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TREATING ANXIETY IN THE PRESENCE OF MEDICAL COMORBIDITY: CALMLY MOVING FORWARD

Bruce L. Rollman, MD, MPH¹ and Jeff C. Huffman, MD²

¹Division of General Internal Medicine, Center for Research on Health Care, University of Pittsburgh School of Medicine, Pittsburgh, PA

²Division of Psychiatry and Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Patients with chronic medical conditions (CMCs) and a co-morbid anxiety or mood disorder tend to report more symptoms and experience poorer treatment outcomes than those without mental health co-morbidity. While the benefits to be derived from treating depression in patients with CMCs have begun to be quantified, particularly among those with cardiovascular disease,¹ our understanding of the benefits of treating anxiety in patients with CMC is far less developed. In part, this may be due to anxiety being overshadowed by discussions of depression or simply dismissed as an artifact of a latent disease process.²

To inform the development of new trials that quantify the benefits of treating anxiety in patients with CMCs and thereby advance the state-of-the-science, evidence is required to determine whether proven-effective and widely generalizable treatments for anxiety: (1) are likely to be as effective in the presence of CMCs; (2) reduce the perceived symptom burden from CMCs; (3) cost-effectively improve health-related quality of life, function, health care utilization, morbidity, mortality and other outcomes valued by patients and providers; and (4) can be sustainably deployed into typical practice settings. The moderator analysis by Campbell-Sills and colleagues from the NIMH-funded multisite Coordinated Anxiety Learning and Management (CALM) Trial published in this issue of *Psychosomatic Medicine* helps address some of these questions and advance our understanding.³

CALM utilized the collaborative care model that has been well-established for treating depression in primary care⁴ and tested in patients with cardiovascular disease,^{5,6} but less well studied for anxiety.^{7,8} Its preferential treatment design allowed patients to choose whether to receive pharmacotherapy, counseling, or both under direction of an allied health professional care manager who proactively monitored the patient at regular intervals and proposed adjustments in treatment based on symptom changes under the supervision of a primary care physician who had access to mental health specialty back-up.

While previous trials have demonstrated the effectiveness of collaborative care strategies for treating anxiety, the CALM investigators are to be commended for their ability to provide a consistent and effective intervention that incorporated a novel computerized cognitive behavioral therapy program to a large (N=1,004) and racially diverse (43% non-White) study cohort who had either generalized anxiety, panic, post-traumatic stress, or social anxiety disorders and were enrolled from one of 17 primary care practices located across the U.S. Consistent with previous trials,⁴ the 12-month CALM intervention produced a small to moderate effect size (ES) decrease in anxiety symptoms and functional disability versus

usual care (e.g., 12-month Brief Symptom Inventory ES: 0.31; 95% CI: 0.44-0.18) that persisted, although in diminished strength, following the conclusion of the intervention (18-month Brief Symptom Inventory ES: 0.18; 0.30-0.06).⁹

The new analyses of CALM data by Campbell-Sills and colleagues in this issue confirm earlier reports that described a high rate of co-morbid CMCs among anxious primary care patients (e.g., 37% hypertension, 33% back problems, 58% with two or more CMCs), and higher levels of anxiety symptoms and anxiety-related disability among those with more CMCs. They also advance our understanding of the potential benefits derived from treating anxiety by demonstrating the CALM intervention was as effective among patients with two or more CMCs as in patients with one or no CMCs.³ Yet perhaps most importantly, patients with two or more CMCs tended to have persistently elevated levels of anxiety and anxiety-related disability throughout their 18-month course of follow-up despite treatment for their anxiety disorder. This finding highlights the continued need to develop more powerful interventions, particularly for patients with CMCs.

Strengthening our trust in these new findings are the CALM Trial's large and nationally representative study population, high rates of completed follow-up assessments (80% at 18-months), and the quality and expertise of the investigative team. Yet unreported is whether and to what extent patients received evidence-based care for their CMCs, and the impact of this treatment on health services utilization and related costs of care that might inform policy makers interested in making the business-case to support deployment of the CALM intervention. Indeed, due to the bidirectional adverse impact of mental health disorders on CMCs, we are left to speculate on whether greater attention to treatment of the CMC *in combination* with treatment of the anxiety disorder would have resulted in a stronger and more durable improvement in anxiety symptoms than the CALM Trial's focus on the anxiety disorder alone.

Emerging evidence indicates that integrated or “blended” collaborative care strategies that treat *both* the psychiatric and physical conditions together tend to produce greater improvements in mood symptoms and control of CMCs than programs that target the psychiatric condition alone. Most notably, Katon and colleagues’ landmark *TEAMcare Trial* of “blended” collaborative care for depression and diabetes reported a medium to large 0.67 ES decrease in mood symptoms versus usual care that was much stronger than that reported by a systematic review of 79 collaborative care trials for depression involving 24,308 participants (ES: 0.34; 0.41-0.27⁴) as well as significant improvements in glycemic control, blood pressure, and LDL cholesterol vs. “usual care” that were as good or better than those produced by more targeted diabetes programs (e.g., 0.42% improvement in HbA1c described in a meta-analysis of diabetes trials¹⁰ vs. 0.58% in *TEAMcare*).¹¹ By contrast, their earlier *Pathways Trial* of collaborative care for depression in diabetic patients reported much a smaller 0.24 ES decrease in mood symptoms consistent with other collaborative care trials,⁴ and no improvements in control of diabetes or cardiovascular risk factors.¹²

Trials of “blended” collaborative care strategies for treating anxiety and one or more clusters of related CMCs modeled on TEAMcare have yet to be evaluated in randomized trials. However, Campbell-Sills and colleagues’ report may enable investigators to propose such a trial now, rather than devote research efforts and funds to first conduct a *Pathways*-like trial for treating anxiety in a population with medical comorbidity. Moreover, “blended” interventions could be developed and tested for such related clusters of conditions as anxiety, depression, insomnia, chronic pain, tobacco, and alcohol abuse and targeted to patients at high-risk for nonresponse to depression treatment¹³ and increased mortality.¹⁴ Critically, these blended models also have the advantage of potentially being delivered via existing CMC programs for diabetes, cardiovascular disease, cancer, organ transplant, and

other high-cost conditions, rather than through a new and parallel system that may be difficult to launch and sustain given pressures on the health care system to reduce costs.

Improving care for patients with CMCs is one of the *major challenges* facing medicine today as patients with multiple chronic diseases account for the majority of health care costs. The added value of collaborative care programs partly depends on the nature of the health care system, health insurance and provider reimbursement structures. In the United States collaborative care has yet to be implemented widely and is generally not available beyond a few large integrated health-care delivery organizations. While this may be due, in part, to costs that are presently not covered by most health insurance systems (e.g., care manager time), patient-centered medical homes and pay-for-performance models that reimburse primary care physicians for providing high-quality chronic illness care have increased interest in their deployment.¹⁵ The report by Campbell-Sills and colleagues in this issue of *Psychosomatic Medicine* shines new attention on anxiety disorders and lays the groundwork for evaluating new collaborative care strategies that are potentially more powerful, scalable, cost-effective and readily delivered through existing CMC programs.

References

1. Rutledge T, Redwine LS, Linke SE, Mills PJ. A meta-analysis of mental health treatments and cardiac rehabilitation for improving clinical outcomes and depression among patients with coronary heart disease. *Psychosom Med*. 2013; 75:335–349. [PubMed: 23630306]
2. Thurston RC, Rewak M, Kubzansky LD. An anxious heart: anxiety and the onset of cardiovascular diseases. *Prog Cardiovasc Dis*. May-Jun;2013 55:524–537. [PubMed: 23621962]
3. Campbell-Sills L, Stein MB, Sherbourne CD, et al. Effects of Medical Comorbidity on Anxiety Treatment Outcomes in Primary Care. *Psychosomatic Med*. July. 2013; 25:2013.
4. Archer J, Bower P, Gilbody S, et al. Collaborative care for depression and anxiety problems. 2012; 10(4):CD004274, CD006525.
5. Rollman BL, Belnap BH, LeMenager MS, et al. Telephone-delivered collaborative care for treating post-CABG depression: a randomized controlled trial. *JAMA*. 2009; 302:2095–2103. [PubMed: 19918088]
6. Huffman JC, Mastromauro CA, Sowden G, Fricchione GL, Healy BC, Januzzi JL. Impact of a depression care management program for hospitalized cardiac patients. *Circ Cardiovasc Qual Outcomes*. Mar.2011 4:198–205. *Cardiovascular Quality & Outcomes*. [PubMed: 21386067]
7. Rollman BL, Belnap BH, Mazumdar S, et al. A randomized trial to improve the quality of treatment for panic and generalized anxiety disorders in primary care. *Arch Gen Psychiatry*. 2005; 62:1332–1341. [PubMed: 16330721]
8. Roy-Byrne PP, Katon W, Cowley DS, Russo J. A randomized effectiveness trial of collaborative care for patients with panic disorder in primary care. *Arch Gen Psychiatry*. 2001; 58(9):869–876. [PubMed: 11545671]
9. Roy-Byrne P, Craske MG, Sullivan G, et al. Delivery of Evidence-Based Treatment for Multiple Anxiety Disorders in Primary Care: A Randomized Controlled Trial. *JAMA*. 2010; 303(19):1921–1928. [PubMed: 20483968]
10. Shojania KG, Ranji SR, McDonald KM, et al. Effects of quality improvement strategies for type 2 diabetes on glycemic control: a meta-regression analysis. *JAMA*. 2006; 296:427–440. [PubMed: 16868301]
11. Katon WJ, Lin EHB, Von Korff M, et al. Collaborative Care for Patients with Depression and Chronic Illnesses. *N Eng J Med*. 2010; 363:2611–2620.
12. Katon WJ, Von Korff M, Lin EH, et al. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry*. 2004; 61:1042–1049. [PubMed: 15466678]
13. Celano CM, Mastromauro CA, Lenihan EC, Januzzi JL, Rollman BL, Huffman JC. Association of baseline anxiety with depression persistence at 6 months in patients with acute cardiac illness. *Psychosom Med*. 2012; 74:93–99. [PubMed: 22210240]

14. Watkins LL, Koch GG, Sherwood A, et al. Association of anxiety and depression with all-cause mortality in individuals with coronary heart disease. *J Am Heart Assoc.* 2013; 2:e000068. [PubMed: 23537805]
15. Katon WJ, Unützer J. Health reform and the Affordable Care Act: The importance of mental health treatment to achieving the triple aim. *J Psychosom Res.* 2013; 74:533–537. [PubMed: 23731753]