Bereavement and the Diagnosis of Major Depressive Episode in the National Epidemiologic Survey on Alcohol and Related Conditions

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ABSTRACT

Objective: Bereavement-related depression is excluded from a diagnosis of major depressive episode (MDE) in *DSM-IV*, unless the syndrome is prolonged or complicated. The objective of this study is to assess the validity of the bereavement exclusion by comparing characteristics of bereavement-related episodes that are excluded from a diagnosis and bereavement-related episodes that qualify for a diagnosis (complicated bereavement) to MDE.

Method: We used data from 2 waves of the National Epidemiologic Survey on Alcohol and Related Conditions (n = 43,093) to compare bereavement-excluded depression and complicated bereavement to MDE with respect to indicators of preexisting risk for psychopathology (antecedent indicators) and indicators of disorder severity measured at baseline and at the study's 3-year follow-up interview (consequent indicators). The primary outcome measure was the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV.

Results: Compared to individuals with MDE, individuals with bereavement-excluded depression had lower risks of preexisting psychiatric disorders (eg, 0.44 lower odds of social phobia, $P = .006$), fewer depressive episodes (recurrence rate 0.37 times lower, $P < .001$), less psychosocial impairment ($P < .001$), a 0.18 times lower odds of seeking treatment ($P < .001$), and a lower risk of psychiatric disorders during a 3-year follow-up period. Unexpectedly, this same pattern of differences was observed between individuals with complicated bereavement and MDE.

Conclusions: Despite the presence of a clinically significant depressive episode, bereavement-excluded depression is in many ways less indicative of psychopathology than MDE. However, complicated bereavement was more similar to bereavement-excluded depression than to MDE. We therefore question whether the *DSM-IV* criteria validly distinguish between nondisordered loss reactions (bereavement-excluded depression), pathological loss reactions (complicated bereavement), and nonloss-related MDE.

J Clin Psychiatry 2012;73(2):208–215

Submitted: *February 25, 2010; accepted October 25, 2010.*
Online ahead of print: *August 23, 2011 (doi:10.4088/JCP.10m06080).*
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DSM-IV-TR excludes individuals experiencing "an expectable and culturally sanctioned response to a particular event, for example, the death of a loved one"[1(p. xxxi)] from receiving a psychiatric diagnosis. This rule is incorporated into the diagnostic criteria for major depressive episode (MDE) by excluding syndromes of short duration that occur in the context of bereavement.[2–4] *DSM-IV* also recognizes that some depressive episodes following a loss are sufficiently extreme that they are pathological and therefore provides for an exception to this exclusion.

There is emerging evidence that depression following bereavement does not differ from depression that is unrelated to bereavement (or other types of stressors).[5–8] There is also evidence that bereavement-related depression improves following antidepressant and psychotherapeutic treatments,[9–12] suggesting a clinical benefit to assigning a diagnosis of MDE even if it occurs in the context of bereavement. It is therefore important to clarify the ambiguous status of bereavement vis-à-vis the diagnosis of depression.

Accordingly, this study investigates the diagnostic *exclusion* for bereavement-related depression, as well as the *exception* to this exclusion. We compare individuals with depression who are excluded from a diagnosis of MDE because of bereavement ("bereavement-excluded depression") to individuals who qualify for a diagnosis of MDE despite their depression occurring in the context of bereavement ("complicated bereavement") and to individuals with MDE that is unrelated to bereavement. We use as comparators 2 types of indicators of psychopathology: (1) antecedent indicators[13] of pre-existing vulnerability to psychopathology (eg, family history, prior psychiatric disorders) and (2) consequent indicators of clinical course (eg, recurrence risk).[14] The expectation, based on the *DSM-IV* criteria, is that individuals with bereavement-excluded depression would score lower on each of the antecedent and consequent indicators because their depression would be more indicative of nondisordered sadness than of MDE. In contrast, individuals with complicated bereavement are expected to score similarly on the disorder indicators as those with MDE.

METHOD

Study Sample

Data for this analysis come from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a 2-wave, nationally representative household survey conducted by the National Institute on Alcohol Abuse and Alcoholism.[15,16] The wave 1 sample included 43,093 adult participants. The wave 2 survey, conducted approximately 3 years later, included 39,959 of the wave 1 participants. The combined response rate for both waves was 70.2%.[17]

Measures

Lifetime MDE was assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS).[18] The AUDADIS

Clinical Points

- Depressive episodes following bereavement are excluded from a *DSM-IV* diagnosis unless they are prolonged or complicated.
- In a population-based sample, individuals with bereavement-related depression had fewer external indicators of psychopathology than individuals with depression that was unrelated to bereavement.
- There was no evidence to support the diagnostic distinction between complicated bereavement and bereavement not identified as complicated.

is a fully structured diagnostic interview administered by trained nonclinician interviewers.[19–21] The AUDADIS algorithm for MDE requires ≥ 5 clinically significant symptoms of depression occurring during a 2-week period of sadness or anhedonia.[22] If participants reported symptoms of an MDE that began to happen just after someone close to them died, a diagnosis of MDE is excluded; we classified these participants in the bereavement-excluded depression group (unless they had the "complicated" features described below).

Depression occurring in association with the loss of a loved one qualifies for a *DSM-IV* diagnosis if it persisted for 2 months or more or exhibited marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychomotor retardation, or psychotic symptoms, which we term *complicated bereavement*. This is not what has been referred to as either "complicated grief" or "prolonged grief," which is a separate condition that is phenomenologically distinct from depression.[23–25]

Except for the duration requirement, there is no guidance in *DSM-IV* for operationalizing the criteria for complicated bereavement. For example, it is unclear how marked functional impairment differs from the generic requirement of clinically significant distress or impairment in social or occupational functioning.[26,27] We defined complicated bereavement as a depressive episode following the loss of a loved one that either persisted for at least 2 months or was accompanied by one of the following symptoms: marked functional impairment, suicidal ideation, or psychomotor retardation. We considered marked functional impairment to be present if respondents endorsed all 3 of the NESARC's impairment items that reference functional impairment ("arguments or friction with friends, family, people at work," "trouble doing things you were supposed to do," and "couldn't do the things you usually did or wanted to do"). Suicidal ideation was based on endorsement of suicide attempt, thoughts of suicide, desire to die, or frequent thoughts of one's own death. Psychomotor retardation was based on the item "move or talk MUCH more slowly than usual, most days for at least 2 weeks." We did not operationalize 2 of the criteria for complicated bereavement: psychotic symptoms, which were not assessed in the NESARC, and morbid preoccupation with worthlessness, which we interpret to imply a higher degree of severity than the general MDE criterion of "feelings of worthlessness." The NESARC assessed symptoms of depression that were present during participants' worst period of depression. Accordingly, the diagnoses that were compared in the current study refer to participants' worst or (for single-episode cases) only lifetime episode.

Antecedent Indicators of Psychopathology

A high family history loading of depression and alcoholism was defined as being in the top decile of a measure indexing the proportion of first- and second-degree relatives with each disorder, weighted by their degree of genetic relatedness to the respondent.[20,28] History of panic disorder, generalized anxiety disorder, social phobia, and alcohol dependence prior to the first onset of depression was determined by comparing the lifetime histories and ages at onset for each of these disorders to the age at first depression onset. *DSM-IV* personality disorders were assessed on a lifetime basis as described previously.[29]

Consequent Indicators of Psychopathology

The number of lifetime depressive episodes was assessed by a single item asking about the number of episodes lasting at least 2 weeks that were separated by a 2-month period of improvement in mood. Psychosocial impairment was defined as the number of difficulties that respondents associated with their depression, not counting those items that were used in the definition of marked functional impairment described above. Treatment seeking was based on participants' reports of seeking professional help to improve one's mood, being hospitalized, seeking emergency room care, or being prescribed medications for mood. Finally, we investigated the risk of MDE, panic disorder, generalized anxiety disorder, social phobia, and alcohol dependence in interval between the wave 1 and wave 2 interviews.

Statistical Analysis

The analyses of antecedent indicators involved comparisons of individuals with complicated bereavement and with bereavement-excluded depression to individuals with MDE. Comparisons were made using multinomial logistic regression models in which the dependent variable was the type of diagnosis, and antecedent indicators were entered as predictors.

In contrast, regression models for consequent indicators treat the consequent indicators as dependent variables and the diagnosis as predictor. Analyses of consequent indicators were conducted by fitting regression models for the number of lifetime depressive episodes (using Poisson regression), mean impairment scores (using linear regression), the likelihood of treatment seeking (using logistic regression), and the risk of psychiatric disorders at wave 2 (using logistic regression). Poisson regression coefficients, when exponentiated, indicate differences in the recurrence rate of depressive episodes between individuals with MDE and those with either complicated bereavement or bereavement-excluded depression. Linear regression coefficients indicate

mean differences in psychosocial impairment scores across groups. Finally, odds ratios obtained from the logistic regression models indicate differences in the odds of treatment seeking and odds of wave 2 disorders across groups.

The analysis sample comprised participants with a lifetime history of depressive symptoms that are required for a *DSM-IV* diagnosis of MDE. We made comparisons in this sample between individuals with MDE, complicated bereavement, and bereavement-excluded depression. However, we included all NESARC participants in the analyses of wave 2 disorders, wherein we added a fourth comparison group: individuals with no lifetime history of depression.

We conducted the analyses using SUDAAN,[30] which adjusts variances and point estimates for the multistage sampling design and differential selection probabilities used to ascertain the NESARC sample. Missing data on wave 1 covariates (approximately 1% of the sample) and on psychiatric disorders among wave 2 nonparticipants (approximately 20% of the sample) were imputed using the method of multiple imputation as implemented in IVEware,[31] with adjustments made for the complex sampling design of the NESARC.[32]

Table 1. Demographic Characteristics of the National Epidemiologic Survey on Alcohol and Related Conditions Sample (n = 43,093), and Characteristics of Participants With Lifetime Major Depressive Episode (MDE), Complicated Bereavement, and Bereavement-Excluded Depression[a]

Characteristic	Sample Distribution, % (n)	MDE, % (n)	Complicated Bereavement, % (n)	Bereavement-Excluded Depression, % (n)
Total	100 (43,093)	18.3 (7,864)	1.2 (566)	0.5 (196)
Sex				
Male	47.9 (18,518)	13.2 (2,437)	0.9 (179)	0.3 (57)
Female	52.1 (24,575)	23.0 (5,426)	1.5 (387)	0.6 (139)
Race/ethnicity				
White	70.9 (24,507)	20.0 (5,072)	1.2 (304)	0.5 (128)
Black	11.1 (8,245)	13.5 (1,152)	1.6 (137)	0.6 (39)
Other	18.0 (10,341)	14.5 (1,640)	1.2 (126)	0.3 (30)
Age				
18–29	21.8 (8,666)	18.5 (1,636)	1.2 (116)	0.4 (40)
30–44	30.9 (13,382)	19.4 (2,620)	1.5 (189)	0.5 (57)
45–64	31.1 (12,840)	21.1 (2,727)	1.2 (172)	0.5 (58)
≥ 65	16.2 (8,205)	10.5 (881)	0.9 (89)	0.6 (43)
Marital status				
Married	61.6 (22,081)	16.4 (3,452)	1.2 (259)	0.4 (93)
Separated, widowed, or divorced	17.5 (11,117)	25.0 (2,554)	1.6 (178)	0.6 (57)
Never married	20.9 (9,895)	18.2 (1,857)	1.2 (129)	0.5 (46)
Education				
Less than high school	15.7 (7,849)	17.1 (1,269)	1.4 (122)	0.2 (26)
High school or GED	29.3 (12,547)	17.4 (2,184)	1.4 (189)	0.4 (50)
Some college or higher	55.0 (22,697)	19.1 (4,411)	1.1 (255)	0.6 (121)

[a]Percentages are weighted; *n*'s indicate the actual number of participants averaged across multiple imputed datasets and do not always sum to the total in the first row due to rounding.
Abbreviation: GED = General Education Development.

RESULTS

Prevalence of MDE, Complicated Bereavement, and Bereavement-Excluded Depression

The lifetime prevalence of MDE was 20.0% (95% CI, 19.2%–20.8%; n = 8,626). The majority of cases were unrelated to bereavement (91.5%, n = 7,864) and thus classified as MDE; 6.2% of cases (n = 566) were bereavement-related but qualified for a diagnosis of MDE because of being complicated bereavement; and 2.3% of cases (n = 196) were excluded from a diagnosis because of bereavement. Prevalences of MDE, complicated bereavement, and bereavement-excluded depression are shown according to participant characteristics demographic in Table 1.

Differences in Antecedent Indicators of Psychopathology Between MDE, Complicated Bereavement, and Bereavement-Excluded Depression

Results of multinomial logistic regression models predicting MDE (reference category), complicated bereavement, or bereavement-excluded depression are presented in Table 2. Virtually all of the odds ratios were less than 1, indicating that the antecedent indicators of psychopathology are less likely to precede complicated bereavement and bereavement-excluded depression than they are to precede MDE. For example, a high family history loading of depression (first row of Table 2) was associated with a 0.85 lower odds of complicated bereavement (95% CI, 0.65–1.13) and a 0.81 lower odds of bereavement-excluded depression (95% CI, 0.54–1.21) relative to MDE. Statistically significant associations in Table 2 were observed for a diagnosis of social phobia prior to depression onset, and for lifetime diagnoses of avoidant, obsessive-compulsive, paranoid, and schizoid personality disorders.

Differences in Consequent Indicators of Psychopathology Between MDE, Complicated Bereavement, and Bereavement-Excluded Depression

Relative to individuals with MDE, those with complicated bereavement (rate ratio = 0.52; 95% CI, 0.38–0.70) and bereavement-excluded depression (rate ratio = 0.37; 95% CI, 0.30–0.46) reported fewer depressive episodes over their lifetimes (Table 3). Complicated bereavement and bereavement-related depression were also associated with significantly less psychosocial impairment, and a lower likelihood of seeking treatment, than MDE. Further, individuals with complicated bereavement and bereavement-related depression had a 0.32 (95% CI, 0.25–0.42) and 0.23 (95% CI, 0.14–0.39) lower odds of being prescribed medication for their depression, respectively, than individuals with MDE.

Risks for Wave 2 Psychiatric Disorders

The prevalences of depression, panic disorder, social phobia, and generalized anxiety disorder during the 3-year

Table 2. Associations Between Antecedent Indictors of Psychopathology and Major Depressive Episode (MDE), Complicated Bereavement, and Bereavement-Excluded Depression in the National Epidemiologic Survey on Alcohol and Related Conditions (n = 8,626)[a]

Indicator	Complicated Bereavement (vs MDE), OR (95% CI)	Bereavement-Excluded Depression (vs MDE), OR (95% CI)	χ^2_2	*P*
High family history loading of psychiatric disorder				
Depression	0.85 (0.65–1.13)	0.81 (0.54–1.21)	2.7	.265
Alcoholism	0.83 (0.62–1.11)	0.58 (0.32–1.07)	4.3	.117
Disorder prior to depression onset				
Panic	0.83 (0.47–1.49)	1.43 (0.50–4.05)	0.9	.627
Generalized anxiety	0.72 (0.33–1.57)	0.48 (0.19–1.21)	2.9	.230
Social phobia	0.53 (0.34–0.84)	0.44 (0.20–0.97)	10.1	.006
Alcohol dependence	1.08 (0.76–1.53)	1.07 (0.55–2.06)	0.3	.883
Personality disorder				
Avoidant	0.48 (0.28–0.82)	0.24 (0.08–0.70)	13.4	.001
Obsessive-compulsive	0.62 (0.46–0.84)	0.54 (0.33–0.88)	15.8	< .001
Paranoid	0.59 (0.42–0.82)	0.53 (0.25–1.13)	12.3	.002
Schizoid	0.55 (0.36–0.83)	0.20 (0.07–0.54)	18.6	< .001
Histrionic	0.57 (0.33–1.00)	0.76 (0.26–2.18)	4.2	.123
Antisocial	0.90 (0.59–1.39)	0.50 (0.14–1.81)	1.3	.525

[a]Results from multinomial logistic regression analyses of depression category, with MDE as the reference, adjusting for age, sex, marital status, race/ethnicity, and educational attainment. Odds ratios indicate the likelihood of either complicated bereavement or bereavement-excluded depression, relative to MDE, associated with each antecedent indicator. Each row presents the results from a separate model.
Abbreviation: OR = odds ratio.

Table 3. Associations Between Consequent Indicators of Psychopathology and Major Depressive Episode (MDE), Complicated Bereavement, and Bereavement-Excluded Depression in the National Epidemiologic Survey on Alcohol and Related Conditions (n = 8,626)[a]

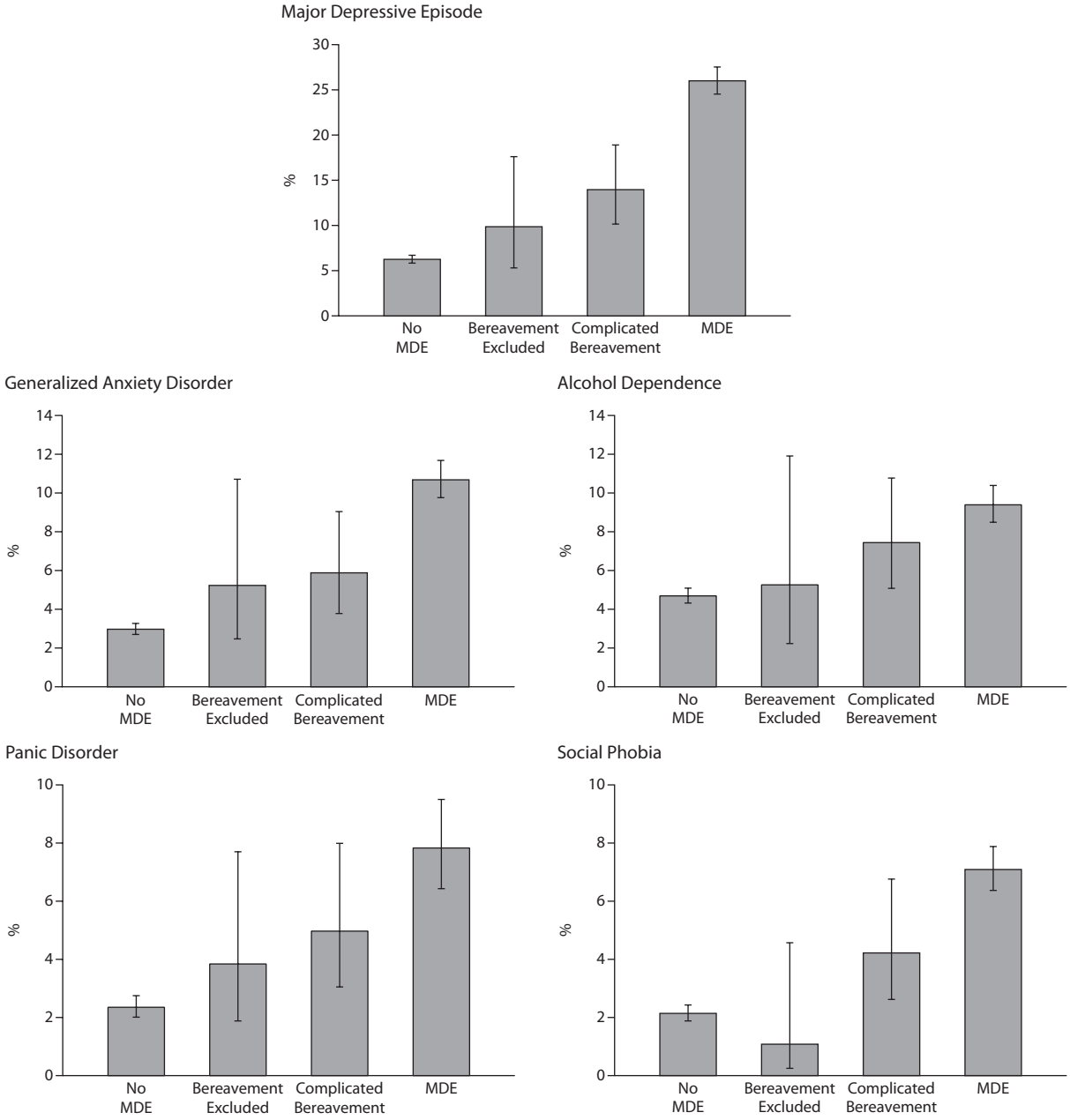
Variable	Complicated Bereavement (vs MDE), Rate Ratio (95% CI)	Bereavement-Excluded Depression (vs MDE), Rate Ratio (95% CI)	χ^2_2	*P*
No. of lifetime depressive episodes[b]	0.52 (0.38 to 0.70)	0.37 (0.30 to 0.46)	103.9	< .001
	Mean Difference (95% CI)	Mean Difference (95% CI)	F_2	
Psychosocial impairment[c]	−0.29 (−0.43 to −0.15)	−0.77 (−0.98 to −0.57)	36.9	< .001
	OR (95% CI)	OR (95% CI)	χ^2_2	
Treatment seeking for depression[d]				
Any treatment	0.32 (0.26 to 0.41)	0.18 (0.12 to 0.30)	144.5	< .001
Sought treatment from mental health professional	0.29 (0.23 to 0.38)	0.15 (0.09 to 0.24)	136.2	< .001
Hospitalized for depression	0.58 (0.36 to 0.95)	0.09 (0.02 to 0.42)	13.8	.001
Visited emergency room for depression	0.56 (0.35 to 0.90)	0.10 (0.02 to 0.58)	13.2	.001
Prescribed medication for depression	0.32 (0.25 to 0.42)	0.23 (0.14 to 0.39)	103.0	< .001

[a]Models predicting consequent indicators adjusting for age, sex, marital status, race/ethnicity, and educational attainment.
[b]Poisson regression model of the number of lifetime depressive episodes. Rate ratios indicate the ratio of number of depressive episodes between individuals with complicated bereavement or bereavement-excluded depression and individuals with MDE.
[c]Linear regression model of psychosocial impairment scores across groups. Regression coefficients indicate mean differences in psychosocial impairment scores between individuals with complicated bereavement or bereavement-excluded depression and individuals with MDE.
[d]Logistic regression models of indicators of treatment seeking. Odds ratios indicate the difference in the odds of seeking treatment for depression between individuals with complicated bereavement or bereavement-excluded depression and individuals with MDE.
Abbreviation: OR = odds ratio.

interval between the wave 1 and wave 2 interviews are shown in Figure 1, with the vertical bars representing disorder status at wave 1. The general pattern that emerges is an increasing risk of disorders, ranging from lowest to highest, among individuals with no lifetime depression at wave 1, bereavement-related depression, complicated bereavement, and MDE.

Logistic regression analyses were then conducted for each disorder (Table 4). As would be expected, individuals without a lifetime history of depression at wave 1 had a substantially lower risk of future disorders compared to individuals with MDE (column 1, ORs ranging from 0.21 to 0.46). Similarly, bereavement-excluded depression was also associated with a lower risk of subsequent depression (OR = 0.33; 95% CI, 0.16–0.65) and other disorders (ORs for bereavement-excluded depression were statistically significant for depression and social phobia). However, contrary to what would be predicted by the *DSM-IV* diagnostic criteria, individuals with complicated bereavement (column 2) also had lower risks for subsequent disorders than individuals with MDE (ORs were statistically significant for 3 of 5 disorders: depression, social phobia, and generalized anxiety disorder). None of the tests comparing the odds ratios for bereavement-excluded depression to the odds ratios for no lifetime depression (fourth column) and for complicated bereavement (fifth column) were statistically significant. Thus, while MDE at wave 1 was associated with an increased risk for psychiatric disorders over a 3-year follow-up interval, this was not true for bereavement-excluded depression at wave 1 nor for complicated bereavement at wave 1.

Figure 1. Prevalence of Psychiatric Disorders During the 3-Year Follow-Up Period Among Participants (n = 43,093) in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) According to Diagnosis Category at the Baseline Assessment[a]



[a]Baseline diagnosis categories on the x-axis are no MDE, bereavement-excluded depression, complicated bereavement, and MDE. The y-axis indicates the percentage of individuals with each disorder during the NESARC follow-up period, assessed at the wave 2 interview.
Abbreviation: MDE = major depressive episode.

DISCUSSION

We sought to assess the validity of the bereavement exclusion in MDE, and theorized that if bereavement-excluded depression represents a loss reaction distinct from other cases of MDE, it would be associated with a lower level of the psychopathology indicators than both complicated bereavement and MDE.

Bereavement-excluded depression was less indicative of underlying psychopathology than MDE on the basis of psychiatric history, lower number of lifetime depressive episodes, lower levels of psychosocial impairment, lower likelihood of treatment seeking, and a reduced risk of subsequent disorders. These results might argue in favor of maintaining the distinction between MDE and bereavement-excluded depression in the diagnostic criteria. However, a problem with this argument is that individuals with bereavement-excluded depression still had a clinically significant depressive episode, which, based on accumulating evidence, may benefit from psychiatric treatment.[9–12] We therefore do not interpret

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Table 4. Odds Ratios (ORs)[a] for Psychiatric Disorders During the 3-Year Follow-Up Period Among Participants in the National Epidemiologic Survey on Alcohol and Related Conditions (n = 43,093) According to Diagnosis Category at the Baseline Assessment

	Diagnosis Category at Baseline			Contrast Between Bereavement-Excluded Depression and no MDE (3 vs 1)		Contrast Between Bereavement-Excluded Depression and Complicated Bereavement (3 vs 2)	
Disorder	(1) No Lifetime Depression (vs MDE), OR (95% CI)	(2) Complicated Bereavement (vs MDE), OR (95% CI)	(3) Bereavement-Excluded Depression (vs MDE), OR (95% CI)	χ^2_1	*P*	χ^2_1	*P*
Depression	0.21 (0.19–0.23)	0.46 (0.32–0.66)	0.33 (0.16–0.65)	1.7	.199	0.3	.373
Panic	0.32 (0.23–0.46)	0.63 (0.36–1.08)	0.52 (0.24–1.13)	1.6	.211	0.2	.686
Social phobia	0.31 (0.26–0.37)	0.59 (0.36–0.97)	0.15 (0.04–0.68)	0.9	.348	2.9	.087
Generalized anxiety	0.29 (0.25–0.33)	0.53 (0.33–0.86)	0.48 (0.22–1.04)	1.7	.191	0.1	.819
Alcohol dependence	0.46 (0.40–0.52)	0.78 (0.51–1.21)	0.60 (0.25–1.43)	0.4	.526	0.3	.575

[a]Odds ratios obtained from separate logistic regression models predicting each disorder, adjusting for age, sex, marital status, race/ethnicity, and educational attainment.

the results of this study to argue against providing professional treatment (psychotherapy, medication, or both) to individuals with clinically significant depressive symptoms that occur after a loss.

Despite the presence of symptoms that invoke the *DSM-IV* exception to the bereavement exclusion, complicated bereavement was rated similarly lower on the antecedent and consequent disorder indicators as was bereavement-excluded depression. Under the current diagnostic framework, the validity of the bereavement exclusion rests in part on the validity of its exception—allowing for a diagnosis to be made for bereavement-related depressions that are extreme. Therefore, if the bereavement exclusion were to be maintained, the exception for complicated bereavement should be strengthened so that cases of complicated bereavement more closely resemble MDE than bereavement-excluded depression.

Finally, the prevalence of bereavement-excluded depression in the NESARC was low in the overall sample (0.5%) and comprised a small proportion of individuals meeting symptom and impairment criteria for depression (2.3%). Though this finding is based on participants' reports of their symptoms during their worst lifetime episode, which are subject to measurement error, it does not support the concern that has been expressed regarding a "massive pathologization of normal sadness"[33(p103)] in epidemiologic studies applying *DSM-IV* criteria.

There are several recent studies on the role of bereavement and other stressors in the diagnosis of MDE. Karam et al[5] observed minimal differences between individuals with bereavement-related versus nonbereavement episodes of depression.[5] Bock et al[34] and Kessing et al[35] also found no differences in preexisting psychiatric vulnerability and in the long-term course of first-onset depression between patients whose depression was preceded by the loss of a loved one, other stressful life events, or no events. In population-based samples, Wakefield et al[7] and Kendler et al[6] found substantially more similarities than differences between individuals with bereavement-related depression and individuals whose depression was related to other types of stressful life events. Corruble et al[36] investigated the severity of depression in a large case-control study of patients who sought treatment for depression. In contrast to the other studies mentioned, Corruble et al[36] found that bereavement-excluded subjects had more severe depression than MDE controls without bereavement.

There are important differences in the designs used and specific questions posed between our study and those just cited. Karam and colleagues' study[5] is most similar to ours, comparing bereavement-related depression to nonbereavement depression in an epidemiologic sample unselected for seeking depression treatment. Kendler et al[6] and Wakefield et al[7] questioned whether or not the bereavement exclusion should be extended to cover other types of events or losses and therefore compared bereavement-related depression to other event-related depression. The studies by Bock et al,[34] Kessing et al,[35] and Corruble et al[36] were based on treatment-seeking samples and may overrepresent severe cases; however, they benefited from standardized interviews using validated scales of depressive symptoms and from diagnoses of depression made by clinicians. In contrast, our study compares the groups specifically referenced in *DSM-IV* (bereavement-related depression that is excluded from a diagnosis, bereavement-related depression that qualifies for a diagnosis—complicated bereavement, and MDE).

Limitations

Our study is based on the framework proposed by Robins and Guze,[14,37–39] which posits that the validity of the diagnostic criteria can be established on the basis of phenomenological coherence and correlations with external indicators of psychiatric illness. Although we included a wider range of diagnostic indicators than Robins and Guze originally proposed, their approach to validation remains an indirect one. There are also alternative explanations for differences between groups on some of the diagnostic indicators used. For example, differences in rates of treatment seeking may be more reflective of cultural biases toward ignoring or normalizing one's own depressive symptoms in the context of a recent loss than they are of differences in the pathological nature of depression.

There are limitations in our assessment of complicated bereavement. We were unable to implement the exceptions for morbid preoccupation with worthlessness and psychotic symptoms, and as a consequence, some cases

of complicated bereavement were incorrectly classified as bereavement-excluded depression. Therefore, our analyses could underestimate the true differences between groups (because presumably more "severe" cases of depression were categorized along with the "less severe" group). Due to the skip patterns used in the NESARC interview, we could not determine the presence of the "complicated" symptoms for all cases of bereavement-related depression. Further research is needed using prospective follow-up and standardized clinical interviews to capture the extent of phenomenological variation in depressive episodes associated with the loss of a loved one, other stressful life events, or no identifiable stressors.

Finally, our comparisons were between different types of depressive episodes that were regarded as the participant's worst episode (or, for single-episode cases, the participant's only episode). The validity of these comparisons rests on the accuracy of participants' recall of the timing of their depressive episodes relative to the experience of a loss, which may weaken over time.[40,41] We also could not investigate the patterns of diagnostic indicators for different episodes in multiepisode cases, nor establish the temporality of all diagnostic validators with respect to the participant's worst episode.

CONCLUSIONS

Bereavement-excluded depression is in many ways less indicative of psychopathology than MDE, but so is complicated bereavement. Our results showed marked differences in the magnitude of disorder indicators between individuals with MDE and those with bereavement-excluded depression and complicated bereavement. However, the same pattern of differences that we observed between bereavement-excluded depression and MDE existed between complicated bereavement and MDE, and there were no detectable differences in disorder indicators *between* bereavement-excluded depression and complicated bereavement.

One interpretation of these findings, as explained above, is that bereavement-excluded depression should continue to be distinguished from MDE. This interpretation assumes maintaining the current diagnostic framework that has a bereavement exclusion and a complicated bereavement exception. However, our results suggest that the *DSM-IV* criteria cannot differentiate between nondisordered bereavement reactions and bereavement reactions that evolve into a psychiatric disorder. This is not surprising, given that psychiatric nosology since publication of *DSM-III* has been designed to be "theory neutral"[42] and rejects classifying disorders based on their supposed causes.

Therefore, an alternative conclusion is that the exclusion-exception framework should be abandoned and the diagnosis of MDE made solely based on symptoms, duration, and impairment, without regard to environmental precipitants. Doing so avoids the need to distinguish between episodes that are "understandable reactions to stressors"[43(p1847)] and episodes that are pathological because they are disproportionate reactions, which requires making causal attributions for an individual's symptoms—ie, determining that the *content* of the symptoms is directly connected to a loss.[44–46]

For example, it is not simply the presence of suicidal ideation that currently separates MDE from bereavement; rather, the suicidal ideation must consist of "thoughts of death other than the survivor feeling that he or she would be better off dead or should have died with the deceased person;"[1(p741)] similarly, the psychotic symptoms that separate MDE from bereavement include "experiences other than thinking that he or she hears the voices of, or transiently sees the image of, the deceased person."[1(p741)] Therefore, the bereavement exclusion in MDE is contradictory with our phenomenologically based nosology that purports not to incorporate assumptions about causal mechanisms into the diagnostic criteria.[1]

Emerging evidence on the role of stressful life events in MDE, as well as supporting evidence for the role of stressors in neurobiological models of depression,[47] suggests the possibility of advancing toward an etiologically based psychiatric nosology. Until then, however, incorporating hypothesized causes of disorders into the diagnostic criteria risks imposing theoretical and methodological challenges on research that aims to investigate those hypothesized causes.

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Potential conflicts of interest: **Dr Fava** has received research support from Abbott, Alkermes, Aspect Medical Systems, AstraZeneca, BioResearch, BrainCells, Bristol-Myers Squibb, Cephalon, CeNeRx BioPharma, Clinical Trials Solutions, Clintara, Covidien, Eli Lilly, EnVivo, Euthymics Bioscience, Forest, Ganeden Biotech, GlaxoSmithKline, Icon Clinical Research, i3 Innovus/Ingenix, Johnson & Johnson Pharmaceutical Research & Development, Lichtwer Pharma GmbH, Lorex, National Alliance for Research on Schizophrenia & Depression (NARSAD), National Center for Complementary and Alternative Medicine, National Institute of Drug Abuse, National Institute of Mental Health, Novartis AG, Organon, PamLab, Pfizer, Pharmavite, Photothera, Roche, RCT Logic, Sanofi-Aventis, Shire, Solvay, Synthelabo, and Wyeth-Ayerst; has received advisory/consulting fees from Abbott, Affectis AG; Alkermes, Amarin Pharma, Aspect Medical Systems, AstraZeneca, Auspex, Bayer AG, Best Practice Project Management, BioMarin, Biovail, BrainCells, Bristol-Myers Squibb, CeNeRx BioPharma, Cephalon, Clinical Trials Solutions, CNS Response, Compellis, Cypress, DiagnoSearch Life Sciences (P), Dainippon Sumitomo Pharma, Dov, Edgemont, Eisai, Eli Lilly, ePharmaSolutions, EPIX, Euthymics Bioscience, Fabre-Kramer, Forest, GenOmind, GlaxoSmithKline, Grunenthal GmbH, i3 Innovus/Ingenis, Janssen, Jazz, Johnson & Johnson Pharmaceutical Research & Development, Knoll, Labopharm, Lorex, Lundbeck, MedAvante, Merck, MSI Methylation Sciences, Naurex, Neuronetics, NextWave, Novartis AG, Nutrition 21, Orexigen Therapeutics, Organon Otsuka, PamLab, Pfizer, PharmaStar, Pharmavite, PharmoRx Therapeutics, Precision Human Biolaboratory, Prexa Pharmaceuticals, Puretech Ventures, PsychoGenics, Psylin Neurosciences, Rexahn, Ridge Diagnostics, Roche, RCT Logic, Sanofi-Aventis, Sepracor, Servier Laboratories, Schering-Plough, Solvay, Somaxon, Somerset, Sunovion, Supernus, Synthelabo, Takeda, Tal Medical, Tetragenex, TransForm, Transcept, and Vanda; has received speaking/publishing fees from Adamed, Advanced Meeting Partners, American Psychiatric Association, American Society of Clinical Psychopharmacology, AstraZeneca, Belvoir Media Group, Boehringer Ingelheim GmbH, Bristol-Myers Squibb, Cephalon, CME Institute/Physicians Postgraduate Press, Eli Lilly, Forest, GlaxoSmithKline, Imedex, Massachusetts General Hospital (MGH) Psychiatry Academy/Primedia, MGH Psychiatry Academy/Reed Elsevier, Novartis AG, Organon, Pfizer,

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PharmaStar, United BioSource, and Wyeth-Ayerst; has equity holdings in Compellis; receives copyright royalties for the MGH Cognitive & Physical Functioning Questionnaire, Sexual Functioning Inventory, Antidepressant Treatment Response Questionnaire, Discontinuation-Emergent Signs & Symptoms, and SAFER; and has a patent application for a combination of azapirones and bupropion in major depressive disorder. Dr Fava also has a patent for Sequential Parallel Comparison Design (SPCD) and a patent for research and licensing of SPCD with RCT Logic; Lippincott, Williams & Wilkins; and World Scientific Publishing. In the past 3 years, **Dr Smoller** has consulted to Eli Lilly, Herman Dana Trust, and RTI International. **Drs Gilman**, **Breslau**, **Trinh**, and **Murphy** report no financial or other conflicts of interest related to the subject of the article.

Funding support: This work was supported in part by National Institutes of Health grants MH087544, DA080887, and MH66057.

Previous presentation: A prior version of this work was presented at the 42nd annual meeting of the Society for Epidemiologic Research; June 23–26, 2009; Anaheim, California.

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