CHAPTER 5

ALCOHOL-USE DISORDER SEVERITY PREDICTS FIRST-INCIDENT OF DEPRESSIVE DISORDERS
ABSTRACT

Background | Previous studies suggested that alcohol-use disorder severity, defined by the number of criteria met, provides a more informative phenotype than dichotomized DSM-IV diagnostic measures of alcohol use disorders. Therefore, this study examined whether alcohol-use disorder severity predicted first-incident depressive disorders, an association that has never been found for the presence or absence of an alcohol use disorder in the general population.

Methods | In a national sample of persons who had never experienced a major depressive disorder (MDD), dysthymia, manic or hypomanic episode (n=27,571), we examined whether a version of DSM-5 alcohol-use disorder severity (a count of three abuse and all seven dependence criteria) linearly predicted first-incident depressive disorders (MDD or dysthymia) after 3-year follow-up. Wald tests were used to assess whether more complicated models defined the relationship more accurately.

Results | First-incident of depressive disorders varied across alcohol-use disorder severity and was 4.20% in persons meeting no alcohol-use disorder criteria versus 44.47% in persons meeting all ten criteria. Alcohol-use disorder severity significantly predicted first-incident of depressive disorders in a linear fashion (OR=1.14, 95% CI=1.06-1.22), even after adjustment for sociodemographics, smoking status and predisposing factors for depressive disorders, such as general vulnerability factors, psychiatric comorbidity and subthreshold depressive disorders. This linear model explained the relationship just as well as more complicated models.

Conclusions | Alcohol-use disorder severity was a significant linear predictor of first-incident depressive disorders after 3-year follow-up, and may be useful in identifying a high-risk group for depressive disorders that could be targeted by prevention strategies.

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INTRODUCTION

Cross-sectional studies have often revealed a strikingly high prevalence of depressive disorders in persons with DSM-IV alcohol use disorders (AUDs; alcohol abuse [AA] and alcohol dependence [AD]). Persons with lifetime AD have a 2- to 4-fold increased risk of lifetime depressive disorders in general population studies (Ross, 1995; Kessler et al., 1997; Hasin et al., 2005; Hasin et al., 2007), whereas the prevalence of depressive disorders appears to be even higher in clinical samples of persons with AD (Lynskey, 1998). In contrast, no associations have been found for lifetime AA (Kessler et al., 1997; Hasin et al., 2005). Among alcohol dependent persons, those with a comorbid depressive disorder are significantly more disabled and have poorer treatment outcomes (Burns et al., 2005). Therefore, prevention of depressive disorders in alcohol dependent persons has the potential to enhance mental health care.

However, the nature of the relationship between AUDs and depressive disorders remains poorly understood. Although strong cross-sectional associations were found for AD and depressive disorders (Ross, 1995; Kessler et al., 1997; Lynskey, 1998; Hasin et al., 2005; Hasin et al., 2007), retrospective general population and twin studies that attempted to take time order into account did not find significant associations (Hettema et al., 2003; Kuo et al., 2006). In addition, AUDs did not prospectively predict the incidence of major depressive episodes in midlife women (Bromberger et al., 2009). In contrast, other prospective studies showed that AUDs (Rohde et al., 2001) and drug and alcohol dependence (Marmorstein et al., 2010) in late adolescence predicted the presence of major depressive disorder in young adulthood. Given these contrasting findings, general population studies examining the first-incidence of depressive disorders are essential for unraveling the time order of comorbidity, a necessary step towards understanding whether there is a causal relationship. To our knowledge, only two large general population prospective studies examined AUDs as predictors of first-incident depressive disorders, one in the United States (Grant et al., 2009) and the other in the Netherlands (De Graaf et al., 2002). These studies failed to find AUDs as significant predictors of future depressive disorders.

One possible explanation for this lack of predictive value is the way AUDs were defined. Both studies characterized AUDs according to DSM-III-R or DSM-IV criteria, i.e., AA and AD, as two separate and hierarchical disorders with AD taking precedence over AA if criteria for both are met. While DSM-IV AD diagnoses are reliable and valid, the reliability and validity of AA is lower and more variable (Hasin, 2003; Hasin et al., 2006a). At the same time, many studies show that most AA and AD criteria form a single latent dimension, with AA and AD criteria interspersed across an underlying severity spectrum (Kahler and Strong, 2006; Martin et al., 2006; Saha et al., 2006; Keyes et al., 2010; Shmulewitz et al., 2010). Moreover, the simple count of criteria forms a linear dimension of alcohol-use disorder severity (Hasin and Beseler, 2009; Dawson et al., 2010; Dawson and Grant, 2010), leading to plans to combine AA and AD criteria into one diagnosis in DSM-5 with different severity levels (www.dsm5.org). This research and the resulting diagnostic
changes suggest that a dimensional approach to AUDs may provide a more informative phenotype than dichotomized measures based on artificially imposed thresholds.

Since incidence rates of psychiatric disorders are generally low, first-incidence studies require large samples and highly reliable, valid and informative predictors. We will therefore examine whether alcohol-use disorder severity predicts first-incident depressive disorders (major depressive or dysthymic disorder) after 3-year follow-up using prospective data from a large, national sample (Grant et al., 2001; Grant et al., 2007). Note that this is one of the samples that did not find a significant association of AUDs defined in a binary manner and first-incident major depression (Grant et al., 2009). Although alcohol-use disorder severity has been linearly associated with various alcohol measures (Hasin and Beseler, 2009), no other study has ever examined its prospective association with psychiatric comorbidity such as depressive disorders. Our aim was, therefore, to examine whether a continuum of alcohol-use disorder severity (as a count of criteria, range 0-10) predicts first-incident depressive disorders in a linear fashion, and test whether more complicated models better describe the association. Analyses adjust for well-known depression risk factors such as smoking status, general vulnerability factors (family history of depressive disorders, family history of alcohol dependence and childhood trauma), psychiatric comorbidity (conduct disorder and anxiety disorder) and subthreshold depressive disorders.

**METHOD**

Sample
The present study is based on the baseline (Wave 1: 2001-2002) and 3-year follow-up (Wave 2: 2004-2005) data of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). The NESARC surveyed a representative sample of the adult (≥18 years) civilian population, residing in household and group quarters, oversampling black and Hispanic people and young adults aged 18-24, with data adjusted for oversampling and household- and person-level nonresponse. The weighted data were then adjusted to represent the U.S. civilian population based on data from the 2000 census. A detailed description of the NESARC study design and sampling procedures can be found elsewhere (Grant et al., 2001; Grant et al., 2007). Face-to-face interviews were conducted with 43,093 respondents at the baseline measurement, yielding an overall response rate of 81.0%. The follow-up measurement involved face-to-face re-interviews with all participants in the baseline interview. Excluding respondents ineligible for the follow-up interview because they were deceased (n=1,403), deported, mentally or physically impaired (n=781) or on active duty in the armed forces throughout the follow-up period (n=950), the response rate at 3-year follow-up was 86.7%, reflecting 34,653 completed interviews. The cumulative response rate at the follow-up measurement was the product of the baseline and follow-up response rates, or 70.2%. The mean interval between baseline and follow-up interviews was 36.3 (SE=2.62) months. All potential NESARC respondents were informed in writing about the nature of the survey, the statistical uses of the survey.
data, the voluntary aspect of their participation, and the federal laws that provide for the confidentiality of identifiable survey information. Respondents who gave consent were then interviewed.

To examine the first-incidence of depressive disorders after 3-year follow-up, we excluded all participants with a lifetime major depressive (n=4,785), dysthymic (n=1,166), bipolar I (n=1,172), bipolar 2 (n=428) and/or hypomanic (n=428) disorder at the baseline measurement. In total, we excluded 7,082 of the 34,653 participants with complete data on the baseline and follow-up measurement, leaving a sample of 27,571 participants for the current analyses. To be consistent with previous first-incidence studies on depressive disorders (De Graaf et al., 2002; Grant et al., 2009), no restrictions regarding lifetime or current alcohol consumption were applied. Mean age of the present sample is 45.9 (SE=0.20) years, 49.5% were female and 69.7% were white, 11.6% African-American, and 12.2% Hispanic.

Diagnostic interview
The diagnostic interview was the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV Version (AUDADIS-IV; Grant et al., 1995), a structured interview designed for experienced lay interviewers. Computer diagnostic programs implemented DSM-IV criteria for the disorders using AUDADIS-IV data. The depressive and anxiety diagnoses in this report are DSM-IV independent diagnoses, i.e., diagnoses of mental disorders that are not substance-induced and not due to a medical condition. In differentiating primary from substance-induced disorders, the DIS, UM-CIDI, and WMH-CIDI rely on the respondent’s opinion of the cause of individual symptoms. An important AUDADIS improvement in this differentiation is the use of specific questions about the chronological relationship between intoxication or withdrawal and questions about the full depressive syndrome. Specific questions about chronology improve the reliability and validity of MDD diagnoses in substance abusers. The DIS, UM-CIDI, and WMH-CIDI also relied on the respondent’s opinion in differentiating primary disorders from those due to a medical condition. The AUDADIS-IV offers a similar improvement: specific questions about chronology of the mental disorder and the medical condition. Diagnoses of major depressive disorder presented in this report also ruled out bereavement. Axis I criteria and disorders were assessed identically in the baseline and follow-up versions of the AUDADIS-IV except for the time frames.

Depressive disorders
In our sample of persons without a lifetime major depressive disorder, dysthymic disorder, manic episode or hypomanic episode, we examined the first-incidence of depressive disorders using a diagnosis of a past-year depressive disorder (major depressive or dysthymic disorder) at the 3-year follow-up interview, comparable to previous first-incidence studies on depressive disorders (De Graaf et al., 2002; Grant et al., 2009).
Alcohol-use disorder criteria
Extensive AUDADIS-IV questions covered all DSM-IV criteria for AA and AD, among all participants that were ever drinkers. Clinical as well as general population studies showed that the reliability (Grant et al., 1995; Chatterji et al., 1997; Hasin et al., 1997a; Hasin et al., 1997b; Grant et al., 2003) as well as the validity (Hasin et al., 1997b; Cottler et al., 1997; Pull et al., 1997) of AUDADIS-IV alcohol diagnoses ranged from good to excellent. In general, AD diagnoses are reliable and valid. The reliability and validity of AA is often lower and more variable when diagnosed hierarchically, as required in DSM-IV (Hasin, 2003), although AA also has excellent reliability when diagnosed without DSM-IV hierarchical requirements (Hasin et al., 2006a).

Based on empirical evidence (Keyes et al., 2010; Dawson et al., 2010), the DSM-5 workgroup proposed to eliminate the AA criterion involving alcohol-related legal problems but retain the remaining three DSM-IV AA criteria and all seven DSM-IV AD criteria into one diagnosis of an alcohol-use disorder with different levels of severity. Consequently, a DSM-5 diagnosis of an alcohol-use disorder was based on the following AA and AD criteria: failure to fulfill major role obligations (AA), recurrent hazardous use (AA), persistent social or interpersonal problems (AA), tolerance (AD), withdrawal or withdrawal avoidance (AD), drinking more or longer than was intended (AD), persistent desire or unsuccessful attempts to quit reduce drinking (AD), great deal of time drinking or recovering from its effects (AD), giving up or reducing occupational, social and/or recreational activities to drink (AD), and continued drinking despite physical or psychological problems (AD). The DSM-5 workgroup has also proposed to add a criterion concerning alcohol craving to these ten existing criteria, but this information was not assessed at the NESARC baseline interview. However, previous studies showed that the other criteria, without alcohol craving, represented the latent variable very well because of the redundancy of craving with the remaining criteria (Keyes et al., 2010). For the present study, alcohol-use disorder severity was based on the simple count of these ten criteria that were present in the year preceding the baseline interview and was a valid indicator of alcohol-use disorder severity compared to a scale based on item weights according to item response theory measures of severity (Dawson et al., 2010; Dawson and Grant, 2010).

Covariates
The following baseline characteristics were used as sociodemographic covariates: age (18-29, 30-39, 40-49, 50+ years), gender, race/ethnicity (white, Hispanic, black, Asian, Native American), education (any college versus other) and marital status (married versus other). The operationalization of covariates is consistent with other NESARC papers. Analyses were additionally adjusted for baseline smoking status (never smoked, former smoker and current smoker) and three clusters of predisposing factors for depressive disorders: 1) general vulnerability factors (family history [FH] of depressive disorders, FH of alcohol dependence and childhood trauma); 2) psychiatric comorbidity (conduct disorder and anxiety disorder); and 3) subthreshold depressive disorders. From the general vulnerability factors, FH of depressive disorders and FH of alcohol dependence were considered positive
if experienced by parents or siblings as reported by participants. Physical abuse, physical neglect, emotional abuse, emotional neglect and sexual abuse before the age of 18 years were assessed to determine the presence (0, 1, 2, 3+ types) of childhood trauma. Baseline psychiatric comorbidity included lifetime DSM-IV conduct disorder and anxiety disorder (panic disorder with/without agoraphobia, generalized anxiety disorder, social phobia and specific phobia) as assessed with the AUDADIS-IV. Analyses were also adjusted for subthreshold depressive disorders as assessed as the number of lifetime MDD symptoms as well as the number of lifetime dysthymia symptoms.

Statistical analyses
Due to the NESARC complex sample design, analyses were conducted using SUDAAN, Version 9.0 (Research Triangle Institute, 2004), a software package that uses Taylor series linearization to adjust variance estimates for complex, multistage sample designs. All analyses were adjusted for gender, age, race, education and marital status. Analyses were additionally adjusted for baseline smoking status and predisposing factors for depressive disorders, such as general vulnerability factors, psychiatric comorbidity and subthreshold depressive disorders.

First, we reported on the first-incidence rates of depressive disorders across alcohol-use disorder severity levels (count of criteria; range 0-10) using descriptive statistics (%, 95% confidence intervals of %). Then logistic regression analyses were used to explore the nature of the prospective relationship between alcohol-use disorder severity at baseline and first-incidence of depressive disorders after three year follow-up. To determine whether a linear trend explained the relationship between alcohol-use disorder severity and first-incident depressive disorders, we tested a linear model in which one predictor represented a simple count of 0-10 criteria. Then, we tested whether this linear model deviated from more complicated models, an analytic method used previously by others (Martin et al., 2006; Hasin et al., 2006b; Beseler & Hasin, 2010). One of these models, the dummy variable model, comprised ten dummy variables representing all separate levels of alcohol-use disorder severity. Variables were created based on groups defined by the number of alcohol-use disorder criteria met at the baseline interview (0, 1, 2, etc.), using those with no criteria as the reference group. The partially linear model included a linear trend for 0-8 criteria, and a category representing the most severe level for 9-10 criteria. This latter model was created based on visual inspection of the graph representing the dummy variable model (see Results section). To test whether these two more complicated models produced significantly different estimates compared to the linear model, we used the Wald statistic. Little or no difference (p>.05) would support the use of a linear model, as it is most parsimonious in terms of number of parameters.
RESULTS

The overall first-incidence of depressive disorders after 3-year follow-up was 4.34% (SE=0.15; results not tabulated) with considerable variation between persons with different alcohol-use disorder severity levels. Table 1 shows that the first-incidence of depressive disorders was low in persons meeting no alcohol-use disorder criteria (4.20%, 95% CI=3.90-4.53%) and much higher in persons meeting 9 (25.93%, 95% CI=4.03-74.46%) or 10 criteria (44.47%, 95% CI=7.72-88.45%).

A linear model of alcohol-use disorder severity, as the simple count of 0-10 criteria, significantly predicted first-incidence of depressive disorders after adjustment for sociodemographics (OR=1.14, 95% CI=1.06-1.22, p=0.0006; see Table 2). Even after taking into account the effects of smoking status and depression risk factors such as general vulnerability factors, psychiatric comorbidity and subthreshold depressive disorders at the baseline interview, the linear model of alcohol-use disorder severity was a significant predictor of first-incident depressive disorders (OR=1.10, 95% CI=1.01-1.19, p=0.02).

To explore whether this linear model deviated from the two more complicated models in predicting the log odds of first-incident depressive disorders, a graph (Figure 1) was plotted to visualize the coefficient from the linear model (slope coefficient of 0.13, SE=0.04; shown as a line) relative to the ten coefficients from a dummy variable model representing all separate levels of severity (shown in symbols: ⌂). No significant difference in explained variance was found between the two models (χ²=13.36, p=0.15). Since Figure 1 suggested that another partially linear model with a linear trend for 0-8 criteria and a separate category for 9-10 criteria might better describe the association, we also tested whether this partially linear model better explained the relationship than the linear model, but this was not the case. These results confirmed that a linear model best and most simply explained the relationship between the count of alcohol-use disorder criteria and first-incident depressive disorders. As Figure 1 might suggest that the significant slope of the linear model could be explained by the high log odds ratios for persons meeting 9-10 criteria, we also tested the linear model, adjusted for sociodemographics, in a subsample of persons meeting 0-8 criteria. In this sensitivity analysis, the linear model was still a significant predictor of first-incidence of depressive disorders (OR=1.10, 95% CI 1.03-1.18, p=0.004), showing that our findings were not exclusively due to the high first-incidence rates in persons meeting 9 or 10 criteria.

DISCUSSION

To our knowledge, this is the first study examining the role of alcohol-use disorder severity as a risk factor of first-incident depressive disorders. The first-incidence of depressive disorders after three years of follow-up varied from 4.2% in persons meeting no alcohol-use disorder criteria to 25.9% and 44.5% in persons meeting nine or all ten criteria, respectively. The count of alcohol-use disorder criteria predicted the first-incidence of depressive disorders in a linear fashion with an OR of 1.14. This means that
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<tr>
<td>10</td>
<td>6</td>
<td>44.47</td>
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Table 1 First-incidence of depressive disorders across alcohol-use disorder severity levels

*Weighted percentages taking into account the weighted sample.

**Figure 1** Alcohol-use disorder severity predicting first-incidence of depressive disorders

Linear model shown by a line, dummy variable model shown in symbols (♦). Adjusted for sex, age, race/ethnicity, education and marital status.
Predictor at baseline | OR | 95% CI | p | OR | 95% CI | p
--- | --- | --- | --- | --- | --- | ---
Alcohol-use disorder severity | 1.14 | 1.06-1.22 | 0.0006 | 1.10 | 1.01-1.19 | 0.02

**Sociodemographics**

Female gender | 2.22 | 1.92-2.63 | <0.0001 | 2.04 | 1.72-2.44 | <0.0001
Age: | | | | | | |
18-29 years | 1.52 | 1.24-1.86 | 0.0001 | 1.68 | 1.36-2.07 | <0.0001
30-39 years | 1.40 | 1.16-1.70 | 0.0008 | 1.40 | 1.14-1.72 | 0.002
40-49 years | 1.53 | 1.26-1.85 | <0.0001 | 1.43 | 1.17-1.75 | 0.0006
50+ years | Reference | Reference | Reference | Reference | Reference | Reference

Race/ethnicity:

| | | | | | | |
| | | | | | | |
| Hispanic | 1.16 | 0.95-1.40 | 0.14 | 1.19 | 0.98-1.43 | 0.07
| Black | 0.79 | 0.64-0.98 | 0.03 | 0.80 | 0.64-1.00 | 0.05
| Asian | 0.76 | 0.53-1.09 | 0.14 | 0.87 | 0.61-1.25 | 0.45
| Native American | 1.53 | 0.92-2.53 | 0.10 | 1.39 | 0.83-2.32 | 0.21

Education: some college or beyond | 0.80 | 0.69-0.93 | 0.004 | 0.83 | 0.71-0.96 | 0.02
Marital status: married | 0.82 | 0.71-0.94 | 0.005 | 0.82 | 0.71-0.94 | 0.005

**Smoking**

Smoking status: | | | | | | |
Never | - | - | - | Reference
Former smoker | - | - | - | 1.16 | 0.93-1.45 | 0.22
Current smoker | - | - | - | 1.15 | 0.97-1.36 | 0.15

**General vulnerability factors**

FH of depressive disorders (yes) | - | - | - | 1.17 | 0.98-1.40 | 0.09
FH of alcohol dependence (yes) | - | - | - | 1.04 | 0.88-1.23 | 0.64
Childhood trauma: | | | | | | |
No | - | - | - | Reference
1 type | - | - | - | 1.65 | 1.38-1.96 | <0.0001
2 types | - | - | - | 1.90 | 1.49-2.43 | <0.0001
3+ types | - | - | - | 3.01 | 2.37-3.81 | <0.0001

**Psychiatric comorbidity**

Conduct disorder (yes) | - | - | - | 0.55 | 0.32-0.94 | 0.03
Anxiety disorder (yes) | - | - | - | 1.48 | 1.21-1.82 | 0.0003

**Subthreshold disorders**

| | | | | | | |
| # of lifetime MDD symptoms | - | - | - | 1.11 | 1.09-1.14 | <0.0001
| # of lifetime dysthymia symptoms | - | - | - | 1.04 | 0.96-1.13 | 0.33

Table 2 Alcohol-use disorder severity predicting first-incidence of depressive disorders

a Adjusted for sociodemographics.
b Adjusted for sociodemographics, smoking status, general vulnerability factors, psychiatric comorbidity and subthreshold depressive disorders.
the risk of first-incident depressive disorders is slightly higher in persons meeting only one criterion but gradually increases with the number of alcohol-use disorder criteria met. Taken together, alcohol-use disorder severity appeared to be useful in identifying persons with an increased risk of developing depressive disorders who could be targeted by prevention strategies.

Our study demonstrated that alcohol-use disorder severity prospectively predicted first-incidence of depressive disorders. Alcohol use disorders have been hypothesized to cause the onset of major depression (Hasin and Grant, 2002; Wang & Patten, 2002; Fergusson et al., 2009) due to their interpersonal and social consequences (Swendsen and Merikangas, 2000). This may indirectly be supported by our finding that the risk of first-incident depressive disorders increases with alcohol-use disorder severity and is highest in persons meeting nine or ten criteria. Alcohol-use disorder criteria involving interpersonal and social consequences (i.e. social or interpersonal problems [AA], giving up or reducing activities [AD] and failure to fulfill roles [AA]) have shown to be the most severe criteria and are more likely to be present in persons meeting many other criteria (Dawson et al., 2010). Although some note that heavy alcohol consumption pharmacologically induces depressive symptoms (Swendsen and Merikangas, 2000), AUDADIS-IV questions on symptoms of major depression were designed to screen out substance-induced depressive disorders, so this is not a likely explanation of our finding.

Shared genetic and environmental risk factors may independently cause the onset of alcohol problems and depressive disorders (e.g., Kendler et al., 1993; Prescott et al., 2000) and, therefore, explain their comorbidity. However, we found that the association between alcohol-use disorder severity and first-incident depressive disorder could not be explained by shared risk factors such as sociodemographics, smoking status, family history of depressive disorders, family history of alcohol dependence, childhood trauma, psychiatric comorbidity and subthreshold depressive disorders because inclusion of these factors in the models did not substantially change the results. These findings may be additional support for a causal model in which alcohol problems result in the development of depressive disorders.

Contrasting findings have been reported by previous studies on the prospective relationship between AUDs and depressive disorders (Rohde et al., 2001; De Graaf et al., 2002; Hettema et al., 2003; Kuo et al., 2006; Grant et al., 2009; Marmorstein et al., 2010). One possible explanation for this may be the heterogeneity (e.g., severity) of AUD diagnoses in the various studies. This is supported by our study showing a significant association between alcohol-use disorder severity and first-incident depressive disorders, whereas a previous study on binary categorical AUDs in the same population did not (Grant et al., 2009). In general, mild disorders are far more prevalent in general population studies than severe disorders (Cohen and Cohen, 1984) and, as the risk of first-incident depressive disorders gradually increased with alcohol-use disorder severity, these mild disorders are less likely to predict first-incident depressive disorders. On the other hand, persons with severe disorders are likely to be overrepresented in clinical studies and may explain the stronger cross-sectional relationship between AUDs and depressive
disorders as reported in clinical versus community samples. A substantial proportion of persons with a severe alcohol-use disorder receive some form of treatment; for example, in our sample 50.7% of persons meeting nine or ten criteria had received some kind of addiction treatment in the year before the baseline interview. While the prevalence of severe alcohol-use disorders is low when considered in the context of the entire general population, individuals with such severity are likely to be under supervision of a health care professional and, therefore, may be reached more easily with prevention strategies for depressive disorders. Assessment of alcohol-use disorder severity by the simple count of positive criteria may be a very simple strategy for identification of persons at a high risk for developing these disorders. This screening method has the potential to be highly effective as one-third of those persons with a severe alcohol-use disorder are likely to develop a depressive disorder.

The heterogeneity of alcohol use disorders highlights the importance of using a more informative phenotype as severity rather than categorical diagnoses based on artificially imposed thresholds. As the count of alcohol-use disorder criteria form a single dimension of severity (see also Hasin & Beseler, 2009; Dawson et al., 2010; Dawson & Grant, 2010), DSM-5 will offer a dimensional approach, the details of which are still under development. Our findings support the plan in DSM-5 to distinguish different levels of severity within diagnoses.

This study has strengths and limitations. Strengths of our study include that we were the first in prospectively examining whether alcohol-use disorder severity predicted first-incidence of depressive disorders after 3-year follow-up. We used data of a very large representative general population study and a highly informative phenotype of alcohol-use disorder severity. Our finding that alcohol-use disorder severity linearly predicted first-incident depressive disorders was robust as a linear model for 0-8 criteria also had a significant slope and, thus, our findings were not only due to the high log odds ratios for 9 and 10 criteria. A limitation is that all diagnostic questions are subject to recall, self report and social desirability bias. Second, no information about alcohol craving was assessed at the NESARC baseline interview. As the DSM-5 workgroup has to add ‘alcohol craving’ to the ten existing criteria, this would have been valuable information. However, previous studies have reported that the 10 criteria, without craving represented the latent variable of alcohol-use disorder severity very well, because of the high cohesion (in fact, redundancy) of craving with the other criteria (Keyes et al., 2010). Another important limitation may be the limited power to test whether the linear model deviated from more complicated models (e.g., the dummy variable model) as especially the number of respondents at the severe end of the alcohol-use disorder severity spectrum was small. Therefore, studies among persons with more severe alcohol-use disorders, for example in high risk or clinical samples, are needed. Future studies might provide important additional information by not only operationalizing alcohol-use disorder severity as a count of criteria, but also as defined in alternative ways such as level of social, occupational or physical impairment, quantity of alcohol consumption, or age of onset of drinking.
In conclusion, we found that alcohol-use disorder severity predicted first-incidence of depressive disorders in a linear fashion, even after taking into account important depression risk factors as potential confounders. This means that the risk of first-incident depressive disorders gradually increases and that alcohol-use disorder severity may be a useful indicator of a high-risk group for depressive disorders and an important target for the prevention of depression.
REFERENCES


GRANT BF, Harford TC, Dawson DA, Chou PS, Pickering RP. The Alcohol Use Disorder and


HASIN DS, Goodwin RD, Stinson FS, Grant BF. Epidemiology of Major Depressive Disorder: Results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Archives of General Psychiatry 2005; 62:1097-1106.

HASIN DS, Grant BF. Major depression in 6050 former drinkers. Archives of General Psychiatry 2002; 59:794-800.


HASIN DS, Stinson FS, Ogburn E, Grant BF. Prevalence, correlates, disability and comorbidity of DSM-IV alcohol abuse and dependence in the United States – Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Archives of General Psychiatry 2007; 64:830-842.


SAHA TD, Chou SP, Grant BF. Toward an alcohol use disorder continuum using item response theory: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychological Medicine 2006; 36:931-941.


WANG J, Patten SB. Prospective study of frequent heavy alcohol use and the risk of major depression in the Canadian general population. Depression and Anxiety 2002; 15:42-45.