disorder — Alcohol use disorder, which in DSM-5 replaced DSM-IV defined alcohol abuse and dependence, is characterized by a problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by 11 specific psychosocial, behavioral, or physiologic criteria [9]. (See 'Diagnosis' below.)

EPIDEMIOLOGY

Alcohol use — Alcohol use is common in adults. As an example, among individuals over the age of 12 years in the United States who participated in the 2019 National Survey on Drug Use and Health [10]:

- 80 percent used alcohol in their lifetime
- 51 percent used alcohol at least once in the past 30 days
- 24 percent reported a heavy drinking episode (five or more drinks on one occasion) in the past month (ie, binge episode)
- 6 percent reported heavy alcohol use (more than five drinks on five or more occasions) in the past month

Levels of alcohol consumption in resource-rich countries, such as the United States, have stabilized; however, evidence suggests that alcohol consumption is increasing in many resource-limited countries, raising the concern that these countries will be facing increasing alcohol-related health problems [11].

Unhealthy and risky use — Nearly 3 in 10 adults in the United States use alcohol in an unhealthy manner and therefore require some form of intervention as part of their health care. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) reports rates of alcohol consumption among United States adults [7] (see 'Risky use' above):

- 28 percent exceed NIAAA thresholds for risky use
  - 19 percent exceeding just the daily limit
  - 9 percent exceeding both the daily and weekly limits
- 72 percent never exceed NIAAA thresholds for risky use

DSM-5 alcohol use disorder — Data from the third National Epidemiologic Survey on Alcohol and Related Conditions showed that 14 percent of adults (>18 years old) met criteria for a current alcohol use disorder and 29 percent had met criteria for an alcohol use disorder in their lifetime [12].

Risk factors — Risk factors for lifetime alcohol use disorder include [13]:

- Male gender
- Age 18 to 29
- Native American and white ethnicity
- Significant disability
- Other substance use disorder
- Mood disorder (eg, major depression, bipolar disorder)
- Personality disorder (eg, borderline or antisocial personality)

Higher than average rates of alcohol use disorder have also been reported among transgender populations; one survey suggested that among transgender adults, heavy drinking episodes (binges) were associated with transphobic discrimination (adjusted odds ratio 4.13) [14].

Genetic risk factors are discussed below. (See 'Genetics' below.)

PATHOGENESIS

The pathogenesis of alcohol use disorder is not known, but its development may be the result of a complex interplay of:

- Genetics – It has been estimated that genetic factors are responsible for approximately 50 percent of the vulnerabilities related to alcohol use disorder [15].
- Environmental influences – Environmental influences can be categorized as intra-familial influences, including prenatal exposure and parenting patterns, and peer influences [16-18].
- Specific personality traits – Personality phenotypes implicated in association with alcohol use disorder includes neuroticism, impulsivity, and extroversion [19].
- Cognitive functioning – Disorders of cognition, especially cognitive dysfunction, may be associated with the development of alcohol use disorders [20].

Several theories have emerged to explain why some drinkers go on to develop an alcohol use disorder. [19,21]. Four theories, below, have received empirical support. That they are not mutually exclusive may help to explain the variable trajectory of the presentation of alcohol use in the population.

- Positive-affect regulation is described as drinking for positive reinforcement, which is directly related to alcohol's neurochemical effect on the brain's reward centers.
- Negative-affect regulation is defined as drinking to relieve negative feelings (ie, the self-medication hypothesis).
- Pharmacological vulnerability postulates that individuals differ in response to alcohol's acute and chronic effects and some people may be more prone to development of alcohol-related difficulties.
- Deviance proneness proposes that alcohol consumption is part of an overall picture of social deviance arising in childhood and resulting from deficient socialization, rather than consumed to provide reinforcement, regulate mood, or because of individual vulnerability of alcohol use.

Pooled data from six cohort studies of over 39,000 participants found that risky alcohol use over time is associated with increasing extraversion, and decreased emotional stability, agreeableness, and conscientiousness [22]. (See 'Risky use' above.)

Genetics — Genetic influences produce alcohol-related phenotypes that, in combination with environmental factors, result in increased risk for alcohol-related problems [23]:

- A low level of response to alcohol
- Personality characteristics, such as impulsivity and behavioral disinhibition
- Alcohol-related psychiatric symptoms

Genetic factors may lead to a decreased risk for alcohol use disorder. As an example, a flushing reaction occurs in individuals homozygous for the gene that codes the enzyme, aldehyde dehydrogenase (ALDH2), which breaks down acetaldehyde, one of the byproducts of alcohol metabolism [24]. Various specific genes have been proposed as important in these and other factors related to the genetic risk for alcohol problems. These genes include the *GABRG1* and *GABRA2* genes that encode the gamma 1 and alpha 2 subunits of the GABA-A receptor [25], *COMT Val158Met* and *DRD2 Taq1A*, which may affect dopamine receptor sensitivity [26], and *KIAA0040* [27]. Genes may influence which individuals are more susceptible to important alcohol-related comorbidities, such as alcoholic liver disease [28].

CLINICAL MANIFESTATIONS

Medical consequences of alcohol drinking may manifest in any organ system of the body. Unhealthy alcohol use is often associated with psychological consequences and may have serious impact on social well-being. Behavioral, psychiatric, social, or medical manifestations of unhealthy drinking that are seen in general medical settings include [29-31]:

- Trauma or injury
- Anxiety, depression, suicidality
- Comorbid substance-use disorders
- Hypertension
- Gastrointestinal symptoms
- Cardiac symptoms
- Central or peripheral neurologic symptoms
- Electrolyte disturbance
- Sleep disturbance
- Increased liver enzymes, including elevated gamma-glutamyl transpeptidase
- Bone marrow suppression
- Macrocytosis
- Malignancies of various organ systems (eg, oropharynx, gastrointestinal breast)
- Social or legal problems

Clinical manifestations of unhealthy alcohol use range in severity from mild in patients with risky drinking to severe in patients with alcohol use disorder.

Patients with unhealthy alcohol use may present asymptomatically in general medical settings, or with a range of signs or symptoms that they may not readily relate to their alcohol use. As examples, patients may present with:

- Sleep disturbance
- Gastrointestinal reflux
- Hypertension
- An incidental finding of abnormal liver enzymes

Patients with alcohol use disorder may display or describe symptoms or behaviors related to their alcohol use, including [9] (see 'Diagnosis' below):

- Recurrent drinking resulting in failure to fulfill role obligations
- Recurrent drinking in hazardous situations
- Continued drinking despite alcohol-related social or interpersonal problems
- Evidence of tolerance
- Evidence of alcohol withdrawal or use of alcohol for relief or avoidance of withdrawal
- Drinking in larger amounts or over longer periods than intended
- Persistent desire or unsuccessful attempts to stop or reduce drinking
- Great deal of time spent obtaining, using, or recovering from alcohol
- Important activities given up or reduced because of drinking
- Continued drinking despite knowledge of physical or psychological problems caused by alcohol
- Alcohol craving

Patients with alcohol use disorder may present in states of acute alcohol intoxication or withdrawal. Signs and symptoms of acute ethanol intoxication vary with severity and can include slurred speech, nystagmus, disinhibited behavior, incoordination, unsteady gait, hypotension, tachycardia, memory impairment, stupor, or coma. Signs and symptoms of withdrawal, seen in patients who abruptly stop or reduce alcohol intake range from tremulousness to hallucinations, seizures, and death. Symptoms generally occur between 4 and 72 hours after the last drink or after a reduction in drinking amounts, peak at about 48 hours, and may last up to 5 days. Alcohol intoxication and withdrawal are addressed in detail separately. (See "Ethanol intoxication in adults" and "Management of moderate and severe alcohol withdrawal syndromes".)

COURSE

The severity of patients' alcohol use patterns in alcohol use disorder does not appear to be strongly correlated with the natural history of the disease. A longitudinal epidemiologic study of male drinkers found that for a large proportion of patients, the severity of their initial diagnosis (using DSM-IV criteria for alcohol abuse and alcohol dependence) was not associated with the patients' clinical status four years later [32]:

Of drinkers initially meeting criteria for **DSM-IV alcohol abuse**:

- 46 percent were in remission
- 24 percent continued to meet abuse criteria
- 30 percent went on to meet criteria for alcohol dependence

Of drinkers initially meeting criteria for **DSM-IV alcohol dependence**:

- 39 percent were in remission
- 15 percent met criteria for abuse only
- 46 percent continued to meet dependence criteria

Many adolescents who exhibit signs of alcohol use disorder have normative drinking patterns or abstain from alcohol consumption in adulthood [33]. Some studies have found that patterns of maladaptive alcohol consumption in adolescence may persist at least into young adulthood [34]. Adolescents with problematic alcohol use short of a disorder had a two-fold increased risk of having an alcohol use disorder in young adulthood, compared with adolescents with non-problematic alcohol use. Adolescents with a diagnosed alcohol use disorder had an additional two-fold increased risk of an alcohol use disorder persisting into young adulthood, compared with adolescents with problematic alcohol use.

ADVERSE CONSEQUENCES

Alcohol use disorder has been found to be associated with higher rates of morbidity and mortality.

Mortality

Mortality rates — Excessive alcohol consumption is the third leading preventable cause of death in the United States. More than 85,000 deaths a year in the United States are directly attributed to alcohol use [3,35]. Excessive drinking, defined as binge drinking, heavy weekly

alcohol consumption, and drinking while underage or pregnant, has been found to result in 1 in 10 deaths among working age adults [5].

Causes — Deaths related to excessive alcohol use include suicide, exacerbation of medical comorbidities, and fatal accidents.

Suicide — Encounters in health care settings are important opportunities to identify active suicidality in patients with unhealthy alcohol use. In persons with alcohol use disorder, suicide is often preceded by recent health care encounters in primary care or specialty outpatient clinics. As an example, a Swedish national survey study of over 250,000 adults with alcohol use disorder examined the health care utilization of 2601 adults in the cohort who died by suicide [36]. The study found that of those persons with alcohol use disorder who died by suicide, 40 percent had a health care encounter within the prior two weeks and 76 percent had an encounter within the prior three months (compared to 6 percent and 25 percent of controls.) A meta-analysis of 31 studies pooling data from over 400,000 participants found an association between alcohol use disorder and suicidal ideation (odds ratio 1.86, 95% CI 1.38, 2.35), suicide attempt (odds ratio 3.13, 95% CI 2.45, 3.81), and completed suicide (odds ratio 2.59, 95% CI 1.95, 3.23 and risk ratio 1.74, 95% CI 1.26, 2.21) [37]. The lifetime rate of suicide attempts among frequent alcohol users in the United States was 7 percent, well above the United States general adult population rate of 1 percent [38-40].

Medical comorbidities — Pooling data from 83 prospective studies, a 2018 analysis of individual participant data from almost 600,000 patients found a dose response relationship between increased alcohol consumption and cardiovascular disease other than myocardial infarction and lower life expectancy. This study suggests that alcohol consumption thresholds should be lower than many published guidelines and less than 100 grams per week (correlates to roughly seven drinks per week) as this is associated with the lowest all-cause mortality [41].

Fatal accidents — Nearly 10,500 traffic fatalities in the United States in 2015 were related to alcohol use, 28 percent of all traffic fatalities [42]. The risk of drowning has been reported to be 3.5 times greater for people who drink than for age-adjusted controls [43].

Medical morbidity — Alcohol can be a significant contributing factor to many medical conditions [31,44,45]. Common medical and psychiatric comorbidities associated with unhealthy alcohol use include:

General medical conditions

- Hypertension
- Cardiovascular disease

- Liver disease
- Pancreatitis
- Gastritis
- Esophagitis
- Bone marrow suppression
- Peripheral neuropathy
- Chronic infectious diseases
- Pneumonia
- Several malignancies, including cancers of the mouth, esophagus, throat, liver, and breast
- HIV

Psychiatric disorders

- Depressive disorders
- Anxiety disorders
- Posttraumatic stress disorder
- Eating disorders
- Other substance use disorders
- Sleep disturbances

SCREENING

It is recommended that all adult primary care patients be screened for unhealthy alcohol use [46,47]. (See "Screening for unhealthy use of alcohol and other drugs in primary care".)

ASSESSMENT

The clinician should carefully assess alcohol use in any patients presenting with social or legal problems, trauma or injury, mood or anxiety disorders, comorbid substance use disorders, along with common alcohol-related medical problems such as hypertension, gastrointestinal issues, increased liver enzymes including elevated gamma-glutamyl transpeptidase, bone marrow suppression, or macrocytosis.

History — Assessment of a patient with suspected unhealthy alcohol use should include asking the patient and collateral sources of information about [48]:

- Current and past alcohol use and treatment

- Family history of alcohol problems and treatment
- Detailed history regarding the quantity and frequency of alcohol use
- Symptoms and behaviors associated with:
  - Criteria for alcohol use disorder. (See 'Diagnosis' below.)
  - Medical complications. (See 'Medical morbidity' above.)
  - Psychiatric complications (eg, depression, anxiety, irritability). (See 'Medical morbidity' above.)
  - Behavioral complications (eg, controlling temper, risky sexual encounters, impulsivity).
  - Other substance use. (See "Opioid use disorder: Epidemiology, clinical features, health consequences, screening, and assessment" and "Cocaine use disorder: Epidemiology, clinical features, and diagnosis" and "Methamphetamine use disorder: Epidemiology, clinical features, and diagnosis" and "Cannabis use disorder: Clinical features, screening, diagnosis, and treatment".)

Physical examination — Physical features accompanying unhealthy alcohol use range from a normal physical examination to features of alcohol withdrawal (tremor, agitation, clouding of the sensorium) to features of advanced liver disease (eg, spider angiomata, palmar erythema, hepatic or splenic enlargement). It can also include findings related to any of the common co-occurring medical and psychiatric disorders along with findings related to less common alcohol-related complications. (See 'Medical morbidity' above.)

Laboratory evaluation — There are several laboratory tests or "biomarkers" related to alcohol consumption, alcohol use disorder or liver disease. None are sensitive for unhealthy use. They all tend to require heavy and repeated recent consumption to be elevated. Most are nonspecific, but some have greater specificity.

Although not sensitive or specific for alcohol use, in the absence of other explanations for alterations in these tests, the following lab tests may be helpful in the assessment of unhealthy alcohol use:

- Liver enzymes – Aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, and albumin to test for liver damage. An AST:ALT ratio of 2:1 is suggestive of alcohol-induced liver disease.

- Hemoglobin, complete blood count – To determine the presence and severity of anemia, pancytopenia, and macrocytosis. A mean corpuscular volume >100 fL constitutes macrocytosis. Pancytopenia and macrocytosis usually require very heavy prolonged use and often liver disease.

- Gamma-glutamyltransferase (GGT) – An indicator of excessive alcohol use when elevated (normal reference ranges: 8 to 40 units/L for females and 9 to 50 units/L for males).

Other tests are more accurate indicators of excessive alcohol use, but are not widely available. If available, these tests may be useful for specific purposes, eg, if elevated from the start they can be used to monitor progress with treatment:

- Carbohydrate deficient transferrin (CDT) – A CDT level above 0.12 suggest chronic excessive alcohol use. CDT is fairly specific for excessive use though can be elevated by rarer liver diseases, such as primary biliary cirrhosis. This is more useful than a GGT, but not routinely available and used mostly by specialists.

- Phosphatidal ethanol (PEth) – PEth is specific for ethanol use and currently mostly in research protocols. A concentration greater than 20 ng/dl is evidence of intoxication; it can detect excessive alcohol intake within a two-week period.

DIAGNOSIS

Alcohol use disorder in DSM-5 replaced two psychiatric disorders in DSM-IV, alcohol abuse and alcohol dependence in 2013. Alcohol use disorder can be specified as mild, moderate, or severe, based on the number of DSM-5 criteria present. Alcohol dependence in DSM-IV is best represented by moderate to severe alcohol use disorder in DSM-5; alcohol abuse is similar to the mild subtype of alcohol use disorder.

DSM-5 diagnostic criteria for alcohol use disorder are described in a table (table 1) [9].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Alcohol use disorders and withdrawal" and "Society guideline links: Alcohol consumption".)

SUMMARY AND RECOMMENDATIONS

- **Terminology** – Terms used to describe alcohol use and alcohol-related problems and disorders include the following (see 'Terminology' above):

  - **Unhealthy alcohol use** – Encompasses the spectrum of alcohol use that can result in health consequences including risky use and alcohol use disorder. Nearly 3 in 10 adults in the United States use alcohol in an unhealthy manner. (See 'Unhealthy alcohol use' above.)

  - **Risky use** – This refers to consumption of an amount of alcohol that puts the individual at risk for health consequences. (See 'Risky use' above.)

  - **Alcohol use disorder** – A disorder characterized by a problematic pattern of alcohol use leading to distress or impairment. (See 'Alcohol use disorder' above.)

  - **Binge drinking** – Drinking so much within two hours that the blood alcohol concentration reaches 0.08g/dL. (See 'Binge drinking' above.)

- **Pathogenesis** – Alcohol use disorder is believed to stem from the interplay of genetics, environmental influences, and specific personality traits. It has been estimated that genetic factors are responsible for approximately 50 percent of the vulnerabilities related to the disorder. (See 'Pathogenesis' above.)

- **Clinical manifestations** – Individuals with unhealthy alcohol use seen in the general medical setting may present with injury/trauma, depression or anxiety, hypertension, abuse of other substances, gastrointestinal symptoms, increased liver enzymes, macrocytosis, and social or legal problems. (See 'Clinical manifestations' above.)

  Individuals with unhealthy alcohol use may present asymptomatically in general medical settings, or with a range of signs or symptoms that they may not readily relate to their alcohol use.

  Physical features accompanying unhealthy alcohol use range from a normal examination to features of alcohol withdrawal, to features of advanced liver disease.

- **Laboratory data** – Laboratory data including liver enzymes, complete blood count, hemoglobin level, gamma-glutamyltransferase, carbohydrate deficient transferrin, and phosphatidyl ethanol, may be helpful in identifying unhealthy alcohol use. (See 'Laboratory evaluation' above.)

- **Mortality** – Excessive alcohol consumption is the third leading preventable cause of death in the United States. More than 85,000 deaths a year in the United States are directly

attributed to alcohol use, including resulting medical illness, traffic fatalities, drowning, and suicide. (See 'Adverse consequences' above.)

- **Screening** – We recommend screening all adults in primary care settings for unhealthy alcohol use. (See 'Screening' above and "Screening for unhealthy use of alcohol and other drugs in primary care".)
- **Assessment** – We include the patient and collateral sources, when possible, in our assessment of the individual with suspected unhealthy alcohol use. We ask about current and past alcohol use and treatment, family history of alcohol problems and treatment, a detailed history regarding the quantity and frequency of alcohol use, and symptoms and behaviors associated with alcohol use disorder, related medical and psychiatric conditions, and use of other substances. (See 'Assessment' above.)

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