



## Research paper

## Major depression and alcohol use disorder in adolescence: Does comorbidity lead to poorer outcomes of depression?



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## ABSTRACT

**Background:** Comorbid major depression (MD) and alcohol use disorder (AUD), particularly in adolescents, have been shown to be associated with poorer subsequent MD outcomes.

**Methods:** Longitudinal data were used to model associations between a four-level classification of MD/AUD during the period 15–18 years (neither; MD-only; AUD-only; comorbid MD/AUD) and MD over the period 18–35 years. These associations were then adjusted for confounding by a series of factors measured in childhood.

**Results:** The three disorder groups had rates of adult MD during the period 18–35 years that were significantly ( $p < .05$ ) higher than that of the group with no disorder. Furthermore, those in the comorbid MD/AUD group had significantly ( $p < .05$ ) higher rates of adult MD than those in the AUD-only group, and marginally ( $p < .10$ ) higher rates of adult MD than those in the MD-only group. After adjustment for confounding, the difference in rates of adult MD between the MD-only group and the MD/AUD group were no longer statistically significant. The factors that explained the associations were gender, childhood behavior problems, and exposure to physical and sexual abuse.

**Limitations:** The data were obtained by self-report, and may have been subject to biases.

**Conclusions:** The results of these analyses suggest that marginally higher rates of depression to age 35 amongst the comorbid MD/AUD group were explained by increased exposure to adverse childhood circumstances amongst members of the comorbid group. Adolescent MD/AUD comorbidity is likely to be a risk marker, rather than a causal factor in subsequent MD.

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## 1. Introduction

The association between alcohol use disorders (AUDs) and mental disorders is well-recognized and has been the subject of a large number of recent studies (Hasin and Delker, 2015). The comorbidity between AUDs and major depression (MD) has received considerable attention, with a number of studies finding that MD and AUD comorbidity is common (Grant and Harford, 1995; Grant et al., 1996; Teesson et al., 2009) and in particular comorbidity at earlier stages of development (Beesdo-Baum et al., 2015; Langenbach et al., 2010; Wittchen et al., 1996). A key question arising from this literature is the extent to which comorbidity early in the developmental sequence predicts worse outcomes than non-comorbid depression at early stages (Essau, 2011; Kaminer et al., 2007).

A number of studies have suggested that early MD/AUD comorbidity predicts poorer subsequent MD outcomes. Hasin and Grant (2002), using data from the US National Longitudinal Alcohol Epidemiologic Survey, found that prior AUD significantly increased the risk of subsequent MD, despite not consuming alcohol at the time of measurement. Fein (2013) reported that individuals with both short- and long-term histories of alcoholism had greater risks of both lifetime and current MD, in a study using retrospective data. Similar findings were reported by Di Sclafani et al. (2007), in a group of long-term abstinent alcoholics.

On the other hand, some evidence suggests that comorbidity is not predictive of a higher risk of later depression. For example, in a large longitudinal study of comorbidity in adolescence and early adulthood, the difference in depressive symptom severity between those with high and low alcohol problems diminished over time, and was minimal by early adulthood (Marmorstein, 2009). Brière et al. (2014), using longitudinal data, also reported that comorbidity was not associated with increased risk of subsequent MD. Relatedly, there is evidence from clinical data in adults

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suggesting the presence of alcohol or substance use disorder comorbidity does not worsen the outcome of treatment for depression (Davis et al., 2010; Mulder et al., 2006).

There may, however, be several issues arising from the previous literature that lead to difficulties in interpretation of these discrepant findings. For example, many studies in this area have relied on clinical, small or selected samples (Davis et al., 2010; Di Sclafani et al., 2007; Fein, 2013; Mulder et al., 2006), or have employed a limited range of variables to test for potential confounding (e.g. Brière et al., 2014; Grant et al., 1996; Marmorstein, 2009). One way to address these issues is to employ data from a longitudinal study employing a general population sample, with repeated measurements of MD over time, and with data pertaining to a wide variety of possible confounding factors.

In this study we used data from a longitudinal birth cohort study to investigate the effect of comorbidity between MD and AUD in adolescence on MD outcomes in adulthood, net of confounding factors. In particular, the study examined: a) whether individuals with comorbid MD/AUD in adolescence had higher rates of adult MD than individuals with either disorder, or no disorder; and b) the extent to which a series of individual and environmental factors could account for increased rates of MD in adulthood amongst individuals with comorbid MD/AUD in adolescence. This was achieved by comparing rates of MD during the follow-up period (18–35 years) between four groups: those with comorbid MD/AUD; those with MD or AUD alone; and those with neither condition; during the period 15–18 years.

## 2. Methods

### 2.1. Participants

The data were gathered from the Christchurch Health and Development Study (CHDS). In this study a birth cohort of 1265 children (635 males, 630 females) born in the Christchurch (New Zealand) urban region in mid-1977 has been studied at birth, 4 months, 1 year and annually to age 16 years, and again at 18, 21, 25, 30 and 35 years (Fergusson and Horwood, 2001; Fergusson et al., 1989). The original cohort was comprised of 97% of all individuals born in Christchurch during the study entry period. All study information was collected on the basis of signed consent from study participants and is fully confidential. All aspects of the study have been approved by the Canterbury (NZ) Ethics Committee. Sample sizes ranged from 1025 (age 18) to 962 (age 35), representing 79% to 82% of the surviving sample at each observation. The primary driver of sample loss over the course of the study has been emigration from New Zealand, with loss of contact.

### 2.2. Late adolescent major depression/alcohol use disorder classification (ages 15–18)

At the assessments at ages 16 and 18 years, participants were interviewed using items from the Composite International Diagnostic Interview (CIDI) (World Health Organization, 1993), in order to assess DSM-III-R (age 16) (American Psychiatric Association, 1987) and DSM-IV (age 18) (American Psychiatric Association, 1994) criteria for major depression (MD) and alcohol abuse/dependence (alcohol use disorder; AUD). This information was used to classify participants into four groups, based on their history of MD and AUD during the period 15–18 years. These groups were: Neither MD nor AUD (comparison group); AUD-only; MD-only; and MD/AUD. Sample sizes at these ages were n=982 (age 16) and n=1025 (age 18).

### 2.3. Outcome measure - Major depression in adulthood (ages 18–21; 21–25; 25–30; 30–35 years)

At the assessments from ages 21 to 35 years, cohort members were interviewed concerning symptoms of MD that had occurred since the previous assessment, again using items from the CIDI to assess DSM-IV criteria for major depression. On this basis, cohort members who met DSM-IV criteria for MD at any time during an assessment period (18–21 years; 21–25 years; 25–30 years; and 30–35 years) were classified as having MD during that period. Sample sizes at these assessments were: n=1011 (age 21); n=1003 (age 25); n=987 (age 30); and n=962 (age 35).

### 2.4. Covariate factors

A number of potential confounding factors were abstracted from the study database, on the basis that they have been shown to be related to both MD and AUD in adolescence and adulthood. These factors included:

#### 2.4.1. Childhood socioeconomic and demographic factors

2.4.1.1. *Gender*. Measured at birth.

2.4.1.2. *Maternal age*. Measured at birth.

2.4.1.3. *Family living standards*. (ages 0–10). At each year a global assessment of the material living standards of the family was obtained via interviewer rating on a five point scale that ranged from 1 = “very good” to 5 = “very poor”. These ratings were summed over the 10 year period to give a measure of family living standards during this period.

#### 2.4.2. Childhood family dysfunction

2.4.2.1. *Parental maladaptive behaviour (alcohol problems/criminal offending)*. At age 15, the parents of cohort members were questioned concerning their history of alcoholism or alcohol problems and criminal offending. On this basis, 11.9% of the sample were classified as having a parental history of alcoholism/alcohol problems, and 12.4% of the sample as having a parental history of criminal offending.

2.4.2.2. *Exposure to family adversity (0–15 years)*. A measure of family adversity was calculated using a count of 38 different measures of family disadvantage during the period 0–15 years, including measures of disadvantaged parental background, poor pre-natal health practices and perinatal outcomes, and disadvantageous child-rearing practices (Fergusson et al., 1994).

#### 2.4.3. Childhood behaviour problems (conduct, attention, anxious/withdrawn, ages 7–9)

At ages 7–9 years, information on child behavior problems was obtained from parental and teacher report. Parental reports were obtained from an interview with the child's mother using a behavior questionnaire that combined items from Rutter et al. (1970) and Conners (1970) questionnaires. Also, the child's class teacher completed a combined version of the Rutter et al. (1970) and Conners (1969) teacher questionnaires. Factor analysis of the item-level report data showed these reports formed uni-dimensional scales reflecting the extent of parent-reported and teacher reported behavior problems in three domains (Fergusson and Horwood, 1993; Fergusson et al., 1991): a) conduct problems (aggressive, oppositional, and conduct disordered behaviour); b) attentional problems (restless, inattentive, or hyperactive behaviours); and c) anxious/withdrawn behaviors (shy, anxious or withdrawn behaviour). For the purposes of the present analysis, the parent and teacher reports were summed for each domain and

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