Psychological Medicine (2013), **43**, 1401–1414. Cambridge University Press 2012

doi:10.1017/S0033291712002309

ORIGINAL ARTICLE

Subsyndromal depression in the United States: prevalence, course, and risk for incident psychiatric outcomes

R. H. Pietrzak[1,2]*, J. Kinley[3], T. O. Afifi[4], M. W. Enns[5], J. Fawcett[6] and J. Sareen[7]

[1] *National Center for Posttraumatic Stress Disorder, Veterans Affairs Connecticut Healthcare System, West Haven, CT, USA*
[2] *Department of Psychiatry, Yale University School of Medicine, New Haven, CT, USA*
[3] *Department of Psychology, University of Manitoba, Winnipeg, Manitoba, Canada*
[4] *Departments of Community Health Sciences, Psychiatry, and Family Social Sciences, University of Manitoba, Winnipeg, Manitoba, Canada*
[5] *Department of Psychiatry, University of Manitoba, Winnipeg, Manitoba, Canada*
[6] *Department of Psychiatry, University of New Mexico School of Medicine, Santa Fe, NM, USA*
[7] *Departments of Psychiatry, Psychology, and Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada*

Background. Subsyndromal depression (SD) may increase risk for incident major depressive and other disorders, as well as suicidality. However, little is known about the prevalence, course, and correlates of SD in the US general adult population.

Method. Structured diagnostic interviews were conducted to assess DSM-IV Axis I and II disorders in a nationally representative sample of 34 653 US adults who were interviewed at two time-points 3 years apart.

Results. A total of 11.6% of US adults met study criteria for lifetime SD at Wave 1. The majority (9.3%) had <5 total symptoms required for a diagnosis of major depression; the remainder (2.3%) reported $\geqslant 5$ symptoms required for a diagnosis of major depression, but denied clinically significant distress or functional impairment. SD at Wave 1 was associated with increased likelihood of developing incident major depression [odds ratios (ORs) 1.72–2.05], as well as dysthymia, social phobia, and generalized anxiety disorder (GAD) at Wave 2 (ORs 1.41–2.92). Among respondents with SD at Wave 1, Cluster A and B personality disorders, and worse mental health status were associated with increased likelihood of developing incident major depression at Wave 2.

Conclusions. SD is prevalent in the US population, and associated with elevated rates of Axis I and II psychopathology, increased psychosocial disability, and risk for incident major depression, dysthymia, social phobia, and GAD. These results underscore the importance of a dimensional conceptualization of depressive symptoms, as SD may serve as an early prognostic indicator of incident major depression and related disorders, and could help identify individuals who may benefit from preventive interventions.

Received 12 July 2012; Revised 5 September 2012; Accepted 10 September 2012; First published online 31 October 2012

Key words: Co-morbidity, depression, disability, epidemiology, incidence.

Introduction

Depression is the leading cause of disability in the developed world, and is associated with considerable morbidity and mortality (Insel & Charney, 2003; Hasin *et al*. 2005; Celano & Huffman, 2011; Pan *et al*. 2011). Subsyndromal depression (SD), which is characterized by clinical symptoms of major depression that are not of sufficient severity to meet diagnostic criteria for this disorder (Fergusson *et al*. 2005), is also associated with adverse functional outcomes, as well as increased risk for incident psychiatric disorders, and economic and societal cost (Wells *et al*. 1989; Broadhead *et al*. 1990; Johnson *et al*. 1992, 2009; Gotlib *et al*. 1995; Judd *et al*. 1994, 1997, 1998*b*, 2002, 2004; Angst & Merikangas, 1997; Kessler *et al*. 1997; Kessler & Walters, 1998; Pincus *et al*. 1999; Pine *et al*. 1999; Lewinsohn *et al*. 2000; Cuijpers *et al*. 2004; Cuijpers & Smit, 2004; Hermens *et al*. 2004; Chopra *et al*. 2005; Fergusson *et al*. 2005; Fogel *et al*. 2006; Wiktorsson *et al*. 2010; Judd, 2012). However, limited data are available regarding the prevalence, course, and correlates of SD in the general population.

* Address for correspondence: R. H. Pietrzak, Ph.D., M.P.H., National Center for Posttraumatic Stress Disorder, VA Connecticut Healthcare System, Yale University School of Medicine, 950 Campbell Avenue 151E, West Haven, CT, 06516, USA.
(Email: robert.pietrzak@yale.edu)

Results of this study were presented at the Annual Conference of the Anxiety Disorders Association of America, Washington, DC, 14 April 2012.

Several conclusions may be drawn from extant research on SD. First, while differences in operational definitions of SD employed across studies have resulted in markedly variable prevalence estimates of SD that range from 2% to 32%, population-based estimates indicate a prevalence of 7–12%. Second, SD is associated with functional impairment and reduced quality of life, as well as greater health service utilization and economic costs. Third, SD increases the risk of developing major depressive and other mood and anxiety disorders, as well as suicidal ideation and attempts. Taken together, these findings underscore the utility of conceptualizing depressive disorders along a dimensional continuum. Given the importance of detecting the earliest manifestations of psychiatric conditions (Insel, 2009), identification of early markers of incident psychiatric illness, such as SD, may help identify at-risk individuals who may benefit from preventive interventions.

While this literature has advanced understanding of SD, it has several limitations. First, there are scarce data on the prevalence, course, and co-morbidity of SD in large, contemporary, population-based, and nationally representative samples. Second, although some studies have examined the relationship between SD and incident major depression, few have evaluated whether SD may also increase risk for the development of other mood, anxiety, and substance use disorders. Third, little attention has been given to the potentially confounding influence of co-morbid psychiatric disorders when evaluating the relationship between SD and incident major depressive and related psychiatric morbidities. Consequently, it is unknown whether SD or Axis I or II disorders associated with SD increase risk for incident major depressive and related disorders. Fourth, little is known about prognostic factors associated with the development of incident major depression among individuals with SD. Additional research using data from large, contemporary, population-based prospective studies is needed to address these limitations.

In the present study, we evaluated the prevalence, co-morbidity, and longitudinal course of SD; and the relationship between SD and incident mood, anxiety, and substance use disorders over a 3-year period in a large, nationally representative sample of US adults. We used data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), one of the largest prospective, population-based psychiatric epidemiologic surveys, which conducted structured diagnostic interviews of a contemporary sample of 34 653 US adults. It also assessed a broad range Axis I and II disorders at two time-points (2001–2002 and 2004–2005), thereby providing an opportunity to examine patterns of a broad range of psychiatric disorders that co-occur with SD; the course of SD over time; and the relationship between SD and incident major depressive and other psychiatric disorders. We had four aims: (1) to estimate the lifetime prevalence of SD in the US adult population; (2) to examine a broad range of Axis I and II disorders that might co-occur with SD; (3) to assess the relationship between SD and incident major depressive, other mood, anxiety, and substance use disorders; and (4) to characterize factors associated with the development of incident major depressive disorder and related disorders among individuals with SD.

Method

Sample

The NESARC is a representative sample of the civilian non-institutionalized adult population residing in the US and was conducted by the United States Census Bureau under direction from the National Institute on Alcohol Abuse and Alcoholism (NIAAA; Grant *et al*. 2004). Wave 1 was conducted in 2001–2002 by face-to-face interviews administered to 43 093 people aged $\geqslant$18 years (response rate 81%). Wave 2 involved follow-up interviews with all eligible respondents from Wave 1 in 2004–2005 and achieved a response rate of 86.7%, which resulted in a final sample of 34 653 (cumulative response rate 70.2%; Grant *et al*. 2009). Ineligible respondents consisted of those who were deceased or deported, individuals judged to be too mentally or physically impaired, or being on active military duty during the follow-up period (3134 individuals). Once weighted for oversampling, design characteristics, and non-response characteristics (sociodemographic variables and the presence of any lifetime Wave 1 NESARC substance use or other psychiatric disorder), the data were representative of the national population at that time.

Measures

Diagnostic assessment

The Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version (AUDADIS-IV; Grant *et al*. 2001) was administered by experienced lay interviewers and assessed alcohol and drug abuse and dependence, major depression, dysthymia, mania, hypomania, panic disorder, social phobia, specific phobia, and generalized anxiety disorder (GAD) at both Waves 1 and 2. In Wave 2, post-traumatic stress disorder (PTSD) was also assessed using timing of symptoms to create variables for PTSD occurring prior to Wave 1 and since Wave 1. Incident disorders were defined as those meeting diagnostic criteria since

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Wave 1 with no lifetime history of that specific disorder at Wave 1. AUDADIS-IV diagnoses for alcohol and substance use disorders have excellent test–retest reliability and extensively documented validity (Grant *et al*. 1995, 2003; Hasin *et al*. 1997; Pull *et al*. 1997; Ustün *et al*. 1997). Diagnoses of DSM-IV mood and anxiety disorders have produced reliability estimates ranging from fair to good (Canino *et al*. 1999; Grant *et al*. 2003), and good convergent validity (Canino *et al*. 1999; Grant *et al*. 2004, 2005*a*, *b*, *d*, 2006; Hasin *et al*. 2005). Lifetime Axis II disorders assessed at Wave 1 included avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial personality disorders. At Wave 2 borderline, schizotypal, and narcissistic personality disorders were assessed. Personality disorders are chronic conditions that begin by age 18 years. Therefore, we treated each Axis II disorder as lifetime and assumed that the onset would have occurred by Wave 1, as all respondents were aged $\geqslant$18 years. Reliability of the personality disorder diagnoses is comparable to that of semi-structured personality interviews (Zimmerman, 1994) with good to excellent convergent validity (Canino *et al*. 1999; Grant *et al*. 2004, 2005*c*).

Level of depressive symptoms

All participants were asked two questions: 'In your entire life, have you ever had a time when you felt sad, blue, depressed, or down most of the time for at least 2 weeks?' (i.e. depressed mood) and 'In your entire life, have you ever had a time, lasting at least 2 weeks, when you didn't care about the things that you usually cared about, or when you didn't enjoy the things you usually enjoyed?' (i.e. loss of interest). If either of these screening questions were endorsed, the participants were asked about specific symptoms that they experienced during the time that their mood was the lowest or they cared about things the least. If they endorsed at least four of the other depression symptoms they were asked about the impact that these symptoms had on their life (e.g. Did you have trouble doing things you were supposed to? Were you upset by these experiences?).

Participants who did not endorse either depressed mood or loss of interest were classified as the asymptomatic or 'None' group for level of depression. Participants who endorsed at least one of these symptoms but did not endorse four or more of the more specific symptoms were classified as the 'Subsyndromal depression: limited symptoms' group. Those who endorsed at least five of the individual symptoms (including at depressed mood and/or loss of interest), but did not meet the distress or impairment criterion for major depression were classified as the 'Subsyndromal depression: no distress' group. Those meeting the distress or impairment criterion were included in the 'Major depression' group. Individuals who endorsed both of the screening questions, as well as three additional symptoms would technically have enough symptoms to meet criteria for major depression. However, the skip-out rules of the interview did not direct these individuals to the distress/impairment questions, making it impossible to accurately categorize them. Therefore, these individuals were not included in the analyses.

'Incident' suicide attempts

Wave 1 of the NESARC only asked respondents about suicidal behavior in the depression module once one of the screener questions was endorsed and within the context of a depressive episode. In Wave 2, all respondents were asked about lifetime suicidal behavior. To create an 'incident' suicide attempt variable, we removed anyone who had endorsed a suicide attempt at Wave 1 in the depression module, and only examined the relationship in the three groups with some level of depressive symptoms.

Mental and physical health status

The Short Form 12 Health Survey version 2 (SF-12v2) is a revised second version of the short-form of the SF-36 Health Survey (Ware *et al*. 1996). The SF-12v2 contains 12 questions and yields physical and mental health composite scores, which range from 0 to 100 and a mean of 50 and a standard deviation of 10; higher scores reflect better health.

Sociodemographic variables

Sociodemographic variables examined in this study included age (18–29, 30–44, 45–64, $\geqslant$65 years), sex, household income in the last 12 months (US$0–19 999, $20 000–34 999, $35 000–59 999, $\geqslant$$60 000), education (less than high school, high school or equivalent, more than high school), current marital status (married or cohabitating, previously married, never married), and race/ethnicity (White, Black, American Indian/Alaska Native, Asian/Native Hawaiian/Pacific Islander, Hispanic/Latino).

Statistical analysis

We first examined the frequency of the outcome variables across the different levels of depression symptoms descriptively with cross-tabulations. The cell sizes presented are unweighted and the percentages are weighted to be representative of the US adult population. We then examined these associations

using multivariable logistic regression analyses with level of depression symptoms entered as the main predictor variable. Separate sets of analyses were conducted to evaluated associations between depression level and (1) sociodemographic characteristics; (2) co-occurring psychiatric disorders at Wave 1; and (3) incident psychiatric disorders and suicide attempts at Wave 2. For all analyses, odds ratios (ORs) and adjusted odds ratios (aORs) are presented with 95% confidence intervals (CIs). In the latter two sets of analyses, the first adjusted model (aOR) included sociodemographic variables as covariates. The second adjusted model (aOR2) additionally included the presence of Axis I disorders at Wave 1 (any other mood disorder, any substance use disorder, and any anxiety disorder), as well as any Axis II disorder. The relationship between depression level and SF-12v2 scores was evaluated using multivariable linear regression analyses, with these same two sets of covariates. Finally, to evaluate the relationship between depression level at Wave 1 and risk for incident major depression, we conducted a multivariable logistic regression analysis with incident major depression entered as the outcome variable and variables hypothesized to be related to this outcome entered as predictor variables. All analyses were conducted using SUDAAN (Shah *et al*. 1995), which employs Taylor series linearization, a variance estimation procedure that uses statistical weights and stratification variables to account for the complex design of the NESARC.

Results

At Wave 1, a total of 6594 (18.7%) respondents had major depression; 3232 (9.3%) had SD with limited symptoms; 817 (2.3%) had SD without distress/impairment; and 23 214 (69.4%) did not meet study criteria for subsyndromal or major depression in their lifetimes.

Table 1 shows demographic characteristics by lifetime depression level at Wave 1. SD with limited symptoms was more common among female, White, and previously married respondents; and less common among 18- to 44-year-old respondents with high school or less education. SD without distress/impairment was more common among female respondents, and those previously married and with household income <US$20 000/year. Major depression was more common among respondents aged 18–64 years, females, those with income <US$35 000/year, and among previously or currently married, and White and American Indian/Alaska Native respondents; and less common among those with high school or less education, married/cohabitating, and Native Hawaiian/Pacific Islander respondents.

Table 2 shows lifetime Axis I and II disorders associated with lifetime depression level at Wave 1. Results of these analyses generally suggested a positive monotonic association between depression level and likelihood of co-morbid disorders, as evidenced by non-overlapping 95% CIs for OR estimates comparing the SD with limited symptoms group to the SD without distress/impairment group; and the SD without distress/impairment group to the major depression group for most of disorders.

Of respondents who were asymptomatic at Wave 1, 5.3% developed major depression at Wave 2, 1.4% developed SD without distress/impairment, 5.8% developed SD with limited symptoms, 86.5% continued to be asymptomatic, and 1.0% could not be categorized because of missing data. Of respondents with SD with limited symptoms at Wave 1, 8.8% developed incident major depression at Wave 2, 2.2% developed SD without distress/impairment, 11.5% continued to experience SD with limited symptoms, 76.4% were asymptomatic, and 1.1% could not be categorized. Of respondents with SD without distress/impairment at Wave 1, 14.5% developed incident major depression at Wave 2, 4.3% continued to experience SD without distress/impairment, 7.3% developed SD with limited symptoms, 72.2% were asymptomatic at Wave 2, and 1.7% could not be categorized. Of respondents with major depression at Wave 1, 26.4% continued to experience major depression at Wave 2, 4.9% had SD without distress/impairment, 9.3% had SD with limited symptoms, 57.4% were asymptomatic, and 2.0% could not be categorized.

Table 3 shows incident psychiatric outcomes at Wave 2 by depression level at Wave 1. After adjusting for sociodemographic variables, and Axis I disorders from Wave 1 and all Axis II disorders, SD with limited symptoms and without distress/impairment were both significantly associated with incident major depression (aOR2 1.72, 95% CI 1.39–2.13 and aOR2 2.05, 95% CI 1.39–3.01, respectively), as well as with incident dysthymia, and social phobia, and GAD (aOR2s 1.41–2.92). Major depression was associated with increased incidence of all disorders assessed except panic disorder, specific phobia, and alcohol and drug use disorders. However, with the exception of specific phobia, all of these associations, as well as the association between major depression and incident suicide attempts, were significant until the final adjusted model.

Table 4 shows SF-12v2 scores by depression level at Waves 1 and 2. At both Waves 1 and 2, mental disability scores decreased as a function of depression level. At Waves 1 and 2, physical disability scores

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 1. *Sociodemographic variables by depression level at Wave 1*

	None 23 214 (69.4%)	Subsyndromal depression: limited symptoms 3232 (9.3%)	Subsyndromal depression: no distress 817 (2.3%)	Major depression 6594 (18.7%)
Age (years)				
18–29	4571 (22.2%)	539 (19.3%)	150 (20.3%)	1329 (22.3%)
OR (95% CI)	1.00	0.76 (0.66–0.87)***	0.99 (0.75–1.31)	1.91 (1.66–2.20)***
30–44	7372 (30.7%)	906 (27.3%)	242 (31.1%)	2254 (33.3%)
OR (95% CI)	1.00	0.77 (0.68–0.88)***	1.09 (0.86–1.38)	2.05 (1.82–2.32)***
45–64	6924 (29.6%)	1073 (33.2%)	278 (32.4%)	2359 (35.2%)
OR (95% CI)		0.97 (0.84–1.13)	1.18 (0.92–1.52)	2.26 (2.02–2.53)***
⩾65	4347 (17.5%)	714 (20.2%)	147 (16.2%)	652 (9.3%)
OR (95% CI)	1.00	1.00	1.00	1.00
Sex				
Male	10 745 (52.5%)	1299 (45.9%)	241 (33.9%)	1973 (34.4%)
Female	12 469 (47.5%)	1933 (54.1%)	576 (66.1%)	4621 (65.6%)
OR (95% CI)	1.00	1.30 (1.18–1.44)***	2.15 (1.78–2.60)***	2.11 (1.96–2.27)***
Household income (US$)				
0–19 999	6020 (21.3%)	930 (23.3%)	287 (28.5%)	1943 (24.0%)
OR (95% CI)	1.00	1.14 (1.00–1.30)	1.41 (1.12–1.78)**	1.24 (1.10–1.39)***
20 000–34 999	4914 (19.8%)	699 (20.6%)	154 (16.6%)	1429 (20.3%)
OR (95% CI)	1.00	1.09 (0.95–1.24)	0.88 (0.66–1.18)	1.13 (1.01–1.26)*
35 000–59 999	5863 (25.8%)	760 (24.3%)	183 (23.5%)	1633 (25.5%)
OR (95% CI)	1.00	0.98 (0.86–1.13)	0.96 (0.73–1.25)	1.08 (0.97–1.21)
⩾60 000	6417 (33.1%)	843 (31.8%)	193 (31.5%)	1589 (30.2%)
OR (95% CI)	1.00	1.00	1.00	1.00
Education				
Less than high school	3982 (15.1%)	513 (13.5%)	151 (15.4%)	996 (14.0%)
OR (95% CI)	1.00	0.84 (0.73–0.96)*	1.02 (0.80–1.31)	0.87 (0.77–0.98)*
High school or equivalent	6841 (29.8%)	889 (27.7%)	247 (29.3%)	1786 (27.3%)
OR (95% CI)	1.00	0.87 (0.78–0.97)*	0.98 (0.81–1.18)	0.86 (0.79–0.93)***
More than high school	12 391 (55.1%)	1830 (58.8%)	419 (55.3%)	3812 (58.8%)
OR (95% CI)	1.00	1.00	1.00	1.00
Marital status				
Married or cohabitating	13 068 (65.7%)	1574 (59.0%)	370 (56.2%)	3016 (56.5%)
OR (95% CI)	1.00	0.91 (0.80–1.04)	0.89 (0.69–1.15)	0.86 (0.80–0.93)***
Previously married	5019 (13.8%)	962 (20.8%)	262 (24.1%)	2082 (22.9%)
OR (95% CI)	1.00	1.54 (1.35–1.75)***	1.83 (1.42–2.35)***	1.67 (1.52–1.84)***
Never married	5127 (20.6%)	696 (20.2%)	185 (19.7%)	1496 (20.5%)
OR (95% CI)	1.00	1.00	1.00	1.00
Race/ethnicity				
White	12 835 (68.7%)	1947 (72.2%)	488 (70.8%)	4361 (77.7%)
OR (95% CI)	1.00	1.25 (1.05–1.50)*	1.21 (0.87–1.69)	1.66 (1.46–1.89)**
Black	4755 (12.0%)	610 (11.0%)	175 (12.7%)	915 (7.8%)
OR (95% CI)	1.00	1.09 (0.88–1.36)	1.24 (0.84–1.84)	0.96 (0.81–1.13)
American Indian/Alaska Native	322 (1.9%)	51 (2.1%)	18 (2.5%)	169 (3.4%)
OR (95% CI)	1.00	1.36 (0.92–2.01)	1.60 (0.88–2.88)	2.68 (2.07–3.46)***
Asian/Native Hawaiian/Pacific Islander	746 (4.9%)	83 (4.1%)	16 (3.3%)	109 (2.5%)
OR (95% CI)	1.00	1.01 (0.75–1.36)	0.79 (0.44–1.43)	0.76 (0.58–0.98)*
Hispanic or Latino	4556 (12.6%)	541 (10.6%)	120 (10.8%)	1040 (8.6%)
OR (95% CI)	1.00	1.00	1.00	1.00

OR, Odds ratio; CI, confidence interval.
n is total number; % are weighted.
* $p<0.05$, ** $p<0.01$, *** $p<0.001$.

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 2. *Lifetime co-morbidity by depression level at Wave 1*

	None 23 214 (69.4%)	Subsyndromal depression: limited symptoms 3232 (9.3%)	Subsyndromal depression: no distress 817 (2.3%)	Major depression 6594 (18.7%)
Any mood disorder	574 (2.5%)	220 (6.4%)	129 (13.7%)	2429 (36.5%)
OR (95% CI)	1.00	2.71 (2.22–3.32)***	6.29 (4.85–8.17)***	22.83 (19.92–26.16)***
aOR (95% CI)	1.00	2.81 (2.30–3.44)***	6.37 (4.94–8.21)***	23.06 (20.18–26.37)***
Dysthymia	94 (0.4%)	86 (2.5%)	41 (4.0%)	1507 (22.2%)
OR (95% CI)	1.00	7.24 (4.86–10.80)***	12.0 (7.40–19.37)***	81.24 (61.83–106.73)***
aOR (95% CI)	1.00	6.95 (4.68–10.33)***	10.84 (6.70–17.55)***	75.59 (57.99–98.53)***
Hypomania	268 (1.2%)	75 (2.2%)	54 (5.8%)	455 (6.7%)
OR (95% CI)	1.00	1.89 (1.40–2.57)**	5.14 (3.57–7.42)***	6.06 (4.97–7.38)***
aOR (95% CI)	1.00	2.05 (1.50–2.80)***	5.64 (3.89–8.17)***	6.31 (5.15–7.73)***
Mania	227 (1.0%)	72 (2.0%)	45 (4.8%)	920 (14.2%)
OR (95% CI)	1.00	2.10 (1.48–2.98)**	5.07 (3.33–7.71)***	16.70 (13.61–20.49)***
aOR (95% CI)	1.00	2.21 (1.55–3.16)***	5.19 (3.42–7.88)***	16.82 (13.64–20.75)***
Any anxiety disorder	2335 (9.7%)	514 (15.7%)	231 (28.3%)	2808 (43.8%)
OR (95% CI)	1.00	1.74 (1.52–2.00)**	3.69 (3.00–4.54)***	7.28 (6.66–7.96)***
aOR (95% CI)	1.00	1.70 (1.48–1.96)**	3.37 (2.72–4.16)***	6.42 (5.87–7.02)***
Panic disorder	542 (2.3%)	135 (4.4%)	71 (9.4%)	1156 (17.7%)
OR (95% CI)	1.00	1.94 (1.52–2.46)**	4.38 (3.12–6.13)***	9.08 (7.90–10.45)***
aOR (95% CI)	1.00	1.86 (1.47–2.37)**	3.87 (2.75–5.47)***	7.66 (6.62–8.85)***
Social phobia	555 (2.4%)	136 (4.6%)	48 (5.7%)	954 (15.2%)
OR (95% CI)	1.00	1.92 (1.48–2.49)**	2.44 (1.66–3.57)***	7.23 (6.21–8.41)***
aOR (95% CI)	1.00	1.92 (1.48–2.49)**	2.34 (1.59–3.45)***	6.67 (5.72–7.78)***
Specific phobia	1461 (5.9%)	298 (8.5%)	153 (18.9%)	1429 (22.3%)
OR (95% CI)	1.00	1.49 (1.25–1.76)**	3.70 (2.90–4.70)***	4.57 (4.13–5.06)***
aOR (95% CI)	1.00	1.46 (1.23–1.74)**	3.35 (2.61–4.29)***	4.00 (3.60–4.44)***
GAD	247 (0.9%)	87 (2.3%)	56 (6.1%)	1192 (18.6%)
OR (95% CI)	1.00	2.48 (1.85–3.32)**	6.87 (4.66–10.13)***	24.03 (20.15–28.66)***
aOR (95% CI)	1.00	2.35 (1.73–3.15)**	6.12 (4.16–9.01)***	21.23 (17.62–25.36)***
PTSD	787 (3.0%)	153 (4.2%)	81 (9.3%)	950 (13.6%)
OR (95% CI)	1.00	1.41 (1.14–1.75)**	3.26 (2.42–4.39)***	5.04 (4.45–5.72)***
aOR (95% CI)	1.00	1.34 (1.08–1.66)**	2.78 (2.05–3.77)***	4.26 (3.72–4.89)***
Any substance use disorder	6143 (28.4%)	948 (31.4%)	254 (33.6%)	3026 (47.9%)
OR (95% CI)	1.00	1.16 (1.05–1.27)*	1.28 (1.05–1.56)*	2.32 (2.15–2.51)***
aOR (95% CI)	1.00	1.27 (1.14–1.41)*	1.61 (1.32–1.96)**	2.78 (2.57–3.02)***
Alcohol use disorder	5753 (26.7%)	884 (29.5%)	243 (32.3%)	2780 (44.0%)
OR (95% CI)	1.00	1.15 (1.04–1.27)*	1.31 (1.07–1.60)**	2.16 (2.00–2.34)***
aOR (95% CI)	1.00	1.25 (1.13–1.39)*	1.66 (1.36–2.03)**	2.59 (2.38–2.81)***
Drug use disorder	1653 (7.6%)	293 (9.6%)	74 (9.7%)	1321 (21.2%)
OR (95% CI)	1.00	1.29 (1.09–1.52)*	1.30 (0.95–1.78)	3.26 (2.95–3.61)***
AOR (95% CI)	1.00	1.39 (1.18–1.64)*	1.47 (1.06–2.05)**	3.40 (3.04–3.79)***
Any Axis II disorder	3617 (14.7%)	678 (21.1%)	263 (31.4%)	2980 (44.9%)
OR (95% CI)	1.00	1.54 (1.38–1.73)**	2.65 (2.18–3.23)***	4.71 (4.36–5.08)***
aOR (95% CI)	1.00	1.65 (1.47–1.85)**	2.88 (2.37–3.49)***	5.10 (4.70–5.53)***

OR, Odds ratio; aOR, adjusted odds ratio; CI, confidence interval; GAD, generalized anxiety disorder; PTSD, post-traumatic stress disorder.

n is total number, % are weighted.

aOR adjusted for age, income, sex, education, marital status, and race/ethnicity.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 3. *Incident Axis I disorders and suicide attempts by Wave 1 depression level*

	None 23 214 (69.4%)	Subsyndromal depression: limited symptoms 3232 (9.3%)	Subsyndromal depression: no distress 817 (2.3%)	Major depression 6594 (18.7%)
Any mood disorder	624 (2.5%)	118 (3.3%)	40 (4.4%)	427 (6.4%)
OR (95% CI)	1.00	1.32 (1.05–1.67)*	1.79 (1.13–2.82)**	2.65 (2.22–3.16)***
aOR (95% CI)	1.00	1.38 (1.09–1.74)*	1.69 (1.06–2.70)*	2.50 (2.08–3.01)***
aOR2 (95% CI)	1.00	1.51 (1.09–2.09)*	1.74 (0.87–3.48)	2.93 (2.19–3.92)***
Major depression	1297 (5.3%)	283 (8.8%)	115 (14.5%)	
OR (95% CI)	1.00	1.72 (1.46–2.03)**	2.99 (2.28–3.92)***	–
aOR (95% CI)	1.00	1.73 (1.46–2.05)**	2.67 (2.03–3.51)***	–
aOR2 (95% CI)	1.00	1.72 (1.39–2.13)**	2.05 (1.39–3.01)***	–
Dysthymia	137 (0.5%)	40 (0.9%)	11 (1.3%)	140 (2.0%)
OR (95% CI)	1.00	1.94 (1.33–2.82)***	2.65 (1.21–2.82)**	4.25 (2.99–6.03)***
aOR (95% CI)	1.00	1.94 (1.33–2.82)***	2.42 (1.11–5.27)**	3.97 (2.80–5.65)***
aOR2 (95% CI)	1.00	2.51 (1.46–4.30)***	2.92 (1.85–10.03)***	4.63 (2.85–7.51)***
Hypomania	212 (0.9%)	39 (1.1%)	15 (1.7%)	112 (1.6%)
OR (95% CI)	1.00	1.25 (0.81–1.93)	1.86 (0.95–3.64)	1.81 (1.35–2.43)***
aOR (95% CI)	1.00	1.32 (0.86–2.03)	1.81 (0.91–3.59)	1.75 (1.29–2.38)***
aOR2 (95% CI)	1.00	1.60 (0.95–2.71)	2.13 (0.77–5.92)	2.39 (1.45–3.94)**
Mania	296 (1.2%)	46 (1.4%)	17 (2.08%)	201 (3.1%)
OR (95% CI)	1.00	1.14 (0.78–1.68)	1.71 (0.94–3.11)	2.53 (1.98–3.23)***
aOR (95% CI)	1.00	1.20 (0.82–1.76)	1.59 (0.87–2.93)	2.30 (1.78–2.97)***
aOR2 (95% CI)	1.00	0.90 (0.45–1.78)	1.21 (0.37–3.98)	1.81 (1.07–3.08)*
Anxiety disorder	1379 (5.7%)	222 (7.1%)	79 (9.9%)	832 (12.2%)
OR (95% CI)	1.00	1.26 (1.06–1.50)*	1.81 (1.37–2.39)*	2.28 (1.98–2.62)***
aOR (95% CI)	1.00	1.26 (1.05–1.50)*	1.62 (1.23–2.15)**	1.93 (1.66–2.33)***
aOR2 (95% CI)	1.00	1.21 (0.97–1.51)	1.48 (0.99–2.22)	1.48 (1.18–1.86)**
Panic disorder	334 (1.4%)	61 (2.2%)	17 (2.3%)	213 (2.9%)
OR (95% CI)	1.00	1.59 (1.11–2.29)*	1.63 (0.87–3.03)	2.10 (1.68–2.62)***
aOR (95% CI)	1.00	1.62 (1.13–2.33)*	1.45 (0.77–2.72)	1.75 (1.38–2.21)***
aOR2 (95% CI)	1.00	1.20 (0.74–1.92)	1.19 (0.48–2.93)	1.32 (0.88–1.97)
Social phobia	280 (1.1%)	55 (1.8%)	17 (2.5%)	191 (2.8%)
OR (95% CI)	1.00	1.65 (1.16–2.56)*	2.38 (1.30–4.34)**	2.65 (2.00–3.51)***
aOR (95% CI)	1.00	1.65 (1.16–2.36)*	2.18 (1.20–3.98)**	2.21 (1.65–2.96)***
aOR2 (95% CI)	1.00	2.13 (1.34–3.38)**	2.91 (1.23–2.72)**	1.67 (1.03–2.72)*
Specific phobia	530 (2.3%)	66 (1.8%)	19 (2.2%)	180 (2.6%)
OR (95% CI)	1.00	0.81 (0.59–1.11)	0.96 (0.56–1.63)	1.15 (0.91–1.45)
aOR (95% CI)	1.00	0.80 (0.58–1.09)	0.85 (0.50–1.45)	0.97 (0.75–1.24)
aOR2 (95% CI)	1.00	0.82 (0.54–1.24)	0.59 (0.27–1.25)	1.07 (0.74–1.54)
GAD	521 (2.2%)	90 (3.1%)	42 (4.9%)	424 (6.2%)
OR (95% CI)	1.00	1.42 (1.08–1.86)*	2.25 (1.56–3.25)***	2.90 (2.44–3.45)***
AOR (95% CI)	1.00	1.41 (1.07–1.85)*	2.00 (1.39–2.88)***	2.41 (1.99–2.92)***
AOR2 (95% CI)	1.00	1.41 (1.01–1.99)*	1.92 (1.05–3.51)*	2.00 (1.41–2.84)**
PTSD	228 (0.9%)	29 (1.0%)	17 (1.9%)	165 (2.3%)
OR (95% CI)	1.00	1.11 (0.62–2.01)	2.19 (1.23–2.01)**	2.61 (2.06–3.31)***
aOR (95% CI)	1.00	1.14 (0.63–2.06)	2.00 (1.12–3.58)*	2.37 (1.85–3.02)***
aOR2 (95% CI)	1.00	1.44 (0.65–3.15)	1.74 (0.70–4.31)	2.52 (1.70–3.75)***
Substance use disorder	1196 (5.4%)	154 (5.0%)	31 (4.8%)	313 (5.1%)
OR (95% CI)	1.00	0.92 (0.73–1.17)	0.89 (0.56–1.42)	0.94 (0.80–1.11)
aOR (95% CI)	1.00	0.97 (0.77–1.24)	0.96 (0.62–1.50)	0.96 (0.81–1.14)
aOR2 (95% CI)	1.00	0.92 (0.68–1.24)	1.02 (0.58–1.79)	0.91 (0.71–1.17)

[*continued overleaf*

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 3 (*cont.*)

	None 23 214 (69.4%)	Subsyndromal depression: limited symptoms 3232 (9.3%)	Subsyndromal depression: no distress 817 (2.3%)	Major depression 6594 (18.7%)
Alcohol use disorder	988 (4.4%)	131 (4.1%)	20 (3.1%)	208 (3.4%)
OR (95% CI)	1.00	0.94 (0.73–1.21)	0.69 (0.42–1.21)	0.76 (0.62–0.93)*
aOR (95% CI)	1.00	1.00 (0.77–1.29)	0.74 (0.45–1.24)	0.78 (0.63–0.96)*
aOR2 (95% CI)	1.00	0.99 (0.71–1.38)	1.13 (0.63–2.03)	0.90 (0.67–1.20)
Drug use disorder	298 (1.4%)	35 (1.4%)	15 (2.5%)	129 (2.2%)
OR (95% CI)	1.00	1.00 (0.66–1.51)	1.81 (0.96–3.40)	1.61 (1.25–2.08)**
aOR (95% CI)	1.00	1.04 (0.69–1.58)	1.97 (1.07–3.62)*	1.63 (1.26–2.12)**
aOR2 (95% CI)	1.00	1.04 (0.63–1.71)	1.52 (0.55–4.19)	1.29 (0.78–2.13)
Suicide attempts	–	72 (2.2%)	24 (3.0%)	309 (4.6%)
OR (95% CI)	–	1.00	1.37 (0.72–2.58)	2.09 (1.47–2.99)***
aOR (95% CI)	–	1.00	1.22 (0.65–2.32)	1.70 (1.18–2.45)**
aOR2 (95% CI)	–	1.00	1.14 (0.48–2.72)	1.43 (0.81–2.52)

OR, Odds ratio; aOR, adjusted odds ratio; CI, confidence interval; GAD, generalized anxiety disorder; PTSD, post-traumatic stress disorder.

n is total number, % are weighted.

aOR adjusted for age, income, sex, education, marital status, and race/ethnicity.

aOR2 adjusted for sociodemographic variables and the presence of co-morbid disorders at Wave 1.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

were significantly lower in the major depression group relative to the asymptomatic/none group; at Wave 2, these scores were also lower in the SD: no distress group than the asymptomatic/none group.

Table 5 shows variables associated with incident major depression among respondents with SD at Wave 1. Any Axis II disorder was associated positively with both incident major depression and greater mental functioning at Wave 1 was negatively associated with this outcome for both SD groups. *Post-hoc* analyses of Axis II personality clusters associated with incident major depression revealed that any Cluster B disorder was strongly positively associated with incident major depression in both groups (OR 2.94, 95% CI 1.88–4.60, and OR 3.30, 95% CI 1.56–6.98, respectively). In the SD with limited symptoms group, any Cluster A disorder was additionally positively associated with incident major depression (OR 1.94, 95% CI 1.25–3.37); and any Cluster C disorder was negatively associated with this outcome (OR 0.47, 95% CI 0.27–0.82).

Discussion

We evaluated the prevalence, co-morbidity, and longitudinal course of SD; the relationship between SD and incident major depressive and other disorders; and factors associated with the development of incident major depression among individuals with SD over a 3-year period in a large, nationally representative sample of US adults. Results suggested that: (*a*) in addition to 18.7% of US adults who meet criteria for a DSM-IV diagnosis of major depression in their lifetimes, an additional 11.6% experience SD; (*b*) SD is associated with significantly increased odds of co-morbid mood, anxiety, substance use, and Axis II disorders, as well as increased psychosocial disability; (*c*) SD is associated with significant increased likelihood of developing a new-onset diagnosis of major depression, dysthymia, social phobia, and GAD; and (*d*) among respondents with lifetime SD at Wave 1, Cluster A and B personality disorder, as well as worse mental functioning at Wave 1 were independently related to the development of incident major depression at Wave 2.

The finding that 11.6% of US adults had lifetime SD is consistent with prior general population-based studies, which have similarly observed that the prevalence of SD typically ranges from 7% to 12% (Judd *et al*. 1994; Kessler *et al*. 1997; Fergusson *et al*. 2005; Meeks *et al*. 2011). Of note, we employed two operationalizations of SD in the current study, with most respondents classified as having SD (9.3% of the total sample) characterized by depressed mood and/or anhedonia, but fewer than five total symptoms; the remainder of respondents with SD (2.3% of the total

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 4. *SF-12v2 scores by depression level*

	None 23 214 (69.4%), mean (S.E.)	Subsyndromal depression: limited symptoms 3232 (9.3%), mean (S.E.)	Subsyndromal depression: no distress 817 (2.3%), mean (S.E.)	Major depression 6594 (18.7%), mean (S.E.)
Wave 1				
Mental Disability Scale				
Unadjusted mean (S.E.)	54.53 (0.08)	52.07 (0.20)***	49.88 (0.42)***	46.29 (0.16)***
Adjusted mean2 (S.E.)	54.58 (0.08)	52.81 (0.21)***	51.52 (0.45)***	50.09 (0.20)***
Physical Disability Scale				
Unadjusted mean (S.E.)	51.48 (0.11)	50.67 (0.23)***	49.78 (0.46)***	49.12 (0.21)***
Adjusted mean2 (S.E.)	51.44 (0.09)	51.12 (0.23)	50.96 (0.45)	49.57 (0.26)***
Wave 2				
Mental Disability Scale				
Unadjusted mean (S.E.)	52.78 (0.10)	51.05 (0.20)***	49.43 (0.46)***	46.94 (0.18)***
Adjusted mean2 (S.E.)	53.12 (0.10)	51.90 (0.20)***	50.77 (0.49)***	50.28 (0.22)***
Physical Disability Scale				
Unadjusted mean (S.E.)	50.89 (0.11)	49.83 (0.24)***	48.95 (0.53)***	48.34 (0.20)***
Adjusted mean2 (S.E.)	50.88 (0.09)	50.50 (0.22)	49.52 (0.52)*	48.93 (0.24)***

SF-12v2, Short Form 12 Health Survey version 2; S.E., standard error.
n is total number, % are weighted.
Adjusted mean adjusted for age, income, sex, education, marital status, and race/ethnicity.
Adjusted mean2 adjusted for sociodemographic variables and the presence of co-morbid disorders at Wave 1.
Significant difference in means relative to 'None' group: * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

sample) had five or more symptoms required for a diagnosis of major depression, including depressed mood and/or anhedonia, but denied significant distress or functional impairment associated with these symptoms. A 'dose–response' pattern of association was observed for magnitudes of associations between depression level and co-morbid Axis I and II disorders, and suicide attempts, with increasing severity of depression level associated with incrementally increasing odds of co-morbid psychopathology. Given that confidence intervals for these odds ratios generally did not overlap, the classification of depression level in this study appeared to reflect an underlying dimensionality of depressive symptom severity that exhibited a positive monotonic association with co-morbid psychopathology. Of note, even respondents with the least severe categorization of SD (i.e. 1–4 symptoms of major depression) had significantly elevated rates of co-morbid disorders, with magnitudes of these associations ranging from 1.25 for alcohol use disorder to 6.95 for dysthymia.

Compared to 5.3% of respondents in the asymptomatic group who developed major depression at Wave 2, 8.8% of the SD: limited symptoms group and 14.5% of the SD: no distress group developed major depression at Wave 2. After adjustment for sociodemographic variables and the presence of co-morbid disorders at the Wave 1 assessment, SD was associated with a 72–205% increased likelihood of developing major depression at Wave 2. However, as has been observed in prior studies (Hermens *et al*. 2004), most (>70%) respondents with SD at Wave 1 were no longer symptomatic at Wave 2. Both classifications of SD were additionally associated with incident dysthymia, social phobia, and GAD. These findings accord with prior population-based studies, which have similarly found that SD is associated with incident major depression, as well as anxiety disorders (Lewinsohn *et al*. 2000; Fergusson *et al*. 2005; Johnson *et al*. 2009). Magnitudes of the associations between SD and incident major depression were generally lower than those observed in these prior studies, which may be related to different time-frames of assessments employed across studies and/or the more conservative approach to covariate modeling employed in the current study, which adjusted for sociodemographic characteristics, as well as the presence of Wave 1 mood, anxiety, and substance use, and any Axis II disorder.

Of note, while some studies have found that SD was associated with increased likelihood of incident substance use disorders (Lewinsohn *et al*. 2000), we did not replicate this finding. Possible explanations for this finding include the relatively brief follow-up

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

Table 5. *Profile of individuals with Wave 1 subsyndromal depression who developed major depression at Wave 2*

	Incident major depression	
	Subsyndromal depression: limited symptoms 283 (8.8%)	Subsyndromal depression: no distress 115 (14.5%)
Wave 1 mood disorder	26 (6.5%)	27 (18.4%)
aOR (95% CI)	0.75 (0.42–1.37)	0.76 (0.35–1.64)
Wave 1 anxiety disorder	63 (23.5%)	42 (37.8%)
aOR (95% CI)	1.08 (0.92–1.28)	1.09 (0.85–1.39)
Wave 1 substance use disorder	80 (32.6%)	38 (34.5%)
aOR (95% CI)	1.01 (0.70–1.46)	0.84 (0.45–1.58)
Any Axis II disorder	115 (38.8%)	60 (55.1%)
aOR (95% CI)	2.18 (1.52–3.13)***	2.83 (1.55–5.15)***
SF-12v2 physical (mean, S.E.)	48.24 (1.05)	49.12 (1.47)
aOR (95% CI)	0.99 (0.97–1.00)	1.00 (0.97–1.03)
SF-12v2 mental (mean, S.E.)	43.18 (0.72)	40.96 (1.71)
aOR (95% CI)	0.93 (0.92–0.94)***	0.91 (0.89–0.94)***
Parental history of depression	94 (35.0%)	42 (34.8%)
aOR (95% CI)	1.16 (0.82–1.64)	0.59 (0.33–1.06)
Stressful life events count (mean, S.E.)	1.92 (0.10)	2.47 (0.25)
aOR (95% CI)	1.02 (0.93–1.13)	1.06 (0.90–1.25)

aOR, Adjusted odds ratio; CI, confidence interval; SF-12v2, Short Form 12 Health Survey version 2; S.E., standard error.

n is total number, % are weighted.

aOR adjusted for all sociodemographic variables and variables presented in the table.

*** Significant association with incident major depression, $p < 0.001$.

interval employed in the current study; variable duration of time since subsyndromal depressive symptoms were most prominent; and conservative adjustment for psychiatric co-morbidity when assessing these associations. Taken together, these findings suggest that SD is associated with a significantly increased likelihood of developing major depression, as well as dysthymia, social phobia, and GAD over a 3-year period in the US adult population. They further underscore the importance of viewing depressive symptoms on a continuum, as a broader, dimensional conceptualization of depressive symptoms may help identify individuals who may be at risk for developing major depression and related disorders. Such a conceptualization may also have utility in assessing depressive symptoms among individuals with major depression. For example, data from the NIMH Collaborative Study on Depression (Keller *et al*. 1992) suggest that during a major depressive episode, most of the episode (68%) is characterized by subsyndromal symptoms, while syndromal symptoms are present only 32% of the time. Further, residual SD among individuals with an initial diagnosis of major depression is associated with a more rapid relapse to major depression compared to individuals with an asymptomatic pattern of recovery (Judd *et al*. 1998*a*). These findings further highlight the utility of dimensional approaches in assessing, monitoring, and treating depressive symptoms in affected individuals (Judd, 2012). Given the importance of detecting the earliest manifestations of psychiatric disorders (Insel, 2009), characterization of early prognostic risk factors such as SD for incident major depression and related disorders may help identify individuals who may benefit from preventive interventions (Judd *et al*. 2004; Cuijpers *et al*. 2007; Rosenberg *et al*. 2010).

Results of this study have implications for the classification of SD in DSM-5 (APA, 2011). While the operationalization of SD in the current study differed slightly from the proposed DSM-5 operationalization (i.e. clinically significant distress/functional impairment related to having less than five MDD symptoms

https://doi.org/10.1017/S0033291712002309 Published online by Cambridge University Press

was not assessed), both operationalizations of SD in the present study were associated with increased mental disability relative to asymptomatic respondents, and this level of disability was maintained over the 3-year study period. Further, the finding that both operationalizations of SD were associated with elevated odds of co-morbid disorders underscores the clinical significance of this categorization, even the less severe category of SD that was characterized by 1–4 symptoms of major depression. Taken together, results of this study corroborate earlier work of Judd and colleagues (Judd *et al*. 1998*b*, 1994, 1997; Judd, 2012) to suggest that SD, even when characterized by only 1–4 symptoms of major depression, represents a level of depressive symptomatology that has both clinical and prognostic significance.

Among individuals with SD at Wave 1, having a Cluster A or B personality disorder was associated with increased likelihood of developing a first episode of major depression at Wave 2, and greater mental functioning at Wave 1 was associated negatively with this outcome. This finding is consistent with recent studies using data from NESARC, which found that borderline and schizotypal personality disorders were associated with the development of incident mood, anxiety, and substance use disorders (Grant *et al*. 2009) and that borderline and schizotypal personality disorders were related to chronic major depression (Skodol *et al*. 2011). Personality disorders (Newton-Howes *et al*. 2006; Bock *et al*. 2010) have also been linked to greater likelihood and chronicity of major depression in other samples. Taken together, these results in combination with this prior work highlight the importance of assessing Axis II psychopathology and mental functioning among individuals with SD, as these factors may help identify individuals at risk for developing major depression.

Methodological limitations of this study must be noted. First, due to the skip-out rules used in the AUDADIS-IV structured diagnostic instrument, classifications of SD were on the basis of lifetime, not more recent (e.g. past year) time-frames. Consequently, the reliability of this assessment, as well as our ability to compare our study results to prior work on SD, which has predominantly employed recent time-frames, may be limited. Further, because of these skip-out rules, data regarding the age of onset, duration, and other clinical characteristics of SD were not available. This information will be important to obtain in future work, as it is not clear whether depression symptom level/severity or chronicity of these symptoms, or both, are associated with disability and/or dysfunction. An additional limitation of the skip-out rules is that they precluded us from evaluating our research questions among respondents with SD who may have had clinically significant distress and/or functional impairment related to these symptoms. Second, the classifications of SD used in this study may differ from classifications used in prior research, so additional research is needed to determine the potential generalizability of the findings reported here. Third, the assessment of suicide attempts is limited and may not accurately reflect incident attempts, as Wave 1 assessed suicide attempts only among those respondents who endorsed depressed mood or loss of interest; and Wave 2 asked about lifetime suicide attempts and not attempts restricted to the 3-year follow-up period between Waves 1 and 2 of the NESARC. Fourth, given that only one follow-up assessment was conducted at 3 years after the initial assessment, the relationship between SD and later-onset psychiatric disorders; as well as trajectories of subsyndromal depressive symptoms over longer periods of time, could not be evaluated. Consequently, it is not clear whether SD may be associated with other incident disorders, such as substance use disorder (Lewinsohn *et al*. 2000), which may develop over a longer period of time, or whether SD remains associated with the development of major depression over time or whether individuals with SD show a more fluid, changing course of depressive illness.

Despite these limitations, this study provides the largest, most comprehensive, and most up-to-date assessment of the prevalence, course, and correlates of SD in the US adult population. Results suggest that 11.6% of the US adult population experience SD in their lifetime; that SD is associated with a broad range of co-morbid psychopathology, including mood, anxiety, substance use, and Axis II disorders; and that SD is related to a significantly increased likelihood of developing new-onset major depression, as well as dysthymia, social phobia and GAD over a 3-year period of time. Among individuals with SD at Wave 1, Cluster A and B personality disorder and mental functioning were independently related to the development of incident major depression, thereby highlighting the importance of comprehensive assessment of co-morbid psychopathology and functioning in this population. Further research is needed to evaluate longitudinal trajectories of depressive symptoms over time in large, population-based samples; and to investigate biopsychosocial mechanisms that underlie the development of SD, and that may mediate the transition from SD to major depression and related disorders in the general population.

Acknowledgments

The authors thank the individuals who participated in the NESARC and the U.S. Census Bureau field

representatives who administrated the NESARC interviews. The NESARC is funded by the NIAAA with supplemental support from the National Institute on Drug Abuse.

Preparation of this report was supported in part by the National Center for Posttraumatic Stress Disorder (Dr Pietrzak), a Manitoba Health Research Council Establishment Award (Dr Afifi), and a Manitoba Health Research Council Chair Award (Dr Sareen). The funding sources did not have any role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; or in the preparation, review, or approval of the manuscript.

Declaration of Interest

None.

References

Angst J, Merikangas K (1997). The depressive spectrum: diagnostic classification and course. *Journal of Affective Disorders* **45**, 31–39; discussion 39–40.

APA (2011). DSM-5 development, D 08 other specified depression disorder, 2010 (http://www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=47). American Psychiatric Association. Accessed 24 August 2011.

Bock C, Bukh JD, Vinberg M, Gether U, Kessing LV (2010). The influence of comorbid personality disorder and neuroticism on treatment outcome in first episode depression. *Psychopathology* **43**, 197–204.

Broadhead WE, Blazer DG, George LK, Tse CK (1990). Depression, disability days, and days lost from work in a prospective epidemiologic survey. *Journal of the American Medical Association* **264**, 2524–2528.

Canino G, Bravo M, Ramirez R, Febo VE, Rubio-Stipec M, Fernandez RL, Hasin D (1999). The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. *Journal of Studies on Alcohol* **60**, 790–799.

Celano CM, Huffman JC (2011). Depression and cardiac disease: a review. *Cardiology Review* **19**, 130–142.

Chopra MP, Zubritsky C, Knott K, Have TT, Hadley T, Coyne JC, Oslin DW (2005). Importance of subsyndromal symptoms of depression in elderly patients. *American Journal of Geriatric Psychiatry* **13**, 597–606.

Cuijpers P, de Graaf R, van Dorsselaer S (2004). Minor depression: risk profiles, functional disability, health care use and risk of developing major depression. *Journal of Affective Disorders* **79**, 71–79.

Cuijpers P, Smit F (2004). Subthreshold depression as a risk indicator for major depressive disorder: a systematic review of prospective studies. *Acta Psychiatrica Scandinavica* **109**, 325–331.

Cuijpers P, Smit F, van Straten A (2007). Psychological treatments of subthreshold depression: a meta-analytic review. *Acta Psychiatrica Scandinavica* **115**, 434–441.

Fergusson DM, Horwood LJ, Ridder EM, Beautrais AL (2005). Subthreshold depression in adolescence and mental health outcomes in adulthood. *Archives of General Psychiatry* **62**, 66–72.

Fogel J, Eaton WW, Ford DE (2006). Minor depression as a predictor of the first onset of major depressive disorder over a 15-year follow-up. *Acta Psychiatrica Scandinavica* **113**, 36–43.

Gotlib IH, Lewinsohn PM, Seeley JR (1995). Symptoms versus a diagnosis of depression: differences in psychosocial functioning. *Journal of Consulting and Clinical Psychology* **63**, 90–100.

Grant BF, Dawson DA, Hasin DS (2001). The Alcohol Use Disorder and Associated Disabilities Interview Schedule – DSM-IV version. National Institute on Alcohol Abuse and Alcoholism: Bethesda, MD.

Grant BF, Dawson DA, Stinson FS, Chou PS, Kay W, Pickering R (2003). The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug and Alcohol Dependence* **71**, 7–16.

Grant BF, Goldstein RB, Chou PS, Huang B, Stinson FS, Dawson DA, Saha TD, Smith SM, Pulay AJ, Pickering RP, Ruan WJ, Compton WM (2009). Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the Wave 2 National Epidemiologic Survey of Alcohol and Related Conditions. *Molecular Psychiatry* **14**, 1051–1066.

Grant BF, Harford TC, Dawson DA, Chou PS, Pickering RP (1995). The Alcohol Use Disorder and Associated Disabilities Interview schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. *Drug and Alcohol Dependence* **39**, 37–44.

Grant BF, Hasin DS, Blanco C, Stinson FS, Chou PS, Goldstein RB, Dawson DA, Smith S, Saha TD, Huang B (2005*a*). The epidemiology of social anxiety disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry* **66**, 1351–1361.

Grant BF, Hasin DS, Stinson FS, Dawson DA, Chou PS, Ruan WJ, Pickering RP (2004). Prevalence, correlates, and disability of personality disorders in the United States: results from the national epidemiologic survey on alcohol and related conditions. *Journal of Clinical Psychiatry* **65**, 948–958.

Grant BF, Hasin DS, Stinson FS, Dawson DA, Goldstein RB, Smith S, Huang B, Saha TD (2006). The epidemiology of DSM-IV panic disorder and agoraphobia in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry* **67**, 363–374.

Grant BF, Hasin DS, Stinson FS, Dawson DA, Ruan WJ, Goldstein RB, Smith SM, Saha TD, Huang B (2005*b*). Prevalence, correlates, co-morbidity, and comparative

disability of DSM-IV generalized anxiety disorder in the USA: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychological Medicine* **35**, 1747–1759.

Grant BF, Hasin DS, Stinson FS, Dawson DA, Chou PS, Ruan WJ, Huang B (2005c). Co-occurrence of 12-month mood and anxiety disorders and personality disorders in the US: results from the national epidemiologic survey on alcohol and related conditions. *Journal of Psychiatric Research* **39**, 1–9.

Grant BF, Stinson FS, Hasin DS, Dawson DA, Chou PS, Ruan WJ, Huang, B (2005*d*). Prevalence, correlates, and comorbidity of bipolar I disorder and axis I and II disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry* **66**, 1205–1215.

Hasin D, Carpenter KM, McCloud S, Smith M, Grant BF (1997). The alcohol use disorder and associated disabilities interview schedule (AUDADIS): reliability of alcohol and drug modules in a clinical sample. *Drug and Alcohol Dependence* **44**, 133–141.

Hasin DS, Goodwin RD, Stinson FS, Grant BF (2005). Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. *Archives of General Psychiatry* **62**, 1097–1106.

Hermens ML, van Hout HP, Terluin B, van der Windt DA, Beekman AT, van Dyck R, de Haan M (2004). The prognosis of minor depression in the general population: a systematic review. *General Hospital Psychiatry* **26**, 453–462.

Insel TR (2009). Translating scientific opportunity into public health impact: a strategic plan for research on mental illness. *Archives of General Psychiatry* **66**, 128–133.

Insel TR, Charney DS (2003). Research on major depression: strategies and priorities. *Journal of the American Medical Association* **289**, 3167–3168.

Johnson J, Weissman MM, Klerman GL (1992). Service utilization and social morbidity associated with depressive symptoms in the community. *Journal of the American Medical Association* **267**, 1478–1483.

Johnson JG, Cohen P, Kasen S (2009). Minor depression during adolescence and mental health outcomes during adulthood. *British Journal of Psychiatry* **195**, 264–265.

Judd LL (2012). Dimensional paradigm of the long-term course of unipolar major depressive disorder. *Depression and Anxiety* **29**, 167–171.

Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Paulus MP, Kunovac JL, Leon AC, Mueller TI, Rice JA, Keller MB (1998*a*). Major depressive disorder: a prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. *Journal of Affective Disorders* **50**, 97–108.

Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Paulus MP, Kunovac JL, Leon AC, Mueller TI, Rice JA, Keller MB (1998*b*). A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. *Archives of General Psychiatry* **55**, 694–700.

Judd LL, Akiskal HS, Paulus MP (1997). The role and clinical significance of subsyndromal depressive symptoms (SSD) in unipolar major depressive disorder. *Journal of Affective Disorders* **45**, 5–17; discussion 17–18.

Judd LL, Rapaport MH, Paulus MP, Brown JL (1994). Subsyndromal symptomatic depression: a new mood disorder? *Journal of Clinical Psychiatry* **55** (Suppl.), 18–28.

Judd LL, Rapaport MH, Yonkers KA, Rush AJ, Frank E, Thase ME, Kupfer DJ, Plewes JM, Schettler PJ, Tollefson G (2004). Randomized, placebo-controlled trial of fluoxetine for acute treatment of minor depressive disorder. *American Journal of Psychiatry* **161**, 1864–1871.

Judd LL, Schettler PJ, Akiskal HS (2002). The prevalence, clinical relevance, and public health significance of subthreshold depressions. *Psychiatric Clinics of North America* **25**, 685–698.

Keller MB, Lavori PW, Mueller TI, Endicott J, Coryell W, Hirschfeld RM, Shea T (1992). Time to recovery, chronicity, and levels of psychopathology in major depression. A 5-year prospective follow-up of 431 subjects. *Archives of General Psychiatry* **49**, 809–816.

Kessler RC, Walters EE (1998). Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the National Comorbidity Survey. *Depression and Anxiety* **7**, 3–14.

Kessler RC, Zhao S, Blazer DG, Swartz M (1997). Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *Journal of Affective Disorders* **45**, 19–30.

Lewinsohn PM, Solomon A, Seeley JR, Zeiss A (2000). Clinical implications of 'subthreshold' depressive symptoms. *Journal of Abnormal Psychology* **109**, 345–351.

Meeks TW, Vahia IV, Lavretsky H, Kulkarni G, Jeste DV (2011). A tune in 'a minor' can 'b major': a review of epidemiology, illness course, and public health implications of subthreshold depression in older adults. *Journal of Affective Disorders* **129**, 126–142.

Newton-Howes G, Tyrer P, Johnson T (2006). Personality disorder and the outcome of depression: meta-analysis of published studies. *British Journal of Psychiatry* **188**, 13–20.

Pan A, Lucas M, Sun Q, van Dam RM, Franco OH, Willett WC, Manson JE, Rexrode KM, Ascherio A, Hu FB (2011). Increased mortality risk in women with depression and diabetes mellitus. *Archives of General Psychiatry* **68**, 42–50.

Pincus HA, Davis WW, McQueen LE (1999). 'Subthreshold' mental disorders. A review and synthesis of studies on minor depression and other 'brand names'. *British Journal of Psychiatry* **174**, 288–296.

Pine DS, Cohen E, Cohen P, Brook J (1999). Adolescent depressive symptoms as predictors of adult depression: moodiness or mood disorder? *American Journal of Psychiatry* **156**, 133–135.

Pull CB, Saunders JB, Mavreas V, Cottler LB, Grant BF, Hasin DS, Blaine J, Mager D, Ustun BT (1997). Concordance between ICD-10 alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI and SCAN: results of a cross-national study. *Drug and Alcohol Dependence* **47**, 207–216.

Rosenberg D, Depp CA, Vahia IV, Reichstadt J, Palmer BW, Kerr J, Norman G, Jeste DV (2010). Exergames for subsyndromal depression in older adults: a pilot study of a novel intervention. *American Journal of Geriatric Psychiatry* **18**, 221–226.

Shah BV, Barnswell BG, Bieler GS (1995). *SUDAAN User's Manual: Software for Analysis of Correlated Data: Release 6.40*. Research Triangle Institute: Research Triangle Park, NC.

Skodol AE, Grilo CM, Keyes KM, Geier T, Grant BF, Hasin DS (2011). Relationship of personality disorders to the course of major depressive disorder in a nationally representative sample. *American Journal of Psychiatry* **168**, 257–264.

Ustün B, Compton W, Mager D, Babor T, Baiyewu O, Chatterji S, Cottler L, Göğüş A, Mavreas V, Peters L, Pull C, Saunders J, Smeets R, Stipec MR, Vrasti R, Hasin D, Room R, Van den Brink W, Regier D, Blaine J, Grant BF, Sartorius N (1997). WHO Study on the reliability and validity of the alcohol and drug use disorder instruments: overview of methods and results. *Drug and Alcohol Dependence* **47**, 161–169.

Ware JJ, Kosinski M, Keller SD (1996). A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical Care* **34**, 220–233.

Wells KB, Stewart A, Hays RD, Burnam MA, Rogers W, Daniels M, Berry S, Greenfield S, Ware J (1989). The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. *Journal of the American Medical Association* **262**, 914–919.

Wiktorsson S, Runeson B, Skoog I, Ostling S, Waern M (2010). Attempted suicide in the elderly: characteristics of suicide attempters 70 years and older and a general population comparison group. *American Journal of Geriatric Psychiatry* **18**, 57–67.

Zimmerman M (1994). Diagnosing personality disorders. A review of issues and research methods. *Archives of General Psychiatry* **51**, 225–245.