RESEARCH REPORT

Validity of the bereavement exclusion criterion for the diagnosis of major depressive episode

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Since the publication of DSM-III in 1980, the official position of American psychiatry has been that the presence of bereavement is an exclusion criterion for the diagnosis of a major depressive episode (MDE). However, the empirical validity of this exclusion has not been well established. As DSM-V is now being planned, it is timely to reexamine the bereavement exclusion, particularly in the light of new evidence since the last reviews of this subject. This paper evaluates the relative validity of two competing hypotheses: 1) the bereavement exclusion for the diagnosis of MDE is not valid because, using validating criteria, bereavement related depression (BRD) within the first two months after the death of a loved one resembles non-bereavement related depression (SMD); 2) the bereavement exclusion for the diagnosis of MDD is valid because, using validating criteria, BRD within the first two months after the death of a loved one does not resemble SMD. The prevailing evidence more strongly supports Hypothesis 1 than Hypothesis 2. Thus, the bereavement exclusion for the diagnosis of MDE may no longer be justified.

Key words: Major depression, bereavement, DSM-V, diagnostic validators

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Consider the following cases:

1) *Allen is a 49 year old man who has been sad and unhappy for the past 5 weeks. In addition, he has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of being fired from his job of 25 years due to down-sizing of the work force.*

2) *Beth is a 49 year old woman who has been sad and unhappy for the past five weeks. In addition, she has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of her husband filing for divorce.*

3) *Cole is a 49 year old man who has been sad and unhappy for the past five weeks. In addition, he has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms seemed to come out of the blue when everything was going well.*

4) *Diane is a 49 year old woman who has been sad and unhappy for the past five weeks. In addition, she has lost interest in normally enjoyable activities, sleeps four hours less than usual, has lost 10 pounds, has difficulty concentrating, limited energy, and no zest for life. These symptoms began within days of her husband's death from pancreatic cancer.*

Now consider the following question: which of the four individuals described above does not have a major depressive episode (MDE)? If you answered "Diane", you are correct according to the DSM-III, DSM-III-R, DSM-IV and DSM-IV-TR. But is Diane's depressive syndrome really different from the others? Is it less likely to be associated with impaired health or functioning, or with a chronic or recurrent course than the others? Is she less deserving of treatment or less likely to respond to standard treatments for MDE? This paper examines the available empirical data to help answer these important questions. The answers will help determine the validity of the DSM's nosological convention to isolate recent bereavement as the one life event that may exclude the diagnosis of MDE.

Since publication of DSM-III in 1980, the official position of American psychiatry has been that the presence of bereavement is an exclusion criterion for the diagnosis of MDE. However, the empirical validity of this exclusion has not been established. In addition, the other major psychiatric nosological system, the ICD-10, does not recognize this exclusion (2). According to the ICD-10, all of the cases described above would be diagnosed with MDE. As work toward DSM-V has begun, it is timely to re-examine the DSM's bereavement exclusion, particularly in the light of new evidence since the last reviews of this subject (3-5).

According to DSM-IV-TR, the "bereavement" exclusion criterion "can be used when a focus of attention or treatment is a *normal* reaction to the death of a loved one". The manual further states that a full depressive syndrome is a *normal* reaction to such a loss, with feelings of depression and such associated symptoms as poor appetite, weight loss and insomnia. To more carefully differentiate bereavement from MDE, the DSM-IV-TR identifies several features more characteristic of one than the other: 1) a bereaved individual typically regards the depressed mood as "normal", although the person may seek professional help for relief of associated symptoms such as insomnia or anorexia; 2) the diagnosis of MDE is generally not given

unless the symptoms are still present at least 2 months after the loss; and 3) MDE should be considered in the presence of certain symptoms that are not characteristic of a "normal" grief reaction, such as *guilt* about things other than actions taken or not taken by the survivor at the time of the death, *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, morbid preoccupation with *worthlessness*, marked *psychomotor retardation*, prolonged and marked *functional impairment*, and *hallucinatory experiences* other than thinking that he or she hears the voice of, or transiently sees the image of, the deceased person.

We recently reviewed the literature bearing on the question "Does bereavement related depression (BRD) resemble standard, non-bereavement related depression (SMD)?". We concluded that the predominance of the published literature supported the similarity of BRD to SMD (1). Since most of the studies reviewed did not describe or follow individuals with BRD specifically within the first two months of bereavement (the period of time the DSM-IV-TR demarcates as excluding the diagnosis of MDE), we were unable to draw definitive conclusions about the validity of the bereavement exclusion. In the present paper, we focus on evaluating the validity of the bereavement exclusion by examining published data on predictors, course, clinical characteristics, consequences, biology and treatment of depression syndromes occurring within the first two months of bereavement. The central question addressed is: "Is BRD occurring within the first two months following the death of a loved one the same as or different from SMD on key validators?".

METHODS

We evaluated the relative validity of two competing hypotheses: 1) the bereavement exclusion for the diagnosis of MDE is not valid because, using validating criteria, BRD within the first two months after the death of a loved one resembles SMD; 2) the bereavement exclusion for the diagnosis of MDD is valid because, using validating criteria, BRD within the first two months after the death of a loved one does not resemble SMD.

We examined three classes of potential validators (6,7), with subclasses as follows: 1) antecedent validators (family studies; past history of MDE; demographic factors); 2) concurrent validators (health; social support; associated clinical features; biological variables); 3) predictive validators (diagnostic consistency over time; treatment outcome).

Articles were located with Medline searches up to December 2006, English language only. Exploded searches, using "grief or bereavement" and "depression" as key words, were employed. Bibliographies of located articles were searched for additional studies. Publications were selected if they included individuals diagnosed with MDE or meeting threshold levels for clinically significant depression based on validated depression interviews or scales. One or more systematic comparison groups were included in most of the selected studies. If the same sample was presented in more than one publication, only the most relevant or inclusive one was considered. The only exception to this general rule is in the categories of family and past history studies, where two different studies from Paula Clayton's series of widowhood investigations were included because of the different control groups used (8,9).

While it would have been ideal to conduct a formal meta-analysis of the literature, this was not feasible. Very few primary reports provided confidence intervals (or standard errors) of the estimates or primary data (i.e., contingency tables or correlations).

RESULTS

Antecedent validators

Two of the most consistently noted predictors of SMD are family history (10) and past personal history of SMD (11). The demographic factors most strongly associated with risk for SMD are female gender and young adult age (12).

Of the two studies that evaluated family history and past personal history of MDE, one supported Hypothesis 1 (that the bereavement exclusion is not valid because early BRD resembles SMD) (13), and one supported Hypothesis 2 (that the bereavement exclusion is valid because early BRD does not resemble SMD) (14).

One of four studies that evaluated gender supported Hypothesis 1 (15) and three did not (3,9,16). In contrast, each of the three studies that evaluated age provided support for Hypothesis 1 (3,5,15).

Overall, then, it does not appear that the antecedent validators of family and past personal histories of MDE or gender or age provide consistent evidence for or against the bereavement exclusion.

Concurrent validators

A number of environmental, clinical and biological features characterize SMD. Two important concurrent risk factors for SMD are poor physical health (17) and low social support (18). Some of the clinical features that are associated with SMD are characteristic symptoms (19), dysfunction and disability (20), and suicidality (21). Biological factors that often are seen in SMD include adrenocortical dysregulation (22), immune dysfunction (23) and sleep architecture disruption (24).

In studies assessing BRD within two months of the death of a loved one, BRD was associated with poor health (25,26) and low social support (25,27,28). In addition, compared to bereaved individuals without BRD, those with BRD had significantly more suicidal thoughts, feel-

ings of worthlessness and psychomotor disturbances, suggesting that these symptoms are not common manifestations of normal early bereavement (3,29-31). Instead, these symptoms are similar to those found in hospitalized patients with SMD (32). Thus, BRD resembles SMD more than it resembles "uncomplicated bereavement".

The four studies that evaluated biological parameters within the first two months of bereavement mostly supported the similarity of BRD with SMD. Two found immunologic changes in BRD to resemble those reported in SMD (33,34). Importantly, in the former study, immunologic changes were seen in bereaved women with BRD but not in a matched bereaved control group without MDE. One study in adults with BRD (33) and another in children with BRD (32) found non-suppression on the dexamethasone suppression test (DST) in recently bereaved individuals to correlate with depression symptom severity, while one study found DST non-suppression more associated with anxiety than with depressive symptoms in recently bereaved widows and widowers (35). In no case does it appear that DST non-suppression is commonly seen in uncomplicated bereavement.

Predictive validators

One of the hallmark characteristics of SMD is that it tends to be a chronic and/or recurrent illness (20,36-39). Another is that about 50-70% individuals with SMD respond to antidepressant medications (40,41).

Each of the studies that assessed BRD at or within two months of bereavement found that the rate of persistence of BRD was high and virtually identical to persistence rates of SMD (5,13,25,31,42-45). The only treatment study focusing exclusively on individuals who met criteria for MDE during the first two months of bereavement found a high rate of response to antidepressant medication, similar to that seen with SMD (46).

DISCUSSION

Normal grief is a highly dysphoric state, characterized by intense sadness, a variable mix of other negative emotions (e.g., anxiety, guilt, anger) and a tendency to turn inward and withdraw from the outside world. The fact that these symptoms resemble those of MDE has caused confusion regarding whether and when MDE should be diagnosed in a bereaved person. However, people experiencing normal grief, even when very intense, often have a full range of affect and are capable of warm joyous feelings, even if transient. Dysphoria often occurs in waves of "pangs of grief". Most do not meet criteria for MDE. These observations raise questions about the validity of excluding all people bereaved less than two months from the diagnosis of MDE. Furthermore, accumulating evidence suggests that early treatment of depression may be vitally important. For example, a recent study demonstrated that both lack of a partner and time in depression were significant predictors of suicidality among people meeting criteria for MDE (21). These findings, along with data indicating that early depression responds well to antidepressant medication, underscore the fact that the validity of the bereavement exclusion for the diagnosis of MDE is not an academic issue.

We reviewed studies assessing antecedent, concurrent and predictive validators. Although none of these studies was designed specifically to answer the question of whether the bereavement exclusion is valid, their data do at least address its validity empirically, albeit indirectly. We attempted to organize the available information to evaluate two competing hypotheses: Hypothesis 1 (that the bereavement exclusion is not valid because early BRD resembles SMD) and Hypothesis 2 (that the bereavement exclusion is valid because early BRD does not resemble SMD). Table 1 summarizes the results of this empirical literature review from the perspectives of these two hypotheses.

As might be expected given a range of methodological differences across the studies, results were not entirely consistent. However, a clear and relatively impressive trend is observed. Hypothesis 1 receives considerably more empirical support than Hypothesis 2. From the perspective of multiple validators, early BRD appears to be closely related to SMD. Like SMD, BRD is particularly frequent in bereaved individuals who are young, have past personal or family histories of SMD, and have poor social supports and compromised health. In addition, BRD has clinical characteristics reminiscent of SMD, including impaired psychosocial functioning, comorbidity with a number of anxiety disorders, and symptoms of worthlessness, psychomotor changes and suicidality. Moreover, the latter symptoms, mentioned in the DSM-IV-TR as unlikely to occur in nor-

Table 1 Summary of evidence for Hypothesis 1 (the bereavement exclusion is not valid because early BRD is similar to SMD) vs. Hypothesis 2 (the bereavement exclusion is valid because early BRD is not similar to SMD)

Antecedent validators	
Family history of MDE	±
Past history of MDE	±
Gender	±
Age	H1
Concurrent validators	
Health	H1
Social support	H1
Clinical features	H1
Immunologic studies	H1
Predictive validators	
Persistence over time	H1
Treatment	H1

BRD - bereavement related depression; SMD - non-bereavement related depression; MDE - major depressive episode; ± - data are inconclusive; H1 - data support Hypothesis 1

mal bereavement, can be long lasting and do not predict which individuals with BRD develop chronic or recurrent depression. BRD also has biological characteristics that reflect similarities with SMD: increased adrenocortical activity and impaired immune function. Like SMD, early BRD is common, long-lasting and recurrent. Finally, BRD appears to respond to antidepressant medication.

One can argue that early BRD is not the same as SMD in that it is often mild, may remit spontaneously, is not self-perceived as an illness, and shares many symptoms with uncomplicated bereavement. But those features often characterize community samples of depressed individuals, as well (37,39,47). The diagnosis of MDE may be difficult to make, especially soon after the death, as many symptoms of normal grief overlap with those of MDE. Nevertheless, all such diagnostic challenges are also present in other instances of MDE and should not mitigate diagnostic precision.

Why should bereavement be singled out as the only stressful life event that excludes the diagnosis of MDE when all other features are present? With all substantial stressors, including the death of a loved person, one may experience the onset or exacerbation of depression (47-50). Thus, a variety of other serious stressors, like divorce (51), illness and disability (52), to name a few, have been found to increase the risk for MDE in vulnerable or sensitive individuals. Kendler et al (53) reported high rates of the onset of MDE following the death of a close relative (OR=16.0), and comparably high rates for several other stressful life events, such as assault (OR=15.0), serious marital problems (OR=12.3) and divorce/break-up (OR=12.3). But in none of these cases, other than death of a loved one, does the presence of the stressor negate the diagnosis of MDE. If someone has met the criteria for MDE for more than two weeks after assault, divorce or myocardial infarct, we do not say that he is not depressed or call his depressive syndrome a "normal stress response"; instead, we make the diagnosis of MDE and consider the most appropriate treatment options (54,55). With one exception, a post-hoc study suggesting that divorce-related depression is similar to SMD but BRD is not (8), it is not clear why bereavement has become the one stressor that negates the diagnosis of MDE (17).

The major limitation of this paper is that so few studies examined depressive syndromes restricted to the first few months after bereavement, the period identified by the DSM to exclude the diagnosis of MDE. The "bereavement exclusion" was instituted to prevent clinicians from diagnosing MDE when the individual was instead experiencing a "normal" grief reaction. Recognizing that true MDE could be triggered by the loss of a loved one, guidelines were given to allow a MDE to be diagnosed following the loss of a loved one if certain features were present: duration of more than two months and/or the presence of specific symptoms characteristic of a true MDE (suicidal ideation other than wishes to join the lost loved one, morbid preoccupation with worthlessness, beyond remorse related to the relationship to the loved one, and psychomotor retardation). Thus, the ideal study to test our hypotheses would simultaneously compare: a) individuals meeting criteria for MDE beginning less than two months after the death of a loved one; b) early bereaved individuals who do not meet criteria for MDE and c) individuals with MDE of similar duration whose onset is unrelated to the death of a loved one. Unfortunately, we found no such studies in the literature. Early BRD, as conceptualized in this paper, is likely a mixture of cases including: those with "bereavement" as defined by the DSM-IV; those that start out with DSM-IV "bereavement" and evolve into true MDE; and others whose onset may precede the actual death of a loved one or be delayed for several months after the death. Although this paper suggests that bereavement-associated MDE is probably quite similar to MDE beginning in other contexts, definitive work clarifying the relationship between "normal grief" and MDE remains to be done.

Several additional caveats are important to note. First, the majority of studies reviewed here dealt with widowhood and included a preponderance of mid-life and older participants. Only two of the studies involved children (losing parents) or adolescents (losing friends to suicide). Data on individuals throughout the life span, experiencing bereavement following loss of different close relationships under a range of circumstances, are needed to fully examine our hypotheses. Second, the primary source of studies included in this paper was a Medline search followed by searching the bibliographies of identified manuscripts. Abstracts, posters, reviews and non-data based chapters were not included. This method may not have captured all relevant information. Third, some subjectivity may have influenced which studies were included and how some of the data have been interpreted. Few of the available studies used structured interviews, and even fewer incorporated the most appropriate control groups to answer our key questions. Only one small study of what might be the most interesting perspective – directly comparing MDE after bereavement with MDE after other kinds of severe events – was identified, and the results of that study support Hypothesis 2. Finally, few studies used control groups ideally suited to test our hypotheses: matched groups of persons with SMD or groups experiencing stressors other than bereavement. With these caveats in mind, our conclusions must be interpreted with caution.

In summary, this paper evaluated studies that bear on the validity of the "bereavement" exclusion for the diagnosis of MDE. Although the definitive study has yet to be completed, the preponderance of available data suggests that excluding recently bereaved individuals from the diagnosis of MDE, when all other symptomatic, duration and functional impairment criteria for MDE are met, may no longer be justified. Given the highly heterogeneous nature of both BRD and SMD, the most propitious conclusion may be that, on average, these two syndromes appear to be closely related. Neither is a true "natural kind", but, with

the very rough kind of syndromal data available, it looks as if these categories are both examples of the same broad syndrome.

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