# Alcohol Use and Depression: Public Health and Clinical Implications

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**Abstract:** Alcohol is used on a national level as a social relaxant. Yet, misuse of alcohol can lead to considerably harms. In clinical psychiatry, the presence of comorbid alcohol abuse and depression are commonly encountered. This presents a challenging scenario for clinicians in terms of diagnostic conundrums, prognostic issues and treatment paradigms. This article reviews findings of key studies in the subject and offers practical suggestions to workers in the field. It also highlights the need for governments and public health agencies to focus on this important and highly prevalent problem.

**Keywords:** Depression, Alcohol Treatment, Co-morbidity, Epidemiology.

Alcohol has been used for millennia in many cultures in social settings. It promotes feelings of well-being, relaxation and mild euphoria. Economically, the production and sale of alcohol generates substantial employment, retail activity, export income and tax revenue. However, it is also associated with states of intoxication, dependence and associated social and mental health problems. The subject of alcohol misuse is of serious concern to health authorities such as those in Australia, where in spite of declining per capita consumption, there is still elevated consumption by world standards [1]. The cost of alcohol misuse to Australian society including costs to the health and hospital system, lost workplace productivity and crime was estimated to be $15.3 billion (27% of all costs from substance misuse) in 2004-5 [2]. Alcohol misuse is linked to violent crime, road traffic accidents and diseases of all major systems of the body including malignant neoplasms, neuropsychiatric conditions, cardiovascular and gastrointestinal system as well as intentional self-injury [3]. Exposure to alcohol during pregnancy, regardless of the level of consumption, has been linked with negative health outcomes including birth defects and disability such as foetal alcohol spectrum disorder [4, 5].

These concerns are mirrored in other countries such as the United States where alcohol dependence ranks third on the list of preventable causes of morbidity and mortality, costing $185 billion in 2000 [6]. The World Health Organization (WHO) identifies this to be a global concern with alcohol being the world's third largest risk factor for disease and disability and the single greatest risk factor in middle-income countries for the same [7]. High rates of alcohol are seen in high income countries and the former socialist countries [3, 7]. Social and general health concerns aside, this article examines the association between alcohol abuse and depressive disorders and identifies emerging treatment strategies.

## DIAGNOSTIC ISSUES IN ALCOHOL USE DISORDER AND DEPRESSION

The most recent revision of the Diagnostic and Statistical Manual of Mental Disorders (5th edition) includes key changes in the classification of alcohol use disorders [8]. Whereas the 4th Edition (DSM-IV) allowed two types of substance use disorders, namely alcohol *abuse* or *dependence*, the 5th edition combines them into *alcohol use disorder* [8, 9]. Key features of classifying alcohol use disorders include impaired control, social impairment and pharmacological criteria including tolerance and withdrawal; the term addiction is not used due to negative connotation [8].

Comorbidity of alcohol and major psychiatric disorder has been identified in repeated studies. The diagnosis of Major Depressive Disorder (MDD) has been a source of controversy in psychiatric research. This has led to various theories regarding the relationship where comorbidity exists: research concepts include distinguishing 'primary' versus 'secondary', 'organic' and 'non-organic' as well as 'substance induced' expected effects of intoxication and withdrawal [10]. The DSM-5 states that a primary mood disorder could be considered over alcohol induced mood disorder where the mood disorder preceded the alcohol use disorder and continues more

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than one month after cessation or withdrawal of the alcohol [8].

Structured diagnostic instruments have been developed to aid differentiation of primary and substance induced disorders in research settings. These have varied in their ability to successfully make this distinction. The Structured Clinical Interview for DSM IV-TR Axis I Disorders (SCID-I, research version) relies on the interviewer to determine, based on the subject's response whether the diagnosis of depression should be primary or secondary to alcohol use [11]. The Semi-Structured Assessment for the Genetics of Alcoholism aims to differentiate 'primary' and 'secondary' mood disorders based on ages of onset and offset of both disorders, mood state during periods of abstinence and has good kappa score on test-retest reliability studies [12]. The psychometric instrument that most closely correlates with the DSM-IV criteria for substance induced psychiatric disorders is the Psychiatric Research Interview for Substance and Mental Disorders (PRISM), which delineates three subtypes: MDD onset prior to substance use disorder, MDD during periods of abstinence and 'substance induced' MDD. Its psychometric properties suggest increase reliability in the measurement of MDD in substance abusers [13]. Regardless of the challenges in establishing aetiological links between depression and alcohol abuse, what is clear is that the two are highly correlated and this has implications for prognosis and treatment.

The association between alcohol use disorders and depression has been the subject of speculation [14]. The association has been proposed to be either causal, of shared aetiology or artefactual. Causal mechanisms may be direct or indirect. A direct mechanism may be alcohol abuse inducing depressive symptoms, thereby mimicking a depressive syndrome. An indirect mechanism may be due to alcohol dependence leading to social problems such as divorce or unemployment, which in turn lead to a depressive syndrome. Shared aetiology may result from genetic and environmental factors (such as disrupted early childhood/family) that may lead to depression. Family and adoption studies have not consistently confirmed the shared aetiology hypothesis [15]. There have been no studies to suggest that the co-occurrence of these two disorders is an artifact of misdiagnosis [16].

Studies in this area have been limited by a number of factors. These have included small sample sizes, cross sectional nature of studies and reliance on self-report in order to quantify the frequency and severity of alcohol consumption. In spite of this, there are a number of high quality studies that provide detailed information on the relationship between depression and alcohol use disorders. The National Comorbidity survey (NCS) [16] and the Epidemiological Catchment Area (ECA) [17] study are large studies conducted in the United States to assess comorbidity. These studies revealed that between 2.5% (NCS) and 3.5% (ECA) of respondents were diagnosed with lifetime alcohol abuse. The rates of alcohol dependence were also consistent between the two studies with lifetime rate of 7.9% (ECA) and 12 month rate of 7.9% (NCS). Almost one third of alcohol dependent patients (27.9%) were likely to have suffered with major depressive disorder in the previous year, which was an odds ratio of 3.9. The NCS also found that psychiatric disorders were reported to precede addictive disorders by 10 years, except in males where almost three quarters reported that alcohol use disorder preceded their mood disorder. A recent study of older adult men reported that the probability of depression decreased with increasing consumption of alcohol up to about 2 standard drinks per day, after which the probability of depression increased rapidly in an almost linear fashion with increasing alcohol use, particularly beyond six standard drinks per day [18]. A study of 6,050 former alcohol dependent patients who had generally not used substances for two years indicated a fourfold increased risk of MDD, suggesting that alcohol intoxication or withdrawal was not the cause of ongoing depressive symptoms [19]. A more recent study examined 1,369 patients with current depression and/or anxiety and alcohol abuse and/or dependence [20]. Severe alcohol dependence was correlated with 95% persistence of depression and/or anxiety in a two year prospective follow up, whereas those with current, previous or no lifetime history of alcohol abuse had a persistence of depression and/or anxiety disorder at lower rates between 46% to 53%. This association remained significant after adjustment for severity of depression and anxiety, psychosocial factors and treatment factors. Another published study of 2329 persons revealed that 20.3% of those with anxiety/depression also had comorbid alcohol dependence compared to controls (5.5%). Alcohol abuse was not a statistically significant risk factor in presence of depression/anxiety compared to non-depressed controls (both groups had 12% prevalence of alcohol abuse) [21]. Conversely, suffering with depression is a risk factor for returning to drinking and alcoholism with persons suffering depression three times more likely to return to

substance dependence [22]. In summary, it is acknowledged that the two disorders are intertwined, with each disorder increasing the risk of development of the other, increasing the severity of the other, and prolonging the clinical course and conferring a worse outcome of the other [23]. The health outcomes of comorbid depression and substance use are worse, and the risk of suicide is increased [24].

## CLINICAL IMPLICATIONS

Given that the relationship between alcohol and mood disorders is complex and multifactorial with genetic and environmental risk factors, treatment should be tailored to individual needs and level of commitment to change. In the first instance, at risk drinkers need to be identified through a detailed history about the pattern of drinking, associated family history and current mental state. Negotiating a lower level of drinking may be an initial practical goal that is more achievable for many patients rather than total abstinence. This needs to be coupled with psychosocial or brief intervention, which is the mainstay of treatment. Given that alcohol abuse and/or dependence can mimic symptoms of depressive disorders, those suffering with comorbid disorders should be detoxified safely and their mental state should be observed over ensuing weeks to see if symptoms of depression improve in the absence of alcohol abuse or dependence [25, 26].

In spite of these interventions, up to 70% of patients resume drinking within 12 months [27] and therefore a combination of behavioral therapies and pharmacotherapy has been recommended for those suffering with alcohol dependence [28]. Three pharmacological agents are commonly used in clinical practice for this suffering severe alcohol use disorder: disulfiram, naltrexone and acamprosate. Naltrexone is an opioid receptor antagonist with proven efficacy in time to relapse into drinking, reduced alcohol consumption and reduced severity of alcohol dependence and craving [29]. Patients treated with acamprosate, a modulator of glutamate neurotransmission at metabotropic-5 glutamate receptor) achieved greater rates of complete abstinence, longer times to first drink and longer periods of abstinence [30]. Not all studies are equivocally positive however, with a recent multicenter trial concluding no benefit of either of these two medications over placebo in the primary analysis [31]. The efficacy of these agents is modest with up to 40% of patients in remission at 2 years compared to 15% in remission from alcohol dependence in the absence of pharmacotherapy with up to half of patients discontinuing pharmacotherapy in clinical trials [32]. A recent overview suggests Naltrexone may reduce craving whereas acamprosate may have a differential effect on abstinence [33]. Disulfiram is an inhibitor of aldehyde dehydrogenase and frequently requires the supervision of another support person to ensure compliance. It leads to aversive reactions even with the consumption of unintentional small amounts of alcohol such as those found in cough mixtures. It is usually reserved where other treatment options have failed. Other emerging off-label treatments for alcohol dependence include topiramate, baclofen and ondansetron [34].

Studies have shown equivocal results in the antidepressant treatment of depression in the context of alcohol abuse. One study based on a cross-sectional interview and self report concluded that antidepressant medication helped reduced alcohol intake in depressed men, although the same outcome was not observed in women [35]. It showed that depression was associated with higher levels of alcohol consumption. Recent meta-analyses have supported this notion, concluding that there may be an improvement in levels of alcohol consumption in patients with depression who are given Selective Serotonin Reuptake Inhibitor antidepressant medications (SSRIs) [36]. Others have suggested that antidepressant medications may worsen the outcome of alcoholism in some individuals [37, 38]. A systematic meta-analysis which looked at 14 double blind randomized controlled trails consisting of 848 patients concluded that the beneficial effect of SSRIs is modest in improving depressive symptoms and should not be stand-alone treatment [39]. A recent randomized double-blind placebo controlled trial aimed to evaluate the efficacy of sertraline and naltrexone compared to each treatment alone and to placebo over 14 weeks [40]. The combined sertraline and naltrexone group had the highest rate of abstinence at the end of the trial (54%) compared to the other three groups combined (24%). There was a greater reduction of depression scores in this group, although it fell short of statistical significance. Hence, SSRIs generally do not appear to reduce alcohol consumption in these studies when used as monotherapy. Therefore, it is recommended that evidence based treatment for both alcohol use disorder and mood disorder are provided in tandem when they co-occur [33]. Prior to instituting pharmacotherapy of mood disorders, it would be ideal if abstinence or significantly reduced drinking could be

enforced for several weeks. Given the co-occurrence of both disorders, integrated services where treatment for both disorders could be delivered together would be most helpful in terms of engaging patients and maintaining them in treatment.

Pharmacological therapies aside, psychosocial therapies also have a role in managing alcohol abuse and dependence. A review suggested that Alcoholics Anonymous (AA) may help by providing external supervision, substitute dependency, new caring relationships and increased spirituality [41]. Whilst acknowledging that it is difficult to obtain empirical research on the efficacy of this organization, the author points to multiple studies that attest to the correlation between good clinical outcome and attending meetings of AA. Project Match was a controlled study involving almost 2000 patients with alcohol dependence which showed AA attendance in the first year to be as effective as cognitive behavior therapy and motivational enhancement therapy and increased attendance at AA meetings led to improved outcomes [42]. Another study which undertook a 8 year follow up of self-selected alcohol dependent patients who returned to controlled drinking, most positive outcomes came from those who were abstinent and attending AA [43]. However, a recent Cochrane review that attempted to analyse studies in this area suggested that most studies were of such low quality with limited data to the extent that firm conclusions could not be drawn [44]. This is supported by older reviews which observe that less intensive community based treatments for alcohol dependence are as equally effective as prolonged inpatient care [45].

## SUMMARY

Since the occurrence of alcohol use disorders and mood disorders are major public health issues, there is much scope for government policy to address these problems on a population based level, with preventative measures being a priority [7]. The World Health organization is leading a Global Strategy to Reduce the Harmful Use of Alcohol, which recommends target areas for government action worldwide to address this [7]. In spite of inconsistencies and heterogeneity of the studies in this field, it is possible to recommend that clinicians address both the alcohol use disorder and depressive disorder in a holistic manner, deploying an array of pharmacological and psychosocial interventions tailored to the individual.

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