Unipolar minor depression in adults: Management

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INTRODUCTION

The continuum of clinical depression ranges in severity from subsyndromal symptoms to the syndromes of minor depression and major depression [1-3]. Unipolar minor depression is characterized by two to four depressive symptoms that are present during the same two-week period, along with distress or psychosocial impairment (table 1). Compared with major depression, minor depression tends to have shorter episodes, less comorbidity, less psychosocial and physical impairment, and fewer recurrences [1,2,4].

Nevertheless, minor depression is a common syndrome that causes clinically significant distress and impairs functioning [5-9]. In addition, minor depression is associated with somatic symptoms [6,10], comorbid psychiatric and general medical disorders [6,10], and substantial healthcare utilization and costs [1,10,11]. Most patients with minor depression do not seek treatment from a mental health clinician, but are frequently seen in primary care [5,12]. Although minor depression is at least as prevalent as major depression, fewer patients with minor depression are accurately diagnosed by primary care clinicians [6,13].

This topic reviews the management and treatment of minor depression. The epidemiology, pathogenesis, clinical manifestations, assessment, and diagnosis of minor depression are discussed separately, as are the clinical features, diagnosis, treatment, and prognosis of major depression:

- (See "Unipolar minor depression in adults: Epidemiology, clinical presentation, and diagnosis".)

- (See "Unipolar depression in adults: Assessment and diagnosis".)
- (See "Unipolar major depression in adults: Choosing initial treatment".)
- (See "Unipolar depression in adults: Choosing treatment for resistant depression".)
- (See "Unipolar depression in adults: Course of illness".)

TERMINOLOGY

The term “depression” can refer to a mood state, syndrome, or specific disorder. (See "Unipolar depression in adults: Assessment and diagnosis", section on 'Definitions of depression'.)

Minor depression is a syndrome that is characterized by two to four depressive symptoms that are present during the same two-week period, along with distress or psychosocial impairment (table 1). Other terms have been used to describe minor depression, including [12,14,15]:

- Mild depression
- Subthreshold depression
- Subsyndromal depression
- Subclinical depression
- Depressive symptoms
- Other specified depressive disorder

The definition of minor depression varies among different studies [12]. In the most widely used definitions, the number of concurrent symptoms ranges from one to three [1,16] or two to four [2,7], the symptoms cause clinically significant distress or psychosocial impairment, and the minimum duration of the syndrome is two to four weeks [12,17,18]. The diagnosis of minor depression (table 1) is discussed separately. (See "Unipolar minor depression in adults: Epidemiology, clinical presentation, and diagnosis", section on 'Diagnosis'.)

GENERAL PRINCIPLES

Treatment strategies and goals — In addition to watchful waiting, treatment options for minor depression include psychotherapy and pharmacotherapy [19]. However, the benefits of these interventions are often modest [17,20-22].

The primary goal of treatment is to alleviate depressive symptoms and improve functioning. Additional goals include reducing other symptoms, such as anxiety and somatic symptoms, as well as preventing minor depression from progressing to major depression.

Primary care patients and collaborative care — Most outpatients with depression are treated by primary care clinicians [23]. In some cases, treatment occurs within collaborative (integrated) care, which integrates psychiatric treatment into primary care settings. Collaborative care is administered by a team that generally includes a primary care clinician and mental health specialist; the team educates patients about depression, teaches skills for managing it, provides psychotherapy and/or pharmacotherapy, and systematically monitors patients. (See "Unipolar depression in adult primary care patients and general medical illness: Evidence for the efficacy of initial treatments".)

Measurement based care — Measurement based care is the systematic and quantitative assessment of symptoms with rating scales during treatment. Although routine monitoring with rating scales may perhaps identify nonresponders, detect residual or prodromal symptoms, and help patients recognize improvement, this is not standard clinical practice. There is no evidence demonstrating that measurement based care improves outcomes for minor depression; this may be due in part to the scarce literature and the limited amount of improvement that is required for the minor depressive episode to resolve.

Additional information about measurement based care is discussed separately. (See "Using scales to monitor symptoms and treat depression (measurement based care)".)

Referral — Most minor depressive episodes are treated by internists, family physicians, and other primary care clinicians [24], sometimes in conjunction with psychotherapists. However, for moderate to severe episodes that are unresponsive to multiple (eg, two to three) treatment trials, we suggest referral to a psychiatrist. In addition, referral is typically indicated for suicidal patients.

CHOOSING TREATMENT

We suggest that acute treatment of minor depression proceed according to the sequence described in the subsections below. Patients start with initial treatment and progress through each step until they respond:

- Initial treatment – Psychotherapy with demonstrated efficacy for minor depression (eg, cognitive-behavioral therapy [CBT])
- Treatment-resistant patients – Switch to a different psychotherapy
- Treatment-refractory patients – Switch to or add-on an antidepressant

Antidepressants are often prescribed as initial treatment for minor depression, especially for patients who do not have convenient access to psychotherapy or who prefer pharmacotherapy.

Initial treatment — For patients with minor depression, we suggest structured, time-limited psychotherapy as initial treatment, based upon its efficacy in multiple randomized trials. We typically use CBT because it is the most widely studied option and is frequently more available than other psychotherapies. However, reasonable alternatives to CBT include behavioral activation, cognitive therapy, interpersonal psychotherapy, and problem-solving therapy. All of these therapies are structured according to a treatment manual, and are typically administered over a period of two to four months in either an individual or group format. Due to the time-limited nature of these psychotherapies, patients generally receive a full course of therapy, regardless if nonresponse persists through the middle phases of treatment. Therapeutic response and adherence to homework assignments are monitored at each session. Evidence supporting the use of psychotherapy in general, as well as the principles and evidence for each specific psychotherapy, are discussed below. (See 'Evidence of efficacy' below.)

However, watchful waiting is a reasonable alternative to psychotherapy for minor depression of recent onset, especially for patients who prefer this approach and do not have suicidal ideation or relatively severe functional impairment [25]. During watchful waiting, the patient is monitored every two to six weeks to ensure that symptoms are not worsening and a major depressive episode has not ensued [26]. It is also helpful to educate patients about depression, including the connections between stress, depressive symptoms, and physical symptoms such as abdominal discomfort, fatigue, or headache. If symptoms worsen during watchful waiting, or do not resolve satisfactorily after 6 to 12 weeks of watchful waiting, we actively treat patients.

Evidence supporting the use of watchful waiting includes prospective observational studies of patients (n = 111, 180, and 226) who received watchful waiting for one month prior to random assignment of treatment [18,21,27]. At the end of watchful waiting, remission of minor depression occurred in 6 to 22 percent. Indirect evidence regarding the benefit of watchful waiting includes a meta-analysis of six randomized trials that compared antidepressants with placebo in 468 patients with minor depression who were treated for 6 to 12 weeks [20]. The number of patients who responded (reduction of baseline symptoms ≥50 percent) to antidepressants or placebo was comparable (41 and 38 percent).

Evidence of efficacy — Most randomized trials that evaluated psychotherapy for minor depression did not adequately control for the nonspecific effects of psychotherapy. Trials that are adequately controlled are less likely to yield positive effects, because a substantial portion of control-group patients improve. In addition, no head-to-head trials have compared psychotherapy with pharmacotherapy.

Evidence supporting the use of psychotherapy to alleviate minor depression includes a meta-analysis of 14 randomized trials (number of patients not reported), which compared psychotherapy (CBT in eight of the trials) with control conditions (typically waiting list or usual care) [28]. The analyses found a significant, small to medium clinical effect favoring psychotherapy. The number needed to treat was five, meaning that treatment of approximately five patients with psychotherapy yielded a beneficial response in one additional patient that would not have occurred with the control condition. A subsequent meta-analysis of 32 randomized trials (total n >5700 patients) found that psychotherapy was more effective than control conditions, and the clinical effect was large [29].

In addition, multiple randomized trials indicate that psychotherapy can prevent progression of minor depression to major depression [22,30-32]; the following studies found that the number needed to treat ranged from 6 to 13:

- A meta-analysis of five randomized trials compared psychotherapy (CBT in four of the trials) with usual care in 480 patients with minor depression [28]. Follow-up at six months found that major depression was less likely to occur in patients who received psychotherapy, and the clinical advantage favoring psychotherapy was moderate to large. The number needed to treat was 10.

- A meta-analysis of 17 randomized trials compared psychotherapy with control conditions in patients with minor depression (sample size not reported) and found that the subsequent risk of developing major depression was reduced with psychotherapy (incident rate ratio 0.7, 95% CI 0.6-0.9) [33]. The number needed to treat was 13.

- A subsequent, open label randomized trial enrolled patients receiving usual primary care for minor depression (n = 406) and assigned them to psychotherapy based upon CBT and problem-solving therapy, or to psychoeducation about depression [34]. Both treatments were web-based, self-help interventions. Psychotherapy consisted of six sessions that each lasted 30 minutes, and was supported by an online trainer. The sample included patients receiving antidepressants. During 12 months of follow-up, the estimated cumulative incidence of major depression was less with psychotherapy than psychoeducation (32 versus 47 percent). The number needed to treat was six. In addition, symptoms of anxiety improved more with psychotherapy.

One meta-analysis (eight randomized trials, 1087 patients), which compared psychotherapy with a control condition, found that psychotherapy did not prevent minor depression from progressing to major depression [35]. However, in the largest trial (240 patients), which found that psychotherapy was not beneficial, half of the patients had subthreshold anxiety rather than

minor depression [36]. In addition, active treatment consisted of a stepped care program that administered multiple elements such as watchful waiting prior to the use of psychotherapy at month 6 of the study.

The remaining material in this section briefly describes specific psychotherapies that can help patients with minor depression, and the evidence supporting their use:

- **CBT** – CBT combines cognitive therapy and behavioral therapy. Cognitive therapy attempts to modify the dysfunctional thoughts, beliefs, and attitudes (eg, "I'm no good," "there's nothing I can do," or "my situation is hopeless") that underlie behaviors associated with depression. Behavioral therapy focuses upon modifying the patient's problematic behavioral responses (eg, social isolation and inactivity) to environmental stimuli or dysfunctional thoughts.

  Evidence that CBT can improve minor depression includes multiple randomized trials. As an example, a meta-analysis of eight trials (number of patients not reported) compared CBT with usual care or a waiting list [28]. Improvement of minor depression at the end of treatment was superior with CBT than the control conditions, and the difference was clinically small to moderate. The number needed to treat was four. A subsequent meta-analysis of 16 randomized trials (number of patients not reported) found that CBT was more efficacious than usual care, and the clinical effect was moderate to large [29].

- **Behavioral activation** – Behavioral therapy is one component of CBT, and behavioral activation is a type of behavioral therapy. Behavioral activation focuses on re-engaging with positive environmental stimuli and increasing rewarding activities, reducing avoidance behavior, promoting behaviors that decrease rumination, and improving problem-solving skills. The therapy makes use of interventions that include identifying depressive behaviors, analyzing triggers and consequences of depressive behaviors, setting goals, self-monitoring, structuring and scheduling daily activities consistent with one's goals, problem solving, and establishing routines.

  Evidence supporting the use of behavioral activation for minor depression includes randomized trials:

  - An eight-week randomized trial compared behavioral activation with usual care in patients age 65 years and older (n = 705) [22]. Behavioral activation was administered weekly by a nurse or psychologist as part of collaborative care in a primary care setting; most sessions were conducted by telephone and the average length of each session was 30 minutes. The sample included patients receiving antidepressants. Follow-up assessments four months after study entry found that improvement of depression was

greater with behavioral activation/collaborative care than usual care, and the clinical effect was small to moderate; the benefit of active treatment persisted 12 months after study entry. In addition, progression to major depression at the 12-month assessment occurred in fewer patients who received behavioral activation than usual care (16 versus 28 percent). Symptoms of anxiety and health related quality of life also improved more with behavioral activation. However, attrition by month 4 was more than twice as large among patients who received active treatment than usual care (24 versus 10 percent).

- A five-week randomized trial compared behavioral activation with no treatment in 118 university students aged 18 to 19 years [37]. Behavioral activation was conducted weekly, with each session lasting 60 minutes. Improvement of depression was greater in the behavioral activation group, and the clinical benefit was large.

- An eight-week randomized trial compared group-based behavioral activation with usual care in 183 primary care patients with minor depression [38]. Active treatment consisted of eight, two-hour weekly sessions and included training in mindfulness skills. At the follow-up assessment 12 months after randomization, improvement of symptoms was greater with behavioral activation than usual care and the clinical benefit was moderately large. In addition, the incidence of unipolar major depression was less in patients who received active treatment than controls (11 versus 27 percent).

- **Cognitive therapy** – Cognitive therapy is one component of CBT, and cognitive therapy appears to be efficacious for minor depression. As an example, a four-week randomized trial compared cognitive therapy with an active control in 41 university students aged 18 to 24 years with minor depression [39]. Both study treatments were administered daily (28 sessions) by computer. Cognitive therapy focused upon modifying the tendency of depressed patients to selectively attend to negative information (eg, angry, hopeless, or sad information). Improvement of depression was greater with cognitive therapy than the active control, and neuroimaging revealed that improvement was associated with changes in connectivity in specific neural circuits.

- **Interpersonal psychotherapy** – Interpersonal psychotherapy focuses upon improving problematic interpersonal relationships or circumstances that are directly related to the current depressive episode. Interpersonal relationships and depressive symptoms appear to affect each other in a reciprocal manner. Improvement of interpersonal functioning reduces symptoms, which leads to additional spontaneous improvement of interpersonal functioning, which in turn reduces depressive symptoms further. There are four categories of interpersonal foci that are identified in interpersonal psychotherapy as associated with

the onset or maintenance of depression: grief over loss (eg, death of a spouse), role disputes (eg, conflicts at work or home about expectations from the relationship), role transitions (eg, childbirth, divorce, or retirement), and interpersonal skills deficits (pervasive problems starting and maintaining relationships, and chronically impoverished, contentious, and unfulfilling relationships). Additional information about interpersonal psychotherapy is discussed separately. (See "Interpersonal Psychotherapy (IPT) for depressed adults: Indications, theoretical foundation, general concepts, and efficacy" and "Interpersonal Psychotherapy (IPT) for depressed adults: Specific interventions and techniques".)

Evidence supporting the use of interpersonal psychotherapy for minor depression includes a meta-analysis of five randomized trials (number of patients not reported), which compared interpersonal psychotherapy with control conditions [31]. During follow-up periods ranging from 3 to 18 months, worsening of symptoms leading to onset of major depression was less likely to occur in patients treated with interpersonal psychotherapy (odds ratio 0.3, 95% CI 0.1-0.9). The number needed to treat was seven.

- **Problem-solving therapy** – Problem-solving therapy incorporates some CBT strategies and is based upon the principle that depression is related to social problems. One goal of therapy is to develop rational and effective problem-solving skills. Patients learn to identify and define their problems, and for each problem, consider the barriers to its resolution, set an achievable goal, list and evaluate the advantages and disadvantages for all available solutions (brainstorming), choose one option, develop an action plan and implement it, and evaluate the outcome [27].

  Evidence that problem-solving therapy can improve minor depression includes randomized trials:

  - A six-week trial compared problem-solving therapy with usual care in 29 primary care patients; active treatment included six sessions administered by telephone, with each session lasting 20 minutes [40]. Improvement was greater with problem-solving therapy.

  - A nine-week trial (n = 151 primary care patients) compared problem-solving therapy (six sessions, each lasting 30 minutes) with usual care and found that improvement was greater with problem-solving therapy [27].

  - An eight-week randomized trial enrolled 230 low income mothers with depressive symptom rating scale scores that on average indicated a mild level of severity below the threshold for major depression; the sample included patients receiving

antidepressants [32]. The mothers were assigned either to usual community case management services or to problem-solving education (six sessions, each lasting 30 to 60 minutes) administered by lay trainers who were not licensed clinicians. During 12 months of follow-up, episodes of moderately severe depressive symptoms occurred in fewer mothers who received problem-solving education than usual services (incident rate ratio 0.6, 95% CI 0.4-0.9).

Treatment-resistant patients — If patients with unipolar minor depression do not respond to initial treatment, we suggest the following steps:

- Verify that the patient has unipolar minor depression rather than a different condition. (See "Unipolar minor depression in adults: Epidemiology, clinical presentation, and diagnosis", section on 'Differential diagnosis'.)
- Ask about adherence with treatment because nonadherence is common during treatment of psychiatric disorders; improving adherence with psychotherapy homework can convert nonresponders to responders.
- Establish whether there are significant life stressors (eg, nonsupportive partner) that need to be addressed.
- Determine if comorbid psychopathology (eg, anxiety disorder, personality disorder, or substance use disorder) is present. If a disorder other than minor depression is more salient, treatment should refocus upon the primary problem. (See "Unipolar minor depression in adults: Epidemiology, clinical presentation, and diagnosis", section on 'Comorbidity'.)

If the diagnosis of minor depression is confirmed as the primary focus of treatment and nonadherence has been ruled out, we suggest a second course of a different psychotherapy for patients who do not respond to an initial course of psychotherapy. The specific options are discussed above. (See 'Initial treatment' above.)

Treatment-refractory patients — Patients with minor depression may not respond to multiple courses of different psychotherapies. For these treatment-refractory patients, as well as patients who do not have access to psychotherapy, we suggest antidepressants, either as add-on treatment with psychotherapy or as monotherapy, based upon randomized trials. This approach is consistent with practice guidelines from the United Kingdom National Institute for Health and Clinical Excellence [41,42].

Many clinicians use antidepressants for minor depression [36]. Among patients with minor depression who enrolled in randomized trials, 12 to 23 percent of patients were currently taking antidepressants at the time of study entry [22,32,34].

In addition, antidepressants are often acceptable to patients with minor depression. A meta-analysis of two randomized trials in 186 patients found that the dropout rate for any reason was comparable for antidepressants and placebo (27 and 25 percent) [20].

Although several different antidepressants are available and reasonable to use, we suggest a selective serotonin reuptake inhibitor (SSRI) such as fluoxetine. SSRIs have been studied more often for minor depression than any other class of antidepressants [20] and SSRIs are generally well tolerated. Additional information about choosing a specific antidepressant for treating unipolar depression is discussed separately in the context of unipolar major depression. (See "Unipolar major depression in adults: Choosing initial treatment", section on 'Antidepressant pharmacotherapy'.)

Depressed outpatients started on antidepressants should generally be seen one to two weeks after starting an antidepressant and subsequently monitored (by phone or visit) at least every two to four weeks for six to eight weeks, depending upon the clinical urgency. Therapeutic response, adverse effects, and adherence should be assessed, with particular attention given to symptoms of suicidal ideation and behavior. Following response, the frequency of assessments can be tapered.

We generally treat minor depression for 6 to 12 weeks before deciding whether a regimen has sufficiently relieved symptoms. However, for patients who show no improvement or are deteriorating after two to three weeks, we increase the dose within the therapeutic range or augment with a second drug. If improvement is modest (eg, reduction of baseline symptoms ≤25 percent) after four to six weeks, it is reasonable to increase the dose, augment with a second drug, or switch to a different antidepressant. Additional information about the duration of an adequate treatment trial, and choosing next step treatment with a different antidepressant, is discussed separately in the context of unipolar major depression. (See "Unipolar major depression in adults: Choosing initial treatment", section on 'Duration of an adequate trial' and "Unipolar depression in adults: Choosing treatment for resistant depression", section on 'Next step treatment'.)

The duration of treatment for patients with minor depression who respond to antidepressants has not been well studied. We typically provide maintenance treatment according to practices established for major depression. (See "Unipolar depression in adults: Continuation and maintenance treatment", section on 'Duration'.)

Whereas randomized trials have consistently supported using psychotherapy to treat minor depression (see 'Evidence of efficacy' above), the evidence for using antidepressants is mixed. However, psychotherapy trials have typically compared active treatment with control conditions such as usual care or a waiting list control, which did not adequately control for nonspecific effects such as attention [28]. By contrast, pharmacotherapy trials have compared antidepressants with placebos, which controlled for attention. It is plausible that if antidepressants were compared with usual care or a waiting list control, the benefit of antidepressants would be comparable to that for psychotherapy.

Multiple randomized trials suggest that antidepressants are generally not beneficial for minor depression [43-45]:

- A meta-analysis of six randomized trials compared antidepressants with placebo in 468 patients who were treated for 6 to 12 weeks; the antidepressants included amitriptyline, fluoxetine, isocarboxazid, and paroxetine. Response (reduction of baseline symptoms ≥50 percent) was comparable for the two groups (41 and 38 percent) [20].

- In a subsequent 12-week randomized trial that compared citalopram (20 mg/day) with placebo in 47 patients, improvement of symptoms was comparable [46].

However, the largest trial in the meta-analysis found that fluoxetine (10 to 20 mg/day) was superior to placebo for minor depression [18,47]. The trial included 157 patients, who constituted 34 percent of the patients in the meta-analysis. During the 12-week trial, improvement of depression was greater with fluoxetine than placebo across multiple outcome measures, suicidal ideation was less likely to worsen with fluoxetine, and fluoxetine was well tolerated.

Additional evidence that may possibly support using an antidepressant for minor depression includes analyses that focused upon the subgroup of patients with more severe symptoms and functional impairment:

- An 11-week randomized trial that compared paroxetine (10 to 40 mg/day) with placebo in 138 primary care patients found that improvement was comparable for the two groups [48]. However, a separate analysis divided patients into three groups according to the severity of depressive symptoms and functional impairment; in the group with the greatest severity, improvement was superior in patients who received the antidepressant rather than placebo.

- A six-week randomized trial compared amitriptyline (median dose 125 mg/day) with placebo in 141 primary care patients with major or minor depression who completed at

least four weeks of treatment, and found that improvement was superior with active drug. In a separate analysis, patients were divided into three groups according to symptom severity; among patients with either the greatest or intermediate level of severity, amitriptyline was beneficial [49,50].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Depressive disorders".)

SUMMARY AND RECOMMENDATIONS

- Minor depression is a syndrome that is characterized by two to four depressive symptoms that are present during the same two-week period, along with distress or psychosocial impairment (table 1). (See 'Introduction' above and 'Terminology' above and "Unipolar minor depression in adults: Epidemiology, clinical presentation, and diagnosis".)

- In addition to watchful waiting, treatment options for minor depression include psychotherapy and pharmacotherapy. However, the benefits of these interventions are often modest. (See 'General principles' above.)

- For patients with minor depression, we suggest structured, time limited psychotherapy as initial treatment, rather than antidepressants or watchful waiting (**Grade 2C**). However, watchful waiting is a reasonable alternative to psychotherapy for minor depression of recent onset, especially for patients who prefer this approach and do not have suicidal ideation or relatively severe functional impairment. (See 'Initial treatment' above.)

- When psychotherapy is chosen, we often use cognitive-behavioral therapy (CBT) because it is the most widely studied option and is frequently more available than other psychotherapies. Reasonable alternatives to CBT include behavioral activation, cognitive therapy, interpersonal psychotherapy, and problem-solving therapy. (See 'Evidence of efficacy' above.)

- Our suggested approach for patients who do not respond to an initial course of psychotherapy is to administer a second course of a different psychotherapy. (See 'Treatment-resistant patients' above.)

- Patients with minor depression, who do not respond to multiple courses of different psychotherapies or do not have access to psychotherapy, are often treated with antidepressants. (See 'Treatment-refractory patients' above.)

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