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Introduction: Chronic Medical Conditions and Depression: the View from Primary Care

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Abstract

Martin Hickman† maneuvered his way into the office and pulled up his sleeve as the medical assistant put the brake on his wheelchair and attached the blood pressure cuff around his oversized upper arm. A bulky 56-year-old man with a heavy shock of gray hair teetering on the edge of his forehead, his problem list included type 2 diabetes, chronic obstructive pulmonary disease, hypertension, obesity, and hyperlipidemia. For the past 15 years he has used a wheelchair due to T4 paraplegia from a gunshot wound. He has also suffers from bouts of major depression that respond to sertraline but never fully remit. As the medical assistant inflated the cuff, Mr. Hickman smiled weakly and maintained a cheerful façade even after she informed him that his blood pressure was 164/88 mm Hg and his glucose was 267 mg/dl (both well above goal). Later, on more careful questioning by his primary care physician, Hickman admitted that he was feeling “more down than usual” and that he sometimes neglected to take his diabetes medicine and blood pressure pills. Thinking back over the years he had cared for this patient, the physician recalled that December tended to be a particularly bad month. Social isolation, tolerable for most of the year, became painful around the holidays. December also happened to mark the anniversary of Hickman's spinal cord injury.

The clock was running, the waiting room was full, and the physician realized he was already falling behind.

Keywords

depression; comorbid; chronic medical conditions; primary care

The role of primary care and of the roughly 220,000 primary care physicians in the United States is still being worked out as part of an ongoing national dialog.¹ Shrinking resources, tight reimbursement policies, diminished interest among medical students, and poor clinician morale have created what some have called a “crisis in primary care.”²⁻⁴ Nevertheless, primary care remains the setting where most Americans receive most of their medical care, most of the time.⁵ Perhaps nowhere is primary care more central than in the care of patients like Mr. Hickman who have coexisting chronic medical illness and depression.

Depending on the setting, primary care physicians are responsible for monitoring population health, delivering preventive services, diagnosing and treating acute disease, recognizing and stabilizing emergencies, performing minor procedures, providing end-of-life care, and acting

†Patient name is fictitious.

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as gatekeepers to specialty and high-tech services. Arguably, the most important role of the primary care physician is to coordinate the care of the 90 million Americans with 1 or more chronic medical conditions.⁶ Although considerable progress has been made in expanding the biomedical armamentarium, less attention has been paid to ensuring that effective treatments are delivered reliably to real patients in real-world settings.⁷ Of equal importance, systems for helping physicians and patients manage complex coexisting conditions are incompletely developed and poorly disseminated. As a consequence, patients like Mr. Hickman suffer.

Depression is common and disabling, with an estimated lifetime prevalence of 16%¹ and a huge impact on disability-adjusted life years.² Chronic medical conditions and depressive disorders frequently co-occur; a large worldwide population-based study found that people with chronic physical conditions were significantly more likely to have depression than those without chronic conditions ($P < .0001$).⁸ Depression alone impaired health to a greater degree than the 4 common chronic physical diseases studied (ie, angina, arthritis, asthma, and diabetes). Additionally, depression occurring concomitantly with other chronic diseases incrementally worsened health compared with depression alone, with any of the chronic diseases alone, and with any combination of chronic diseases without depression.

Chronic illness raises the risk of depression, with depressive disorders roughly 2-fold more prevalent among patients with diabetes, coronary artery disease, HIV infection, and stroke than among patients free of chronic illness.⁹ Conversely, depression appears to raise the risk of developing various chronic diseases. For example, depression has been associated with a doubling of the risk of type 2 diabetes^{10,11} and a 64% increase in the risk of coronary artery disease.¹² In short, depression and chronic medical conditions have a reciprocal relationship; depression affects the prevalence, severity, and management of co-occurring chronic medical conditions and vice versa. With the aging of the US population, the prevalence of chronic illness will continue to increase. Addressing co-occurring depression and chronic medical illness is thus a critical challenge for primary care physicians, who are on the front lines of caring for people with both mental and physical health conditions.

In the remainder of this introductory essay, we discuss implications of chronic medical conditions for the treatment of depression and implications of depression for treatment of chronic medical illness. We then explore opportunities to improve care for both physical and mental health conditions through an integrated chronic care model. We conclude by considering some of the many unanswered questions in need of further research.

Characteristics of Patients With Chronic Medical Conditions That Influence Depression Care

Treating depression in patients with chronic medical conditions presents at least 3 separate challenges. First, the physical and emotional burden of chronic illness can make depression more difficult to recognize, diagnose, and manage. Some diseases (particularly neurologic syndromes such as stroke or Parkinsonism) directly affect brain chemistry.¹³ Others impact sleep, appetite, physical functioning, and ability to socialize, thereby exacerbating depressive symptoms while interfering with adjunctive interventions and social engagement. On an existential level, severe physical illness can rob patients of valued capabilities and impose a cap on hopefulness.

Second, patients with co-occurring depression and chronic medical conditions may tacitly collude with their physicians to “focus on the physical,” putting off care of depression for weeks, months, or longer. While it may sometimes make sense to attend to physical symptoms before treating depression, undue delay not only complicates efforts to secure remission of depression but, paradoxically, makes treatment of the physical condition more difficult.

Waiting to get the blood pressure below 130/80 and the glycosylated hemoglobin under 7 % before initiating or escalating treatment for depression may be the medical equivalent of waiting for Godot. The good news is that depressed patients with medical comorbidities tend to be seen more frequently than medically ill patients without depression, which means that the physician has more opportunities to screen, monitor, adjust, and intensify depression-related therapy.

The third major challenge is that many chronic medical illnesses are increasingly treated with complex pharmacologic regimens. In the mid 1990s, about one third of community dwelling elders were taking 5 or more medications¹⁴; adding pharmacological treatment for depression increases the probability of drug-drug interactions in patients already medicated for comorbidities (Table 1). Most antidepressants are metabolized in the liver; metabolism by the isoenzymes of the cytochrome P450 system, including CYP2D6, CYP3A3/4, and 2C19 are responsible for many drug-drug interactions in the clinical setting.¹⁵ For instance, the metabolism of donepezil, a commonly prescribed treatment for Alzheimer's disease, may be affected by antidepressants that inhibit CYP450.

Furthermore, some antidepressant agents may have specific properties potentially affecting antidepressant treatment choice in the presence of a comorbid chronic condition (Table 2). For example, some SSRIs cause weight gain,¹⁵ an effect that would be particularly deleterious for patients with diabetes, and venlafaxine has been associated with elevated blood pressure in elderly patients.¹⁶ Conversely, tricyclic antidepressants, duloxetine, and venlafaxine have demonstrated efficacy in treating diabetic neuropathy¹⁷ and escitalopram or problem-solving therapy was associated with decreased 12-month incidence of poststroke depression.¹⁸

Characteristics of Patients With Depression That Influence Care of Chronic Medical Conditions

Just as chronic medical conditions affect the treatment of depression, depressive symptoms can complicate treatment of chronic medical illness. Patients with depression share 2 characteristics that potentiate the challenges of chronic disease care. First, even without *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV)¹⁹ somatization, depressed patients have a tendency to amplify somatic symptoms.²⁰ This tendency may manifest as a “positive review of symptoms,” increased experience of and reporting of pain, excessive anxiety around disease susceptibility, or a tendency to “catastrophize” after experiencing setbacks in disease control. Such tendencies can disrupt effective chronic disease care by triggering testing cascades,²¹ encouraging over prescribing of potentially harmful medications (eg, opiates, sedative-hypnotics), and interfering with self-care. The downstream result is greater health care utilization, higher costs, and worse health outcomes. Himelhoch et al.,²² for example, have shown that emergency department visits are 2 to 3 times more common among patients with diabetes, hypertension, and heart disease who have depression than among similarly ill patients without depression.

Second, patients with depressive disorders exhibit reduced self-efficacy and “will to function.” Self-efficacy, as defined by Bandura,²³ is confidence in the ability to carry out a behavior or accomplish a task. A growing body of evidence places self-efficacy as a central mediator of health-related behavior. It is influenced by past personal experience with the behavior or task at hand, observation of others (i.e., modeling), and verbal persuasion. Depressed mood and associated feelings of helplessness, hopelessness, and guilt tend to suppress self-efficacy across a broad spectrum of health-related behaviors, thereby disrupting effective chronic disease self-management. For example, all else equal, depressed patients will be less confident in their ability to count carbohydrates, monitor their own blood pressure, or take medications regularly. In addition, depression is associated with a diminution in will to function.²⁴ This concept

developed as an explanation for why patients with similar physiologic derangements function very differently. Depressed patients with impaired will to function manifest greater levels of disability or impairment at a given level of chronic condition severity.

In summary, chronic medical conditions affect depression care by altering brain function, contributing to disability, reinforcing collusive avoidance of depression treatment, and raising the prospect of drug-drug and drug-disease interactions. Depression affects chronic disease care by amplifying somatic symptoms and diminishing self-efficacy and the will to function. The challenges of managing coexisting depression and chronic medical illness are therefore considerable.

The Chronic Care Model: Promises and Limitations

Prompted by studies showing large deficits in quality of care for patients with chronic physical and mental health conditions, Wagner and colleagues promulgated the Chronic Care Model (CCM), a multi-pronged, systems approach to care improvement. The CCM leverages community resources to improve health care organization through self-management support, delivery system redesign, decision support, and clinical information systems (Table 3).²⁵⁻²⁷ In various guises, the CCM has been successfully applied to numerous chronic conditions including diabetes, hypertension, congestive heart failure, and depression. A 2005 meta-analysis of 33 studies evaluating the CCM in depression showed modest but statistically significant improvements in clinical outcomes, quality of life, and process of care.²⁸ However, for the most part, successful CCM programs have been implemented in organized systems of care (such as group-model health maintenance organizations) and have targeted 1 chronic condition at a time. These parameters are a nonstarter for the majority of primary care clinicians. After all, 50% of primary care physicians practice in solo or small groups, and most lack electronic medical records.²⁹ It is unrealistic to expect physicians practicing in such settings to establish separate disease management schemes for even the most common chronic medical and psychiatric conditions (e.g., diabetes, hypertension, congestive heart failure, COPD/asthma, and depression). Integrated approaches that play off commonalities among conditions are more promising.³⁰

Opportunities for Practice Improvement

Recognition of chronic medical condition and depression comorbidity represents an opportunity for primary care physicians to integrate and enhance services while becoming skilled at containing treatment costs and improving patient outcomes. In subsequent articles within this Supplement, content experts will review current evidence regarding treatment of co-occurring depression and cardiovascular disease, neurologic disease, osteoarthritis, and diabetes. Several overarching principles emerge:

- Treat depression and comorbid medical conditions simultaneously
- Set aggressive goals: remission of depression, re-establishment of near normal physiology, good functional status
- Monitor depression status (e.g., use the Patient Health Questionnaire [PHQ]-9³¹ or other standardized instrument) along with blood pressure, body weight, or hemoglobin A1c
- Fight clinical inertia³²: if depression has not remitted or chronic disease parameters are not under control, switch or intensify treatment
- Get help: create real or virtual teams that may include primary care physicians, psychiatrists, medical subspecialists, therapists, nurses, health educators, and office personnel

Applying these principles will require effort, expertise, and resources. Primary care practices need materials and resources to implement an integrative chronic care model that cuts across disease states. The situation is both urgent and remediable. Researchers should focus on developing materials and methods for implementing the CCM in small practices, leaving policymakers to focus on finding the resources to turn academic innovation into practice-based reality. The ultimate goal—improved care for patients like Mr. Hickman—is within reach.

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Table 1

Potential Drug-Drug Interactions Between Antidepressants and Medications Commonly Used to Treat Chronic Comorbid Illnesses¹⁴⁻²²

Comorbidity	Antidepressant Drug	Potential Interaction	Adverse Event Risk(s)
Cardiovascular Conditions	SSRIs, SNRIs	Warfarin, NSAIDs, aspirin, and other drugs that affect coagulation	Increased bleeding
	Fluoxetine, paroxetine, sertraline, duloxetine, bupropion	Type 1C antiarrhythmics (e.g., propafenone, flecainide)	Increased antiarrhythmic plasma levels
	Paroxetine	Phenytoin	Reduced drug plasma concentrations
	Bupropion	Phenytoin	Phenytoin may induce the metabolism of bupropion
	Citalopram, escitalopram, fluvoxamine, venlafaxine	Metoprolol	Increased metoprolol plasma levels; reduced cardioselectivity
Diabetes	Sertraline	Tolbutamide	Decreased clearance of tolbutamide
Neurological disorders	SSRIs, SNRIs, bupropion	MAOIs	Serotonin syndrome
	SSRIs, SNRIs	Triptans	Serotonin syndrome
	Fluoxetine, fluvoxamine, sertraline	Diazepam	Increased diazepam plasma concentrations
	Fluoxetine, paroxetine, duloxetine	Phenothiazines	Increased phenothiazine plasma levels
	Fluoxetine, fluvoxamine, venlafaxine	Lithium	Increased lithium plasma concentrations; serotonin syndrome
Osteoarthritis	SSRIs, SNRIs	Tramadol	Serotonin syndrome
	SSRIs, SNRIs	NSAIDs	Increased bleeding

Table 2
Relatively Compelling Indications and Contraindications for Use of Specific Depression Treatments

Specific Treatment	Indication/Contraindication
Antidepressant Treatments	
Tricyclic antidepressants	<ul style="list-style-type: none"> • Generally contraindicated in organic heart disease due to pro-arrhythmic properties³³ • Contraindicated in severely depressed or suicidal patients due to toxicity in overdose • Contraindicated in Parkinson disease due to anticholinergic side effects and aggravation of PD-associated orthostatic hypotension³⁴ • Limited use in diabetes due to weight gain, cardiac exacerbation, and postural hypotension^{35,36}
Nortriptyline	<ul style="list-style-type: none"> • Demonstrated efficacy in poststroke depression³⁷
SSRIs	<ul style="list-style-type: none"> • Perception that SSRIs may worsen motor function in Parkinson disease³⁴ • Generally safe and well tolerated in patients with coronary heart disease when used with appropriate precautions^{33,38}
Escitalopram	<ul style="list-style-type: none"> • Demonstrated efficacy in preventing poststroke depression¹⁸
Citalopram	<ul style="list-style-type: none"> • Reduced depression in patients with coronary heart disease³⁹ • Demonstrated efficacy in poststroke depression³⁷ • One of the most studied agents in comorbid depression and heart disease
Fluoxetine	<ul style="list-style-type: none"> • Some evidence for depression efficacy and glycemic control in diabetes^{40,41} • Appeared safe and reasonably effective in stable coronary heart disease⁴²
Sertraline	<ul style="list-style-type: none"> • Demonstrated efficacy in poststroke depression³⁷ • One of the most studied agents in comorbid depression and heart disease • Some evidence of antidepressive maintenance efficacy in diabetes⁴³ • Safe to use after an acute coronary syndrome but only modestly efficacious for depression⁴⁴
Bupropion	<ul style="list-style-type: none"> • May be particularly useful in diabetes due to lack of weight gain/weight loss and improved glycemic control⁴⁵ • Effective in the treatment of diabetic neuropathy¹⁷
Venlafaxine	<ul style="list-style-type: none"> • Care should be taken in coronary heart disease due to sustained increases in blood pressure, increased QTc interval, and tachycardia⁴⁶ • Effective in the treatment of diabetic neuropathy¹⁷
Duloxetine	<ul style="list-style-type: none"> • Some evidence for efficacy in comorbid musculoskeletal pain (Kroenke et al) • Effective in the treatment of diabetic neuropathy¹⁷
Nonpharmacologic Therapies	
Cognitive behavioral therapy	<ul style="list-style-type: none"> • CBT has benefits in treating depression in multiple sclerosis • CBT has demonstrated efficacy for depression and long-term glycemic control⁴⁷

Specific Treatment	Indication/Contraindication
	<ul style="list-style-type: none"> • Problem-solving therapy was significantly superior to placebo in preventing poststroke depression for 1 year¹⁸
Interpersonal psychotherapy	<ul style="list-style-type: none"> • No additional improvement with psychotherapy added to citalopram in coronary heart disease
SSRIs, selective serotonin reuptake inhibitors; CBT, cognitive behavioral therapy.	

Table 3
The Chronic Care Model: Components and Interventions

Components of Chronic Care	Interventions
Delivery system redesign	<ul style="list-style-type: none"> • Organize patient care teams that include the physician, nurses, and nonmedical staff • Train nonphysician staff to provide routine assessment, prevention tasks, and self-management support • Allocate tasks • Have ready access to specialist care (eg, medical specialists, nutritionists, social workers) • Use specialist care support as needed • Assure regular patient contact through practice-initiated appointments and follow-up
Physician assisted patient self-management	<ul style="list-style-type: none"> • Assess patient knowledge • Provide patient education • Mutually agree on the definition of the problem • Set realistic goals to target issues of greatest importance to the physician and patient • Develop a personalized intervention plan with patient input • Provide self-management support tools (eg, disease management instructions, behavioral support programs, exercise options) • Arrange for practice-initiated follow-up at regular intervals
Decision support	<ul style="list-style-type: none"> • Conventional referral or consultation • Increase expertise through continuing medical education • Access to recent textbooks and journals • Use of electronic evidence-based medicine resources • Use of PDA-based prescribing resource • Use of treatment algorithms • Use of measurement-based care • Use of electronic decision support systems with audits and reminders
Clinical information systems	<ul style="list-style-type: none"> • Use computerized patient registries to facilitate reminders for follow-up and preventive care • Provide patient-carried medical records and care plans • Use an information system to get patient feedback • Ensure access to longitudinal computerized patient information