The Multifactorial Presentation of Depression in Acute Care

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Depression is by its very nature a heterogeneous disorder; 2 patients with the same diagnosis (ie, major depressive disorder) may have few symptoms in common. This heterogeneity is evidenced by the fact that depression presents in a wide variety forms related to polarity (unipolar vs bipolar), symptoms (melancholic, atypical, psychotic, or anxious), onset (specific events, seasons, or age), recurrence, and severity. These diagnostic specifiers and subgroups can guide treatment decisions in several ways. For example, recognizing a specific depressive subtype in a patient can help the clinician select an appropriate treatment based on that patient's particular presentation. These subtypes can also guide treatment by helping the clinician and patient to identify and discuss factors that help or hinder the achievement of remission and recovery. Although depression specifiers and subtypes are subject to revision and change, many of them provide helpful information about recognition and treatment.
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When some people get depressed, they feel burdened by a gloomy mood, but others may instead feel a loss of interest or pleasure in their usual activities, and still others may experience both symptoms. The *DSM-5* criteria[1] for major depressive disorder (MDD) include having either of those symptoms—depressed mood or anhedonia—for at least 2 weeks, plus 4 or more of the following symptoms:

- Fatigue or low energy
- Insomnia or hypersomnia
- Loss of appetite/weight or increased appetite/weight
- Psychomotor retardation or agitation
- Poor concentration or indecisiveness
- Suicidal ideation
- Pathological guilt or feelings of worthlessness

With so many possible combinations of symptoms, MDD varies so much that 2 people may not even have one symptom in common—that is the heterogeneous nature of the illness. Despite this variability in presentation, clinicians must recognize depression in all its forms and provide appropriate treatment. Unrecognized or poorly treated depressive episodes may lead to recurrent or persistent depression, which increases health care costs and reduces patients' ability to function.

The multifactorial presentation of depression also affects treatment response, with different presentations of depression responding differently to treatment. Various subtypes of depression have been suggested to categorize these different presentations. Subtypes for MDD may be grouped by polarity, symptoms, onset, course of illness, and severity.

POLARITY-BASED SUBGROUPS

By definition, MDD is a unipolar disorder and is distinguished from bipolar disorder, which is defined by the history of mania or hypomania. It is controversial whether or not biological factors, other aspects of clinical course, and symptomatology of these 2 types of depression can be used to reliably differentiate them from one another.[2] Nevertheless, bipolar disorder is characterized by an earlier age at onset, more rapid recurrence, and greater mood variability than unipolar depression, for which episodes are more likely to feature anxiety and agitation.[2] Even patients who have never had a full-blown manic or diagnosable hypomanic episode may still have a bipolar spectrum disorder. Identifying hypomania and more subtly mixed episodes remains a challenge, and missing them may lead to incorrect diagnoses.[3] However, self-assessment screening instruments such as the Mood Disorder Questionnaire and the Hypomania Checklist-32 may help clinicians in this regard.

The distinction between bipolar and unipolar depression affects treatment choice because antidepressant treatment in patients with bipolar disorders can cause mood switches, cycling, agitated states, and treatment resistance.[4] For patients whose illnesses are judged to fall within the bipolar spectrum, treatment should include a mood stabilizer or an atypical antipsychotic or a combination of the 2, and an antidepressant or electroconvulsive therapy (ECT) can be used adjunctively if needed.[5] As research into the pathogenesis of depression continues, more similarities or differences may emerge between unipolar and bipolar depression, changing the way depression is studied, categorized, and treated.

SYMPTOM-BASED SPECIFIERS

Besides the unipolar/bipolar depression distinction, other subgroups of depression have been identified according to symptom profiles and included as diagnostic specifiers in the new *DSM-5*.[1] These groups include melancholic, atypical, anxious, and psychotic types.

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Clinical Points

- Recognize subgroups of depression based on symptoms, onset, course of illness, and severity.
- Tailor treatment according to depressive subtype, specifier, or other category to achieve the best possible outcome.

Melancholic Depression

Melancholia is the classical prototype of severe depression. The *DSM-5* illness specifier "with melancholic features" requires either anhedonia or lack of mood reactivity to pleasant events, plus 3 or more of the following symptoms: psychomotor retardation or agitation, weight loss, excessive guilt, early-morning sleep disturbances, depressed mood with despair or despondency, and worse mood in the mornings.[1]

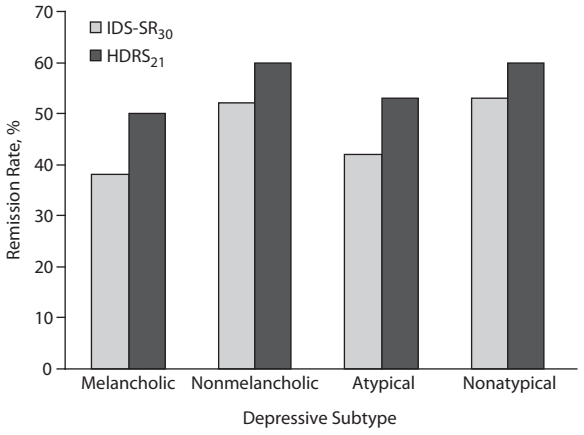
Melancholic depression affects about 25% to 30% of depressed patients.[6] Compared with patients with atypical depression (described below), melancholic patients tend to be older, with a higher number of depressive episodes and depression severity scores (Figure 1).[6]

Patients with melancholic depression are usually unresponsive to placebo treatments and may be somewhat less likely to benefit from psychotherapies and social interventions than patients with milder depressions.[6] Although not all experts are in agreement, many think that melancholia responds better to ECT and tricyclic antidepressants (TCAs) than to selective serotonin reuptake inhibitors (SSRIs).[6] In the STAR*D study,[7] melancholic patients displayed a significantly lower chance of remission with the SSRI citalopram than patients without melancholic features ($P < .0001$). In another large naturalistic study,[6] it was found that melancholic patients were treated more frequently with serotonin-norepinephrine reuptake inhibitors (SNRIs) than SSRIs. Patients with melancholic depression also received more concomitant antipsychotic medications than people with other subtypes of depression, which reflects the treatment resistance of the melancholic subtype.

Atypical Depression

The term *atypical depression*, the historical counterpart to melancholia, was coined by the first generation of intervention researchers to describe patients who presented with a reversal of the "typical" vegetative symptoms, including overeating, weight gain, and oversleeping, as well as other associated symptoms, such as phobic anxiety, chronic pain, and rejection sensitivity.[8] However, in modern context, atypical depression is hardly atypical and—depending on the criteria set used to make the diagnosis—may account for almost 40% of all depressive episodes.[9] In *DSM-5*, the specifier "with atypical features" requires mood reactivity and 2 or more of the following symptoms: weight gain or increased appetite, hypersomnia, leaden paralysis, or interpersonal rejection sensitivity.[1] However, mood reactivity has come under scrutiny as researchers investigate whether or not it is a significant feature of atypical depression.[9] Reversed vegetative symptoms of hypersomnia and overeating/weight gain may be sufficient to accurately identify atypical depression in many patients.[9]

Figure 1. Remission Rates Associated With Depressive Subtypes per Measurement-Based Rating Scales[a]



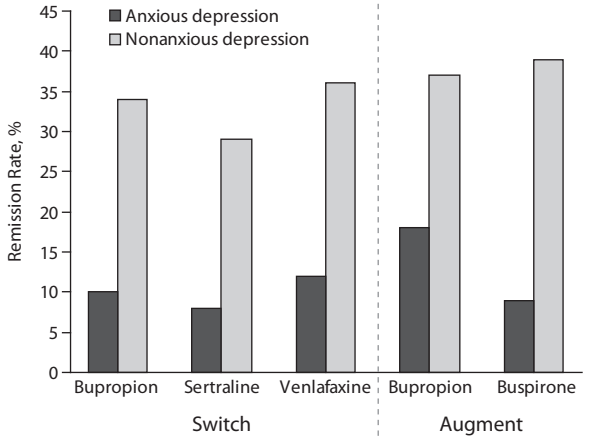
[a]Data from Gili et al.[6]
Abbreviations: $HDRS_{21}$ = 21-Item Hamilton Depression Rating Scale; $IDS\text{-}SR_{30}$ = Inventory of Depressive Symptomatology–Self Rated.

The demographics of atypical depression have proven both heuristically and clinically useful.[10] Compared with other depressed patients, atypical patients generally include a higher percentage of women with an earlier age at onset and a higher rate of suicide attempts.[9] These areas can help clinicians recognize patients with atypical depression and provide timely and appropriate treatment.

Perhaps the most important early validator of the concept of atypical depression was differential treatment response. Specifically, patients with atypical depressions were found to respond better to treatment with monoamine oxidase inhibitors (MAOIs) than TCAs or ECT.[10] In a meta-analysis[11] of randomized controlled trials, the MAOI phenelzine was found to improve response rates in atypical depression better than the TCA imipramine, whereas imipramine was equal to phenelzine only in patients lacking atypical reversed vegetative symptoms. Of course, the MAOIs are associated with side effects and the need to adhere to dietary restrictions, which have limited their use as first-line therapy, and in the modern era it is uncertain if the term *atypical depression* has any practical value for predicting treatment response with first-line therapies. SSRIs appear to be more effective for atypical depression than placebo, but the SSRI fluoxetine did not prove more effective than imipramine in a randomized 10-week trial including 154 patients with atypical depression.[12]

Whatever treatment is chosen, clinicians should measure symptom improvement using an assessment scale. Two commonly used assessment scales, the Hamilton Depression Rating Scale (HDRS) and the Montgomery-Asberg Depression Rating Scale (MADRS), focus primarily on melancholic symptoms, so clinicians may consider other instruments that include atypical symptoms, such as the Inventory of Depressive Symptomatology (IDS).[9]

Figure 2. Remission Rates in Level 2 of STAR*D: Anxious vs Nonanxious Depression[a,b,c]



[a]Data from Fava et al.[16]
[b]Remission rates based on Hamilton Depression Rating Scale scores.
[c]Patients who achieved no symptom remission in Level 1 or who could not tolerate citalopram were randomly assigned either to switch medications or to augmentation of citalopram with bupropion or buspirone.

Anxious Depression

Anxious depression has been defined dimensionally as MDD with high levels of anxiety symptoms and categorically as MDD with a comorbid anxiety disorder.[13] The dimensional approach may be more useful because patients with MDD may have high levels of anxiety symptoms that do not meet criteria for a specific anxiety disorder.[13] The *DSM-5* specifier "with anxious distress" requires 2 or more of the following symptoms: unusual restlessness, tension, poor concentration due to worry, a fear that something awful may happen, and a fear of losing control over oneself.[1]

Anxious depression is common, with 46% of patients in the STAR*D trial[17] and 49% in the German Algorithm Project (GAP3)[18] meeting criteria for anxious depression.[14,15] Both trials noted that patients with anxious depression were more likely than nonanxious patients to be older, unemployed, and more severely depressed and to exhibit melancholic rather than atypical features.[14,15]

Evidence also reveals poorer outcomes with pharmacotherapy for anxious versus nonanxious depressed patients.[13] For example, remission rates for anxious patients were 22% compared with 33% for nonanxious patients treated with citalopram in Level 1 of STAR*D.[16] Likewise, in Level 2, patients with anxious depression had lower rates of response and remission than nonanxious patients in both the switching and augmenting treatment options (Figure 2).[16] These results highlight the need to identify anxiety symptoms in patients with depression and apply flexible or alternate treatments such as adjunctive pharmacotherapy or cognitive therapy to target thoughts and behaviors associated with both depressed and anxious moods.[13]

Psychotic Depression

Psychotic depression is characterized by delusions or hallucinations; approximately 15% to 20% of patients with more severe episodes of major depression have psychotic features.[17] Individuals with psychotic depression tend to experience a higher recurrence rate, more frequent hospitalization, longer episodes, and greater impairment than patients with nonpsychotic depression.[18] For example, Gaudiano et al[19] found that patients with psychotic major depression had greater depression severity, suicidal ideation, and functional impairment at work and in relationships than depressed patients without psychotic features.

Despite the need for urgent, effective treatment, psychotic depression remains difficult to treat. Most treatment guidelines suggest either the combination of an antidepressant with an antipsychotic or ECT for the acute phase treatment of psychotic depression.[20] A 12-week, double-blind, randomized controlled trial[17] comparing olanzapine plus sertraline versus olanzapine plus placebo showed a higher remission rate for combination therapy (42%) versus olanzapine monotherapy (24%). However, a review[21] found that patients treated with vigorous courses of antidepressant therapy may do as well as those who receive combination therapy, although, surprisingly, few studies have been conducted with the SSRIs and second generation antipsychotics.

ONSET-BASED SUBGROUPS

Various subtypes of depression have been developed related to the onset of the major depressive episode. Seasonal affective disorder, peripartum/postpartum depression, and an episode of MDD within the context of recent bereavement are triggered by an event, while age-related depression subtypes are divided into early- versus late-life onset.

Seasonal Affective Disorder

Seasonal affective disorder is diagnosed when recurrent depressive episodes occur during a season, usually fall or winter, and remit during another season, usually spring or summer; the *DSM-5* includes the MDD specifier "with seasonal pattern."[1] Up to 10% of recurrent MDD cases follow a seasonal pattern,[22] and seasonal affective disorder prevalence increases with latitude and is more common in women.[23,24]

Patients with seasonal affective disorder may benefit from maintenance or pretreatment in addition to treatment during the predictable acute phase. Preventative treatment has proven successful with bupropion, according to evidence that demonstrated lower recurrence rates of depressive episodes in patients with seasonal affective disorder.[25] In addition to antidepressant treatment, bright light therapy is well-tolerated and often successful in reducing symptoms, although a study[26] showed that after-treatment costs were lower with fluoxetine than light therapy.

Peripartum and Postpartum Depression

Postpartum depression has historically been defined as a depressive episode occurring within 4 weeks of delivery.[27] Nonpsychotic postpartum depression occurs in an average of 13% of women who deliver,[28] and recurrence rates can be as high as 50% in subsequent pregnancies.[29] However, the onset of depression often actually occurs before delivery, so the

DSM-5[1] updated the relevant specifer to be "with peripartum onset," which includes both pregnancy and the postpartum period.

Screening for mood disorders before and during pregnancy may help clinicians identify women at risk for peripartum depression. Recognition is often complicated by the fact that many women experience mild depressive symptoms, tearfulness, anxiety, irritability, fatigue, and increased sensitivity after childbirth, but these symptoms typically resolve by the 10th postnatal day.[30] Clinicians should also distinguish peripartum and postpartum depression from postpartum psychosis, which is a rare but serious disorder characterized by delusional thoughts such as harming oneself or the baby and which constitutes a medical emergency.

The Edinburgh Postnatal Depression Scale (EPDS), a self-rated, 10-item scale, can be used to screen for postpartum depression and takes only 5 minutes for patients to complete.[31] A large study[32] that screened 10,000 mothers using the EPDS yielded 1,396 women (14%) who had a positive screen. Of the women who received a diagnosis after evaluation with the Structured Clinical Interview for *DSM-IV*, 69% were diagnosed with unipolar depressive disorders and 23% had bipolar disorders. Comorbid generalized anxiety disorder was common among those with unipolar depression. Postpartum depressive episodes were the most common (40%), followed by episodes during (33%) and before (27%) pregnancy. The women with postpartum depression were more likely to be younger, African American, publicly insured, single, and less educated than the women without depression.[32]

Many women with pregnancy-related depression prefer to avoid antidepressants, if possible, and may benefit instead from individual or group therapy. In such cases, a stepped-care approach may be suggested, with antidepressants reserved for those with more severe symptoms or those who do not respond to psychotherapy. Because parents may be concerned about the impact of medication exposure to the baby, the choice of medication, the recommended dosage and duration of therapy, and likely side effects should be carefully discussed.[30] Although most antidepressants are classified by the FDA as Class C with respect to the risk of fetal malformations, to a large extent the evidence collected over the past 20 years has been reassuring. For example, a study[33] of the impact of SSRIs on infant growth during the first year concluded that in utero exposure to SSRIs did not affect weight, length, or head circumference in the 46 infants whose mothers took an SSRI.

Bereavement

One of the most controversial aspects of the *DSM-5* has been the change regarding classification of depressions that occur in close temporal relationship with bereavement. A conservative interpretation of the *DSM-IV-TR* might lead one to conclude that if depressive symptoms begin within 2 months of the loss of a loved one, the patient is experiencing bereavement as opposed to MDD.[27] By contrast, *DSM-5* omits the bereavement exclusion and instead includes notes on distinguishing bereavement from a major depressive episode.[1] According to the *DSM-5*, the expression of "normal" grief following bereavement should not include symptoms such as persistent depressed mood, pervasive unhappiness, self-critical or pessimistic rumination, thoughts of suicide, and feelings of worthlessness. Normal grief, as opposed to a depressive episode, usually comes in waves, is specifically associated with thoughts of the loved one, and decreases in intensity over time.[1] Of course, the *DSM-IV-TR* also permitted clinicians to use their judgment to differentiate bereavement from MDD even within the specified time window and provided examples of when symptom severity, level of functional impairment, or the presence of specific symptoms (such as marked psychomotor disturbances, delusions, or hallucinations) would suggest that MDD was the more appropriate diagnosis.[27] Generally, treatments for MDD are effective in people experiencing a major depressive episode in the context of bereavement.

Early- Versus Late-Onset Depression

Early versus late onset is another common form of subgrouping for depression, but the exact cutoff age has not yet been clarified, making the validity of this delineation hard to determine. In STAR*D, *early onset* was defined as a depressive episode before age 18 years and was reported in about 36% of patients.[34] It was associated with female sex, longer episodes, more suicidality, greater symptom severity, more comorbid psychiatric illnesses, and more sadness, irritability, agitation, and atypical features, as well as lower educational attainment and marriage rates than late-onset depression.[34] A recent review,[35] however, comparing clinical features of early- versus late-onset depression uncovered no distinguishing features between the 2 groups except for a higher frequency of familial mood disorders in the early-onset group. This review covered only studies of adults, not of patients younger than 18 years, and 8 of 10 studies used 60 years as the cutoff age for late-onset depression.

Another study[36] divided 301 adult patients with first-episode depression into early-onset (18–30 years) and late-onset (31–70 years) groups. The early-onset group (33%) had more comorbid personality disorders and neuroticism but fewer stressful life events prior to onset compared with the late-onset group. However, symptom severity, treatment response, and family history of psychiatric illness were not significantly different between groups (Table 1).[36] As the early- versus late-onset subgroups of depression continue to be studied, researchers may uncover more specific clinical features or treatment options based on age at onset; however, agreement on age cutoffs is needed.

COURSE OF ILLNESS SPECIFIERS

Specifying the course of illness can impact treatment decisions, especially regarding whether or not to continue treatment once symptoms remit. Clinicians must ascertain if the patient is experiencing a single depressive episode, recurrent episodes, or a chronic course.

The specifier "recurrent episode" is given when at least a 2-month period of remission separates the current episode

from the previous one.[1] Patients with recurrent MDD experience psychosocial impairments that affect their family, social, and professional roles.[37] Two-year antidepressant maintenance treatment has been shown to improve these areas and overall quality of life in patients with recurrent MDD compared with placebo.[37] Focusing on long-term outcomes and treatment adherence can help patients avoid recurrent episodes.

The *DSM-5*[1] has consolidated the 2 diagnoses of chronic MDD and dysthymia into *persistent depressive disorder (dysthymia)*. The criteria for persistent depressive disorder (dysthymia) omit 4 symptoms that are criteria for a major depressive episode: anhedonia, psychomotor retardation or agitation, suicidal ideation, and excessive guilt. The 1 required symptom is depressed mood for at least 2 years, and patients must also experience at least 2 of the following symptoms: insomnia/hypersomnia, eating too much or too little, low energy/fatigue, poor self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness.

Table 1. Clinical Characteristics of 301 Patients With First-Episode Depression by Age at Onset[a]

Characteristic	Total (N = 301)	Age ≤ 30 Years (n = 99)	Age > 30 Years (n = 202)	P[b]	B/OR (95% CI)[c] Early vs Late Onset (Adjusted for Gender)	P[d]
Severity of depression, N (%)						
Mild	73 (24.3)	19 (19.2)	54 (26.7)		0.6 (0.3–1.2)	.1
Moderate	161 (53.5)	56 (56.6)	105 (52.0)	.4	0.8 (0.4–1.5)	.5
Severe	67 (22.3)	24 (24.2)	43 (21.3)		1.0	
Melancholic features, N (%)	196 (65.1)	58 (58.6)	138 (68.3)	.1	0.7 (0.4–1.2)	.2
Psychotic features, N (%)	13 (4.3)	4 (4.0)	9 (4.5)	.9	1.4 (0.4–5.0)	.6
Suicidal ideations, N (%)	194 (64.5)	69 (69.7)	125 (61.9)	.2	1.6 (0.9–2.7)	.09
Atypical features, N (%)	11 (3.7)	10 (10.1)	1 (0.5)	< .0005	15.4 (1.9–122.9)	.01
Psychiatric comorbidity, N (%)						
Anxiety/OCD	143 (47.5)	53 (53.5)	90 (44.6)	.1	1.2 (0.7–2.0)	.4
Alcohol abuse	45 (15.0)	7 (7.1)	38 (18.8)	.007	0.4 (0.2–0.9)	.03
Drug abuse	22 (7.3)	14 (14.1)	8 (4.0)	.001	4.1 (1.6–10.8)	.004
Somatoform/eating disorders	14 (4.7)	8 (8.1)	6 (3.0)	.05	2.1 (0.7–6.4)	.2
Personality disorders, N (%)						
Any personality disorder	96 (31.9)	55 (55.6)	41 (20.3)	< .0005	4.8 (2.8–8.3)	< .0005
Personality traits, mean (SD)						
Neuroticism score	11.6 (6.3)	14.0 (5.5)	10.5 (6.3)	< .0005	−2.7 (−4.4 to −1.0)	.002
Extroversion score	11.5 (5.4)	11.4 (5.7)	11.5 (5.3)	.9	−0.05 (−1.6 to 1.5)	1.0
Anxiety score, mean (SD)	10.2 (6.2)	10.7 (5.7)	10.0 (6.4)	.4	0.1 (−1.4 to 1.7)	.9
Family history of psychiatric illness in 1 generation, N (%)						
Depression	87 (28.9)	33 (33.3)	54 (26.7)	.2	1.4 (0.8–2.5)	.20
Any psychiatric illness	199 (66.1)	67 (67.7)	132 (65.3)	.7	1.0 (0.6–1.6)	.9
Family history of suicide in 1 generation, N (%)	10 (3.3)	2 (2.0)	8 (4.0)	.4	0.5 (0.1–2.3)	.3
One or more stressful life events, N (%)	189 (62.8)	46 (46.5)	143 (70.8)	< .0005	0.4 (0.2–0.7)	.001

[a]Adapted with permission from Bukh et al.[36] [b]*P* values (2-sided) in univariate analyses comparing patients with early and late onset (χ^2-test categorical data and t-test for continuous data). [c]Correlation coefficients in multiple regression models/odds ratios in logistic regression models; the effect of age-of-onset adjusted for the affect of gender. [d]*P* values (2-sided) in the regression models.
Abbreviations: CI = confidence interval, *DSM* = Diagnostic and Statistical Manual of Mental Disorders, OCD = obsessive-compulsive disorder, OR = odds ratio.

About 20% of patients with MDD develop a chronic course of illness.[38] In the STAR*D study,[38] patients with chronic depressive illness often had comorbid generalized anxiety disorder, greater medical illness burden, and a history of suicide attempts. Other factors associated with chronic depression include childhood mistreatment, low socioeconomic status, and racial/ethnic minority status.[38,39]

A chronic course often becomes difficult to treat, and specific therapies for this subgroup are being explored. Continuation therapy is necessary to reduce the risk of relapse in chronic depression, and clinicians can consider combination therapy for treatment-resistant patients.[40] One study[41] found that the combination of nefazodone and cognitive-behavioral analysis was significantly more effective than either treatment alone ($P < .001$), but another study[42] found that outcomes with individualized pharmacotherapy alone were not significantly different from combination treatment with pharmacotherapy and 1 of 2 forms of psychotherapy. Longitudinal studies are needed to determine optimal treatment for chronic depression.

SEVERITY AND RESPONSE SPECIFIERS

Finally, one can categorize MDD based on illness severity—mild, moderate, or severe—and treatment response—in partial remission or in full remission.[1] An episode is mild if the minimum number of required symptoms is present, the symptoms are distressing but manageable, and the patient's functional impairment is minor. Severe MDD is indicated for a substantial excess of the required number of symptoms for a major depressive episode, symptoms are unmanageable for the patient, and disability in responsibilities is obvious. Moderate severity falls between the mild and severe criteria. Full remission is achieved if a patient remains symptom-free for at least 2 months. If the period is less than 2 months or a few symptoms persist, the patient is in partial remission, according to *DSM-5* criteria.[1]

Severity dictates treatment modality in many guidelines and algorithms. Clinicians should tailor treatments according to patients' individual needs for efficacy and tolerability. For example, a patient with severe MDD may be willing to tolerate more side effects to achieve remission than a patient with mild symptoms who is concerned about issues like weight gain with an SSRI.

CONCLUSION

Depression presents in many forms, and dividing it into subgroups can help clinicians with the recognition and specific treatment of different types. The distinction between unipolar and bipolar depression, for example, affects whether or not antidepressants are used as first-line treatment or as monotherapy. Melancholic depression, in which patients

tend to have decreased appetite and wakefulness, is more responsive to TCAs and ECT than to SSRIs and psychotherapy. Atypical depression is associated with increased appetite and fatigue and responds better to MAOIs and TCAs than to SSRIs or ECT. Symptoms of psychosis and anxiety with depression indicate the need for adjunctive treatments, with an antipsychotic for psychosis and other therapy, including cognitive therapy, for anxiety.

The time of onset of a major depressive episode can also be used to categorize patients. Patients with depression that follows a seasonal pattern, for example, may require light therapy in addition to antidepressant treatment, and preventative treatment may be needed. When women experience peripartum depression, clinicians should be prepared with treatment options that are appropriate for both the mother and the baby.

The persistence of depressive illness also affects treatment because longer continuation therapy may be needed once patients achieve symptom remission. Finally, the severity of MDD should be specified as mild, moderate, or severe to help the clinician and patient weigh the benefits and risks of treatment options.

Although these subgroups have grown and changed in recent years, many of them are helpful for recognition and treatment. As more research is conducted, these groupings may change, perhaps by identifying genes or brain activity specific to various forms of depression.

Drug names: bupropion (Wellbutrin, Aplenzin, and others), citalopram (Celexa and others), fluoxetine (Prozac and others), imipramine (Tofranil and others), olanzapine (Zyprexa and others), phenelzine (Nardil and others), sertraline (Zoloft and others), venlafaxine (Effexor and others).
Disclosure of off-label usage: Dr Thase has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this activity.

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