Evidence-Based Treatment of Dysthymia in Primary Care

Case Study and Commentary, Terry M. Bush, PhD, Wayne Katon, MD, Elizabeth H.B. Lin, MD, MPH, and Evette J. Ludman, PhD

INTRODUCTION
The prevalence of dysthymic disorder in primary care approaches that for major depression [1–4]. Dysthymia, however, is much less likely than major depression to be treated by primary care providers (PCPs), in part because historically it has been thought to be untreatable [5,6]. Recent scientific advances in the treatment of dysthymia may now help PCPs to confidently and effectively care for patients with this condition. Specifically, the increased availability of screening tools may aid in identification of the disorder, and clinicians can now choose from a battery of treatment options, including various antidepressants and psychotherapeutic techniques that have been shown to be effective.

Dysthymia is characterized by chronically depressed mood for most of the day, for more days than not, for at least 2 years [7–9]. Left untreated, more than two thirds of patients remain symptomatic for 10 years or more, with mean durations reported to be as long as 30 years [10–14]. In addition to this personal suffering, dysthymia is associated with high medical utilization and costs and a high degree of somatic, social, and occupational impairment [11,15–20]. The deficits in quality of life, functional impairment, and disability days are similar to or worse than those associated with major depression and cause more impairment than other chronic conditions such as diabetes, asthma, and arthritis [21,22].

PCPs play a critical role in the initial recognition, diagnosis, and treatment of dysthymia and associated mood disorders. Fifty-four percent of depressed patients first seek mental health care in a primary care setting, meaning that PCPs often represent the “point-of-first-contact” with the health care system. Indeed, PCPs are often the only mental health providers for certain subpopulations of patients, such as the elderly and chronically ill, who rarely use specialty mental health care. The purpose of this paper is to provide information about the differential diagnosis of dysthymia and effective pharmacologic and psychotherapeutic treatments presented in the context of a clinical case. The report reviews findings from the Cochrane Collaboration [23–26], the Agency for Healthcare Research and Quality (AHRQ) evidence report on newer pharmacotherapies [27], and more recently published articles.

CASE STUDY
Initial Presentation
A 38-year-old woman presents to her PCP with chronic fatigue.

History
The patient has a prior history of alcohol abuse but has been sober for more than 10 years. At this visit, in addition to reporting feeling tired, she describes a history of poor sleep and decreased concentration but denies other vegetative symptoms. When asked about mood problems, she reports struggling with depressed mood since her early teenage years. She states that she has had 2 severe depressive episodes: the first when she initially left home after high school and the second after her divorce. She describes a family history of alcohol abuse in her father and paternal grandfather and depression in her mother and one sister. Her family life as a child was difficult due to her father’s heavy drinking and mother’s chronic depression.

Diagnostic Workup
The patient’s physical examination is unremarkable. The PCP orders blood tests to rule out potential underlying causes of the patient’s fatigue (eg, infection, anemia, thyroid dysfunction); he also asks about current stress, workload, and use of alcohol, street drugs, and tranquilizers (eg, benzodiazepines). As the patient’s symptoms and history alert the physician to the possibility of a recurrence of depression, he also asks her about other depressive symptoms (loss of interest in activities, feelings of inadequacy), the severity and duration of symptoms, and any associated functional impairment or distress. When asked, the patient acknowledges...
having difficulty at work as an advertising salesperson and having been put on probation due to decreased productivity. When the physician asks about pleasant activities, the patient reports that she no longer enjoys playing tennis or going out with friends.

To be diagnosed with major depressive disorder, a patient must meet the criteria shown in Table 1. Because the patient has had feelings of depression since her teen years and reports fewer than 5 symptoms, the physician suspects that the patient has dysthymia rather than current major or minor depression. Other relevant history includes the patient’s previous history of alcoholism: dysthymia in adolescence is a risk factor for developing alcohol, drug, or nicotine dependence. In dysthymia, as in other affective disorders, alcohol use may be a form of self-medication. High rates of mood and personality disorders in first-degree relatives of patients with dysthymia are also common [28,29].

Although the patient has never been treated for depression, she is receptive to the idea that she is depressed and is eager to find some relief. To make an accurate diagnosis, the physician administers the PRIME-MD questionnaire [21], which includes 2 questions about duration of symptoms to assist in making a diagnosis of dysthymia. Numerous screening instruments, such as the Brief Patient Health Questionnaire (PHQ) [30] (Figure 1), and diagnostic tools such as the PRIME-MD and the Structured Clinical Interview for DSM-IV (SCID) [31] are available and useful [32,33]. When assessing patients for depression, it is important to include a question about functional impairments and distress associated with depressive symptoms (eg, question 3 of the PHQ).

### Table 1. DSM-IV Criteria for Major Depression*

<table>
<thead>
<tr>
<th>Criteria</th>
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<tbody>
<tr>
<td>Depressed mood most of the day, nearly every day</td>
<td></td>
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<tr>
<td>Loss of interest and pleasure in activities</td>
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<tr>
<td>Change in appetite or weight</td>
<td></td>
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<tr>
<td>Insomnia or hypersomnia</td>
<td></td>
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<tr>
<td>Psychomotor retardation or agitation</td>
<td></td>
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<tr>
<td>Fatigue</td>
<td></td>
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<tr>
<td>Feelings of worthlessness or guilt</td>
<td></td>
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<tr>
<td>Diminished ability to concentrate or indecisiveness</td>
<td></td>
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<tr>
<td>Thoughts of death or suicide</td>
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</tbody>
</table>

*Five or more of the symptoms should be present during the same 2-week period; at least one of the symptoms should be (1) depressed mood or (2) loss of interest.


Individuals with dysthymia may describe their mood as sad, “down in the dumps,” or irritable rather than depressed. In children and adolescents, the depression may appear as disruptive, high-risk behavior and the required minimum duration is 1 year.

Two types of dysthymia have been described: early-onset (occurring before the age of 21 years, in some cases as early as age 5) and late-onset (age 21 years or after) [7,10,34,35]. The first type had been previously classified as neurotic depression and was in the past thought to be a form of personality disorder. Compared to patients with late-onset dysthymia, early-onset dysthyms tend to have longer episodes of major depression, higher rates of personality disorders and lifetime substance abuse and, like the case patient, a greater likelihood of family history of mood disorder and a higher risk of childhood adversity (abuse and neglect) [10]. Late-onset dysthymia may represent the long-term sequelae of an untreated major depression. The late- and early-onset types of dysthymia do not appear to differ on severity of symptoms or functional impairment, but early onset may require longer treatment.

Dysthymia is commonly exacerbated by severe episodic mood disorders, particularly major depression [2,15,36–39]. Major depression superimposed on dysthymia (“double depression”) can be distinguished from major depression in partial remission and pure dysthymia using standard diagnostic assessments. It is important to note that for each of these conditions, research supports the use of similar treatment: antidepressant medications and/or psychotherapy, although the dose and duration of treatment may differ. The case patient clearly meets the diagnostic criteria for dysthymic disorder with a prior history of major depressive episodes.

**Dr. Bush:**

The following criteria are essential for a diagnosis of dysthymia [7]:

- **Depressed mood**
- At least 2 of the following additional symptoms: poor appetite or overeating, insomnia or hypersomnia, fatigue or lack of energy, low self-esteem, feeling hopeless, or poor concentration or difficulty making decisions
- Symptoms last most of the day for more days than not for at least 2 years
- No period of time without symptoms for more than 2 months


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**What are the diagnostic criteria for dysthymia?**

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### Brief Patient Health Questionnaire

This questionnaire is an important part of providing you with the best health care possible. Your answers will help in understanding problems that you may have.

Name ___________________ Age _______ Sex: ☐ Female ☐ Male Today’s Date ________________

1. Over the last 2 weeks, how often have you been bothered by any of the following problems?
   - a. Little interest or pleasure in doing things .........................
   - b. Feeling down, depressed, or hopeless ..............................
   - c. Trouble falling or staying asleep, or sleeping too much ........
   - d. Feeling tired or having little energy .................................
   - e. Poor appetite or overeating ...........................................
   - f. Feeling bad about yourself — or that you are a failure or have let yourself or your family down ..............................
   - g. Trouble concentrating on things, such as reading the newspaper or watching television .................................
   - h. Moving or speaking so slowly that other people could have noticed. Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual ..........................
   - i. Thoughts that you would be better off dead or of hurting yourself in some way ............................................

2. Questions about anxiety.
   - a. In the last 4 weeks, have you had an anxiety attack — suddenly feeling fear or panic? ............................. NO YES
      If you checked “NO”, go to question #3.
   - b. Has this ever happened before? ........................................
   - c. Do some of these attacks come suddenly out of the blue — that is, in situations where you don’t expect to be nervous or uncomfortable? ........................................
   - d. Do these attacks bother you a lot or are you worried about having another attack? .................................
   - e. During your last bad anxiety attack, did you have symptoms like shortness of breath, sweating, your heart racing or pounding, dizziness or faintness, tingling or numbness, nausea or upset stomach? ............................................

3. If you checked off any problems on this questionnaire so far, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
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</tbody>
</table>

**Figure 1.** First page of Brief Patient Health Questionnaire (PHQ) [30], a self-administered version of the PRIME-MD screening instrument for mental disorders. Users of the PHQ have the choice of using the entire 4-page instrument, the 3-page diagnostic portion, a 2-page version, or only the first page of the 2-page version (covering only mood and panic disorders), shown here. Although the instrument is not specific for dysthymia, it can be used in conjunction with asking about duration of symptoms. (Reprinted with permission from Pfizer Inc.)
• Should PCPs screen all patients for dysthymia?

**Dr. Bush:**

Dysthymia is often missed during routine primary care visits, possibly because patients with dysthymia tend not to mention characteristic symptoms such as feeling hopeless [40]. Instead, like the case patient, they may present with chronic fatigue, stress, headaches, and unexplained pain or gastrointestinal disturbances. Because of the insidious onset of symptoms at an early age, many patients report that they “have always felt this way.”

An awareness of dysthymia and use of a brief, standardized set of screening questions can increase recognition and subsequent treatment rates. Note, however, that guidelines recommend routine screening for depression (or dysthymia) only among those at risk for affective disorders [41]. People who are shy, avoidant, overly dependent on others, over-reactive to criticism or rejection, or who have low self-esteem may be prone to depression [28,42]. A major risk factor for developing dysthymia appears to be adverse childhood experiences (abuse, battered mother, mentally ill or incarcerated household members, parental divorce). These early experiences may lead to substance use and dependence as well as increased feelings of sadness and depression [43]. At least one third of individuals with dysthymia report a history of substance abuse [10,22,44–46].

• What are treatment recommendations for patients with dysthymia?

**Dr. Bush:**

Before implementing a treatment plan, the physician and patient should thoroughly discuss the diagnosis of dysthymia and the treatment options available. Therapy with an antidepressant should be an initial consideration, along with medication counseling to ensure adherence (Table 2). If this is the patient’s first experience with antidepressants, a selective serotonin reuptake inhibitor (SSRI) should be prescribed. Follow-up visits should be scheduled every 2 to 4 weeks until

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**Table 2. Therapeutic Dose Ranges and Side Effects* of Antidepressant Medications Used to Treat Depression and Anxiety**

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Therapeutic Dose Range, mg/day</th>
<th>Sedation, Fatigue</th>
<th>Anticholinergic</th>
<th>Dizziness</th>
<th>Insomnia, Agitation</th>
<th>Headache</th>
<th>Weight Gain</th>
<th>Gastrointestinal</th>
<th>Anorgasmia</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>20–60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>0</td>
<td>1+</td>
<td>2+</td>
</tr>
<tr>
<td>Sertraline</td>
<td>50–200</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>2+</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>20–50</td>
<td>1+</td>
<td>1+</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2+</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>150–300</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>1+</td>
<td>2+</td>
<td>2+</td>
</tr>
<tr>
<td>Citalopram</td>
<td>20–40</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1+</td>
</tr>
<tr>
<td>Bupropion</td>
<td>300–450</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>75–300</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>300–500</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>30–60</td>
<td>2+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Heterocyclics</td>
<td></td>
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<td></td>
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<tr>
<td>Maprotiline</td>
<td>75–300</td>
<td>4+</td>
<td>2+</td>
<td>0</td>
<td>0</td>
<td>1+</td>
<td>2+</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Trazodone</td>
<td>150–600</td>
<td>3+</td>
<td>0</td>
<td>2+</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Tricyclics</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>40–200</td>
<td>2+</td>
<td>2+</td>
<td>1+</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>0</td>
<td>1+</td>
</tr>
<tr>
<td>Imipramine</td>
<td>75–300</td>
<td>2+</td>
<td>3+</td>
<td>3+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>75–300</td>
<td>2+</td>
<td>2+</td>
<td>3+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>2+</td>
</tr>
<tr>
<td>Protriptyline</td>
<td>20–60</td>
<td>1+</td>
<td>3+</td>
<td>1+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>75–300</td>
<td>3+</td>
<td>3+</td>
<td>3+</td>
<td>0</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Desipramine</td>
<td>75–300</td>
<td>1+</td>
<td>1+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Doxepin</td>
<td>75–300</td>
<td>3+</td>
<td>3+</td>
<td>3+</td>
<td>1+</td>
<td>0</td>
<td>2+</td>
<td>1+</td>
<td>1+</td>
</tr>
</tbody>
</table>

*0 = absent/rare; 1+, 2+, 3+ = in between; 4+ = relatively common
SSRIs = selective serotonin reuptake inhibitors. (Adapted from reference 41).
an adequate response to treatment is noted; if there is a lack of response, consider increasing the dose, switching medications, or augmenting with additional medication. Psychiatric comorbidities such as substance abuse, if present, need to be treated. Also, it is important to encourage patients to schedule pleasant activities and avoid social withdrawal. If residual symptoms and chronic social stressors are present, psychotherapy may be added, or, in some patients, can be used as a first-line treatment. Continue treatment for at least 4 to 6 months from the time of recovery. Long-term maintenance treatment (ie, for 2 or more years) with combined medications and/or psychotherapy can be considered. Provision of effective psychotherapeutic treatment for depression or dysthymia depends on the availability of suitably trained and experienced therapists. A summary of the evidence that supports these recommendations is provided in Table 3. Note that much of the scientific evidence regarding effective treatments is derived from studies conducted with psychiatric patients.

### Treatment and Follow-up

The patient is prescribed fluoxetine 20 mg/day. The PCP warns the patient about potential side effects of the medication, noting that some patients who start an SSRI may feel as if they have had 2 or 3 cups of coffee. A return appointment is scheduled for 2 weeks. Results of the blood tests are normal.

At the 2-week follow-up visit, the patient reports that after 3 days on fluoxetine she felt nauseous and jittery, so she stopped the medication. The PCP explains that these side effects are not dangerous and usually subside within a week or two. The physician suggests taking half the dosage to minimize side effects (ie, fluoxetine 10 mg) and to take the medication with food and avoid coffee and tea the first 10 days of treatment. The physician encourages the patient to try the medication again for the next 2 weeks, slowly increasing the dose to 20 mg, and to phone the clinic if she has further problems or concerns. The physician also asks...
about pleasant activities that the patient has been doing and encourages continued efforts to meet with friends.

The patient continues to abstain from alcohol. Her current life stresses include her work and dealing with her family. She is worried about attending a family wedding in 2 months. She continues to feel tired and lethargic and has a tendency to overeat. She finds very little enjoyment in her usual leisure activities.

- Is watchful waiting a treatment option in this patient?

**Dr. Lin:**

Watchful waiting would have been appropriate for this patient if the depressive symptoms were of recent onset (no prior history of depression) and not severe. Had there been evidence of abnormalities from the blood tests, the physician would have treated the underlying disorder (eg, thyroid dysfunction or infection) and observed for symptom response. If symptoms remained, the physician would have treated the dysthymia with an SSRI.

- What patient education and counseling should PCPs provide dysthymic patients?

**Dr. Lin:**

Studies of depressed primary care patients have shown that specific educational messages provided by the PCP improved adherence to antidepressant medication [74,75]. It might be helpful to give patients the following brief educational messages [74]:

- Take medication every day
- Wait 2 to 4 weeks for a noticeable effect
- Continue medication even when feeling better
- Don’t stop without first checking with physician
- Schedule pleasant activities
- Stay on medications for at least 6 months

Due to the high discontinuation rates for those started on antidepressants (16% to 32%), the physician must closely follow patients (at least every 2 weeks) until a clinical response is obtained. It is helpful to encourage patients to phone the clinic if they have problems or concerns with the medications. More frequent initial visits have been shown to improve clinical outcomes [41,76]. It is important for the physician to spend ample time discussing positive activities such as exercise or going to lunch with a friend during the first few weeks of treatment with antidepressants, when side effects may appear to outweigh beneficial effects. Encourage patients to set small, achievable goals. Be specific. Ask patients what they want to do, when and how often. Ask the patient to take out his or her diary and mark down a specific time for next week’s pleasant activities (see Primer, page 53).

**Dr. Katon:**

It is also helpful to draw a graph for patients showing the side effect versus therapeutic effect curves (Figure 2). This graph shows that patients may develop annoying side effects with SSRIs such as jitteriness, headache, and nausea in the first week of treatment, which then tend to decrease over the second week. On the other hand, beneficial effects such as improved mood, sleep, energy, and concentration tend to occur over a 1- to 3-week period. The major educational point is to emphasize that because side effects may occur before beneficial effects, patients may get discouraged and prematurely stop their medication. This is the time to emphasize the importance of scheduling pleasant activities into their daily routine. It might benefit patients to read a pamphlet about reasons for treatment, the use of antidepressants, side effects and their management, the need to continue treatment for 6 months, and actions to take in the event of forgetting a dose [76]. However, educational materials alone without close follow-up have little effect on adherence [75].

- Are antidepressant medications safe to use in patients with hypertension?
PRIMER: SELF-MANAGEMENT OF DYSTHYMIA AND OTHER CHRONIC CONDITIONS

Evette J. Ludman, PhD

The case study illustrates straightforward ways that providers can support patients in the self-care, or self-management, of their dysthymia. The term self-care refers to the fact that in chronic disease, it is the patients themselves, along with their families, who are the primary caregivers in the day-to-day management of their illness [111]. Self-care tasks that are important for the management of depression and dysthymia include interacting with health care providers, adhering to recommended treatment protocols, and engaging in activities that promote positive mood. Other self-care tasks important to managing depressive disorders include monitoring of symptoms and managing the effects of depression on relationships and ability to function in work and family roles. Ongoing monitoring of symptoms, life events, and behavioral activities can be a particularly potent self-care task because such self-monitoring can help patients see their progress and make connections between the activities they do to try to feel better and how well these strategies work. Patients can share their self-monitoring journals with their providers.

Primary care providers or care managers (ie, primary care team members such as nurses or medical assistants) can support patients’ self-care in a variety of ways. Sometimes, the line separating self-management support and psychotherapy can seem blurred, especially because discouragement, inactivity, and disability are characteristics of depressive disorders. Health care providers can incorporate brief strategies of problem-solving therapy or cognitive behavior therapy into their visits and calls with patients. For instance, providers can help enhance patients’ hopefulness, motivation, and confidence in their ability to manage their depression by offering a variety of options for treatment, helping patients set targeted goals that are meaningful and important to them, and coaching patients to identify options and steps toward problem-solving life difficulties or barriers to adherence. Providers can help patients create incremental, realistic action plans for self-care tasks, anticipate and plan for obstacles, and provide ongoing supportive follow-up.

Providers can also help patients’ self-care by connecting patients with peer and community resources for themselves and their families and by providing encouragement through sharing the success stories of others. Practice teams should keep an updated list of available resources in their community (eg, local chapters of the National Depressive and Manic-Depressive Association) and have organization literature on hand to distribute to patients at the time of office visits. Reputable internet sites and “virtual” online communities are options in regions lacking in local resources.

Contact information:
National Depressive and Manic-Depressive Association
730 N. Franklin St., Suite 501
Chicago, IL 60610
1-800-836-3632
www.ndmda.org
National Institute of Mental Health
1-800-421-4211
www.nimh.nih.gov

Dr. Katon:
SSRIs can raise the serum levels of other medications because they are highly protein bound and may also affect liver metabolism. The safest course for patients who are taking medications where serum levels are required (ie, coumadin, theophylline, dilantin, digoxin) is to recheck the serum level within 10 to 14 days after starting an SSRI. An elevated serum level should lead the clinician to decrease the dosage of the medication or to switch to a different medication such as citalopram.

Dr. Bush:
In mild to moderate cases of dysthymia, cognitive behavioral therapy (CBT) or problem-solving therapy (PST) should be tried first. Home visits from nurses or midwives, 24-hour hotlines, and scheduled telephone calls to the physicians have
also been shown to improve depressive symptoms among pregnant women [77]. For women who do not respond to psychotherapy or those with severe depression, antidepressants should be considered. The benefits of treatment outweigh the potential risks of using medications. Maternal depression is associated with poor nutrition, weight loss, risk of suicide, low birth weight, postpartum depression, and lack of maternal bonding.

SSRIs and tricyclic antidepressants (TCAs) appear to be safe in the second and third trimesters but are not recommended in the first trimester. Dosage should be carefully tapered just prior to delivery to avoid symptoms of withdrawal in the infants. In a recent review, Wisner et al [78] reported that exposure to TCAs and SSRIs did not increase the risk for intrauterine death or major birth defects. Note that physiologic changes during pregnancy may alter drug clearance so that higher doses may be required to achieve therapeutic levels [78].

• Are antidepressants safe to use in adolescents?

Dr. Katon:
There is insufficient evidence from trials to evaluate the effectiveness of antidepressant medications among youths with dysthymia. Among youths aged 7 to 17 with major depression, antidepressants have been shown to be safe and effective, but the drop-out rates in many studies are high (18% to 25%) [79–81]. The use of antidepressants for children has become common, but there are few randomized trials to inform clinical decisions. CBT has been shown to be effective for the treatment of adolescents with major depression or dysthymia [82–83] and should be the first line of treatment for youth with dysthymia. Antidepressants may be appropriate for adolescents with psychosis, bipolar depression, severe depression, and those who do not respond to an adequate trial of psychotherapy.

• What about St. John’s wort?

Dr. Bush:
There is some evidence in controlled studies of adult patients with mild to moderate depression or dysthymia that hypericum (St. John’s wort) is more effective than placebo and equally effective as antidepressants for short-term treatment [26].

Telephone Follow-up
Two weeks later, a follow-up phone call is made to the patient by a clinic nurse. The patient reports that she has been able to slowly increase her dose of fluoxetine from 10 to 20 mg. Although she reports feeling better, she has symptoms of fatigue and difficulty concentrating that continue to impact her job. The nurse urges the patient to stay on the medication, monitor her symptoms, and avoid situations that are likely to precipitate depression. The nurse asks about specific activities that the patient had previously enjoyed (taking walks, playing tennis, and going out with friends). She encourages her to continue to make time for pleasant activities and asks her to schedule an office visit within the next 2 weeks.

• Can telephone case management improve outcomes in dysthymia?

Dr. Bush:
Results from 2 randomized trials have shown that telephone case management by a nurse or case manager improves depression outcomes and patient satisfaction [84,85]. Although not specifically tailored to dysthymic patients, these studies advanced the field of depression treatment by providing evidence that depression-specific case management delivered by telephone is cost-effective and convenient. This case management technique improves care for patients with access barriers and is proactive (initiated by the practice team, rather than relying upon patients who may or may not seek help when symptoms are exacerbated).

Follow-up Visit at 6 Weeks
The patient returns after 6 weeks of medication treatment and feels about 50% better on fluoxetine 20 mg/day. Her mood is a little better and she has noticed that her tendency to overeat has diminished, but she still finds work increasingly difficult due to irritability and lack of interest and motivation. The PCP recommends increasing the fluoxetine to 30 mg/day this week and, if the patient is not completely better, to 40 mg/day 3 weeks later. The physician raises the issue of psychotherapy, noting that some patients with incomplete recovery benefit from a specific form of psychotherapy in addition to the medication. The physician further explains that this form of therapy targets negative thought patterns (eg, I’m a failure, I’ll never improve or be happy). The PCP provides a referral for a course of CBT.
Dr. Bush:
Individuals with dysthymia are prone to an exacerbation of symptoms during times of stress or changes in routine. Psychotherapy as an adjunct to pharmacotherapy may be particularly effective in resolving residual symptoms such as negative affectivity, cognitive distortions, and social isolation [50] and in providing adaptive coping strategies. Research has shown that the most profound changes after treatment were in patients’ ability to cope with daily hassles without being overwhelmed [51]. Deficits in major social roles (work, family, life, intimate relations, social and leisure time) are also common with dysthymia [11,53,60,61,86]. Successful treatment of clinical symptoms is likely to alleviate these social impairments. Addressing functional limitations and soliciting family support may help the patient achieve treatment goals.

Primary care patients may be reluctant to follow up with referral for psychotherapy treatment. This may be due to a variety of factors including social stigma, inconvenience, costs, or negative expectations about the effectiveness of psychotherapy. PCPs may also be reluctant to refer patients if they lack positive experiences from previous referrals. To address some of the barriers to making and accepting referrals to mental health, brief, on-site, depression-focused psychotherapies have been developed specifically for primary care patients and tested in randomized clinical trials. For example, 2 studies demonstrated that patients with major depression experienced improved depression outcomes and better patient satisfaction with such primary care–based treatments delivered in collaboration with their PCPs [87,88]. Regardless of whether or not a patient is referred, it is important to share with patients evidence from controlled trials reporting the benefits of behavioral activation interventions and to encourage patients to plan daily pleasurable activities.

Guidelines recommend referring patients with severe symptoms, suicide risk, comorbid medical or psychiatric conditions, substance abuse, or failure to respond to treatment within 12 weeks [41].

Follow-up Visit at 10 Weeks
The patient is feeling more energetic. She has experienced no apparent side effects with the increased dose of fluoxetine (40 mg/day). She has attended 2 sessions of CBT with a psychologist and has agreed to continue with the 6-week course. The patient also has made a concerted effort to plan pleasant activities. In the past week, she walked in her neighborhood on 3 evenings and met with friends on the weekend.

- When will benefits from treatment be seen?

Dr. Bush:
The scientific literature reports treatment response using a variety of definitions. To address this problem, a working group of experts in the field recommend the use of these standardized definitions [32]:

- **Response**: clinically significant reduction in symptoms
- **Remission**: improvement such that an individual no longer meets criteria and has no more than minimal symptoms
- **Recovery**: remission sustained for at least 6 months

Among dysthymic patients, treatment response with fluoxetine (20 mg/day) or CBT has been reported at 8 weeks with further improvement at 16 weeks [55]. Remission of dysthymia can be achieved with antidepressants by 12 weeks [42,52,89,90]. In some depressed patients, drug response can be detected as early as 2 weeks [91]. Response to psychotherapy has been reported within 6 weeks of treatment (after 2 sessions) among patients with subclinical depression (75% had dysthymia) [69]. McCullough [13] treated dysthymia until remission and noted that this required an average of 31 sessions of CBT (10 patients). However, the lack of a full response after 6 weeks of treatment is not unusual.

Patients with lifetime pure dysthymia may respond more slowly to antidepressants than those with concurrent major depression, but the long-term outcomes may be similar [10,14,36,37,92–94]. Medical comorbidity [95], comorbid personality disorder, and substance abuse may also decrease treatment response [45,93]. Some dysthymic patients may discontinue treatment before complete remission of symptoms because in their minds they have returned to what they consider to be normal.

AHRQ guidelines recommend that response to medication be evaluated between 4 and 6 weeks and suggest switching medication or augmenting if at least a 25% reduction in symptom severity has not occurred [41]. It is helpful to monitor clinical response with reliable measures such as the PHQ (Figure 1), a self-report version of the PRIME-MD [30]. This brief scale provides a measure of severity and includes a list of specific symptoms of depression, the number of days the symptoms are present, and the impact of the symptoms on functioning. The Beck depression inventory (short form) is also commonly used to measure treatment response [96]. At each follow-up visit, it is also important to ask about daily functioning.

- How long should treatment last?
DYSTHYMIA

Dr. Katon and Dr. Lin:

Once treatment response is achieved, clinicians must discuss with their patients the duration of treatment, risks of recurrence, and ways to prevent a relapse. The evidence shows that patients with dysthymia who remain on medication (fluoxetine or trazodone) maintain improvement over time compared with dysthymic patients who discontinue their medications [48,60,61,68,93]. Discontinuation of antidepressants in a 4-year maintenance study among patients with chronic depression resulted in an 89% rate of relapse [37]. These and other studies have led most experts to recommend maintenance therapy in their patients with dysthymia. Evidence suggests that adding psychotherapy at this time will decrease the relapse rates. Although maintenance treatment with older or newer antidepressants appears to be safe, there may be unwanted side effects such as sexual dysfunction (SSRIs) or weight gain [97]. If a patient and doctor decide to discontinue medications, it is important to slowly taper doses over 4 to 8 weeks. Common symptoms of abrupt SSRI discontinuation are dizziness, headache, nausea, vomiting, diarrhea, insomnia, irritability, electric shock sensations, and depressed mood and anxiety [98].

• Is a complete remission among patients with dysthymia possible?

Dr. Bush:

Adequate pharmacologic treatment and/or psychotherapy have been shown to result in complete resolution of symptoms in many patients with dysthymia [52,59,89,90]. Furthermore, the psychosocial functioning of those who respond to treatment are comparable to community normal controls even as far out as 40 months from treatment initiation [11,53,60,61,99,100]. However, others have reported significant psychosocial deficits among dysthymics even after symptom recovery [47,67,93]. It is important for providers to recognize the difficulty in maintaining the beneficial treatment effects among dysthymic patients.

• What are the cost benefits of treating dysthymia?

Dr. Bush:

Dysthymia is associated with a lifetime of suboptimal psychosocial functioning, recurrent major depression, substance abuse, chronic medical illness, lost productivity, interactions with the criminal justice system, and disruption in one’s family life [22,44,46,101,102]. It is likely that these relationships are bidirectional. Relatives of depressed patients also suffer, as demonstrated by increased levels of stress, dysfunction, and psychiatric disorders and decreased school performance [103–105]. The individual, societal, and health care costs associated with dysthymia are enormous [15,99,100,106,107]. Treatment of dysthymia significantly reduces clinical symptoms as well as functional limitations at work, home and school even among mildly depressed individuals where the need for antidepressants might be questioned [11]. Cost-effectiveness analyses of proven interventions for depression (some of which include dysthymia) show modest increases in outpatient treatment costs [108–110]. The costs of medication and/or psychotherapy for the treatment of major depression or dysthymia may be offset by savings from reduced disability days or workdays lost.

SUMMARY

Dysthymia develops over years and is likely to persist unless treatment is initiated and outcomes are monitored to ensure that treatment response is achieved and sustained. Systematic care involving regularly scheduled visits is essential to establish patients’ trust, monitor progress, and adjust treatment. For patients with dysthymia, provision of adequate dose and duration of treatment greatly increases their chance of recovery. Prompt and aggressive treatment may prevent development of a more severe disorder and the associated high prevalence of drug and alcohol abuse. Long-term pharmacotherapy and the addition of depression-specific psychotherapy may be necessary for patients with dysthymia because relatively low degrees of stress or disruptions in lifestyle may trigger an episode of depression.

Antidepressant medications, while proven effective for treating most patients with dysthymia, may have adverse side effects, and some are expensive. Nonpharmacologic treatments with little risk and demonstrated benefits may provide a useful addition to depression management. While psychotherapy apparently works and is long-lasting, the psychotherapy that has been shown to be effective is not feasible within primary care unless trained and competent psychotherapists are integrated into the setting and allowed at least 30 minutes for each visit. Some patients may require a full 16- to 30-week treatment to benefit from psychotherapy. With each form of treatment, the drop-out rates can be discouraging. Assessing a patient’s beliefs about the effectiveness of the treatment may help guide physicians in ways to boost adherence.

In summary, evidence of effective treatments for patients with dysthymia is encouraging. Even more promising are the positive effects of treatment on psychosocial functioning and the evidence that the function restored is comparable to normal controls. Although fewer studies have been conducted on maintenance phase treatments for dysthymia, the available evidence documents the prophylactic effects of long-term use of pharmacotherapy and/or psychotherapy.
After 18 months of continuous treatment with fluoxetine, the patient tapers off of the medication (reducing the dose by 10 mg/week). Two months after stopping treatment, the patient is symptom-free, working full-time, and has enrolled in a class at the local community college with the goal of finding employment more amenable to her personality. She has completed a 6-week course of CBT and feels the therapy was particularly helpful with her negative thinking and low self-esteem. She agrees to follow a relapse prevention plan, which involves monitoring her mood and prompt notification if symptoms return.

DYSTHYMIA


