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Predictors of first-episode unipolar major depression in individuals with and without sub-threshold depressive symptoms: A prospective, population-based study

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ABSTRACT

Background: The aim of this study is to assess predictors of first-episode major depression in a community-based sample of adults with and without sub-threshold depression.
Method: Data were from Waves 1 and 2 of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC). Participants meeting criteria for a sub-threshold depressive episode (sMDE; $n=3901$) reported lifetime depressed mood/loss of interest lasting at least two weeks and at least two of the seven other DSM-IV symptoms of MDD. Predictors of MDE 3 years later were compared in those with and without ($n=31022$) sMDE.
Results: Being female, history of alcohol or substance use, and child abuse increased the odds of developing MDD to a greater degree in individuals without sMDE relative to those with sMDE. Among those with sMDE and additional risk factors (low education, substance use), younger age was associated with marginally increased risk of MDD.
Conclusion: Several demographic risk factors may help identify individuals at risk for developing MDD in individuals who have not experienced an sMDE who may be candidates for early intervention. Future work should assess whether preventative interventions targeting substance/alcohol use and child abuse could reduce the risk of depression.

1. Introduction

Major depressive disorder (MDD) is among the most common mental disorders. MDD is associated with significant impairment in individual functioning, as well as a costly burden in terms of economic expenditures (McLaughlin, 2011; WHO Organization, 2008). Importantly, the public health impact of depression is likely much wider than estimates based on full syndromal MDD, as there is a growing recognition of the negative impact of sub-threshold depression (Lewinsohn et al., 2000; Pincus et al., 1999). Lifetime prevalence rates of sub-threshold depression may be as high as 26% (Lewinsohn et al., 2004) and symptoms of sub-threshold depression are associated with significant impairment in functioning (Lewinsohn et al., 2000). In at least one study, impairment associated with sub-threshold depression is comparable to that of MDD (Gotlib et al., 1995). Sub-threshold depression is also associated with elevated risk for developing MDD (Georgiades et al., 2006; Keenan et al., 2008; Pine et al., 1999; Shankman et al., 2009). However, not all individuals with sub-threshold symptoms escalate to full syndrome MDD. Identifying individual factors that further specify the nature of risk for developing MDD has the potential to improve the accuracy and efficiency of screening procedures and target prevention programs in a manner that is most likely to reduce the risk of symptom escalations.

Surprisingly, relatively few studies have utilized longitudinal designs to identify the characteristics of individuals with sub-threshold symptoms who are more likely to develop MDD. A study of adults in primary care found an 18.35% rate of MDE onset after one year. Severity of depressive symptoms, family history of MDD, and having a chronic general medical illness were associated with increased risk of onset (Cuijpers et al., 2005). In a subsequent study of older adults with elevated scores on a depression screening measure, Cuijpers et al. found that 20.1% of individuals developed MDD or dysthymia by 6 year follow-up. Low appetite and trouble sleeping conferred a higher likelihood of developing a mood disorder (Cuijpers et al., 2006). More recently, predictors of escalation to full-syndrome depressive disorders were examined

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in a community sample of 225 adolescents with a conversion rate from sub-threshold to major depression of 67% (Klein et al., 2009). Severity of depressive symptoms, medical conditions/symptoms, history of suicidal ideation, history of anxiety disorder, and familial loading for MDD predicted escalation. A later study from the same project investigated specific combinations of risk factors to improve the sensitivity and specificity of predicting MDD onset (Hill et al., 2014). Adolescents with a history of sub-threshold depression were at highest risk of escalation to MDD if they fell into either of two clusters; those with friend support and an anxiety or substance use disorder, or those with better friend support, but multiple major life events, and an anxiety disorder.

Although existing studies have helped to identify common demographic and clinical risk factors for the transition from sub- to full-threshold depression, several important methodological gaps remain. First, the generalizability of previous findings is unclear, as there is an essential lack of studies based on nationally representative community samples with a prospective follow-up. Findings from age-specific cohorts, or from individuals seeking treatment in primary care, may not be representative of the overall population. Second, the onset of MDD is not necessarily predated by a sub-threshold depressive episode. Data from existing studies do not clarify whether variables that predict the first onset of MDD are unique to individuals with sub-threshold symptoms, or are risk factors for MDD across all individuals. Third, risk factors for MDD may vary as a function of age (Jaffee et al., 2002). Individuals with adolescent or young adult onset are likely to be more severe (Korten et al., 2012), thus rates and risk factors for conversion to MDD may be magnified during certain periods in adulthood. An ideal sample is one that is well powered to assess the moderating effect of age on rates and risk factors across the lifespan.

The aims of the current study are three-fold. To aid in replication efforts we will first examine prospective predictors of first episode MDD over a three-year follow-up period using the National Epidemiological Survey of Alcohol and Related Conditions (NESARC; (Grant et al., 2007, 2003), a large, nationally representative, community-based sample. The primary aim is to examine whether predictors of first episode MDD pertain more strongly to individuals who experienced a sub-threshold depressive episode (sMDE) or broadly predict the development of a first major depressive episode (MDE) in individuals regardless of whether they have experienced an sMDE. Next, we will evaluate whether predictors of MDD onset vary according to age. Predictors were selected that were associated with escalation in previous studies (e.g. medical burden, family history (Cuijpers et al., 2006, 2005; Klein et al., 2009)), part of a standard mental health assessment (anxiety, substance/alcohol use, child abuse), or are typically assessed in routine clinical screenings (demographics). Importantly, any positive findings from the selected predictors have the potential for immediate clinical translation and impact since they represent characteristics that are common, affordable, and feasible to assess.

2. Method

2.1. Study design

Data for this study were sourced from the 1st and 2nd waves of the NESARC (Grant et al., 2007, 2003). Full details regarding data acquisition methods have been reported previously (Grant et al., 2007, 2003). Briefly, this nationally representative sample was drawn from non-institutionalized individuals across the United States using a combination of face-to-face and computer-assisted interviews. The Wave 1 survey was administered between 2001 and 2002. 43,093 respondents completed the Wave 1 survey with an overall response rate of 81%. A longitudinal follow-up to the Wave 1 survey was conducted approximately 3 years later. In Wave 2, all Wave 1 participants were re-interviewed, barring those unavailable due to death, migration, active military duty during follow-up period, or physical/mental incapacity. 34,653 individuals completed follow-up interviews with an overall response rate of 86.7%.

2.2. Participants

Participants were 18 years or older at time of enrollment in Wave 1. Individuals met criteria for the sMDE group at Wave 1 if they ever in their life experienced an episode of depressed mood or loss of interest or pleasure lasting at least two weeks during which they also experienced at least two of the seven other DSM-IV symptoms of an MDE, but never experienced any full-syndrome mood disorder (MDD, dysthymia, bipolar I disorder, and bipolar II disorder). This definition is consistent with other studies on sub-threshold depression (Cuijpers et al., 2006, 2005; Hill et al., 2014; Klein et al., 2009). Of the 43,093 respondents who completed the Wave 1 survey, $n=8170$ participants met criteria for a lifetime full-syndrome mood disorder, and were excluded from the analysis. This left a total sample of $N=34,923$ participants. Of these participants, $n=3910$ met criteria for a lifetime sMDE at Wave 1. This resulted in $n=31,022$ participants without a lifetime sMDE or full-threshold mood disorder at Wave 1 as a comparison group. At Wave 2, $n=1314$ of this sample met criteria for a full-threshold unipolar major depressive episode (participants who escalated to bipolar disorder I or II or dysthymia were not included). Demographic and clinical characteristics of the sample are reported in Table 1.

Table 1
Demographic and clinical characteristics of participants with and without sMDE.

	sMDE($n=3901$)		**No mood disorder**($n=31,022$)	
	Esclated to MDD ($n=184$)	No MDD ($n=3717$)	Esclated to MDD ($n=1130$	No MDD ($n=29,892$)
Age$^{M\ (SE)}$	43.13 (.69)	46.85 (.16)	42.01 (.21)	46.02 (.07)
Female	133 (67%)	2410 (61%)	800 (67%)	15,742 (47%)
Race	149 (88%)	2900 (86%)	871 (84%)	22,282 (82%)
Education$^{M\ (SE)}$	9.63 (.07)	9.82 (.02)	9.41 (.03)	9.57 (.01)
LT Anxiety disorder	56 (33%)	853 (23%)	174 (17%)	2715 (9%)
LT Alcohol use disorder	42 (29%)	1162 (35%)	291 (29%)	6910 (26%)
LT Substance use disorder	20 (14%)	403 (12%)	98 (9%)	1890 (7%)
Number of medical conditions$^{M\ (SE)}$	1.67 (.07)	1.93 (.08)	4.37 (.14)	3.47 (.06)
1st Degree family history MDD	84 (52%)	1577 (46%)	267 (27%)	5228 (18%)
Childhood abuse	17 (10%)	193 (5%)	119 (10%)	857 (3%)

Note: All percentages are un-weighted. M (SE) denotes Mean (Standard Error).

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