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## Do reasons for major depression act as causes?

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### Abstract

We make sense of human behavior using reasons, which produce understanding via a subjective empathy-based first-person perspective and causes, which leads to explanations utilizing objective facts about the world assessed scientifically. We evaluate the common sense hypothesis that for episodes of major depression (MD), reasons act as causes. That is, individuals who have highly understandable depressive episodes will have, on average, fewer objective scientifically validated causes than those who have un-understandable episodes. The understandability of a MD as defined by the Diagnostic and Statistical Manual, 4th Edition (DSM IV) experienced in the past year in 630 personally interviewed twins from a population-based registry was rated, with high reliability, from rich contextual information. We predicted, from these understandability ratings, via linear and logistic regression, 12 validated risk factors for MD reflecting genetic and long-term environmental liability. No significant association was observed between 11 of these indices and the understandability of the depressive episode. The only significant finding—higher cotwin risk for MD associated with greater understandability—was opposite that predicted by the reasons-as-causes hypothesis. Our results do not support the hypothesis that reasons for MD act as causes. These findings, unlikely to result from low power, may be explicable from an empirical and/or philosophical perspective. Our results are, however, consistent with ‘the trap of meaning’ hypothesis, which suggests that understanding does not equal explanation and that while reasons may be critical to help us empathize with our patients, they are unreliable indices of objective risk factors for illness.

### Keywords

causes; etiology; major depression; philosophy; reasons

### Introduction

We have two main approaches toward making sense of the behavior of our fellow humans. One approach relies on a first-person subjective perspective and provides *reasons* for behavior. As humans, we are capable of intuiting the reasons for others’ behavior through the process of empathy. Using the terminology adopted by Jaspers<sup>1</sup> (p. 301) such reasons

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#### Conflict of interest

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lead to *understanding*. If a close friend became depressed after a traumatic romantic break-up, we might feel: ‘Oh, of course. He was really in love with her.’ We feel that we understand the origin of his depression.

The second way we comprehend human behavior is by *causes*—that is, objective third-person scientific facts that are established by systematic observation and quantification. For example, studies have consistently found that patients with depression have a threefold increased risk of depression in their relatives.<sup>2</sup> On this basis, we conclude that a positive family history is a contributing cause of major depression (MD). Using Jasper’s terminology, causes lead to *explanation*.

The question that we address in this paper is the relationship between reasons and causes for developing MD. Because understanding how *reasons for MD might act as causes* is so central to this paper, and might seem at first glance odd or abstract, we give two clinical vignettes to ‘ground’ this concept in clinical common sense.

Assume you are evaluating two patients each of whom presents with a depressive syndrome. Like most good clinicians, you carry in your head a list of empirically validated causes of such a presentation including medical disorders (for example, endocrine abnormalities), early environmental exposures (for example, childhood sexual abuse), genetic risk factors and potential psychological vulnerabilities (for example, high levels of neuroticism). Assume that in the early stages of your history taking, patient A tells you that his business recently burnt down with great financial loss and his beloved only child was diagnosed with a potentially fatal childhood cancer. Patient B, whom you know to be a reliable informant, tells you that everything has been going well in her social and family life, and at work, and her depression emerged ‘out of the blue.’ In the terms used in this article, patient A has good reasons to be depressed while patient B does not. That is, at the level of common sense psychology, the depressive episodes of patients A and B appear to be, respectively, quite understandable and rather un-understandable.

Many clinicians would, on hearing the story of patient A, conclude: ‘Yes, it makes sense to me why he became depressed.’ They would assume that the reasons given by this patient for his depression were causes that both ‘made sense’ to them as humans *and* constituted a causal explanation that could be used to guide further evaluation and treatment. Given that they felt they had a good explanation for the episode, they would not spend much further effort pursuing, by history or laboratory tests, other potential causes for this depressive episode. Furthermore, sensing that the depression arose understandably from external stressors, many clinicians might be willing to take a ‘watch and wait’ approach rather than developing a more aggressive treatment plan. By contrast, the workup would be more thorough for patient B because without good reasons for being depressed there ought to be some good causes to be found. Without a good psychological explanation for the emergence of the depression, an active pharmacological treatment approach would more likely be adopted.

### Goals of this paper

The question that we address in this paper is the relationship between reasons and causes for developing MD. More specifically, we evaluate two hypotheses about this relationship: the *reasons are causes* and the *trap of meaning* hypotheses. The above clinical vignettes illustrate the implications of the ‘common-sense’ hypothesis that *reasons are causes*. An unambiguous prediction of this hypothesis is that, on average, individuals with many reasons for developing MD will have fewer causes. That is, in a group of depressed patients, we will observe a robust inverse relationship between the degree of understandability of their MD (which reflects the number and plausibility of their reasons for developing

depression) and the presence of objective causes for MD (for example, personality, genetic loading and exposure to early environmental adversities).

By contrast, our alternative *trap of meaning* hypothesis assumes little to no relationship between reasons and causes. That is, while the reasons patients give us for the emergence of their disorders may help us to empathize with them and improve our emotional relatedness, they actually tell us little about the objective causes of their illness. A recent article about the trap of meaning<sup>3</sup> forcefully argued that physicians do a disservice to their patients by assuming that understandable symptoms do not need further diagnostic evaluation or treatment. Specifically, the trap of meaning hypothesis predicts that in a group of depressed patients, little or no relationship would be found between the degree of understandability of their depressive episode and the presence of objective causes for MD as determined by their personality, their genetic loading and their exposure to early environmental adversities.

In this article, we evaluate the ‘reasons-as-causes’ versus ‘trap of meaning’ hypotheses for MD by examining detailed interviews with 630 twins who experienced an episode of MD in the last year, from a longitudinally assessed population-based registry. These interviews contained rich contextual information that permitted us to rate, with high reliability, the level of understandability (LOU) of their episodes. Furthermore, we have for this cohort detailed information about a range of empirically validated genetic and environmental indices of risk for MD. How would these causes for being at high risk for MD relate to the reasons for their current episode as reflected in our measures of understandability?

## Materials and methods

### Sample and diagnostic assessments

Participants derive from two inter-related investigations in Caucasian twin pairs in VATSPSUD,<sup>4</sup> a sample ascertained from a population-based twin register in the Commonwealth of Virginia. Female–female (FF) twin pairs, born 1934–1974, became eligible if both members responded to a mailed questionnaire in 1987–1988, the response rate to which was ~64%. This sample was interviewed four times over 10 years, with cooperation rates ranging from 85 to 92%. Male–male and male–female (MMMMF) pairs (born 1940–1974) were ascertained directly from registry records by a phone interview with a response rate of 72%. The second interview wave, conducted up to 5 years later, had an 83% response rate. The mean (s.d.) age and years of education of the twins at the first FF (FF1) and second MMMF (MM2) interview were 29.3 (7.7), 13.5 (2.1) and 37.0 (9.1), 13.6 (2.6), respectively. The FF1 and MM2 interviews were completed largely face-to-face while the other interview waves were conducted mostly by telephone. Signed informed or verbal consent was, respectively, obtained before all face-to-face and telephone interviews.

At each interview, we assessed the occurrence over the last year of 14 individual symptoms, representing the disaggregated nine ‘A criteria’ for MD in DSM-IV. For each symptom, we eliminated responses arising from physical illness or medication. The respondents aggregated their symptoms over the last year into co-occurring syndromes reporting months of onset and remission. The diagnosis of MD was made using DSM-IV criteria without the bereavement exclusion. Respondents were asked to report their ‘worst’ episode in the last year. It was that episode on which we focused in our review.

This project began by LJH and KSK together designing a simple scale (Table 1) that assessed the understandability of the depressive episode based on a review of the detailed contextual information available from these interviews. LJH then reviewed and prepared vignettes for all cases from the MM2 and FF1 interviews that met criteria for one or more episodes of MD in the past year with the goal of rating the understandability of the

depressive episode. These interviews were very detailed and included a descriptive summary by the interviewer of the nature, context and key findings from the interview. Interview sections that were consulted included: (i) the subject's determination as to whether the worst MD episode came 'out of the blue' or was attributed to something that happened, and if the latter, a description of what happened; (ii) a range of relationship and social support items, including quality of relationships with spouse/partner, children, other relatives and friends; number of confidants (and whether spouse/partner was one); and degree of involvement in clubs/organizations; (iii) employment status and work difficulties; (iv) financial status and financial problems; (v) health status and any difficulties; (vi) an extensive list of 15 categories of personal and network stressful life events (SLEs) that occurred in the last year and were dated to the nearest month, with a focus in our review of those that occurred during or shortly before the month of onset of the worst depressive episode of that year. In the MM2 but not FF1 interview, the interviewer coded every SLE on a four-point scale of long-term contextual threat.<sup>5</sup>

Table 2 contains examples of the vignettes prepared by LJH—two for each category. Some vignettes were randomly selected for inter-rater reliability trials. In the MM2 sample, 95 cases were jointly rated and the resulting weighted  $\kappa^6$  was +0.89 (95% confidence interval = 0.85–0.94). We also jointly rated 37 cases from the FF1 sample with similar results: weighted  $\kappa = +0.86$  (0.77–0.95).

A total of 866 twins were selected as eligible for this study as they met criteria for MD at some point in the year before interview. In all, 630 were included in this study with the most common reason for exclusion being that the onset of the worst episode was before the last year, so we lacked detailed information about proximal stressors.

Lifetime MD was assessed at personal interview by DSM-III-R criteria in the cotwin and by family history using the Family History-Research Diagnostic Criteria in parents.<sup>7</sup> Neuroticism was assessed by the short form of Eysenck's Personality Questionnaire.<sup>8</sup> Generalized anxiety disorder was diagnosed using DSM-III-R<sup>9</sup> criteria requiring 1 month minimum duration. Phobia was diagnosed using an adaptation of DSM-III criteria<sup>10</sup> requiring one or more unreasonable fears that interfere with the respondent's life. Panic disorder was defined using DSM-III-R criteria, except, because of the rarity of fully syndromal panic disorder,<sup>11</sup> we allowed up to 30 min for symptoms to maximize. We calculated the risk for new depressive onsets within the 1-year prevalence window assessed by our interviews.

For early life risk factors, we examined self-report measures of parental warmth as measured by a shortened version of the Parental Bonding Instrument<sup>12</sup> and childhood sexual abuse (defined as genital contact and/or attempted or completed intercourse).<sup>13</sup>

### Statistical analysis

Depending on whether the dependent variables— all liability indices for MD—were dichotomous or continuous in distribution, we used, respectively logistic or linear regressions in PROC LOGISTIC and PROC REG in SAS<sup>14</sup> with our five-point LOU scale as the key predictor variable. Our initial analyses included age, sex and a dummy variable representing the MMMF versus FF sample as covariates. Because of the highly skewed nature of the distribution, the variable number of prior episodes was reduced to a four category variable: zero, 1–2, 3–10 and > 10 prior MD episodes. Two-tailed *P*-values were reported. Because our sample contained both members of only 31 pairs, we did not formally correct for the correlational structure of the data.

## Results

Of the 630 individuals for whom the level of understandability (LOU) ratings were available, 11.9% were rated not understandable, 19.8% a little understandable, 30.8% somewhat understandable, 26.3% quite understandable and 11.1% totally understandable.

### Impact of number of prior episodes

In Kendler *et al.*<sup>15</sup> and many other samples,<sup>16–18</sup> the association between SLEs and the onset of episodes of MD declines with increasing number of depressive episodes. This has sometimes been called ‘kindling’.<sup>16</sup> The occurrence of such stressful events immediately before the depressive onset formed part of the information used for our LOU ratings. Given the potential importance of controlling for prior depressive episodes, we first examined their association with understandability. Number of prior episodes strongly and *inversely* predicted LOU ( $\chi^2 = 17.4$ ,  $df = 1$ ,  $P < 0.0001$ , odds ratio per category = 0.74, 95% confidence intervals = 0.65–0.85). In addition, age but neither sex nor FF versus MMMF cohort significantly predicted LOU with older age associated with lower LOU. Therefore, number of prior episodes and age were used as covariates for all subsequent analyses.

### Association between LOU and indices of liability to MD

As seen in Table 3, we next examined the ability of our measures of LOU to predict 12 individual risk indices for MD organized into six groups.

**Personality**—The personality trait with the strongest association with risk for MD, mediated substantially by shared genetic factors, is neuroticism.<sup>19,20–24</sup> LOU was unrelated to levels of neuroticism in our sample.

**Comorbidity with anxiety disorders**—Epidemiological and twin studies show that MD and anxiety disorders together form a highly comorbid group of internalizing disorders which share a common genetic diathesis.<sup>25–27</sup> No relationship was found between LOU in our participants and their risk for generalized anxiety disorder, panic disorder or phobias.

**Early age at onset**—Although the familial liability to MD is associated with an early age at onset,<sup>2,28</sup> our ratings of LOU were unrelated to age at onset.

**Childhood risk factors for MD**—In Kendler *et al.*<sup>13,29,30</sup> and other samples,<sup>31,32</sup> the risk for MD was elevated in subjects exposed to low levels of parental warmth, childhood sexual abuse or childhood parental loss. However, LOU did not predict exposure to any of these adversities.

**Indices of genetic/familial risk for MD**—Familial/genetic factors have been conclusively shown to substantially contribute to liability to MD.<sup>2</sup> LOU in this sample was unrelated to risk for MD in the father or mother. However, contrary to the prediction of the reasons-as-causes model, LOU was significantly and *positively* related to risk for MD in the cotwin.

**Risk for future episodes**—As our sample was longitudinal, we were able to assess risk for subsequent depressive episodes, a self-evident index of liability to MD. LOU did not predict risk for future episodes of MD.

## Discussion

The goal of this paper was to evaluate empirically, in a large epidemiological sample of individuals with depressive episodes in the last year, two hypotheses about the relationship between reasons and causes for MD: ‘reasons as causes’ and ‘trap of meaning.’ Reasons were assessed by a reliable five-point scale reflecting the LOU of the depressive episode in the context of a rich description of the individual’s stressors and social resources in the last year. For causes, we examined 12 clinical, personality, genetic and environmental risk factors shown in this and other samples to predict episodes of MD.

Consistent with the trap of meaning but not the reasons–as-causes hypothesis, 11 of the 12 variables, including such prominent risk factors as levels of neuroticism, age at onset, comorbidity with anxiety disorders and history of MD in parents, were unrelated to LOU. The one remaining variable (risk for MD in cotwin) was, contrary to the predictions of the reasons-as-causes hypothesis, *positively* associated with ratings of LOU.

The reasons-as-causes hypothesis—that reasons can not only provide us understanding but also explanation—is deeply intuitive. But our results contradict its central prediction. Individuals with plausible reasons for developing depression did **not** have fewer scientifically validated causes for MD than individuals without such plausible reasons.

Although our results seem puzzling and may arouse skepticism, they are not without precedent. An older literature on ‘reactive’ or ‘situational’ MD shows that situational and non-situational depressed patients do not differ in personality,<sup>33</sup> recovery rates<sup>34</sup> or familial loading.<sup>35,36</sup> A prior study in this sample found no relationship between many of the same indices of liability to MD and the level of long-term contextual threat of precipitating SLEs.<sup>37</sup> Congruent with our results in cotwins, two prior studies found higher rates of familial loading for MD in relatives of either situational MD<sup>38</sup> or cases of MD with onset associated with high levels of psychosocial stressors.<sup>39</sup> In this same sample, we evaluated the understandability of the origin of phobias (for example, did they arise in response to severe traumas, mild traumas or without known environmental precipitants?) and found that this LOU had no relationship with genetic or personality risk factors for phobias.<sup>40</sup>

### Interpretation of findings

While our results contradicting the predictions of the reasons-as-causes hypothesis are clear-cut, their interpretation is not. We suggest one methodological, two empirical and one philosophical explanation for these findings. The methodological explanation is simply that our measure of LOU, while highly reliable and face-valid, is either just noise—signifying nothing— or too superficial to reflect anything useful about human psychological processes. We knew a good deal about the key ‘surface features’ of our subject’s lives— their health, interpersonal relationships, finances, job stressors and satisfaction, losses and conflict. We inquired specifically about what they thought caused their depression. So, we globally assessed both the array of stressors they had confronted and the social resources they had for coping with those stressors. However, we do not know in detail either their inner psychological workings or whether the specific details of their depressive symptoms relate thematically to the stressors that they experienced. So, for some of the cases that we rated as ‘un-understandable,’ a more in-depth inquiry might have yielded meaningful psychological connections between their life experiences and their depression.

We have two responses to this legitimate concern. First, as our vignettes in Table 2 illustrate, the kind of interview we conducted actually captured a large proportion of the losses, stressors and humiliations that reflect our common human understanding of the psychological origins of depression. We do not claim to have captured all of the relevant

experiences, but to argue that our assessments are just noise seems implausible. Second, this interpretation is hard to square with the finding that, although number of prior episodes of depression were not mentioned in the case summaries and therefore had no role in our judgment of understandability, we found a strong inverse association between understandability and the number of past MD episodes. In light of this finding, it is difficult to argue that our measure of LOU is not indexing something important about depression.

We suggest two plausible empirical explanations for our findings. First, the adversity that the subjects report as occurring before their depressive episode (and which formed a substantial part of our understandability ratings) might not actually causally contribute to the depression. Instead, these stressful events and associated financial, interpersonal and medical difficulties could result either from risk factors that are shared with MD or reflect early signs of the depressive episode that was missed by our interview. This interpretation is consistent with some prior findings. A number of the risk factors for MD, including SLEs, low social support and marital conflict, are modestly heritable.<sup>41</sup> The genetic risk factors for SLEs also impact on risk for MD.<sup>42</sup> The association between event exposure and depressive onsets declines when controlling for genetic background<sup>43,44</sup> showing that some proportion of the event-depression association is not causal but results from genetic factors which contribute both to risk for MD and to selection into stressful environments. However, these same studies have shown that this is not the entire story. Even when controlling entirely for genetic effects (studying monozygotic twins discordant for life event exposure), stressful events do still causally impact on risk for MD.<sup>43,44</sup>

Our second empirical explanation for these findings relates to the phenomenon of kindling. Subjects with high levels of risk to MD may have had earlier depressive episodes that were quite understandable. However, by the time we have seen them, their mind/brain had 'learned' to easily shift into a depressive state with little or no external stressors.<sup>15</sup> Such cases characterized by high number of causes for MD but low understandability would certainly attenuate any evidence for the reasons-as-causes hypothesis. In our sample, 268 subjects denied earlier depressive episodes. If our findings resulted entirely from kindling, we should see the pattern of results predicted by the reasons-as-causes hypothesis in this first-onset subsample. We did not. In this subsample, our ratings of LOU did not predict lower rates of exposure to any of our 12 liability indices.

The philosophical interpretation of our findings is that reasons and causes may represent two incommensurable ways of knowing about human behavior. The distinction between these two approaches was clearly articulated by Wilhelm Dilthey, who, in Germany in the latter part of the nineteenth century, rejected the idea that everything useful about human behavior could be obtained through causes and explanation as studied by the natural sciences (*Naturwissenschaften*).<sup>45</sup> Instead, he proposed a separate discipline of the human sciences (*Geisteswissenschaften*) where reasons and understanding were the dominant methodology. Dilthey's conceptualization substantially influenced the psychiatrist/philosopher Jaspers<sup>1</sup> and had a central role in his conceptual framework for psychopathology.

### Trap of meaning hypothesis

While our findings are contrary to the predictions of the reasons-as-causes hypothesis, they are entirely consistent with the trap of meaning hypothesis.<sup>3</sup> While our empathic abilities may be indispensable in permitting us to see the world from another person's perspective, they may not be a good guide to the causes of (at least) MD. While it may seem sensible to stop looking for objective causes of depressive illness when confronted with an intuitively plausible set of reasons, our results support the contention of Lyketsos and Chisolm<sup>3</sup> that this approach may not optimally serve our patients.

## Limitations

As with any study with predominantly negative results, our findings should be interpreted in the context of the statistical power of our experiment. We performed linear and logistic regression with our relatively normally distributed five category predictor variable—LOU. Assuming as we did a two-tailed  $\alpha$  level of 5% for linear regressions, we had, with our sample of 630 subjects, ~70% power to detect a small effect size ( $r = 0.10$ ) and over 99% power to detect anything larger.<sup>46</sup> For logistic regression, we had over 80% power to detect ORs of  $\leq 0.7$  with the rarest of our risk factors—panic disorder and childhood sexual abuse—and 80% or more power at an odds ratio of  $\leq 0.8$  for all other variables. Thus, we were very well powered in this study to detect relationships between reasons and causes that were of moderate or large effect size but could have missed some subtle relationships. However, of our 11 non-significant findings, six were in the direction predicted by the reasons-as-causes hypothesis and five were not. These results are not consistent with an underlying trend in favor of the reasons-as-causes hypothesis that was missed due to inadequate power.

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**Table 1**

## Scale of level of understandability (LOU) of major depressive episode

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1	not understandable (I cannot understand why R would have developed these symptoms)
2	a little understandable (I have only a slight or modest sense of why R would have developed these symptoms)
3	somewhat understandable (I have a general sense of why R might have developed these symptoms—I could see some people, when put in this situation, would react similarly)
4	quite understandable (I can empathize a lot with R's response—many individuals in this situation would react similarly)
5	totally understandable (I can completely empathize with R's response—most people in this situation would react similarly)

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Table 2

Examples of case vignettes scored at each level of understandability<sup>a</sup>*Rating of 1, not understandable*

The respondent (R), a 39-year-old married man, had an 8-month episode of MD that he attributed to the purchase of a car that turned out to have a lot of problems. The only past-year stressful life event occurring before the onset of the MD was the major new expense of this car purchase, followed by several months of trying unsuccessfully to get the dealer to repair it or allow him to return it. R indicated his family has 'more money than we need' and never has trouble affording things. No particular stress was reported at his job of 9 years as a sales manager. His relationships with his wife, other family members and friends are quite good.

R is a 34-year-old married woman with three school-age children. She had a 9-week episode of depression which she said came 'out of the blue.' Very good relationships with spouse, children, other family members and friends were reported. Her job of 9 years as a nurse is secure and only moderately stressful; she reported an expected reorganization of responsibilities at work a few months before her MD onset (minor long-term contextual threat (LTCT)). The only other past-year stressful life events she reported all occurred several months before her MD onset and all were rated minor LTCT—major new expenses related to her husband starting a business, an uncle's expected death and sibling's and friend's personal crises.

*Rating of 2, a little understandable*

R is a 47-year-old never-married man, living with his partner and her 21-year-old son, who had a 2-week episode of past-year MD when his partner entered the hospital for minor gallbladder surgery. R's job was described as fairly highly pressured but secure; finances are tight and his partner does not work outside the home. He reported having an excellent relationship with his partner (his one confidant) and good relationships with six friends as well as family members. No other past-year stressful life events were reported.

R is a 42-year-old never-married woman living with a partner for the past 2 years. She reported a 3-week episode of past-year MD starting just after the new year, which she related to fatigue and overload from work and the holidays. She owns several retail stores and works 60+ hours per week. Past-year stressful life events reported—all rated minor or low moderate LTCT—were difficulty getting along with a subordinate (7 months before MD onset), an employee died of colon cancer (3 months before MD), her car was burglarized (3 months before MD); and her sister had a personal crisis (same month as R's MD onset). Her relationship with her partner was described in positive terms, although he is not one of her two confidants. She reported very good relationships and frequent contact with five friends but not especially close relationships with family members.

*Rating of 3, somewhat understandable*

R is a 46-year-old married woman with one biological and two step-children. She reported an ongoing 8-month episode of past-year MD attributed to conflict with daughter and concern over a cyst in her breast (not coded in health section, just mention of fibrocystic breast disease there). The month before the MD onset, R started having serious trouble getting along with her daughter, who got mixed up with the 'wrong crowd,' flunked out of college, and moved back home (high moderate LTCT). This was also a serious personal crisis for her daughter (low moderate LTCT). That same month R had financial problems (minor LTCT); reportedly her family has 'not enough' money. She indicated she has fairly good relationships with her husband (although he is quite a bit demanding and there is some tension and criticism) and her children (although they often are too dependent, argumentative, do not pay enough attention and do not listen enough), good relationships with two friends and fair relationships with relatives.

R is a 21-year-old full-time college junior who reported a 2-week episode of past-year MD attributed to receiving poor grades (C's and D's) in her engineering courses and hating her planned engineering major. She reported the additional component of feeling like she was a failure and letting down her father, an engineer, when she decided to switch to a business major. R has frequent contact with and very good relationships with seven friends and family (although she is 'afraid' of her father), has four confidants and attends weekly club meetings. No financial, health or other past-year stressful life events were mentioned.

*Rating of 4, quite understandable*

R is a 47-year-old married mother of three. Her worst past-year episode of MD, lasting 9 weeks so far, was attributed to ongoing medical problems (hypertension, pinched nerve in back, permanent nerve damage in foot) resulting in > 3 months in bed. The pinched nerve in her back occurred at work last winter and has worsened over time, aggravating her preexisting foot problem, and eventually causing her to take sick leave starting 2 months before the MD onset. Her activities have been greatly limited and she has been in great pain (severe LTCT). She expects to be out of work for 6–12 months and so far has been unpaid due to slow paperwork processing, resulting in a major reduction in family income (high moderate LTCT). R described her marriage in mostly negative terms and reported serious trouble getting along with her husband (high moderate LTCT). She said her children are often too demanding and dependent and she has had serious trouble getting along with a son (high moderate LTCT). She also reported serious trouble getting along with her mother (high moderate LTCT). In contrast, she has very good relationships with six friends and other family members, with two confidants (not her husband).

R is a 44-year-old married man with a teenage son who reported a 3-month episode of past-year MD, attributed to his dad's stroke of 2 months earlier 'sinking in.' R's 72-year-old father had been in good health when he had a serious stroke resulting in permanent nursing home placement. R had worked with his father in the family business on a daily basis and the stroke took away a main confidant of R's and significantly altered his daily routine (severe LTCT). His father's stroke was also a serious personal crisis for R's twin and three other siblings (all rated minor LTCT). R reported having an excellent relationship with his wife (a confidant) and very good relationships with his son, 10 friends and family members. No work, financial, health or other past-year stressful life was reported.

*Rating of 5, completely understandable*

R is a 45-year-old married man with three children. He reported a 6-month ongoing period of MD starting when his 11-year-old daughter was diagnosed with a rare and life-threatening cancer (severe LTCT). His daughter and wife have been living in another city for several months while his daughter receives experimental treatment; she has been close to death several times. R also has had major new expenses related to his daughter's illness (high moderate LTCT) and he described his family as being poor (R's reported income confirms this). R's wife (low moderate LTCT), son (minor LTCT) and cotwin (minor LTCT) all had serious personal crises related to his daughter's illness. Also in the past

year R's father-in-law died (low moderate LTCT). R reported very good relationships with his wife (his sole confidant) and children, and good relationships with four friends and other family members.

R is a 26-year-old single woman working as a sales representative and living alone. Her worst episode of past-year MD lasted 3 weeks after her partner committed suicide. She had been dating this man for 7 years, they lived together, but she had recently been trying unsuccessfully to extricate herself from this longstanding relationship. R returned home from work 1 day to find her boyfriend hanging from a tree in the backyard. His death also resulted in a major reduction in family income as he had been sharing living expenses; R has 'not enough' money. She called the police that month when her boyfriend's family, who blamed her for his suicide, came into her home to take his things. R reported having good relationships with three friends and family members, with five confidants.

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Abbreviation: MD, major depression.

<sup>a</sup>Small changes in details have been made in all these vignettes to protect the identity of the respondent.

Table 3

Regression to predict variable from understandability rating (five levels) using subjects with MD in last year

Variable	Type	Parameter estimate	95% CI	Odds ratio	95% CI	Statistic (DF)	Statistic value	P-value
Level of neuroticism <sup>a,b</sup>	Linear	-0.048	-0.115, 0.019			<i>t</i>	-1.41	0.1602
Lifetime history of generalized anxiety disorder <sup>b</sup>	Logistic			1.048	0.907, 1.211	$\chi^2(1)$	0.4116	0.5212
Lifetime history of phobia <sup>b</sup>	Logistic			0.971	0.845, 1.115	$\chi^2(1)$	0.1751	0.6756
Lifetime history of panic disorder <sup>b</sup>	Logistic			0.875	0.670, 1.142	$\chi^2(1)$	0.9700	0.3247
Age at onset of MD <sup>a,b</sup>	Linear	-0.011	-0.060, 0.039			<i>t</i>	-0.43	0.6686
Parental warmth <sup>a,b</sup>	Linear	0.066	-0.012, 0.144			<i>t</i>	1.66	0.0968
Childhood sexual abuse <sup>b</sup>	Logistic			1.105	0.920, 1.329	$\chi^2(1)$	1.1404	0.2856
Parental loss <sup>b</sup>	Logistic			0.955	0.819, 1.115	$\chi^2(1)$	0.3351	0.5627
Paternal history of MD <sup>b</sup>	Logistic			1.082	0.901, 1.299	$\chi^2(1)$	0.7113	0.3990
Maternal history of MD <sup>b</sup>	Logistic			1.041	0.898, 1.207	$\chi^2(1)$	0.2794	0.5971
History of MD in cotwin <sup>c</sup>	Logistic			1.177	1.007, 1.376	$\chi^2(1)$	4.1782	0.0409
Subsequent episode of MD <sup>b</sup>	Logistic			0.953	0.810, 1.120	$\chi^2(1)$	0.3432	0.5580

Abbreviations: CI, confidence interval; MD, major depression.

<sup>a</sup> Variable is standardized.<sup>b</sup> Covariates in model are age and previous episode of MD (ordinal).<sup>c</sup> Covariates in model are twin age, twin sex, cotwin sex, zygosity and previous number of episodes of MD (ordinal).