



# A comprehensive model of predictors of persistence and recurrence in adults with major depression: Results from a national 3-year prospective study



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## ABSTRACT

Identifying predictors of persistence and recurrence of depression in individuals with a major depressive episode (MDE) poses a critical challenge for clinicians and researchers. We develop using a nationally representative sample, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; N = 34,653), a comprehensive model of the 3-year risk of persistence and recurrence in individuals with MDE at baseline. We used structural equation modeling to examine simultaneously the effects of four broad groups of clinical factors on the risk of MDE persistence and recurrence: 1) severity of depressive illness, 2) severity of mental and physical comorbidity, 3) sociodemographic characteristics and 4) treatment-seeking behavior. Approximately 16% and 21% of the 2587 participants with an MDE at baseline had a persistent MDE and a new MDE during the 3-year follow-up period, respectively. Most independent predictors were common for both persistence and recurrence and included markers for the severity of the depressive illness at baseline (as measured by higher levels on the general depressive symptom dimension, lower mental component summary scores, prior suicide attempts, younger age at onset of depression and greater number of MDEs), the severity of comorbidities (as measured by higher levels on dimensions of psychopathology and lower physical component summary scores) and a failure to seek treatment for MDE at baseline. This population-based model highlights strategies that may improve the course of MDE, including the need to develop interventions that target multiple psychiatric disorders and promotion of treatment seeking to increase access to timely mental health care.

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## 1. Introduction

Major depression is a leading source of disease burden (Hollon et al., 2005; Lopez et al., 2006) characterized by complex patterns

of recurrence and persistence (Hasin et al., 2005; Kessler et al., 2003; Mueller et al., 1999; Solomon et al., 1997). Persistence and recurrence are common among patients with major depression (Frank et al., 1990; Keller et al., 1983; Mueller et al., 1999). Persistence may be defined by a prolonged time to recovery from an index episode and recurrence by the occurrence of a new episode in a remitted case (Skodol et al., 2011). Identifying predictors of persistence and recurrence in patients with a major depressive episode (MDE) is an important challenge for clinicians and researchers.

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Prior research has implicated several risk factors for MDE persistence or recurrence. They include severity of major depression (Sargeant et al., 1990; Skodol et al., 2011; Spijker et al., 2010; Steinert et al., 2014), number of lifetime MDEs (Skodol et al., 2011; Spijker et al., 2010; Steinert et al., 2014), co-occurring Axis I (Hoertel et al., 2013a, 2013b, 2013c; Keller et al., 1982, 1992; Klein et al., 2006; Manetti et al., 2014; Steinert et al., 2014) and Axis II disorders (Grilo et al., 2005; Skodol et al., 2011), history of suicide attempts (Avery and Winokur, 1978), family history of depression (Patten et al., 2010), concurrent physical health problems and psychosocial difficulties (Lam et al., 2009), early age at onset of first MDE (Hoertel et al., 2013a; Klein et al., 1999), stressful life events (Wang et al., 2012), female gender, older age and being divorced or widowed (Colman et al., 2011; Dowrick et al., 2011; Fava et al., 2007; Gilman et al., 2013; Hardevel et al., 2013a, 2013b; Kornstein et al., 2000; Lam et al., 2009; Patten et al., 2012; ten Doesschate et al., 2010; Wang et al., 2012).

The diversity of these predictors and their frequent co-occurrence suggest the need to develop more powerful statistical approaches. Several integrative predictive models of MDE persistence or recurrence have been examined (Brugha et al., 1997; Dowrick et al., 2011; ten Doesschate et al., 2010; Wang et al., 2014; Fandiño-Losada et al., 2016). However, most of these models have been based on samples of convenience and used relatively small sample sizes. In addition, because MDE often co-occurs with other mental disorders (Kessler et al., 2003, 2005; Manetti et al., 2014), recent theories have proposed a meta-structure of psychiatric diagnoses that organizes disorders into broad dimensions of psychopathology (i.e., internalizing and externalizing dimensions) (Blanco et al., 2013; Eaton et al., 2012; Hoertel et al., 2015a, 2015b; Kotov et al., 2011; Krueger et al., 1998; Krueger and Markon, 2006). Applying this dimensional approach to model disorder comorbidity in a comprehensive model of MDE persistence or recurrence could help clarify whether broad psychopathological liabilities or individual Axis I or Axis II disorders predict persistence or recurrence of MDE.

This report proposes a comprehensive model of the 3-year risk of persistence or recurrence of MDE using a longitudinal nationally representative study, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). We used structural equation modeling to examine simultaneously the effects of four broad groups of clinical factors previously identified as potential predictors of persistence and recurrence of MDE: 1) severity of depressive illness, 2) severity of mental and physical comorbidity, 3) sociodemographic characteristics and 4) treatment-seeking behavior. With this model, we aimed to ascertain readily identifiable characteristics to help clinicians recognize adults with MDE who are at increased risk for recurrent or chronic MDE.

## 2. Method

### 2.1. Sample

Data were drawn from the wave 1 and wave 2 of the NESARC, a nationally representative face-to-face survey of the US adult population, conducted in 2001–2002 (Wave 1) and 2004–2005 (Wave 2) by the National Institute on Alcoholism and Alcohol Abuse (NIAAA) (Grant et al., 2003). The target population included the civilian noninstitutionalized population, aged 18 years and older, residing in the United States. The overall response rate at Wave 1 was 81% and the cumulative response rate at Wave 2 was 70.2%, resulting in 34,653 Wave 2 interviews (Grant et al., 2009). The Wave 2 NESARC data were weighted to adjust for non-response, demographic factors and psychiatric diagnoses, to ensure that the Wave 2 sample approximated the target population, that is, the

original sample minus attrition between the two waves (Grant et al., 2009). The research protocol, including written informed consent procedures, received full human subjects review and approval from the U.S. Census bureau and the Office of Management and Budget. The present analysis includes the 2587 participants who had a DSM-IV diagnosis of MDE during the year preceding the Wave 1 interview and completed interviews at both waves.

### 2.2. Measures

#### 2.2.1. Assessment of the 3-year risk of persistence and recurrence of MDE

Persistence was defined as meeting full criteria for current MDE at Wave 1 and throughout the entire 3-year follow-up period. Recurrence was defined as meeting full criteria for current MDE at Wave 1 and again during the last 12 months in Wave 2 but not during the first 24 months after the Wave 1 interview (Skodol et al., 2011).

#### 2.2.2. Assessments of DSM-IV past-year Axis I and lifetime Axis II diagnoses at Wave 1

Mental disorders were assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule, DSM-IV version (AUDADIS-IV), a structured diagnostic instrument administered by trained lay interviewers (Grant et al., 2009). In accord with DSM-IV criteria, MDE diagnosis required meeting clinical significance criteria (i.e., distress or impairment), having a primary mood disorder (excluding substance-induced or general medical conditions), and ruling out bereavement. Other Axis I diagnoses included substance use disorders (alcohol use disorder, drug use disorder, and nicotine dependence), mood disorders (dysthymic disorder, and bipolar disorder), anxiety disorders (panic disorder, social anxiety disorder, specific phobia, and generalized anxiety disorder), and pathological gambling. For MDE and all Axis I disorders, diagnoses were made in the past 12 months prior to Wave 1. Axis II disorders (including avoidant, dependent, obsessive-compulsive, histrionic, paranoid, schizoid, and antisocial personality disorders) were assessed on a lifetime basis (Grant et al., 2009) at Wave 1. The test-retest reliability and validity of AUDADIS-IV measures of DSM-IV mental disorders are good to excellent for substance use disorders and fair to good for major depressive episode and other disorders (Canino et al., 1999; Chatterji et al., 1997; Grant et al., 1995, 2003; Hasin et al., 1997).

#### 2.2.3. Sociodemographic characteristics in Wave 1

Sociodemographic characteristics included sex, age, marital status (married vs. non-married), race-ethnicity (White vs. non-White) and household income. In addition, participants were asked about 12 stressful life events concerning a variety of occupational, familial, financial, and legal issues and whether they had experienced these events in the year before the Wave 1 interview (Grant et al., 2003).

#### 2.2.4. Treatment-seeking behavior for major depression

Participants with a current MDE who declared “going anywhere or saw anyone to get help for low mood” during the year preceding the interview at Wave 1 were considered as seeking treatment for MDE.

#### 2.2.5. Assessment of prior suicide attempts at Wave 1

To assess a lifetime history of suicide attempts, all individuals with an MDE in the past year of Wave 1 were asked whether they had ever attempted suicide.

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