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Optimizing Outcomes for Patients with Depression and Chronic Medical Illnesses

Daniel E. Ford, MD, MPH

Division of General Internal Medicine, Johns Hopkins School of Medicine, Baltimore, Maryland, USA

ABSTRACT

Depression and comorbid chronic medical conditions such as coronary heart disease, diabetes mellitus, and osteoarthritis are frequently seen in the primary care setting, and the interaction of these illnesses can complicate diagnostic and treatment efforts. Although the etiologies of these bidirectional associations are not well understood, a number of negative outcomes are apparent, and challenges exist at patient, provider, and healthcare system levels to better recognize and treat depression in patients with chronic medical comorbidity. Such patients are more likely to present with somatic complaints, engage in unhealthy behaviors, harbor unhealthy thoughts or cognitions, and are less likely to comply with therapeutic recommendations. Primary care encounters often represent the only opportunities for these patients to address these issues and obtain the professional attention their depression requires. For clinicians, forging empathetic partnerships with patients, prescribing appropriate treatments, and closely monitoring symptoms and therapeutic progress are invaluable for optimal management of both affective and medical disorders. Further opportunities to improve care also exist at the healthcare system level, such as developing, funding, and implementing multimodal collaborative care models in the primary care setting.
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Patients with chronic medical conditions and depression are commonly encountered in primary care and other medical settings such as hospitals and medical specialty offices. This is not surprising in light of the close and complex bidirectional link between medical conditions and depression. Consequences of depression comorbid with chronic medical conditions include greater morbidity, mortality,[1–4] and costs.[5–8] The majority of depression care is delivered by general medical providers,[9–12] so the drive for quality management of these patients cannot be overemphasized, particularly in light of studies suggesting that the general standard of care is currently inadequate.[13–17] The opportunity to diagnose and treat patients early in the course of a depressive illness in the primary care setting is substantial but largely unrealized in the current US healthcare system.[18]

The risk of major depressive disorder (MDD) is increased in patients who have ≥1 chronic medical condition,[19] and its presence is a significant complicating factor in the course and care of chronic medical conditions due to increased functional disability,[20–24] decreased self-care, and worse adherence to medical regimens.[25,26] There is evidence of negative physiologic effects of depression associated with medical illness including decreased heart rate variability,[27,28] increased platelet aggregation,[29–32] higher levels of inflammatory risk markers,[33] and glucose dysregulation.[34]

Approximately two thirds of patients with depression in primary care present with somatic symptoms such as pain or fatigue.[35] Clinicians consequently may overlook[36] or neglect[37] a mood disorder owing to concern over other pathologies. Most studies have found that patients with chronic medical conditions have worse outcomes for depression, but not higher rates of treatment, than patients with no or minimal medical comorbidity.[38]

A study that explored the overall health status of patients with depression alone or as a comorbidity determined that

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Requests for reprints should be addressed to Daniel E. Ford, MD, MPH, Johns Hopkins School of Medicine, 2024 Building, Suite 2-500, 600 North Wolfe Street, Baltimore, Maryland 21287.

E-mail address: dford@jhmi.edu.

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depression generates a significantly greater decrease in health than angina, arthritis, asthma, or diabetes mellitus.[39] When compared with patients who have a chronic medical condition alone, patients with depression or anxiety comorbid with a chronic medical condition report a significantly greater number of medical symptoms when controlling for disease severity.[40] The burden of physical symptoms associated with complications from a medical illness may also be likely to initiate or worsen episodes of depression and/or anxiety.[19]

Unfortunately the clinical data pertaining to depression and comorbid physical illness are scarce because clinical trials frequently exclude participants with concurrent medical disorders.[41] The reports in this supplement to *The American Journal of Medicine* provide reviews of the evidence regarding treatment of depression for patients with selected chronic medical conditions. However, the discrepancy between how primary care is delivered and the needs of patients with chronic medical conditions and depression remains an important consideration. In clinical practice, factors at the patient, physician, and healthcare system levels may serve to limit or optimize treatment for patients with comorbid depression and chronic medical illness.

PATIENT-LEVEL TREATMENT ISSUES

Although the risk of depression is higher for patients with all types of chronic medical conditions, the reasons for this association are not clear. The chronic nature of both depression and medical conditions strains the patient's sense of self, self-confidence, and social relationships. Depressed mood makes it difficult to be optimistic about the future and adherence to treatments for medical and affective conditions may be difficult and burdensome. A quantitative review demonstrated that patients with depression were 3 times as likely to be nonadherent to recommended treatment compared with their nondepressed counterparts.[26] Depression may be associated with poor treatment adherence because a patient with depression may not accurately recognize the potential benefit of treatment.[26] In addition, research suggests that social support is an important component of treatment adherence, and many patients with depression have a restricted support network of family and friends.[42]

Patients with depression have a higher likelihood of participating in unhealthy behaviors, such as tobacco smoking, sedentary lifestyle, and overeating.[19] For example, individuals with depression are more likely to smoke tobacco[43] and depression symptoms significantly reduce the likelihood of quitting.[44] In light of the increased risk for coronary artery disease and stroke associated with depression, helping a patient with depression and tobacco abuse to stop smoking and increase physical activity is among the most important steps toward improving overall health. Smoking cessation should be the number 1 priority for at least some of the visits when taking care of patients who smoke and also have depression.

Unhealthy behaviors may lead to a higher incidence of some medical conditions. In addition, many chronic medical conditions require comprehensive self-management behaviors to ensure optimal treatment. Depression negatively affects self-care behavior in many illnesses.[19] Patients with diabetes and depression have been shown to be less adherent to dietary recommendations and oral hypoglycemic regimens, with attendant poorer functioning and higher treatment costs.[5] In patients with cardiac illness, major depression interferes with exercise rehabilitation[45] and is associated with failure to adhere to a daily aspirin regimen.[25] In general, depression has a negative effect on a patient's ability to adhere to recommendations to taking medications regularly.[18] Depression also has been shown to diminish satisfaction with care,[46] which similarly affects adherence.[47]

Although biological pathways from chronic medical illness to depression most certainly exist, it is important not to forget that psychological adaptation to chronic medical illness can also contribute to patient well-being. Even though Americans increasingly expect they will have to learn to live with chronic medical illnesses, adaptation is often more difficult than they believe. The adaptation process may vary by the age of the patient, but even those aged >70 years will need help adjusting to taking a medication on a daily basis when it is their first experience. Studies have shown that significantly more medical symptoms with unexplained pathology and significantly more functional impairment are reported by patients with chronic medical conditions and comorbid depression or anxiety than by patients with chronic medical conditions alone after controlling for disease severity.[48] Increasing evidence suggests that depression interferes with adaptation to chronic medical illness and creates increased awareness of physical symptoms[19]; patient perception of illness and adaptation are directly relevant to overall patient well-being.

The foundation of cognitive behavioral therapy is based on the premise that individuals feel the way they think. Negative cognitions that interfere with patient progress need to be identified and new approaches developed. If patients are continuously thinking about negative outcomes, they eventually begin to have a generalized feeling of hopelessness and depressed mood. In Table 1, several of the common thoughts or cognitions of patients with chronic medical illnesses are listed. The first 2 cognitions are indicative of patients who want to concentrate on 1 condition at a time or have an unrealistic view concerning the course of most chronic medical conditions.

It is useful for providers to explore with patients their inner view of how to manage their conditions and how they view any relation between their affective and medical illness. The focus should be on adaptation and using compensatory approaches to maximize function from the very beginning. They may not get their diabetes under control unless they are also actively involved in family and social activities. Some patients may believe they can only take a certain number of medications and that antidepressants may need to be delayed. The general approach is to challenge these thoughts and ask the patient about the basis for these

beliefs. Is there another way to think about this? Yes, they may truly be more dependent than others, but do they think less of individuals, like their friends or family members, who have needed help? Maybe they were never quite as independent as a young healthy person as they thought. Another strategy is asking them to take a small step to challenge their views. For example, instead of silently deciding he is only a burden to his wife, recommend to the patient that he communicates these thoughts to his wife and identify ways he can maximize his contribution to the household. Expressing thankfulness for the help they do receive can also be liberating to patients experiencing depression and chronic illness. Equally effective to the cognitive component of cognitive behavioral therapy is behavioral activation. Patients should be encouraged to set goals for regular physical activity and engaging activities that have been enjoyable to them in the past. It may be helpful to use the analogy that people have to exercise the pleasure and reward parts of their brain to help with recovery.

FACILITATING EFFICACY FOR THE PRIMARY CARE PHYSICIAN

Empathy

Patients with depression and chronic medical conditions usually come to the office with an understandable sense of low self-worth and loneliness. In this situation, primary care physicians can provide an invaluable service by considering not only the technical aspects of diagnosis and treatment planning but also by attending to the affective component of the visit. Physicians characterized as empathic, interested in psychiatry, and curious about family and problems at home are more likely to accurately recognize mental illness.[49] Patients are looking for someone who accepts them and legitimizes their predicament. Physicians who suspect the presence of a depressive condition need to spend enough time with the patient to understand the complexity of the situation and make an evaluation. Asking screening questions such as "What are your most troublesome symptoms?" "Which symptoms came first?" or "Have you lost interest in things you usually enjoy?" may provide clues to the presence and severity of depressive symptoms.[50]

While both provider and patient want to find solutions, the patient is also looking for someone to tell them they understand they are in a tough situation, it is not their fault, and they are willing to work with them for as long as it takes to improve their situation. Because many patients with chronic medical illness are seeing multiple providers, a primary care physician's willingness to consider problems from a holistic viewpoint is especially comforting. Simple statements like, "Most of my patients with medical problems and feelings like you have get very frustrated and discouraged—how about you?" or "You have shown a lot of courage facing several problems—how can I help you move ahead?" or "No matter what happens, I will continue to work with you to find the best solutions for you" are of comfort to a patient facing multiple medical and emotional difficulties.

Table 1 Thoughts associated with depression comorbid with chronic medical conditions

- "My depression will get better once I get my [other condition(s)] under control."
- "I cannot lead a full life until my [condition] is cured or under perfect control."
- "With these health problems I'm just a burden to my family."
- "I used to be able to do everything on my own, but not anymore."
- "I can only take [number] medications—1 more is too many."
- "My life is just a series of doctor visits—all I think about is my health."
- "I am afraid of dying."

Treatment Approach

In addition to legitimizing the situation, most patients with depression and chronic medical problems want to have some ability to choose their treatment approach. Evidence is accumulating that primary care patients with depression who indicate that they had a role in their treatment decisions have better outcomes.[51] Treatment decisions for these patients are not easy because cognitive functioning associated with depression may impair the ability to make decisions and follow through with them.[26] Primary care physicians should attempt to understand the patient's view of proposed treatment, provide information to counter misperceptions about depression and its treatment, and discuss the nonaddictive nature of antidepressant pharmacotherapy.[50] Selecting the right treatment for a patient is a critical determinant of adherence; if a patient chooses pharmacotherapy, it is important to select an agent with a once-daily dosing regimen and minimal potential adverse events to improve adherence.[50]

It is appropriate to evaluate adverse event potential in terms of both medication tolerability and relative risk of causing drug–drug interactions. Years of clinical experience with the various antidepressants have allowed distinct tolerability profiles to emerge,[52] which can help clinicians guide patients toward the therapeutic choices that are most appropriate given individual circumstances. Similarly, characterization of antidepressant metabolic profiles yields insight into the relative risks of drug–drug interactions,[53] which represent a particularly important treatment consideration for patients with a comorbid medical illness.

Adherence to treatment is critical to effectively manage depression and medical illness. Primary care physicians should simplify the decision points for patients by providing several options. Important aspects of treatment to explore include side effects, costs, and ability to follow through with the treatment plan. Patients should be asked to select a treatment option and then commit to following through with

the option for a specified period of time. If the patient does not believe that he or she can reliably adhere to the treatment strategy, the next step should be to identify a simpler or more easily accomplished option that has a higher probability of success. The goal should be to develop a series of incremental steps that build self confidence and leads to the agreed upon goal.

Patients with depression and medical comorbidity require the best opportunity to maintain or improve function in all areas; this can be accomplished by providing the highest quality medical care. When patients have multiple health problems that need to be addressed, clinical management, treatment, and physician visits can be complicated. Maximum vascular and brain function can only improve the probability of recovering from depression.[54,55] For example, all patients with comorbid depression and diabetes should have cardiovascular risk factors controlled to the greatest extent possible.[56] Poorly controlled blood pressure may adversely affect recovery from depression because of short- and long-term effects on vascular function.[57,58] Patients with depression are at increased risk for myocardial infarction (MI) and stroke.[59,60] While there are no data available from studies that have tested this strategy, primary care providers should consider targeting lower levels of cardiovascular risk factors in patients with depression. Based on guidelines, physicians target a lower blood pressure of 130/80 mm Hg for patients with diabetes. Good practice should probably target a similar lower blood pressure for patients with depression.

Patients who have had an MI and depression are at increased risk for additional cardiovascular events.[61] Certainly for these patients, normalization of cardiovascular risks is an important strategy. Achieving lower targets may require effort and creativity on the part of the providers, because patients with depression are less likely to adhere to recommendations to stop smoking and take aspirin. Interestingly, at least 1 study found that patients with depression after MI were more likely to have elevated C-reactive protein levels unless they were taking a 3-hydroxy-3 methylglutaryl coenzyme A reductase inhibitor (statin) medication routinely to reduce their low-density lipoprotein cholesterol level. By taking statin medications, patients with depression no longer had elevated C-reactive protein levels.[62]

Physical activity also should not be ignored for patients with depression and comorbid medical conditions. Physical activity, not vigorous exercise, should be the goal for most patients, particularly if they have not been regular exercisers in the past. Physical activity is useful for many cardiovascular conditions, bone health, and weight control. In terms of depression, physical activity as a component of behavioral activation can improve mood, establish a more regular routine that improves sleep, and may promote social interaction. Primary care physicians should encourage physical activity as a positive strategy for treating medical illness as well as depression.

Symptom Monitoring

Patients with depression and comorbid medical illness may not be equally bothered by all symptoms, and a key role of the primary care physician is careful monitoring of these symptoms. While it is important to ask patients which symptoms are most bothersome, difficulty sleeping is commonly among the most distressing symptoms. To many patients insomnia represents just another example that they are no longer in control of their body: The most natural process of falling to sleep is no longer dependable. Studies are currently evaluating whether targeting insomnia improves depression outcomes, but for many patients any strategy to improve insomnia would be welcomed. At this point it seems prudent to monitor and aggressively treat sleep disturbances with both behavioral approaches and medication.[63]

Pain symptoms are relatively common in patients with depression, particularly if they have chronic medical conditions as well.[19] Diagnosis of depression in patients with comorbid illness can be complicated by somatic symptoms, such as pain, that are often amplified.[48] High levels of pain are associated with worse depression outcomes but depression outcomes of patients with comorbid pain are still improved with collaborative models that have focused on the depression symptoms.[64] Management is complicated and requires careful consideration of how pain, depression, and chronic medical conditions are interrelated. Antidepressants may help control pain in patients with depression[65] and are generally safer than opiates. Even though there are not as many evidenced-based approaches to treat pain as we would like, patients' pain should not be ignored. Comprehensive treatment programs targeting both depression and pain symptoms appear to be more effective. The symptom of pain has a clear impact on daily function, and not acknowledging pain is very disruptive to the patient–physician relationship.

Depressive symptoms can be monitored in several ways, but one of the easiest ways is to utilize the Patient Health Questionnaire (PHQ)-9 with an added question on pain. The questionnaire measures the frequency of symptoms in the previous 2 weeks and appears to be sensitive to clinical change.[66] If patients or physicians want a more detailed measurement of symptoms like sleep, it is possible for physicians to work with an individual patient to create a brief checklist that is unique to their specific symptoms and that can be used to monitor change.

Visit Frequency

Patients with complex issues that include both chronic medical issues and depression may make more demands on the primary care physician's time. The complexity of their situation requires more frequent visits than other patients with less comorbidity. They may have to be seen every 2 to 4 weeks to address all of their issues. If possible, visits should be preplanned[50] and the agenda for visits must be carefully managed. Not all problems can be addressed at each visit. It is perfectly acceptable to state at the beginning of the visit "we are only going to address your tobacco smoking today" or "let's concentrate on your depression today." Decision support and checklists to track preventive

care should be particularly helpful. If care managers or nurses in the practice with care management skills are available, they should be assigned to these patients.[50] Finally, it may be useful to try to enlist a family member or friend of the patient with depression and medical comorbidity to help carry out the treatment plans.[50] Work with the patient to identify the best person for this role and establish rules for sharing information.

Prevention Approaches

It is important to realize that outcomes for patients with depression and chronic medical conditions are not optimal, with most studies reporting at best 50% of patients achieving remission of their depression.[67,68] Prevention strategies should not be ignored. For example, if a patient has a history of previous episodes of major depression and a chronic medical condition, it would make sense to begin treatment for depression with the emergence of the first depressive symptoms. The presence of a chronic medical illness is a risk factor for progression of minor depression to MDD. However, the choice to start therapy is not that easy, because the absolute risk of developing MDD is <1 in 3.[19]

Focusing on key symptoms may also act as a preventive strategy for depression. Insomnia may be 1 of those key symptoms. Insomnia is a powerful risk factor for developing depression and the risk is even higher when the insomnia persists. Pharmacologic and cognitive-behavioral approaches may reduce insomnia and lead to a reduction in the development of new episodes of depression. Other preventive strategies that have some evidence of effectiveness include programs to address the unhealthy cognitions of individuals prone to depression. Intentionally enhancing social networks might also be effective for patients with chronic medical syndromes. It also is important to be aware of medications used for treating some medical conditions that might increase the risk for depression, such as corticosteroids and interferon-like medications.

DEPRESSION AND MEDICAL COMORBIDITIES AT THE HEALTHCARE SYSTEM LEVEL

The question of how primary care physicians will be able to optimize medical care for patients with depression and chronic medical conditions remains. Competing demands and time constraints during visits make it difficult to address complex problems.[69] Limitations on third-party coverage for mental illness, formulary restrictions, limited referral networks, lack of access to providers, and poor coordination of services between providers are additional system-level barriers that exist and may contribute to less than optimal patient treatment.[69,70]

Collaborative care for depression is a treatment model that uses a multimodal, structured, evidence-based approach that involves nonmedical specialists to augment primary care treatment; a care manager works with the patient and the primary care physician to help develop a shared definition of problems, provide patient education and support, target treatment goals, detail a specific treatment plan, and provide patient follow-up by tracking adverse events, depression outcomes, treatment adherence, and planning additional visits.[71,72] In addition to a care manager, effective collaborative care models for depression also provide consultation and caseload supervision by a psychiatrist.[72] In contrast to usual care, collaborative care is designed to strengthen and support self-care in chronic illness while providing effective medical, preventive, and health maintenance intervention.[71] Noteworthy studies, such as the Improving Mood–Promoting Access to Collaborative Treatment (IMPACT)[73] and the Pathways Study[34] (Table 2), have demonstrated both treatment efficacy and feasibility of implementing a collaborative care model in a primary care setting. Of note, those patients with higher levels of medical comorbidity also benefited from the collaborative care in the IMPACT study.[74]

Table 2 Additional resources

- The Improving Mood–Promoting Access to Collaborative Treatment (IMPACT) trial (http://impact-uw.org)
- The MacArthur Initiative on Depression and Primary Care (www.depression-primarycare.org/)
- The Pathways Study of collaborative care for depression and diabetes mellitus (http://pathways-uw.org)

A meta-analysis of 37 randomized controlled trials demonstrated that sufficient evidence of the statistically significant benefit of collaborative care, compared with usual care, for patients with depression receiving treatment in primary care had emerged by 2000.[75] The meta-analysis produced important findings pertaining to collaborative care with regard to associated short- and long-term benefits (up to 5 years), enhanced care with either neutral or cost savings effects, and better depression outcomes. These results demonstrate that opportunity exists to institute widespread change in primary care practice. The use of a collaborative care model may be a practical way to integrate evidence-based care for depression into disease management for comorbid chronic medical conditions. Given the success of collaborative care models for depression, research on integrated disease management is warranted due to the preponderance of patients with this common comorbidity in who are seen in primary care.

SUMMARY

Patients with depression and chronic medical illnesses are challenging to treat, but they are exactly the type of patient that can benefit from the expert care of a primary care provider. There is a growing body of evidence that chronic medical conditions and depression are interrelated and that treatment of one condition can affect the outcomes for the other.[76–80] Primary care providers have the long-term perspective to understand how each condition is interrelated and affects the overall function and quality of life of the patient. They also have the skills to balance the treatment requirements and set priorities for each condition. While primary care providers will almost always have a long-term role in coordinating care, they should

not hesitate to ask for the best advice from other medical specialists and mental health specialists in developing the best treatment plan for these complex patients.

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