The Prevalence and Severity of Depressive Symptoms Along the Spectrum of Unipolar Depressive Disorders: A Post Hoc Analysis

Jeffrey J. Rakofsky, MD; Pamela J. Schettler, PhD; Becky L. Kinkead, PhD; Ellen Frank, PhD; Lewis L. Judd, MD; David J. Kupfer, MD; A. John Rush, MD; Michael E. Thase, MD; Kimberly A. Yonkers, MD; and Mark H. Rapaport, MD

ABSTRACT

Objective: To explore which symptoms are common in patients who experience a range of symptom severity that spans minor depression and major depressive disorder (MDD).

Method: A post hoc analysis of subjects entering outpatient, pharmacologic treatment studies for minor depression or MDD who provided baseline data on the Inventory for Depressive Symptomatology-Clinician Rated (IDS-C) was performed in November 2000. The minor depression sample included 161 patients diagnosed according to the National Institute of Mental Health Diagnostic Interview Schedule, while the MDD subjects included 969 subjects diagnosed according to the Structured Clinical Interview for *DSM-III-R*. Descriptive statistics were calculated for the total IDS-C score and for each item-rating score for both groups. The percentages of patients within the low, medium, and high severity groups of minor depression and MDD endorsing each IDS-C item were calculated and used to identify specific patterns of prevalence across the 6 groups: symptoms with high prevalence in all groups (core symptoms), those with increasing prevalence across groups (continuum symptoms), and those that become prominent only at a certain threshold of illness severity.

Results: The mean (SD) IDS-C score was 21.18 (5.37) for minor depression patients, while it was 37.14 (7.27) for the MDD patients ($P = .0001$). Ten items pertaining mostly to mood state and cognition were identified as "core" symptoms of depression based on their high prevalence in all groups. Fourteen items consisting mostly of neurovegetative and somatic symptoms were identified as "continuum" symptoms based on their general pattern of increasing prevalence across the 6 severity groups. Four "threshold" symptoms, including suicidal ideation, psychomotor slowing, gastrointestinal symptoms, and panic/phobic symptoms, were prevalent in only the most severely depressed groups.

Conclusions: The presence of core, continuum, and threshold depressive symptoms indicates central features of both minor depression and MDD as well as symptoms that increase or emerge with depressive illness severity. Some of the core symptoms of minor depression and MDD are not included in *DSM* depressive criteria or traditional assessment rating scales.

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Corresponding author: *Jeffrey J. Rakofsky, MD, Mood and Anxiety Disorders Program, Emory University Department of Psychiatry and Behavioral Sciences, 1256 Briarcliff Rd, 3rd Floor North, Atlanta, GA 30306 (Jrakofs@emory.edu).*

One of the challenges the field of psychiatry has faced is how to determine the lower boundary of a unipolar depressive disorder. No one wants to pathologize brief, evanescent feelings that may be associated with stress, loss, or disappointment, yet one should not ignore a sustained mood disturbance that results in long-lived emotional distress and dysfunction simply because the number of arbitrarily defined symptoms elicited during an interview does not reach a nonempirically developed threshold. This concern has led to a considerable amount of research attempting to define, validate, and delineate depressive disorders that do not meet *DSM-IV* criteria for major depressive disorder (MDD). The largest body of such work investigates minor depression.

Extensive clinical and epidemiologic data suggest that minor depression and MDD exist along a continuum of severity. With increasing numbers of depressive symptoms, patients report worse quality of life,[1,2] worse functional impairment,[1,3–7] greater depressive severity,[1,6] longer depressive episodes,[1,8] worse psychological well-being,[2] greater cognitive dysfunction,[9] and more anxiety disorders.[4,8] Over 2 years, patients with minor depression have a 2-fold higher risk of developing MDD as compared to healthy controls.[4] There is evidence of a within-subject continuum of depressive episode severity from the Epidemiologic Catchment Area community study in which 38% of subjects who were in a major depressive episode at their initial interview had minor depression or dysthymia when interviewed 1 year later.[10] Angst and Merikangas[11] also described substantial bidirectional fluctuation between MDD and subthreshold forms of depression in the Zurich cohort over a 15-year period. We previously reported[12] between-group findings that support the dimensional conceptualization of depressive disorders. We found no difference in intake characteristics or treatment response for minor depression subjects with versus without prior MDD.[12] Minor depression and MDD subjects have a similar age of illness onset.[5] There is a lack of familial aggregation of minor depression among first-degree relatives of community subjects with minor depression[13] that also suggests that the 2 conditions may exist on a continuum rather than being categorically different. Finally, a taxonometric analysis[14] of subjects in a community sample who endorsed at least 1 depressive symptom also concluded that depression exists as a continuously distributed syndrome. Thus, a preponderance of evidence suggests that there may be clinical and scientific value in investigating a wider spectrum of individuals who present with sustained symptoms of a depressive disorder.

Clinical Points

- Clinicians should carefully assess core mood and cognitive symptoms of depression identified in this study; even though not all are currently *DSM* criteria, they are highly prevalent even at the lowest end of the depressive illness spectrum.
- Several vegetative and somatic symptoms show a general pattern of increase with overall depressive severity; however, many of these are as prevalent at the high range of minor depression as at the low range of major depressive disorder (MDD).
- Suicidal ideation, psychomotor slowing, and gastrointestinal symptoms appear to differentiate MDD from minor depression.

The 2 most commonly used clinician-rated depression severity scales are the Hamilton Depression Rating Scale (HDRS)[15] and the Montgomery-Asberg Depression Rating Scale (MADRS).[16] They were developed on the basis of clinical observations about endogenous and melancholic depressed inpatients from the 1950s–1970s. A more recently developed clinician-rated scale, the Inventory for Depressive Symptomatology-Clinician Rated (IDS-C) includes almost all the symptoms of MDD included in the *DSM*, along with other symptoms commonly seen among inpatients *and* outpatients with these disorders.[17]

In this article, we use the IDS-C to describe the occurrence and severity of a broader group of symptoms than those listed in the *DSM* or in standard rating scales in order to explore which symptoms are common (or uncommon) in patients who experience a range of symptom severity that spans minor depression and MDD. To date, no studies have compared minor depression and MDD samples on symptom-item endorsement or severity using a psychiatric rating scale. We hypothesized that minor depression and MDD would share core psychological features but would differ in their severity, while physiological symptoms associated with MDD would be layered onto these psychological features at increasing levels of illness severity.

METHOD

Overview of the Study

Data for this report are derived from post hoc analysis of carefully diagnosed cohorts of participants entering outpatient, pharmacologic treatment studies for minor depression[12] or MDD.[18] Institutional review board approval was obtained at all participating sites before enrollment began. One hundred sixty-one patients from the minor depression study were recruited at 3 sites (University of California, San Diego; University of Pittsburgh; and University of Texas, Southwestern Medical Center). Minor depression was diagnosed by using the depression module of the National Institutes of Mental Health Diagnostic Interview Schedule (DIS). To meet minor depression criteria, subjects had to endorse having at least 2 weeks of both depressed mood/dysphoria/sadness *and* pervasive loss of interest/pleasure in all or almost all activities and at least 1 additional depressive symptom from the DIS, or they had to endorse having at least 2 weeks of depressed mood/dysphoria/sadness *or* pervasive loss of interest/pleasure in all or almost all activities and at least 2 additional depressive symptoms from the DIS. Patients also had to demonstrate functional disability on both the Global Assessment of Functioning scale (≤ 70 in the past month) and the Short-Form Health Survey (≤ 75 on the social role function scale or ≤ 67 on the emotional role function scale in the past month). Minor depression patients with a past history of MDD or dysthymia were included as long as they did not meet criteria for these conditions within 2 years of enrollment. The Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I) was used to exclude individuals with other current Axis I disorders, including adjustment disorder with depressed mood, those with a lifetime history of schizophrenia, bipolar I disorder, and substance use disorders in the last year; personality disorders were excluded as well. Patients were rated at screening with the 30-item IDS-C.

Nine hundred ninety-three nonpsychotic MDD subjects participated in 2 multicenter, placebo-controlled medication trials.[18] These patients were diagnosed by using the Structured Clinical Interview for *DSM-III-R*. To be included, those with recurrent depression had to be in the current episode for ≥ 6 months or had to have a history of depressive episodes lasting ≥ 6 months. For single-episode patients, the current episode had to exceed 1 year in duration. Those with seasonal depression, bipolar disorder, or substance use disorders within the last 6 months were excluded. Baseline MDD severity was assessed by using the 28-item version of the IDS-C.

The IDS-C is a depression rating scale with broad symptom coverage (criteria for MDD, melancholic and atypical features) and has demonstrated high internal validity (Cronbach $\alpha = 0.75–0.94$) and high concurrent validity (Pearson correlation coefficient = 0.81). Additionally, it can reliably distinguish between severe, moderate, mild, and recovered forms of depression.[17,19] Although it contains a broader list of symptoms as compared to the *DSM-IV* criteria for MDD, the IDS-C does not include an item assessing "excessive or inappropriate guilt." Scores of 1 or higher for item 8, "reactivity of mood," indicate increasing difficulty with mood brightening in response to good events. Scores of 1 or higher for item 19, "involvement," refer to a reduction in interest in people and activities. Neither the minor depression nor MDD studies required subjects to have a minimum symptom severity score on the IDS-C or other depression rating scales to qualify for enrollment.

Statistics

Mean and standard deviation values of total 28-item IDS-C score and of the item-rating for each item on the IDS-C scale for the minor depression and the MDD groups were calculated. A 2-group Wilcoxon Rank Sum test was performed by comparing the mean value of each item score between the minor depression and MDD samples. The

Table 1. Comparison of Minor Depression Versus MDD Patients on the 28-Item Inventory for Depressive Symptomatology-Clinician Rated (IDS-C)

IDS-C Symptom	Minor Depression Patients (n = 162), Mean (SD)[a]	MDD Patients (n = 993), Mean (SD)[a]	Significance of Minor Depression—MDD Contrast by Wilcoxon Rank Sum Test		Minor Depression Patients Reporting Any Level of Symptom, %[b]	MDD Patients Reporting Any Level of Symptom, %[b]
			Z	*P*		
(1) Sleep-onset insomnia	0.76 (1.10)	1.56 (1.11)	8.24	.0001	35.8	75.4
(2) Midnocturnal insomnia	1.33 (1.23)	2.05 (1.02)	6.98	.0001	61.7	88.5
(3) Early morning insomnia	0.72 (0.97)	1.28 (1.07)	6.40	.0001	40.7	68.7
(4) Hypersomnia	0.16 (0.43)	0.50 (0.78)	5.41	.0001	13.6	34.3
(5) Sad mood	1.53 (0.66)	2.26 (0.58)	12.35	.0001	93.2	99.7
(6) Irritable mood	1.23 (0.72)	1.74 (0.68)	8.41	.0001	84.6	95.9
(7) Anxious mood	1.10 (0.72)	1.86 (0.65)	11.95	.0001	79.6	97.8
(8) Reactivity of mood	1.02 (0.82)	1.68 (0.75)	9.44	.0001	70.4	93.1
(9) Diurnal mood variation	0.76 (0.98)	1.46 (1.28)	6.66	.0001	43.2	64.8
(10) Quality of mood distinct from bereavement	2.01 (1.08)	2.49 (0.78)	5.89	.0001	85.2	97.9
(11) Appetite decreased	0.11 (0.39)	0.45 (0.70)	6.32	.0001	8.6	33.4
(12) Appetite increased	0.25 (0.61)	0.61 (0.91)	5.05	.0001	16.7	36.8
(13) Weight decrease within last 2 weeks	0.07 (0.32)	0.35 (0.74)	4.95	.0001	4.9	21.3
(14) Weight increase within last 2 weeks	0.23 (0.62)	0.63 (0.92)	5.50	.0001	16.0	37.5
(15) Trouble with concentration/ decision making	1.33 (0.78)	1.70 (0.61)	5.78	.0001	82.7	97.9
(16) Outlook: self	1.01 (0.93)	1.71 (0.90)	8.73	.0001	67.3	94.2
(17) Outlook: future	1.12 (0.68)	1.70 (0.64)	9.49	.0001	82.7	97.8
(18) Suicidal ideation	0.12 (0.35)	1.08 (0.63)	16.90	.0001	11.7	84.2
(19) Involvement	1.24 (0.63)	1.84 (0.75)	9.31	.0001	90.7	97.5
(20) Energy/fatigability	1.22 (0.76)	1.84 (0.58)	10.39	.0001	81.5	98.6
(21) Pleasure/enjoyment (other than sexual)	0.99 (0.57)	1.62 (0.65)	10.83	.0001	83.3	97.0
(22) Sexual interest	1.09 (1.06)	1.70 (0.96)	6.91	.0001	61.7	85.8
(23) Psychomotor slowing	0.33 (0.53)	1.15 (0.65)	14.29	.0001	30.2	87.6
(24) Psychomotor agitation	0.28 (0.45)	0.77 (0.68)	8.80	.0001	28.4	63.9
(25) Somatic complaints	0.65 (0.56)	1.17 (0.63)	9.66	.0001	61.1	90.1
(26) Sympathetic arousal	0.29 (0.48)	0.82 (0.64)	10.06	.0001	27.8	69.4
(27) Panic/phobic symptoms	0.10 (0.31)	0.51 (0.66)	7.69	.0001	10.5	41.7
(28) Gastrointestinal symptoms	0.12 (0.36)	0.64 (0.71)	9.51	.0001	10.5	51.4
IDS-C Total	21.18 (5.37)	37.14 (7.27)	26.77[c]	.0001	NA	NA

[a]Mean value based on item response values 0 (none of symptom) or 1–3 (increasing levels of frequency of the symptom).
[b]Percentage of subjects reporting symptom are based on response values 1–3.
[c]*t* Value.
Abbreviations: MDD = major depressive disorder, NA = not applicable.

percentage of minor depression patients and MDD patients reporting any level of symptom was also calculated.

An analysis of the continuity-discontinuity of each IDS-C item among the low-medium-high severity groups of minor depression and MDD patients was performed. Minor depression and MDD patients were divided into approximately even thirds (within each sample) based on their intake total scores on the IDS-C. Because of nonnormal distribution, a Kruskal-Wallis test of differences across all 6 severity groups was performed and between the minor depression high severity and MDD low severity groups.

The percentages of item endorsement by patients within these severity groups were inspected visually to determine if they fit within predefined symptom clusters including core symptoms (endorsed by a substantial majority of all minor depression and MDD patient severity groups, ie, approximately 60% or more of respondents in each group), continuum symptoms (demonstrating progressively higher rates of endorsement with each increase in group severity level), and threshold symptoms (demonstrating low prevalence in all minor depression severity groups and a considerably higher prevalence in all MDD severity groups or only the highest severity levels within MDD). Analyses were conducted in November 2000.

RESULTS

The mean (SD) score for minor depression patients on the IDS-C was 21.18 (5.37), while the mean for the MDD patients was 37.14 (7.27) ($t_{1.153} = 26.77$; $P = .0001$). All 28 IDS-C symptoms had a statistically significant lower mean rating for minor depression than for MDD patients (for all items, $P = .0001$) (Table 1). For the minor depression sample, mean (SD) item ratings ranged from 0.07 (0.32) (weight decrease, item 13) to 2.01 (1.08) (quality of mood distinct from bereavement, item 10). For the MDD sample, mean item ratings ranged from 0.35 (0.74) (weight decrease, item 13) to 2.49 (0.78) (quality of mood distinct from bereavement, item 10). The percentage of minor depression patients endorsing individual symptom items ranged from 4.9% (weight decrease, item 13) to 93.2% (sad mood, item 5). The percentage of MDD patients endorsing individual symptom items ranged from 21.3% (weight decrease, item 13) to 99.7% (sad mood, item 5).

Within the minor depression sample, the low severity group included 54 patients, with a mean (SD) IDS-C score of 15.54 (2.58); the medium severity group included 50 patients, with a mean IDS-C score of 20.6 (1.54); and the high severity group included 57 patients, with a mean IDS-C

Table 2. Comparison of Symptom Intensity on the 28-Item Inventory for Depressive Symptomatology-Clinician Rated (IDS-C) Across the Spectrum of Severity

	Minor Depression (n = 162)			Major Depressive Disorder (n = 969)		
IDS-C Symptom	Low (n = 54), Mean (SD)	Medium (n = 50), Mean (SD)	High (n = 57), Mean (SD)	Low (n = 334), Mean (SD)	Medium (n = 287), Mean (SD)	High (n = 348), Mean (SD)
(1) Sleep-onset insomnia	0.43 (0.90)	0.64 (1.01)	1.19 (1.22)	1.19 (1.07)	1.54 (1.11)	1.95 (1.03)
(2) Midnocturnal insomnia	0.70 (1.04)	1.34 (1.26)	1.93 (1.08)	1.72 (1.06)	1.97 (1.01)	2.41 (0.87)
(3) Early morning insomnia	0.35 (0.80)	0.68 (0.91)	1.11 (1.03)	0.84 (0.94)	1.27 (1.03)	1.73 (1.04)
(4) Hypersomnia	0.06 (0.23)	0.12 (0.33)	0.30 (0.60)	0.39 (0.69)	0.54 (0.81)	0.56 (0.82)
(5) Sad mood	1.28 (0.74)	1.58 (0.57)	1.72 (0.59)	1.97 (0.55)	2.24 (0.53)	2.56 (0.50)
(6) Irritable mood	0.96 (0.70)	1.22 (0.76)	1.49 (0.63)	1.47 (0.69)	1.77 (0.64)	1.97 (0.60)
(7) Anxious mood	0.78 (0.60)	1.12 (0.69)	1.39 (0.73)	1.62 (0.62)	1.79 (0.62)	2.15 (0.59)
(8) Reactivity of mood	0.61 (0.76)	1.08 (0.78)	1.35 (0.77)	1.28 (0.75)	1.76 (0.66)	1.97 (0.65)
(9) Diurnal mood variation	0.69 (0.89)	0.58 (0.95)	1.00 (1.07)	1.09 (1.13)	1.43 (1.26)	1.86 (1.31)
(10) Quality of mood distinct from bereavement	1.56 (1.19)	2.06 (1.10)	2.39 (0.77)	2.21 (0.91)	2.55 (0.72)	2.71 (0.62)
(11) Appetite decreased	0.13 (0.44)	0.06 (0.24)	0.14 (0.44)	0.31 (0.56)	0.38 (0.64)	0.62 (0.82)
(12) Appetite increased	0.13 (0.44)	0.30 (0.65)	0.33 (0.72)	0.42 (0.76)	0.73 (0.95)	0.73 (1.00)
(13) Weight decrease within last 2 weeks	0.06 (0.30)	0.06 (0.31)	0.09 (0.34)	0.21 (0.57)	0.29 (0.64)	0.51 (0.89)
(14) Weight increase within last 2 weeks	0.07 (0.26)	0.24 (0.69)	0.39 (0.75)	0.46 (0.80)	0.68 (0.96)	0.78 (0.99)
(15) Trouble with concentration/decision making	1.06 (0.79)	1.38 (0.78)	1.53 (0.71)	1.41 (0.58)	1.71 (0.56)	1.97 (0.53)
(16) Outlook: self	0.67 (0.61)	0.90 (0.86)	1.40 (1.08)	1.22 (0.72)	1.66 (0.85)	2.21 (0.83)
(17) Outlook: future	0.89 (0.66)	1.16 (0.68)	1.32 (0.63)	1.34 (0.57)	1.67 (0.57)	2.03 (0.56)
(18) Suicidal ideation	0.07 (0.26)	0.14 (0.40)	0.16 (0.37)	0.88 (0.58)	1.06 (0.62)	1.28 (0.62)
(19) Involvement	1.13 (0.62)	1.16 (0.62)	1.40 (0.62)	1.53 (0.70)	1.80 (0.68)	2.16 (0.71)
(20) Energy/fatigability	1.06 (0.74)	1.20 (0.73)	1.39 (0.77)	1.52 (0.57)	1.92 (0.48)	2.09 (0.52)
(21) Pleasure/enjoyment (other than sexual)	0.87 (0.65)	1.00 (0.53)	1.11 (0.52)	1.23 (0.58)	1.65 (0.54)	1.95 (0.58)
(22) Sexual interest	0.89 (0.92)	0.90 (0.99)	1.47 (1.14)	1.40 (0.96)	1.68 (0.96)	2.03 (0.85)
(23) Psychomotor slowing	0.22 (0.46)	0.30 (0.46)	0.44 (0.60)	0.91 (0.62)	1.15 (0.60)	1.34 (0.63)
(24) Psychomotor agitation	0.15 (0.36)	0.26 (0.44)	0.44 (0.50)	0.66 (0.69)	0.76 (0.68)	0.90 (0.66)
(25) Somatic complaints	0.52 (0.57)	0.52 (0.50)	0.89 (0.52)	0.92 (0.54)	1.17 (0.56)	1.43 (0.66)
(26) Sympathetic arousal	0.17 (0.42)	0.32 (0.47)	0.37 (0.52)	0.56 (0.56)	0.74 (0.56)	1.12 (0.66)
(27) Panic/phobic symptoms	0.00 (0.00)	0.10 (0.30)	0.19 (0.40)	0.25 (0.49)	0.43 (0.59)	0.82 (0.74)
(28) Gastrointestinal symptoms	0.06 (0.23)	0.18 (0.44)	0.12 (0.38)	0.43 (0.61)	0.63 (0.71)	0.86 (0.76)
IDS-C Total	15.54 (2.58)	20.60 (1.54)	27.04 (2.82)	29.44 (4.04)	36.96 (1.38)	44.69 (3.99)

score of 27.04 (2.82). Within the MDD sample, the low severity sample included 334 patients, with a mean IDS-C score of 29.44 (4.04); the medium severity group included 287 patients, with a mean IDS-C score of 36.95 (1.38); and the high severity group included 348 patients, with a mean IDS-C score of 44.69 (3.99) (Table 2).

Ten items fit our definition of core symptoms and occurred in a substantial majority of patients with all levels of minor depression or MDD severity (Table 3). These included sad mood (item 5), irritable mood (item 6), anxious mood (item 7), quality of mood distinct from bereavement (item 10), concentration/decision making (item 15), outlook-self (item 16), outlook-future (item 17), involvement (item 19), energy/fatigability (item 20), and pleasure/enjoyment (nonsexual) (item 21).

Fourteen IDS-C items showed increasing rates of endorsement across the low minor depression to high MDD severity groups, and thus fit our definition for continuum symptoms. These items included sleep-onset insomnia (item 1), midnocturnal insomnia (item 2), early morning insomnia (item 3), hypersomnia (item 4), reactivity of mood (item 8), mood variation (item 9), appetite decrease (item 11), appetite increase (item 12), weight decrease (item 13), weight increase (item 14), sexual interest/pleasure (item 22), psychomotor agitation (item 24), somatic complaints (item 25), and sympathetic arousal (item 26).

Four symptoms fit our definition for threshold symptoms. Suicidal ideation (item 18), psychomotor slowing (item 23), and gastrointestinal symptoms (item 28) demonstrated a substantial discontinuity of endorsement rates for minor depression as compared with any level of MDD, with $P = .0001$ for all comparisons between high minor depression and MDD. Panic/phobic symptoms (item 27) showed an abrupt increase in prevalence between the medium and high levels of MDD severity and were endorsed by the majority of subjects only in that group, so we considered it a threshold symptom at that level. A similar pattern of discontinuity is observed when one studies the mean scores for these items (Table 2).

DISCUSSION

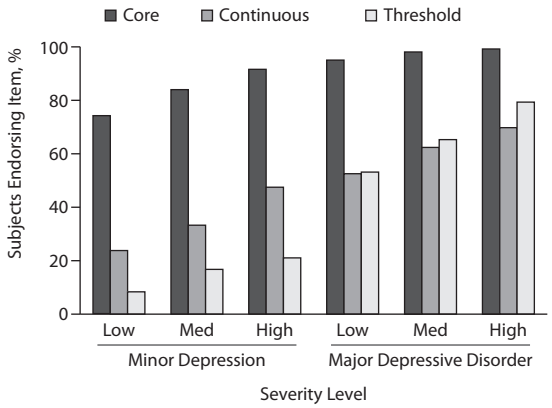
In this first of its kind comparison of minor depression and MDD patients using the individual symptom items from the IDS-C scale, we have identified 3 clusters of symptoms that vary in rates of occurrence and severity across the spectrum of unipolar disorders. Symptoms may be conceptualized as falling into 3 distinct groups based on their pattern of prevalence across the 6 analysis groups: core symptoms, continuum symptoms, and threshold symptoms. For a graphical illustration, see Figure 1. The 10 core symptoms (sad mood, irritable mood, anxious mood, mood quality distinct from bereavement, concentration, outlook-self, outlook-future, involvement, energy, and pleasure) represent mostly mood and cognitive symptoms that are highly endorsed across the range of severity for patients with depressive spectrum disorders, although the severity of those items increases in a monotonic fashion

Table 3. Comparison of Symptom Prevalence on the 28-Item Inventory for Depressive Symptomatology-Clinician Rated (IDS-C) by Depression Subtype and Severity

	Minor Depression (n = 162)			Major Depressive Disorder (n = 969)		
IDS-C Symptom	Low (n = 54), (n) %	Medium (n = 50), (n) %	High (n = 57), (n) %	Low (n = 334), (n) %	Medium (n = 287), (n) %	High (n = 348), (n) %
(1) Sleep-onset insomnia	(12) 22.2	(16) 32.0	(30) 52.5	(216) 64.7	(215) 74.9	(299) 85.9
(2) Midnocturnal insomnia	(20) 37.0	(31) 62.0	(49) 86.0	(272) 81.4	(255) 88.8	(331) 95.1
(3) Early morning insomnia	(10) 18.5	(21) 42.0	(35) 61.4	(178) 53.3	(200) 69.7	(290) 83.3
(4) Hypersomnia	(3) 5.6	(6) 12.0	(13) 22.8	(95) 28.4	(105) 36.6	(130) 37.4
(5) Sad mood[a]	(45) 83.3	(49) 98.0	(56) 98.2	(331) 99.1	(287) 100.0	(348) 100.0
(6) Irritable mood	(41) 75.9	(41) 82.0	(54) 94.7	(308) 92.2	(279) 97.2	(343) 98.6
(7) Anxious mood[a]	(37) 68.5	(42) 84.0	(49) 86.0	(320) 95.8	(282) 98.3	(346) 99.4
(8) Reactivity of mood	(24) 44.4	(38) 76.0	(51) 89.5	(283) 84.7	(276) 96.2	(343) 98.6
(9) Diurnal mood variation	(23) 42.6	(16) 32.0	(31) 54.4	(193) 57.8	(185) 64.4	(253) 72.7
(10) Quality of mood distinct from bereavement	(39) 72.2	(43) 86.0	(55) 96.5	(319) 95.5	(283) 98.6	(346) 99.4
(11) Appetite decreased[a]	(5) 9.3	(3) 6.0	(6) 10.5	(86) 25.8	(85) 29.6	(146) 42.0
(12) Appetite increased	(5) 9.3	(10) 20.0	(12) 21.0	(94) 28.1	(124) 43.2	(142) 40.8
(13) Weight decrease within last 2 weeks	(2) 3.7	(2) 4.0	(4) 7.0	(46) 13.8	(58) 20.2	(101) 29.0
(14) Weight increase within last 2 weeks	(4) 7.4	(7) 14.0	(15) 26.3	(100) 29.9	(113) 39.4	(152) 43.7
(15) Trouble with concentration/decision making	(40) 74.1	(42) 84.0	(51) 98.5	(323) 96.7	(281) 97.6	(346) 99.4
(16) Outlook: self	(32) 59.3	(32) 64.0	(44) 77.2	(296) 88.6	(273) 95.1	(343) 98.6
(17) Outlook: future	(39) 72.2	(43) 86.0	(52) 91.2	(321) 96.1	(281) 97.9	(346) 99.4
(18) Suicidal ideation[a]	(4) 7.4	(6) 11.0	(9) 15.8	(257) 77.0	(240) 83.6	(319) 92.0
(19) Involvement	(47) 87.0	(44) 88.0	(55) 96.5	(321) 96.1	(281) 97.9	(344) 98.8
(20) Energy/fatigability	(41) 75.9	(41) 82.0	(49) 86.0	(326) 97.6	(285) 99.3	(345) 99.1
(21) Pleasure/enjoyment (other than sexual)	(39) 72.2	(43) 86.0	(52) 91.2	(310) 92.8	(284) 99.0	(346) 99.4
(22) Sexual interest	(30) 55.6	(28) 56.0	(42) 73.7	(263) 78.7	(244) 85.0	(325) 93.4
(23) Psychomotor slowing[a]	(11) 20.4	(15) 30.0	(22) 38.6	(256) 76.6	(256) 89.2	(335) 96.3
(24) Psychomotor agitation[a]	(8) 14.8	(13) 26.0	(25) 43.9	(182) 54.5	(184) 64.1	(257) 73.8
(25) Somatic complaints	(26) 48.2	(26) 52.0	(46) 80.7	(272) 81.4	(267) 93.0	(334) 96.0
(26) Sympathetic arousal[a]	(8) 14.8	(16) 32.0	(20) 35.1	(177) 53.0	(196) 68.3	(296) 85.1
(27) Panic/phobic symptoms	(0) 0	(5) 10.0	(11) 19.3	(74) 22.2	(108) 37.6	(223) 64.1
(28) Gastrointestinal symptoms	(3) 5.6	(8) 16.0	(6) 10.5	(123) 36.8	(146) 50.9	(226) 64.9

[a]Wilcoxon rank sum nonparametric test of ranks between minor depression-high and MDD-low was statistically significant at $P = .05$.

Figure 1. Average IDS-C Item Endorsement Rate Within Each Symptom Cluster Across the Depressive Spectrum



Abbreviation: IDS-C = Inventory for Depressive Symptomatology-Clinician Rated.

as the overall severity of the depressive disorder increases. The 14 continuum symptoms represent symptoms that generally increase in both frequency of endorsement and intensity as one progresses through the severity continuum. These symptoms include sleep problems, eating issues, sexual interest, somatic complaints, diurnal variation, and sympathetic arousal. Threshold symptoms occur much more frequently among MDD patients than minor depression patients and demonstrate a discontinuity between these 2 conditions. These include the more extreme symptoms of depression: suicidal ideation, psychomotor slowing, gastrointestinal symptoms, and panic/phobic symptoms. They are present < 40% of the time and, in most cases, < 20% of the time among patients with minor depression, while among those with the most severe MDD, these symptoms are present > 64% of the time.

The pattern of symptom occurrence demonstrated by these 3 symptom clusters adds to the growing evidence that minor depression represents an incipient form of MDD along the spectrum of unipolar depressive illnesses. This relationship is already supported by studies that show an increased risk of developing MDD over time among minor depression patients.[4,11] With increased symptom occurrence, there may be an increased complexity of brain activity, as demonstrated by previous neuroimaging studies. For example, core symptoms, such as depressed mood and anhedonia, are associated with the medial prefrontal cortex, the amygdala, and the ventral striatum.[20–23] Continuous symptoms, such as sleep, appetite, and sexual interest, are driven by connections between the medial prefrontal network, the hypothalamus, periaqueductal gray, and various brainstem targets.[22,23] Threshold symptoms involve the amygdala and the anterior cingulate (suicidal ideation)[22]; amygdala and brainstem nuclei (panic)[22]; dorsal striatum, left prefrontal cortex, and motor cortex (psychomotor retardation)[24]; and the medial prefrontal network, amygdala, hypothalamus, lateral prefrontal cortex, orbitofrontal cortex, and periaqueductal gray (gastrointestinal symptoms).[25]

The wide endorsement of the core symptoms by most minor depression and MDD patients has implications for how we conceptualize and assess depression. First, it suggests that these symptoms are central to unipolar forms of depression, regardless of MDD or minor depression classification. Second, the range of mood quality symptoms within this cluster confirms the presence of a unipolar-polymorphic mood dysregulation among episodically depressed patients, similar to that of patients with borderline or depressive personality disorder.[26,27] Third, irritability and anxious mood are endorsed frequently in this study, yet neither of these is listed as an MDD or minor depression criterion in *DSM*. Interestingly, these 2 symptoms were included in the first organized diagnostic criteria list for depression (the Feighner Diagnostic Criteria),[28,29] but with subsequent iterations of diagnostic schedules, these were eventually removed. Although these 2 symptoms are not listed in the *DSM* criteria (except irritability for children), these 2 items remain in the *DSM*'s narrative description of MDD.[30] These symptoms are not traditionally considered "core" items of MDD yet may be important to identify and treat, especially if they resolve at a different rate than the other symptoms of depression. Patients may be classified as remitted yet still display troubling levels of anxiety or irritability.

Fourth, these findings suggest that the rating scales used most frequently, HDRS and MADRS, may not be capturing the full range of the central elements of depression, and inclusion of these symptoms would be likely to increase sensitivity to detect change. Currently, the HDRS includes the assessment of irritable mood within the psychic anxiety item, merging both irritability and anxious mood into a single item. On the other hand, the MADRS fails to include any item explicitly assessing irritability but does include the item inner tension, a measure of edginess and panic. Additionally, HDRS includes weight loss, which has a low prevalence across all levels of depression in our study and includes hypochondriasis and loss of insight, which have questionable diagnostic value or specificity to depression. While many rating scales include items for some of these core symptoms, they also contain "threshold symptom" items that are endorsed by only a subset of patients—including those with MDD at any level or only the most severe level. Thus, using these rating scales in clinical trials of mildly depressed patients may create a floor effect and may be one explanation for the reported lack of placebo-study drug separation for patients with mild-moderate depression or minor depression.[31–33]

Given that the frequency of endorsement and symptom severity are almost identical between patients in the minor depression–severe and MDD-mild groups, the *DSM* cutoff point of 5 symptoms for distinguishing between minor depression and MDD seems arbitrary and problematic. This observation is particularly important since many times the presence or absence of a diagnosis of MDD may influence both the decision to initiate treatment as well as the likelihood that care will be reimbursed by payers.

The *DSM-IV* Mood Disorders Field Trial,[34] which compared depressive symptom prevalence rates among MDD patients to those among patients with dysthymia, demonstrated that somatic/vegetative symptoms were better than cognitive/affective symptoms at distinguishing the 2 illness groups. These findings parallel our results identifying continuous/threshold symptoms (vegetative and somatic symptoms) that are more common among MDD patients and core symptoms (cognitive and affective symptoms) that are common to both MDD and minor depression patients and, therefore, less distinctive. In one analysis[35] from the Rhode Island Hospital Methods to Improve Diagnostic Assessment and Services (MIDAS) project, the authors reported *DSM-IV* MDD symptom prevalence rates ranging from 55% to 93% among clinic outpatients with MDD. Death/suicidal thoughts and psychomotor change had the lowest prevalence rates, 56.7% and 54.6%, respectively.[35] In our study, prevalence rates for symptoms on the IDS-C ranged from 21% to 99% for MDD patients, with prevalence rates of 84% for suicidal ideation, 87.6% for psychomotor slowing, and 63.9% for psychomotor agitation. These differences in prevalence rates between the MIDAS analysis and our study may be due to the evaluation of different populations (insured, clinic vs clinical trial sample) and/or the use of the IDS-C in our study, which allowed reports of both subthreshold and threshold levels of *DSM* symptoms.

Limitations to this study include the use of a minor depression sample and MDD sample originating from 2 different study cohorts, with a few important differences to mention: comorbid Axis I diagnoses, such as anxiety disorders, were exclusionary for the minor depression sample but allowed for the MDD sample. This difference may have affected IDS-C item endorsement, as symptoms that are part of the comorbid illness and listed on the IDS-C (eg, anxious mood, panic/phobic symptoms) may have been more likely endorsed by the MDD subjects than if the comorbidity had not been permitted. The difference in episode duration inclusion criteria between the minor depression and MDD cohorts might have led to more MDD subjects having received symptom-modifying treatment, though on the basis of their IDS-C scores, they still demonstrated high severity at enrollment. Alternatively, it may have led to an MDD cohort with a higher symptom burden than would be seen among MDD patients with a shorter episode duration. Different IDS-C versions (28-item and 30-item) were used for the 2 groups instead of 1 common version. While it is unlikely that the total number of items would have affected the patient's symptom endorsement, using the 30-item version with both the minor depression and MDD samples would have allowed us to compare 2 atypical features (interpersonal sensitivity, leaden paralysis/physical energy) that are not included on the 28-item version. (The data presented in this article are based on the 28-item scores.)

Setting the threshold for symptom prevalence at a score of 1 on the IDS-C led to the inclusion of symptoms that would be considered subthreshold by *DSM* standards. However, doing so created a broader picture of the varying symptom

intensity and duration that exist among patients who met *DSM* criteria for depressive illnesses. High occurrences of depressed mood and anhedonia among all subjects may be the result of an enrollment bias, as at least 1 of these items is required and sometimes both are used to meet criteria for MDD when using the SCID-I or for minor depression when using the DIS. Additionally, the separation of severity groups into low, moderate, and high was based on creating even numbers within 3 groups instead of using clinically meaningful IDS-C scores. Finally, the generalizability of these results to the larger population of depressed patients is limited by the fact that all minor depression and MDD subjects were pharmacologic, clinical trial participants rather than subjects surveyed in hospitals, outpatient clinics, and the community.

In conclusion, this study contributes to the growing literature suggesting that minor depression and MDD are related conditions within the spectrum of unipolar depressive illnesses. Core mood and cognitive symptoms are common among patients with either minor depression or MDD. The development of continuum and threshold symptoms as the core symptoms increase adds valuable preliminary evidence suggesting a possible layering effect of certain types of symptoms as one progresses from mild minor depression to severe MDD. Clinicians should carefully assess the full range of symptoms analyzed in this study, including those not currently included in the *DSM* criteria for MDD. Finally, our data suggest that the IDS-C provides better coverage of depressive symptoms than other scales traditionally used to assess treatment response.

Author affiliations: Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia (Drs Rakofsky, Schettler, Kinkead, and Rapaport); Department of Psychiatry, University of California, San Diego School of Medicine, San Diego (Drs Schettler and Judd); Department of Psychiatry, University of Pittsburgh School of Medicine (Drs Frank and Kupfer); Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia (Dr Thase), Duke-NUS Graduate Medical School, Singapore (Drs Rush and Thase); and Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut (Dr Yonkers).

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