Research Article

PILOT RANDOMIZED TRIAL OF A CROSS-DIAGNOSIS COLLABORATIVE CARE PROGRAM FOR PATIENTS WITH MOOD DISORDERS

Amy M. Kilbourne, Ph.D., M.P.H.,[1,2]* Decartes Li, M.D.,[3] Zongshan Lai, M.S.,[1,2] Jeanette Waxmonsky, Ph.D.,[4] and Terrence Ketter, M.D.[5]

Objectives: *Chronic care models improved outcomes for persons with mental disorders but to date have primarily been tested for single diagnoses (e.g. unipolar depression). We report findings from a pilot multisite randomized controlled trial of a cross-diagnosis care model for patients with mood disorders.* **Methods:** *Patients (N = 60) seen in one of four primary care or mental health clinics affiliated with the National Network of Depression Centers were randomized to receive a mood disorder care model, Life Goals Collaborative Care (LGCC, N = 29) or usual care (N = 31). LGCC consisted of five group self-management sessions focused on mood symptom coping and health behavior change strategies followed by monthly patient and provider care management contacts for up to 6 months. Outcomes at 3 and 6 months included mood symptoms (Patient Health Questionnaire—PHQ-9, Internal State Scale—well-being, Generalized Anxiety Disorder scale) and health-related quality of life.* **Results:** *Of the 60 enrolled, the mean age was 46.2 (SD = 13.2), 73.3% were female, 16.7% were non-white, and 36.8% had a bipolar disorder diagnosis. LGCC was associated with greater likelihood of depressive symptom remission in 6 months (respectively, 50% versus 19% had a PHQ-9 score ≤9 and 50% reduction in PHQ-9 score, P = .04) and improved well-being (β = 2.66, P ≤ .01, Cohen's D = 0.43).* **Conclusions:** *LGCC may improve outcomes for patients regardless of mood diagnosis, potentially providing a feasible and generalizable chronic care model for routine practice settings. Depression and Anxiety 30:116–122, 2013.* ©

Key words: *mood disorders; collaborative care; self-management*

INTRODUCTION

Chronic mood disorders (bipolar disorder and recurrent unipolar major depressive disorder) are the leading causes of disability worldwide.[1,2] When left untreated, they can lead to premature mortality, particularly from suicide.[1] A recent report by the U.S. Institute of Medicine (IOM) and others documented substantial gaps in evidence-based care for mental disorders,

[1]VA Ann Arbor Center for Clinical Management Research, Ann Arbor, Michigan
[2]Department of Psychiatry, University of Michigan Medical School, Ann Arbor, Michigan
[3]Department of Psychiatry, University of California San Francisco, San Francisco, California
[4]Department of Psychiatry and Depression Center, University of Colorado, Denver, Colorado
[5]Department of Psychiatry, Stanford University, Palo Alto, California

*Correspondence to: Amy M. Kilbourne, VA Ann Arbor Center for Clinical Management Research, North Campus Research Complex, 2800 Plymouth Road, Bldg 14, Ann Arbor, MI 48109. E-mail: amykilbo@umich.edu
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citing poor quality in detection, treatment, and follow-up care.[2] Although unipolar depression is more common, bipolar disorder is more costly on a per patient basis due to its chronic and severe nature.[3]

Collaborative chronic care models[4,5] have demonstrated efficacy and cost-effectiveness in managing unipolar major depressive disorder,[6–10] and more recently, bipolar disorder.[11–14] These care models involve a care manager who provides patient self-management education, coordinated care between primary care and mental health providers, and systematic dissemination of information related to treatment guidelines. Care models have been found to be cost neutral for bipolar disorder, and in depression, cost-effective compared to usual care, suggesting that care models may ultimately prove financially feasible not only in the public but also in the private sector.[6]

However, to date, most care models for mental disorders have been implemented for a single diagnosis such as depression.[6] There is growing demand for cross-diagnosis care models, in order to maximize their reach and to make them more appealing to providers, who might be reluctant to hire multiple care managers for different mental health diagnoses. Combining diagnostic groups also has the potential to decrease waiting time for patients to participate in clinical interventions. Mood disorders serve as an ideal starting point in which to implement a cross-diagnosis care model, notably because they are common, with U.S. population prevalence rates estimated at 16% for unipolar depression[15] and 4% for bipolar spectrum disorders.[16,17] The goal of this pilot randomized controlled trial was to implement a cross-diagnosis care model for patients with mood disorders across a national sample of clinics and determine whether, compared to patients receiving usual care, those randomized to receive LGCC had improved outcomes, notably decreased mood disorder symptoms over a 6-month period.

MATERIALS AND METHODS

This single blind multisite randomized controlled trial compared patients receiving LGCC to those receiving usual care across four sites affiliated with the National Network of Depression Centers (NNDC) at the University of Colorado, University of Michigan, University of California, San Francisco, and Stanford University. One of the sites (Michigan) was a primary care practice whereas the others were mental health specialty programs. Clinics participating in the pilot study identified a mental health clinician "champion" who served as the primary point of contact to help identify potentially eligible patients, and also designated an existing provider to implement LGCC at their clinic. LGCC care managers were existing providers, three of which were master's level clinical social workers and one was a PhD-level psychologist. This study was reviewed and approved by local Institutional Review Boards of the participating institutions, and all patients provided verbal and written informed consent prior to participation.

Patients were eligible if they had a current diagnosis of unipolar major depressive disorder or bipolar disorder (Type I, II, or Not Otherwise Specified), based on screening by the designated clinician, using checklists of mood disorder criteria derived from the text revision of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, American Psychiatric Association, 2000). Exclusion criteria were minimal in order recruit a real-world clinical outpatient mood disorder sample, and included at the time of enrollment having acute alcohol/substance use, psychiatric, or medical disorders that required inpatient treatment, active alcohol/substance intoxication, acute medical illness, dementia, or active suicidal ideation. The clinicians at each site screened patients and eligible patients were asked if they wanted to be part of the study. Patients agreeing to participate provided informed consent and completed an assessment that included questions on symptoms, quality of life, and other clinical and demographic features used in prior studies.[13,14]

INTERVENTION

After agreeing to participate, patients were randomized to receive LGCC or usual care. Life Goals Collaborative Care (LGCC) is based on the care model for bipolar disorder[13,14] expanded to address unipolar depression as well. Those randomized to LGCC were first contacted by the Care Manager who then scheduled intervention sessions. LGCC involved five group self-management sessions that included those diagnosed with either unipolar depression or bipolar disorder, followed by monthly care management contacts with both patients and providers for up to 6 months. LGCC self-management sessions were based on the Life Goals program, described previously,[13,14] and were expanded to include anxiety as well as depressive and manic symptom coping strategies. Sessions lasted approximately 90–120 min each and were semidirective, in which the Care Manager used motivational enhancement and elicited active discussions regarding management of mood symptoms. In particular, sessions covered mood disorder basics and issues around stigma (session 1), personal mood symptom profiles, coping strategies, and healthy behaviors to mitigate mood symptoms (sessions 2–4), and preparing an action plan for mood symptom coping and navigating healthcare appointments (session 5).

LGCC care management consisted of provider support through brief (15–20 min) follow-up phone contacts to the patient and provider by the care manager. During this period, care managers coordinated care with patients' primary care and/or mental health physicians, in particular, cueing providers if there was deterioration or no clinical or functional improvement and providing additional information on bipolar disorder and unipolar depression treatment guidelines if warranted (e.g. bipolar depression, hypomanic symptoms). Additional provider support for evidence-based decision making included the use of an electronic registry by the Care Manager to track symptoms and progress in which summary information on patient status was relayed back to the physician by the Care Manager.

LGCC Care Managers were trained by study investigators that included didactic instruction on management of depression and bipolar disorder along with hands-on training in the LGCC self-management, care management, and registry implementation. Additional training was provided on topics such as the boundary between depression and bipolar II disorder/bipolar disorder not otherwise specified (e.g. how to assess and treat with input from treating psychiatrists) and strategies for managing treatment-refractory depressive symptoms.

Usual care across the four sites was consistent in that it included guideline-informed standard mental health treatment by psychiatrists in the respective clinics (at the University of Michigan, a psychiatrist was co-located at the primary care clinic) but none of the LGCC components. No other psychosocial programs were offered to the patients during the intervention period.

MEASURES

Patients self-completed brief assessments at baseline, 3 months and 6 months. LGCC was designed to reduce mood symptom burden and

improve health-related quality of life based on previous trials.[13,14] The primary outcome was depressive symptoms based on the 9-item Patient Health Questionnaire (PHQ-9), a widely used and previously validated assessment of depressive symptoms.[18] Secondary outcomes included the Quick Inventory of Depressive Symptomatology (QIDS), and 16-item assessment of depressive symptoms,[19] and the Internal State Scale (ISS),[20] an 8-item assessment of manic symptoms and overall well-being that has been strongly correlated clinician ratings of mood disorders and improved quality of life. In addition, anxiety symptoms were assessed based on the Generalized Anxiety Disorder scale (GAD-7),[21] and health-related quality of life was assessed using the short-form 12-item survey (SF-12) in which mental and physical health component scores were generated.[22]

We also assessed potential mediators across the LGCC and UC groups, notably medication adherence and completion of LGCC sessions/contacts. The brief assessment also included a self-completed question on mood disorder medication adherence, based on previously established assessments. Self-reported "good" adherence was defined as response to a question on number of days in which he or she missed any of their antidepressant or mood stabilizer doses in the past 4 days (0, 1, 2, 3, or 4 days). A cutpoint of 0 days was categorized as adherent whereas any missed days was defined as nonadherent This definition (i.e. perfect self-reported adherence) was strongly associated with good adherence based on electronic cap monitoring (≥80% correct cap openings) in a primary care patient population.[23]

ANALYSES

Statistical analyses (intent-to-treat) ascertaining the effect of LGCC were considered exploratory, as this was a pilot study. Thus, a significance threshold of $P < .05$ was used and a correction for multiple comparisons was not applied. Repeated measures analyses were used to determine the effect of LGCC versus usual care on outcomes, adjusting for the baseline value of the outcome, effect of the LGCC, time (3, 6 months), medication adherence, and the interaction of time and LGCC effect. Effect sizes were estimated using Cohen's *D*. In addition, using logistic regression analyses, we compared the probability of remission from depression based on PHQ-9 scores. Depression remission was defined based on two definitions: (1) 50% reduction in PHQ-9 score and 6-month PHQ-9 score of 9 or lower, or (2) PHQ-9 score of 4 or lower (≤5) using established definitions for clinical significance.[18] Finally, sensitivity analyses were conducted in which we stratified repeated measures analyses by mood disorder diagnosis (bipolar disorder, unipolar depression) to assess whether LGCC had a differential effect on these patients.

RESULTS

Out of 92 eligible patients approached, 32 declined to participate, leaving 60 for this pilot study. Of the 60 enrolled, 29 were randomized to LGCC and 31 to usual care, and all 60 completed baseline and 6-month follow-up assessments. Overall, the mean age was 46.2 (SD = 13.2), 73.3% were female, 16.7% were non-white, and 36.8% had a bipolar disorder (type I or II) diagnosis. There were no significant differences in demographic characteristics among those who declined versus those who were enrolled or in those assigned to LGCC versus treatment as usual. Among those randomized to LGCC, the mean (±SD) number of group sessions and follow-up care management contacts were, respectively, 4.0 (±1.7) and 4.1 (±4.0).

Repeated measures analyses (Table 1) found that the effect of LGCC on reductions in depressive symptoms as measured by changes in PHQ-9 scores approached significance ($\beta = -1.56$, $P = .09$; Cohen's $D = 0.18$). However, patients randomized to LGCC versus usual care were significantly more likely to have a 50% reduction in PHQ-9 score and a PHQ-9 score of ≤9 at 6 months (respectively, 50.0% versus 19.1%, OR = 9.4, $P = .04$) based on logistic regression analyses (Table 1). In addition, 36.8% of those enrolled in LGCC achieved a PHQ-9 score of ≤5 compared to 19.1% in the usual care group, but this finding was not statistically significant.

LGCC compared to usual care was also associated with improved well-being ($\beta = 2.66$ $P \leq .01$, Cohen's $D = 0.43$) based on repeated measures analysis (Table 1). These changes appeared to not be attributable to changes in medication adherence: as similar rates of no missed doses were evident for the LGCC and usual care groups at 6 months: respectively, 81.3% versus 80.0%, OR = 1.1, $P = .92$.

Repeated measures analyses stratified by diagnosis (bipolar disorder or unipolar depression) revealed similar trends and larger effects for patients diagnosed with bipolar disorder (Table 2). Among patients diagnosed with unipolar depression, those receiving LGCC reported improved well-being in 6 months compared to those in the UC group.

DISCUSSION

To our knowledge this was the first study of a cross-diagnosis mood disorder care model implemented across different treatment settings (primary care, specialty mental health) by existing providers. The evidence supporting the efficacy/effectiveness of cross-diagnosis cronic care models (CCMs) mental health programs,[25] and depression and co-occurring medical conditions,[26] enhancing the generalizability and overall value of the CCM for mental disorders in routine practice.

This was also the first dissemination of a collaborative care model-based intervention across the NNDC, the largest network of its kind focused on research and treatment related to depression and bipolar disorders. CCMs typically include patient self-management education, coordination of follow-up care by a nonphysician provider, and ongoing symptom monitoring and population management for people with chronic medical or mental health diagnoses. This study provides a template for research and clinical care involving a single network entity, services; ultimately simplifying training and reducing cost and complexity.

We found that LGCC compared to usual care outcomes, notably improved depression remission and overall well-being. Previous trials of care models applied to bipolar disorder had a less effect on depressive than manic symptoms.[11,12] We found that half of patients randomized to LGCC achieved a 50% reduction in PHQ-9 score and a 6-month score of ≤9. The

TABLE 1. Six-month outcomes comparing Life Goals Collaborative Care (LGCC) versus usual care (UC)

	LGCC ($N = 29$)			UC ($N = 31$)			Repeated measures results[c]	
Outcomes ($N = 60$)	Baseline	3 months	6 months	Baseline	3 months	6 months	β (95% CI)	T (P)
Depressive symptom score (PHQ-9)[a]	13.72 (7.51)	9.34 (6.53)	6.26 (4.20)	16.84 (6.51)	14.03 (6.25)	11.86 (6.78)	− 1.56 (−3.37, 0.26)	− 1.72 (.09)
Depressive symptoms: QIDS score[a]	18.66 (8.23)	13.20 (7.17)	10.53 (5.05)	22.87 (6.21)	19.70 (8.65)	17.00 (8.66)	− 1.76 (−4.19, 0.67)	− 1.45 (.15)
Manic/hypomanic symptoms (ISS)[a]	10.29 (8.38)	7.79 (5.43)	9.65 (7.87)	15.74 (12.8)	15.65 (12.8)	16.50 (11.73)	− 0.98 (−3.75, 1.79)	− 0.71 (.48)
Well-being (ISS)[a]	13.00 (7.88)	15.79 (8.27)	20.41 (7.75)	10.18 (6.85)	12.53 (7.81)	12.44 (8.07)	2.66 (0.72, 4.60)	2.76 (<.01)
Anxiety symptoms: GAD-7[a]	9.90 (6.11)	8.10 (6.06)	5.79 (4.52)	12.71 (5.90)	9.99 (5.41)	9.81 (6.13)	− 0.28 (−1.72, 1.16)	− 0.39 (.69)
SF-12 Mental health-related quality of life[b]	30.86 (6.30)	31.12 (7.74)	31.64 (8.45)	25.46 (6.95)	29.26 (7.48)	28.82 (8.97)	0.62 (−2.30, 3.55)	0.43 (.67)
SF-12 Physical health-related quality of life[b]	37.52 (6.74)	38.43 (6.36)	39.05 (8.04)	40.03 (6.83)	36.70 (5.84)	40.86 (4.24)	0.59 (−1.36, 2.56)	0.61 (.54)
PHQ-9 cutpoints[d]		% (95% CI)			% (95% CI)		OR (95% CI)	χ^2 (P)
% with ≥50% drop in PHQ-9 score and PHQ-9 score ≤9 in 6 months	–	–	50.0 (26.0, 73.9)	–	–	19.0 (5.5, 41.0)	9.4 (1.4, 64.0)	4.18 (.04)
% with PHQ-9 ≤ 5	13.8 (3.9, 31.7)	35.0 (15.4, 59.2)	36.8 (16.3, 61.6)	3.2 (0.08, 16.7)	10.0 (1.2, 31.7)	19.1 (5.5, 41.9)	7.1 (0.9, 53.7)	1.58 (.20)

[a]Mood symptom scores were based on the Patient Health Questionnaire (PHQ-9) and Quick Inventory of Depressive Symptomatology (QIDS), and for anxiety symptoms the Generalized Anxiety Disorder scale (GAD) in which a higher score reflects more symptoms for these three measures. For the Internal State Scale (ISS) well-being scale, possible scores range from 0 to 20 and a higher score indicates greater well-being.

[b]Health-related quality of life (SF-12) includes a mental health (MCS) and physical health component score (PCS). Possible scores range from 0 to 100, with higher scores indicating better health scores. For both summary scores, the population $M \pm SD$ is 50 ± 10.

[c]Repeated measures analysis adjusted for the baseline value of the outcome, effect of the Life Goals Collaborative Care (LGCC), time (3, 6 months), medication adherence, and the interaction of time and LGCC effect.

TABLE 2. Six-month outcomes comparing Life Goals Collaborative Care (LGCC) versus usual care (UC) by diagnosis

Bipolar disorder ($N = 21$)		LGCC ($N = 11$)			UC ($N = 10$)		β (95% CI)	T (P)
Depressive Sx score (PHQ-9)[a]	10.05 (5.63)	8.75 (6.76)	4.44 (3.00)	16.80 (5.71)	14.00 (5.21)	9.63 (6.25)	−2.67 (−6.24, 0.91)	−1.57 (.13)
Depressive Sx: QIDS score[a]	17.73 (7.88)	12.38 (5.60)	8.44 (5.34)	22.80 (5.94)	19.38 (10.84)	14.88 (11.41)	−2.47 (−7.78, 2.84)	−0.98 (.34)
Manic Sx (ISS)[a]	12.55 (6.53)	8.67 (6.71)	10.57 (7.98)	19.10 (13.94)	14.33 (5.32)	18.33 (8.29)	−2.31 (−7.27, 2.64)	−0.98 (.33)
Well-being (ISS)[a]	16.82 (6.38)	17.67 (8.76)	25.14 (5.18)	10.55 (5.31)	11.83 (7.41)	16.33 (5.28)	1.76 (−0.57, 4.09)	1.60 (.12)
Anxiety Sx: GAD[a]	7.18 (4.35)	6.88 (4.39)	4.56 (3.78)	11.80 (5.49)	9.75 (5.44)	7.38 (5.71)	−0.32 (−3.00, 2.37)	−0.25 (.80)
		% (95% CI)			% (95% CI)		OR (95% CI)	χ^2 (P)
% with ≥50% drop in PHQ-9 score and PHQ-9 score ≤9 in 6 months	–	–	75.0 (34.9, 96.8)	–	–	25.00 (3.2, 65.1)	57.89 (0.93, 100)	3.71 (.05)
% with PHQ-9 ≤5[d]	27.3 (6.0, 60.9)	37.5 (8.5, 75.5)	55.6 (21.2, 86.3)	0.00 (0.00, 30.9)	12.5 (0.3, 52.7)	25.00 (3.2, 65.1)		
Unipolar depression ($N = 36$)		LGCC ($N = 18$)			UC ($N = 18$)		β (95% CI)	T (P)
Depressive Sx score (PHQ-9)[a]	15.97 (7.76)	9.74 (6.65)	7.90 (4.58)	18.56 (5.98)	14.04 (7.08)	13.23 (6.95)	−2.08 (−4.26, 0.09)	−1.96 (.06)
Depressive Sx: QIDS score[a]	19.22 (8.61)	13.75 (8.25)	12.40 (4.17)	23.89 (6.20)	19.92 (7.37)	18.31 (6.65)	−1.79 (−4.46, 0.88)	−1.38 (.17)
Manic Sx (ISS)[a]	8.82 (9.28)	7.38 (4.99)	9.00 (8.15)	14.33 (11.81)	16.36 (15.69)	15.58 (13.37)	−1.39 (−4.19, 1.41)	−1.02 (.31)
Well-being (ISS)[a]	10.67 (7.95)	14.92 (8.25)	17.10 (7.71)	8.78 (7.01)	12.91 (8.35)	10.50 (8.70)	3.23 (0.25, 6.21)	2.22 (.03)
Anxiety Sx: GAD[a]	11.56 (6.53)	8.92 (7.03)	6.90 (5.02)	14.72 (5.10)	10.15 (5.63)	11.31 (6.10)	−1.03 (−2.89, 0.84)	−1.13 (.26)
		% (95% CI)			% (95% CI)		OR (95% CI)	χ^2 (P)
% with ≥50% drop in PHQ-9 score and PHQ-9 score ≤9 in 6 months	–	–	30.0 (6.7, 65.3)	–	–	15.4 (1.9, 45.5)	26.69 (0.42, 102)	2.40 (.12)
% with PHQ-9 ≤5[d]	5.6 (0.1, 27.3)	33.3 (9.9, 65.1)	20.0 (2.5, 55.6)	0 (0.0, 18.5)	8.3 (0.2, 38.5)	15.3 (1.9, 45.3)	–	–

[a]Symptom (Sx) scores were based on the Patient Health Questionnaire (PHQ-9) and Quick Inventory of Depressive Symptomatology (QIDS), and for anxiety symptoms the Generalized Anxiety Disorder scale (GAD) in which a higher score reflects more symptoms for these three measures. For the Internal State Scale (ISS) well-being scale, possible scores range from 0 to 20 and a higher score indicates greater well-being.

[b]Health-related quality of life (SF-12) includes a mental health (MCS) and physical health component score (PCS). Possible scores range from 0 to 100, with higher scores indicating better health scores. For both summary scores, the population $M \pm SD$ is 50 ± 10.

[c]Repeated measures analysis adjusted for the baseline value of the outcome, effect of the Life Goals Collaborative Care (LGCC), time (3, 6 months), medication adherence, and the interaction of time and LGCC effect.

[d]Small sample sizes precluded accurate effect estimates.

observed clinically significant reduction in well-being also shows that the care model may potentially benefit those with a wider range of persons with mood disorders. Well-being in particular is associated with improved functioning overall and is a potentially generalizable marker for improved outcomes across mental health diagnoses.[2]

In contrast to previous studies, LGCC was not associated with improved health-related quality of life.[11,12] Prior studies found significant differences in mental health physical health-related quality of life,[11,12] after a follow-up period of at least 2 years. Nonetheless, improvements in mood symptoms, particularly depression and well-being, has been shown to be associated with clinically significant changes in outcomes including health-related quality of life, functioning, and survival in previous studies of the care model.[6]

Limitations of the study included a small sample size, which limited statistical power to detect mood benefits, and a relatively short follow-up period, which may have limited our ability to observe potential changes in longer-term outcomes such as quality of life observed in earlier LGCC trials.[10,12] This pilot study also lacked sufficient statistical power to also explore mechanisms of treatment effect, such as bipolar disorder diagnosis or potential diagnosis switching.

Overall, our study provided preliminary evidence that cross-diagnosis care model was feasible to implement and could improve outcomes among diverse mood disorder patients seen in different treatment settings. Our findings suggest that further cross-diagnosis care model research is warranted, including assessments of dissemination of care models across an even wide range of diagnosis (e.g. mood, anxiety disorders) and exploration of the feasibility of reimbursement models in the private sector, as well as the application of technologies such as telemedicine or web-based applications to facilitate the uptake of LGCC and other care models in routine practice.[27] In addition, the potential effectiveness of collaborative care models such as LGCC has implications for healthcare reform, notably in the implementation of Accountable Care Organizations (ACOs).[28] Given the substantial prevalence of mood disorders in general medical care settings, integrated mental healthcare models within ACOs are needed. ACOs have potential to improve care for mood disorders through incentives for better performance and bundled payments that can support care managers who can implement key components of care models (e.g. self-management sessions, measurement-based care). Ultimately, manual-based, cross-diagnosis care models such as LGCC that can be easily adopted by existing providers have the potential to improve efficiency, quality, and outcomes for this vulnerable group across different care settings.[29,30]

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