Full NIH Title: Implementing Health Plan-Level Care Management for Solo & Small Practices
NCT02041962
Protocol # HUM00073753
Protocol version: v5
Protocol date: 3.23.15
PI: Amy Kilbourne, PhD, MPH

I. Objective

The vast majority of primary and behavioral health care services are provided by solo or small practices, yet to date collaborative chronic care models (CCM) have not been implemented in these settings. Mood disorders are common and represent the most expensive mental disorders for commercial health plans and employers. The goal of this study is to implement and test a CCM for mood disorders for solo and smaller practices in partnership with Aetna Health Plan, with an eye towards making the business case and demonstrating value for CCMs for these settings that can reach patients wherever they receive treatment.

II. Specific Aims/Hypotheses

A 2010 HHS report highlighted the prevalence, morbidity, and cost associated with clusters of co-occurring chronic conditions, both physical and mental. The report also underscored the lack of sustainable treatment strategies for these afflicted individuals, and the difficulties in customizing patient-centered interventions.

Collaborative chronic care models (**CCMs**) are effective in treating chronic medical and mental illnesses at little to no net healthcare cost. To date CCMs have primarily been implemented at the facility level and primarily developed for and adopted by larger healthcare organizations. However, we have determined that the vast majority of primary care and behavioral health practices providing commercially insured care are far too small to implement such models. Health plan-level CCMs can address this unmet need.

Chronic mood disorders (e.g., bipolar disorders, depression) are common and are associated with extensive functional impairment, medical comorbidity, and personal and societal costs. While unipolar depression is more common, bipolar disorder is more costly on a per patient basis due to its chronic and severe nature. Moreover, bipolar disorder is the most expensive mental disorder for U.S. commercial health plans and employers. While evidence-based care parameters have been well established for mood disorders, quality of care and health outcomes in general mental health practice are suboptimal. The majority of these patients suffer from clusters of comorbid conditions, both physical and mental. Thus mood disorders represent optimal tracer conditions with which to improve management strategies for individuals with multiple chronic conditions.

Accordingly, we have partnered with Aetna Inc. to develop and implement a CCM designed to improve outcomes for persons with mood disorders for solo or small practices, with an eye towards developing a business case for a generalizable plan-level CCM for chronic disorders. We will conduct an RCT of a health plan-level CCM vs. education control. The population of interest will be Aetna beneficiaries across the country hospitalized for depression or bipolar disorder treated in solo or small primary care or behavioral health practices. Patients will be randomized to one year of outpatient treatment augmented by the CCM or education control, for a total of 344 participantsCCM care management will be fully remote from practice venues and patients, implemented by existing providers (the Aetna care management center). A business case will be developed using the Replicating Effective Programs (**REP**) strategy that identifies generalizable facilitators for CCM spread and value added of CCMs to be vetted to key industry and policy stakeholders.

Our Specific Aims are to:

1. Determine whether individuals with mood disorders treated with a health plan-level CCM demonstrate improved health outcomes and quality of care at 12 months compared to those who are mailed educational material alone (Educational Control-EC).

Our **primary hypothesis** is that compared to EC, the mood CCM will result in a) reduced mood symptoms in 12 months, or b) improved health-related quality of life.

Our secondary hypotheses is that patients receiving CCM vs. EC will have improved guideline-concordant care (e.g., mood disorders treatment, cardiometabolic monitoring), reduced hospitalizations, and improved work productivity within 12 months.

2. To support subsequent CCM dissemination by identifying key organizational, provider, and patient characteristics associated with CCM engagement and outcomes.

3. To conduct a cost-effectiveness analysis of CCM versus EC on changes in patient utilities over 24 months and apply findings to develop a business case for CCMs in smaller practices.

This proposed R18 addresses **AHRQ's research demonstration and dissemination priorities**, particularly around prevention and care management, with an emphasis on vulnerable groups including more rural populations (the majority of Aetna enrollees are seen in smaller practices). It also confronts unanswered organizational and financial questions raised by a recent **AHRQ report** ("A National Agenda for Research on Collaborative Care"). As one of the first cross-diagnosis CCM-based implementation studies focused on small practices, this groundbreaking study is informed by an extensive partnership with a network-model health plan (Aetna). The study also applies a novel implementation framework (REP) in which the CCM is delivered by existing providers. In addition to the specific importance of this practice-research partnership to further implement CCMs among small practices at the health plan level within a natural experiment setting, this study will contribute to the evolution of the business case for CCMs in general, enhance the utility of plan-level panel management focused on vulnerable populations across different treatment settings, and inform remote technologies that will facilitate emerging healthcare initiatives (e.g., accountable care organizations, health IT).

III. Background and Significance

A. Significance.

1. Majority of care for mental disorders is provided by private solo or small practices.

The 2011 HHS report on multiple chronic conditions (1) highlighted the prevalence, morbidity, and cost associated with clusters of co-occurring chronic conditions, and lack of current treatment strategies. A recently completed AHRQ report (2) and meta-analysis by our group (3) concluded that collaborative chronic care models (**CCMs**) are effective in treating chronic medical and mental illnesses at little to no net healthcare cost (4-6). CCMs consist of: (a) patient self-management skill enhancement, (b) expert decision support to providers via evidence-based practice guidelines, and (c) enhanced access and continuity via care managers working in collaboration with physicians to support information flow between patients and providers (7, 8).

Our recent meta-analysis of CCMs also found that they have primarily been implemented at the facility level in publically funded settings (2, 3, 9, 10). Still, between 50-70% of patients with mental health conditions are managed by commercial health plans (11). Moreover, in a recent analysis we have also determined that 85% of those with mood disorders receive care from solo or small practices (12) that are less likely to be able to implement care management processes at the practice level (13).

CCMs will become increasingly important as healthcare delivery systems evolve into accountable care organizations (14, 15), thereby taking on broader responsibility for care coordination and quality while bearing financial risk for complex, chronic conditions. CCMs can provide either the foundation of, or an annex to, emerging medical home methodologies (16-18). However, dissemination of CCMs is limited to larger practice venues with sufficient infrastructure (19, 20). To date CCMs for chronic disorders have been implemented as clinic-based interventions (21) or within integrated healthcare systems, but not in smaller practices (22).

2. Mood disorders are common exemplars for complex patients at high risk in need of CCMs.

Mood disorders (depression and bipolar disorder) are chronic illnesses associated with substantial social dysfunction (23) and rank in the top ten causes of disability worldwide (24). National studies of the U.S. population estimate the lifetime prevalence for bipolar spectrum disorders as 6.4% (25, 26) and 16.6% for major depressive disorder (27). Medical comorbidity is the rule for mood disorders, in which the majority of patients suffer from at least one co-occurring chronic medical illness (28, 29). Persons with mood disorders die younger, mainly from cardiovascular disease (30-32). Quality of care is suboptimal for both chronic medical (33) and mental (34-41) disorders, underscoring the need for coordinated, comprehensive care. Not

surprisingly, the recently released IOM comparative effectiveness priority list includes among its top-quartile priorities research on comprehensive care coordination for chronic diseases (42). While unipolar depression is more common, patients with bipolar disorder incur the most health care costs of any mental illness (43). Up to 70% of direct treatment costs for mood disorders are generated outside the mental health sector, notably in primary care (44-46). In response to extremely high costs and high disease burden associated with mood disorders, Aetna has partnered with us to develop and implement care management methods for this group.

3. Health plan-level cross-diagnosis CCMs can address gaps in quality & outcomes for mood disorders To date CCMs have not been implemented across mood disorder diagnoses (depression or bipolar disorder), nor have they simultaneously addressed medical and psychiatric outcomes in this group. Given these clear public health deficits, there is a need for adaptation and greater reach of care management strategies beyond single diagnoses. The current state-of-the-science indicates that research efforts should focus more on cross-diagnoses models such as the one proposed in this study as well as issues of spread and sustainability. CCMs have been found to be effective in reducing symptom burden and improving health-related quality of life for depression (3, 47-49) and bipolar disorder (7, 8, 50-53) in separate studies and are now recommended in practice guidelines (54, 55). Our preliminary study of a cross-diagnosis CCM for mood disorders also demonstrated improved outcomes (**Section C**). Moreover, long-term CCM treatment for mood disorders can be cost-neutral (51), and effective among patients with co-occurring substance use disorders (56).

Thus adapting CCMs for this population will require population or health plan level intervention. Moving to plan level care management requires primary reliance on remote rather than clinic-based methods, such as telephone contacts with patients and providers. We have identified 14 reports of 10 trials of telephone care management for depression but none for bipolar disorder (2). These studies recommend a combination of rapport-building telephone care manager-patient contacts with tailored health IT modalities (e.g., web-based self-management, EMRs) (57-69). Several initiatives by our study team also hold promise in a health plan-level implementation of the CCM (**Section C**), notably a telehealth program for bipolar disorder and a web-based, tailored medical care management program for mood disorders (40, (70).

B. Innovation

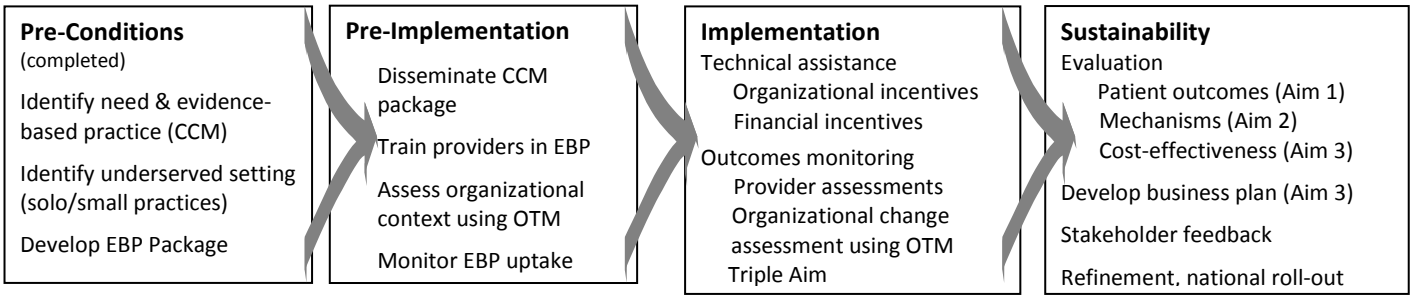
1. To date this is the first study to implement CCMs in solo or small practices, where many patients with mood disorders are seen: CCMs have mostly been implemented at the facility level, and primarily developed for and adopted by larger healthcare organizations. However, 50-70% of Americans with mood disorders are managed by commercial insurance plans such as Aetna. Aetna is one of the largest health plans in the U.S., and among its enrollees >90% were seen in solo or small practices (12). This study also complements ongoing efforts in the public sector to implement CCMs through medical home models (10).

2. Translating CCMs to health plan level models is essential for maximal generalizability: Plan-level CCMs have rarely been tested in rigorous RCTs (31). A focused implementation of a cross-diagnosis CCM at the national level has implications for the tailoring of evidence-based programs to smaller and rural settings, personalized health care, and implementation of health IT. As technologies around large databases become more sophisticated and complete, implementation programs that successfully apply these rich resources to helping vulnerable populations will serve as important milestones in the nation's transition to a more public health model of care. By focusing on measurement dimensions of the Berwick Triple Aim (care, health, and cost), study findings are potentially generalizable across complex patient populations (71).

3. Implement CCM using an established strategy to address organization, financing (Figure 1): We will apply a state of the art framework to implement the CCM across Aetna nationally. Developed by study investigators, the Replicating Effective Programs (**REP**) implementation framework has been used to facilitate the uptake of mood disorder CCMs in prior studies (R01 MH 79994) (72, 73). A variety of implementation frameworks and supporting theories exist (74-78), with relative advantage conferred on those that are (a) theory-based, (b) highly specified operationally, and (c) widely used in relevant contexts. REP is based on the Centers for Disease Control and Prevention's Research Practice Framework (76, 77, 79). Based on Social

Learning Theory (80) and Rogers' diffusion model (81), REP is highly specified operationally into three components that are directly applied to the CCM: Packaging (i.e., translation of CCM materials into user-friendly language), Training, and ongoing facilitated Technical Assistance to address barriers to uptake.

Figure 1: Enhanced Replicating Effective Programs (REP) to Facilitate Implementation of CCMs



Enhanced REP: In a recent implementation of REP (R01 MH79994), community-based administrators and providers made specific recommendations to the Technical Assistance component that would help develop a **business case** for the CCM based on organizational as well as financial incentives (73). This **Enhanced REP** framework includes ongoing assessment of organizational barriers or facilitators to implementation (11, 82-87) based on the **Organizational Transformation Model- OTM** (88) that assesses both context as well as organizational change factors that might influence implementation. The OTM assessment (72) measures organizational processes found to be associated with improved quality (89), including the practice's readiness to implement new programs (e.g., CCM), leadership commitment, degree to which frontline providers are involved in the operationalization of a new program, and alignment of new program goals with existing priorities and day-to-day processes. Enhanced REP emphasizes dissemination of data to health plan leaders and other stakeholders, and aligning CCM components with reimbursement strategies that may inform the implementation of emerging initiatives including accountable care organizations.

4. This proposal represents a true private-public partnership in light of other AHRQ initiatives (90). Community-based providers involved in our previous studies (R01 MH74509, MH79994) have strongly emphasized the need for CCMs across mood disorders from smaller practices (73). Aetna will provide all care management infrastructure, data, and staff while federal research funds are limited to support of training and evaluation. All products developed from this project will be made available in the public domain based on AHRQ guidelines. Finally, this R18 also addresses unanswered questions raised by a recent AHRQ report on setting a National Agenda for Research in Collaborative Care (2).

IV. Preliminary Studies:

Our preliminary studies, including a national study of care management in Aetna and implementation of a cross-diagnosis CCM across the National Network of Depression Centers demonstrate our collective expertise in development and implementation of mood disorder CCMs to improve outcomes across a wide variety of practices, and support the readiness of the mood CCM for a plan-level RCT.

C.1. Mood disorders in Aetna: Identifying and addressing the need in solo/small practices. Aetna Inc. is the fifth largest healthcare insurer in the country, providing benefits through employers in all 50 states, with products and services targeted specifically to small, mid-sized and large multi-site national employers. Aetna Behavioral Health serves approximately 12 million covered lives, with 244,971 providers across 157,523 practices filing claims in the past year. Thus while this specific RCT is sited in a single health plan, Aetna has the size and diversity sufficient to represent a wide range of commercially funded care for mood disorders in the US. Aetna has had a longstanding and stable commitment to implementing disease management for high-prevalence, high-cost mental health conditions, as well as a track record of NIH-funded research (e.g.,

1R01DA029716; 1R01DA026414). Aetna's commitment to sustaining and expanding mental health care management—and the mood disorders CCM in particular—is underscored in the letters from both Dr. Un and Aetna's in-kind contribution outlined in the Budget Justification.

C.2. Most Aetna beneficiaries receive care for bipolar disorder from small or solo practices. Using all Aetna Behavioral Health claims data from 2009, we determined practice size based on number of participating providers linked to the same tax identification number. Unlike the situation for primary care and multi-specialty groups (19, 20, 91), care for bipolar disorder is predominantly provided in small behavioral health practices, with the vast majority of individuals with bipolar disorder treated in solo practices (Table 1). Further, among Aetna patients with bipolar disorder from solo or small practices, **23% (N=2785) were hospitalized** in the past year. This distribution convinced us that it is critical to focus the study on smaller or solo practices in order to truly reach a vulnerable population who to date may not have access to effective care management.

Table 1: Profile of Aetna Enrollees with Bipolar Disorder by Practice Size

Practice Size (# Licensed Independent Providers)	# Behavioral Health Practices (%)	# Psychiatrists (%)	# Patients Treated for Bipolar Disorder Seen in Given Practice Venue Size (%)**	Avg. Bipolar Patient Census
Single Independent Psychiatrist	20,318 (84.1%)	20,318 (45.7%)	20,203 (94.4%)	3.5
Single Psychiatrist Registered as Group*	1,250 (5.2%)	1,250 (2.8%)	111 (0.5%)	1.3
Group Practice with 2-3 Psychiatrists	967 (4.0%)	4,428 (10.0%)	207 (1.0%)	2.3
Group Practice with 4-10 Psychiatrists	1,029 (4.3%)	6,875 (15.4%)	329 (1.5%)	2.0
Group Practice with 11-20 Psychiatrists	380 (1.6%)	5,089(11.4%)	225 (1.1%)	2.4
Group Practice with 21-100 Psychiatrists	214 (0.9%)	5,645(12.7%)	318 (1.5%)	4.5
Group Practice with >100 Psychiatrists	14 (0.1%)	894(2.0%)	18 (0.1%)	18.0
Total Number of Practices	24,172 (100.0%)	44,449 (100.0%)	21,411 (100.0%)	--

*Individual providers could register with Aetna either as an independent practitioner or as a group at their own discretion.
**Analysis of 20,933 unique patients treated for bipolar disorder; 1,675 (0.8%) received care in >1 venue.

C.3. Aetna national RCT of brief phone-based CCM vs. education control for bipolar disorder (N=457)
An IRB-approved feasibility RCT of a brief plan-level care management program (CM) was led by Aetna Behavioral Health Medical Director Dr. Hyong Un and internal Aetna staff. The study involved 457 adult Aetna enrollees or family members with bipolar disorder from 215 distinct practices across all 6 Aetna regions randomized to either CM or educational material mailing control (EC). Inclusion criteria included hospitalization for bipolar disorder type I or II and >= 6 months of prior enrollment in Aetna in order to provide sufficient claims data. Inability to speak or read English was the sole exclusion criterion to enhance generalizability (<10%, or N=48 out of the 505 approached).

EC consisted of 6 biweekly educational mailings about bipolar disorder, and CM consisted of these mailings plus 3 semi-structured, monthly telephone patient contacts provided by a care manager stationed at the Aetna national CM center in Salt Lake City. Telephone contacts focused on: (a) measurement-based clinical assessment, (b) identification and trouble-shooting of patient-identified disease- and treatment-related challenges, and (c) motivational interviewing techniques to support treatment engagement. At the patient's discretion additional sessions were arranged at the end of this 3-month period. This prototype CM model included no provider contacts or participant compensation. Outcomes included several service use and costs (inpatient, outpatient, laboratory, pharmacy) from the economic perspective of the insurer.

Of the 457 randomized, 424 (92.8%) completed the protocol. CM participants completed a mean of 4.4 contacts. Cost data were exported to Dr. Kilbourne for analysis. Despite the modest intensity, there was a

greater reduction in costs among CM vs. EC participants (Cohen's D=0.21) (Table 2). Importantly, outpatient visits were not decreased in the control group, indicating that the protocol did not disrupt usual care. Moreover, care managers identified 4 out of 457 patients who had suicidal ideation and, through established protocols, alerted the provider and arranged emergency evaluation; and no suicide attempts occurred during the study. This study indicates that: (a) participants can be successfully enrolled into a plan-level care manager RCT; (b) care management can be successfully implemented with participants across time zones from a national call center; and (c) claims data suggest that care management may have had beneficial effects.

Table 2: Changes in Costs among Aetna Patients Randomized to CM or EC: National Data

	Care Management (mean $±SD)			Educational Control (mean $±SD)		
	6 Mos Pre	6 Mos Post	Difference	6 Mos Pre	6 Mos Post	Difference
Aetna BH $/member	5,210±8,370	934±2,210	-4,277±7,926	6,048±6,347	3,492±7,621	-2,556±8,461

C.4. NNDC Multisite mood CCM implemented by existing providers improves outcomes. In a randomized controlled pilot study we determined the effectiveness of a cross-diagnosis mood CCM compared to education control in a cohort of outpatients with unipolar depression or bipolar disorder from four sites affiliated with the National Network of Depression Centers (NNDC). NNDC is the nation's largest network of academic and community-affiliated mental health and primary care clinics representing a diverse practice size and patient population. Existing care managers at four NNDC sites (Ann Arbor, Palo Alto, San Francisco, Denver) were trained by study investigators to implement the CCM using Enhanced REP. Sixty patients (mean age=46, 40% bipolar diagnosis, 73% female, 17% African-American) with mood disorders were identified using chart reviews and randomized to CCM or usual care. CCM included phone-based self-management and care management as well as guideline dissemination to providers. Repeated measures analyses comparing changes in 3 and 6-month outcomes revealed clinically significant probability of depression remission (>50% PHQ-9 score reduction and <=9 on PHQ-9 in 6 months): 50.1% for CCM vs. 19.0% for EC group (OR=9.4, p=.04) and improved well-being (positive symptoms based on the Internal State Scale-ISS - Cohen's D=.36).

Table 3: 6-Month Outcomes Comparing CCM vs Education Control (EC): Repeated Measures Analysis

Outcomes(N=60)	CCM (N=29)			EC (N=31)			Repeated measures results		
	Baseline	3-mon	6-mon	Baseline	3-mon	6-mon	Beta	T(p)	Effect(D)
PHQ-9	13.7 (7.5)	9.3 (6.5)	6.3 (4.2)	16.8 (6.5)	14.0 (6.6)	11.9 (6.8)	-1.24	-1.37(.17)	-.22
50% drop: PHQ-9 and PHQ-9 <=9			50.0%			19.0%	OR=9.4; Chi-sq= 4.18; p=.04		
ISS-Wellbeing	13.0 (7.9)	15.8 (8.3)	20.4 (7.8)	10.2 (6.9)	12.5 (7.8)	12.4 (8.1)	2.22	2.35(.02)	.36

V. Methodology

Overview. We will conduct an RCT of the **CCM** for mood disorders vs. an educational mailing control (**EC**). The population of interest will be Aetna adult enrollees and family members (beneficiaries) across the country hospitalized for an episode of unipolar depression or bipolar disorder and belonging to a solo (i.e., single provider) or small practice (2-3 providers). Patients will be randomized to CCM or EC. The CCM will be implemented using Enhanced REP (76, 77, 79) as we have in prior studies (72, 73, 76). CCM care management will be fully remote from practice venues and patients, implemented by Aetna care managers. CCM and EC strategies represent add-ons to ongoing practice, which will not otherwise be altered. Main outcomes include mood symptoms (e.g., PHQ-9) and health-related quality of life (SF-12), accounting for nesting of patients within practices.

C.5.b. Sample recruitment, eligibility, enrollment (Figure 2). The following steps will be taken to enroll participants, provide informed consent, and randomize them. Participant recruitment and treatment will utilize existing Aetna resources.

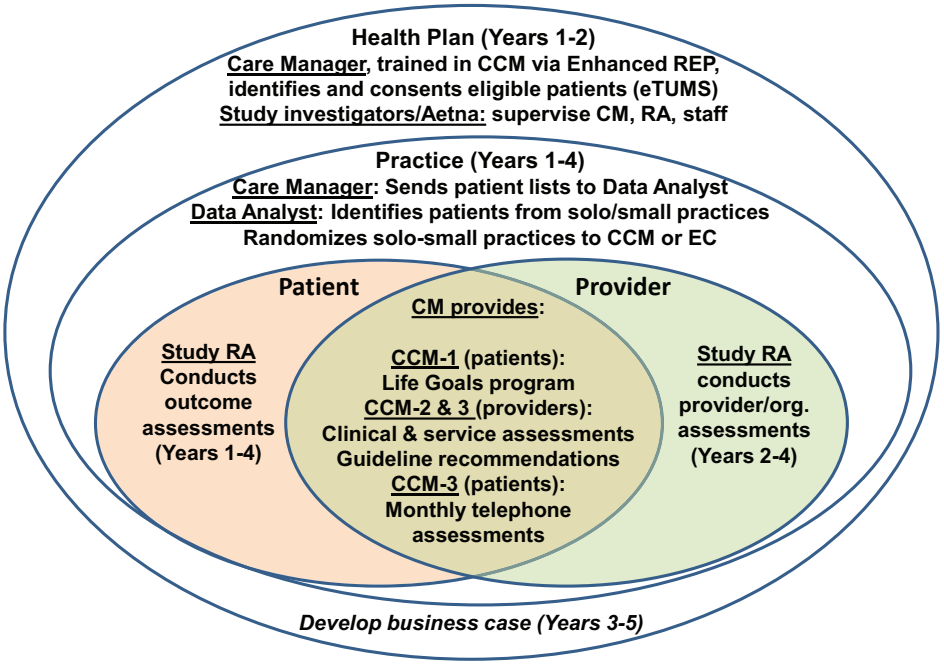
1. Aetna care managers will recruit participants by first screening them based on near-real time information of recent hospitalizations (as with the pilot study). At hospitalization, Aetna is notified for (pre)authorization, typically before or within 48 hours of admission. Care managers will be notified about patient hospitalizations via the Aetna care management registry, eTUMS (Section C.5.c) and will contact the potential participant by phone as in the pilot study (Section C.4.a). Care managers will screen for eligibility and obtain informed consent and authorization to release information to the research team and to coordinate care with their providers. This will be done over the telephone after verbally explaining the protocol, risks, benefits, and safety measures via written script based on previous RCTs (92, 93). Because patients have not been randomized at this point, Aetna care managers will be blind to treatment assignment at baseline.

2. Patient inclusion criteria as determined by the care managers include:

a. Adult patients age 21 years or older from the contiguous United States (lower 48 states)
b. Currently covered by Aetna's HMO or preferred provider products (for whom Aetna provides mental and medical inpatient, outpatient, and pharmacy benefits) for at least 6 months
c. Recent (past 6-month) hospitalization for an acute psychiatric or partial hospital unit with a manic or depressive episode and confirmation of mood disorder diagnosis at discharge (52).
d. Ability to speak and read English and provide informed consent

4. The research associate (RA), who will be external to Aetna to maintain separation of care management and program evaluation, and will be blinded to randomization assignment. (S)he will be trained by Aetna on their well-established call implementation program across time zones (**Section C.5.c**) and by study investigators in human subjects risk reduction procedures used in prior studies (8, 50) that will minimize risk while not compromising study internal validity (8). The initial assessment (described below) will include a brief survey baseline factors, including demographics, employment, whether they were the Aetna enrollee or a family member, and primary clinician who treats their mood disorder (i.e., prescribes psychotropic medications). Comorbidities will be ascertained from Aetna eTUMS chart reviews conducted by the RAs.

Figure 2: Implementation of Mood CCM across Health Plan, Practices, and Patients



C.5.c.Existing Aetna Infrastructure Used in this Study. The following components are of specific relevance:
1. The **registry/database** consists of four main components and will be used to identify potentially eligible patients as well as ascertain utilization and other outcomes data (see variable descriptions below). The Electronic Total Utilization Management System (**eTUMS**), a proprietary care management tool is populated by

claims data augmented by customizable care manager input; major claims events, such as hospitalization, result in automatic care manager notification. The **pharmacy claims database** accrues prescription claims daily, including drug and dose, and is downloaded to eTUMS on a weekly basis. **Laboratory claims data** are similarly downloaded on a monthly basis; laboratory reports contain the name of the test, while reports from larger laboratories also provide results. Thus these registries will provide the data necessary to measure guideline-concordant care (e.g., non-filling of mood disorder prescriptions, non-completion of cardiometabolic laboratory tests). The fourth component, **Aetna claims data**, includes use and cost data for Aim 3.

2. The Aetna **care management infrastructure** is substantial and stable. The masters level Aetna care managers who participated in the pilot will serve as the CCM care managers. They have a minimum of 5 years of care management experience with Aetna, providing short-term or ongoing care management for an average of 300 beneficiaries per year across multiple time zones and patient schedules.

Care manager coverage across time zones: All Aetna care managers function in teams with supervisory care manager and medical oversight. They also work staggered hours (e.g., covering 9am-midnight ET M-F, 10-6pm Sat) in order to make patient calls across different time zones. Biweekly 1:1 supervisor meetings and monthly team meetings provide support and training. Quality is monitored via audit tools that assess both calls and documentation three times per month. Regular Medical Director Rounds are supplemented by reviews when claims or other data indicate that the beneficiary is not doing well.

CM and study staff handling of suicide risk/adverse events: Imminent risk (suicidal or assaultive ideation, significant medication toxicity) are managed via protocols used in prior studies (8, 50, 52). In the pilot study (Section C.3), care managers identified 4 out of 457 who had suicidal ideation and, through established protocols, alerted the provider and arranged emergency evaluation; no suicide attempts occurred during the pilot study. Moreover, CCMs have been shown to reduce suicide (94). Study staff (both University of Michigan and Aetna) will be trained to identify and address suicidal ideation in patients. If the patient articulates thoughts of death or suicidal ideation, the study team member will ask the patient to elaborate on recent suicidal behavior (i.e., ask if he or she has an active plan). Follow-up regarding the situation will be based on the patient's responses and whether the study team member perceives that the patient is in immediate danger (e.g., active plan verbalized). Endorsement of the suicidal thoughts on the survey will also serve as an emergent/urgent situation. The study team member will then ask whether there is another individual with the patient (if over the phone), and will remain on the phone while instructing the other individual to get help. If no one else is present with the patient, the team member direct the patient to his/her local emergency room or, refer to a national suicide hotline that can do further assessment and planning, so the patient can get immediate help. Adverse event reporting is outlined further in the data safety monitoring plan. We will have a adverse events and serious adverse events management plan for this project, as due to the nature of this population, fairly frequent visits to the emergency room that do not require hospitalization and hospitalizations due to their mood disorder exacerbation are to be expected. All adverse events encountered by both University of Michigan and Aetna staff will be reported to the UM IRB according to our management plan (see Data Safety Monitoring Plan document).

C.5.d. Interventions: EC and CCM. The **education control (EC) condition** consists of a self-guided workbook mailed to patients developed by study investigators (95) along with standard care from the practice, but none of the CCM components from the plan-level CM.

Table 4: Mood Disorders CCM Core Elements: Life Goals Collaborative Care

CCM Core Element 1: Life Goals Skills Management Enhancement	**10 weekly 30-min telephonic sessions** utilizing the web-based Life Goals program (52, 95) • Core modules cover management of depressive and manic symptoms • Additional web modules utilized as clinically indicated (e.g., wellness, foods and moods, exercise, substance use, anxiety, psychosis, anger/irritability, metabolic risk)
CCM Core Element 2: Access / Continuity Parameters for Care Manager	**12 monthly patient telephone contacts for 1 year** (in addition to the skills management training above) to trouble-shoot self-management issues and summarize clinical status

	Scheduled and Ad Hoc Clinical Assessments and Registry Data Utilization • Ad hoc contacts at either care manager or participant initiation based on clinical or other concerns, including response to participants within one business day. • "In-reach" to treating clinicians for hospitalization, ER visits, or specialty consultation • Communication of clinical assessment data to mental health provider • Collaboration with family as permitted • Resource referral as needed
CCM Core Element 3: Provider Decision Support via Depression and Bipolar Disorder Clinical Practice Guidelines(96, 97)	**Provider contacts**; care manager elicits preference for mode of communication with provider (e.g., call, email, fax) • Same content as clinic-based CCM • Guidelines based on AHRQ depression in primary care and APA bipolar guidelines • Will alert provider that his/her patient is receiving Life Goals and when he/she completes participation

The mood disorders CCM intervention ("Life Goals Collaborative Care") consists of: (a) a web-based patient self-management skills enhancement (CCM-1), (b) enhanced information flow and continuity of care via a care manager (CCM-2), and (c) decision support, or situation-specific evidence-based clinical practice guideline recommendations for providers (CCM-3)- see Table 4 (98). The CCM will be implemented utilizing telephonic contact with patients and providers by the Aetna care managers who participated in the Aetna care management pilot study, based on a recommended caseload of 80-100 patients each (99). The care managers will also use the Life Goals web portal as a guide for each session.

Care managers will implement the three CCM Core Elements as follows:

CCM-1: Web-based Self-Management Support: The care manager will deliver the Life Goals Program adapted for mood disorders via telephone using a website that contains modules, exercises, and other information for patients and the CM (52, 95). The Life Goals program utilizes psychoeducation based on Social Cognitive Theory, emphasizing Motivational Interviewing and cognitive-behavioral techniques, particularly behavioral activation, to address symptom management and problem-solving skills. Ten core modules will be delivered over 10 weekly telephonic sessions of 30 minutes (59, 100) using content available from the Life Goals website. An additional six modules can be implemented based on patient preferences for other specific self-management topics (101), and will be tracked as part of the CCM engagement index (Section C.5.h). Both the CM and patients will also have access to additional exercises and tailored modules via the Life Goals web portal. For patients with bipolar disorder, at least one of the modules will focus on coping with manic symptoms, while patients with unipolar depression will also receive an additional module on depressive symptoms (100).

CCM-2: Access/Continuity: This core element consists of three components:

- **Patient Clinical Assessment:** During the first 10 weeks, each fourth call (monthly) will also include an assessment of overall clinical and treatment status (~15 minutes). Assessment will include the 9-item Patient Health Questionnaire (PHQ-9)(102, 103) to assess depressive symptoms, the 8-item Internal State Scale (**ISS**; (52, 104-106) to assess manic symptoms and well-being; medication use, adherence (7, 107), and side effects. The intake contact includes identification of care providers and recent contacts, and each follow-up call will include a focus on maintaining engagement/continuity. These calls will continue on a monthly basis for up to one year of participation, with additional phone contacts made to follow up in the event of a hospitalization or emergency room visit based on our RCTs (50-53, 108).
- **Claims Database/Registry Review:** The care manager will also use the eTUMS registry to track inpatient hospitalizations, pharmacy and laboratory status. These data, available in a clinically useful time frame (Section C.5.c), will assist the patient with trouble-shooting illness management, and assist the care manager in identifying opportunities for intervention or quality enhancement.
- **Provider communication:** Care management strategies to date have under-emphasized provider engagement (9). In the mood disorders CCM, the care manager will contact the provider at the time of patient enrollment to introduce the CCM and to determine how best to integrate CCM procedures into the provider's practice needs. This initial contact will identify the optimal mode of communication between

provider and care manager, as well as delineation by the provider for the care manager of the expected care plan going forward (frequency of visits, medications, lab tests such as cardiometabolic monitoring). After this initial engagement and care planning contact, the care manager will contact the provider in the event of hospitalization, emergency room visit, or development of a new clinical issue, as well as to cue them if there is a crisis encounter (e.g., suicidality).

CCM-3: Provider Decision Support: As noted above, the care manager will have obtained clinical assessment data each month plus eTUMS-based data on pharmacy refills (weekly) and laboratory utilization (monthly). Using these multi-component assessment and treatment data, s/he will communicate situation-specific treatment options based on clinical practice guidelines for bipolar disorder (96, 98). For instance in the case of unipolar depression, non-response or partial response to medication (defined as <50% reduction in PHQ-9 score and PHQ-9 <=9) would be followed by the care manager providing a series of treatment options based on current guidelines (97, 109). For those with bipolar disorder and presence of subtherapeutic lithium levels and manic symptoms, the care manager would also outline options based on clinical practice guidelines (110). It is important to note that, as in our prior studies (50-53, 108), the CCM is designed to supplement care and does not replace or control provider decision-making. That is: clinical decision-making remains in the hands of the provider. CCM therefore enhances care processes by: (a) enhancing patient skills to facilitate treatment participation, (b) offering the provider timely information, and (c) outlining situation-specific evidence-based treatment options.

C.5.e. Implementation Procedures. The study will be managed by the **Aetna Joint Operating Committee** led by Drs. Kilbourne and Un and includes William Gillis, PsyD, Aetna Clinical Specialty Programs Head, and Lesa Stevens, RN, Aetna Head of Program Development (Section C.5.k, see support letter from Dr. Un). We will implement the CCM using Enhanced REP (76, 77, 79). Our research implementation infrastructure will provide, keeping with the theme of "light footprint" of research, the customized **package** of CCM procedures (see Appendix), supported by 16 hours of **training** at study initiation, followed by ongoing **technical assistance**. CCM Fidelity monitoring will be incorporated into ongoing Aetna CM audits (Section C.5.c).

Packaging includes an implementation manual for all three CCM components developed by Dr. Kilbourne as well as the secure web-based self-management program for care managers and patients for the CCM-1 component (52, 95).

Training for care managers will follow existing Aetna standard procedures for telephonic and web-based training. This will consist of 16 hours of telephonic training by Dr. Kilbourne and her study team over 2 weeks modeled after our current on-site training package.

Technical assistance will be provided by the Joint Operating Committee and supported by study consultants Dr. Greg Simon (telephonic care management) and Dr. John Fortney (implementation processes). Joint Operating Committee members will conduct conference calls with the care managers (weekly) and supervisors (monthly) to guide the use of CCM components, particularly with regard to interface issues between: care managers and patients; care manager and providers/practices; and patients and providers. The Joint Operating Committee will have separate quarterly and ad hoc calls with consultants for debriefing and advice.

C.5.f. Data Collection and Measures. Key outcomes data will be ascertained from patients (including surveys, medical record- eTUMS reviews, and claims data) and organizational surveys (Table 5).

Patient survey: A concise (15-30 minute) quantitative survey will be collected from patients via phone at baseline, 6, 12, 18, and 24 months thereafter by the research associate (RA). If the RA is unable to reach the patient via phone for follow-up assessments after multiple attempts, a survey will be mailed to the confirmed last known address of the participant as a final attempt to receive this data. Patients will be asked to return this survey without any identifying information on the survey or the envelope. The survey will contain a subject ID number to identify the patient's survey when it is returned via mail. Patient outcomes data will be entered by the RA into an database on a password-protected research computer within a secure network server at the University of Michigan.

Patient utilization and cost data, described below will be ascertained from the Aetna eTUMS and claims databases, and exported securely for merging with survey data and analysis at the University of Michigan.

Table 5: Primary and Secondary Outcomes and Measures – Baseline and Follow-ups

Aims	Key Measures	Source
Aim 1. Primary outcomes	Mood symptoms: PHQ-9	Patient survey
	Health-related quality of life-SF-12	Patient survey
Aim 1. Secondary outcomes	Guideline concordant care- key measures	Medical record (eTUMS)/claims
	Mood tx: % receiving guideline-concordant antidepressants (if unipolar depression) or guideline-concordant anti-manic treatment (bipolar disorder dx) in 6-month period	Medical record (eTUMS)/claims
	Cardiometabolic monitoring: % receiving lipid profile, fasting glucose or HbA1C	Medical record (eTUMS)/claims
	Hospitalizations (ACSC)	Aetna claims data
	Productivity (Work Limitation Questionnaire)	Patient survey
Aim 2	Organizational data: Practice demographics	Aetna data
	Patient: demographics, comorbidities	Patient survey
Aim 3:	CCM costs, patient inpatient, outpatient, ER, Rx use	Aetna claims, provider survey
	Patient utilities (SF-6)	Patient survey

The research associate will be blind to random assignment at baseline. In follow-ups, given the nature of the CCM intervention (CCM-2), there is the possibility that enrolled patients may inadvertently disclose their randomization status with the RA. In pilot studies we found that this is a rare occurrence, but will be mitigated through RA training (e.g., minimizing leading questions that would disclose treatment assignment).

Primary Aim 1 (patient-level quality of life, symptoms) include changes in mood symptoms based on the PHQ-9 (102, 103) or ISS (52, 104-106) and health quality of life via the SF-12 Mental and Physical Health Component Scores (**MCS/PCS**; 85,113).

Patient-level secondary outcomes include guideline-concordant (quality of) care, hospitalizations, as well as self-reported productivity. These measures are based on recommended indicators from the Accountable Care Organization published rules for performance measures and shared savings (111). We will apply previously established quality measures for mood disorders (98, 111, 112), and cardiometabolic management (113, 114) (Table 5). Quality of care data will be gathered from electronic medical records (eTUMS) and **hospitalization data** will be ascertained from Aetna utilization and claims files at the end of patients' 12 and 24-month participation in two prospectively observed 6-month intervals. Preventable hospitalizations over the 12 and 24-month period will be defined using the AHRQ Ambulatory Care Sensitive Condition (ACSC) definition (115), which identifies conditions for which "good" outpatient care can potentially prevent the need for hospitalization or for which early intervention can prevent complications or more severe disease. We will also assess the probability of psychiatric rehospitalization separately. **Patient-level productivity** over the 24-month period will be assessed in the survey using the Work Limitation Questionnaire(116).

Patient factors include CCM engagement ascertained from the patient survey. Engagement is based on the six-item Preference Index for Decision-Making (**API-D**; (117, 118)) which has been used in chronically ill samples to investigate the desire for collaborative care from clinicians. Other patient factors include demographic and clinical information, including co-occurring symptoms (substance use (121, 122), comorbidities (from eTUMS).

Aim 3: Utilization, costs, CEA, and business case: Primary utilization measures of interest, including outpatient services, inpatient (including length of stay), and ER use, and health care costs will be ascertained from Aetna eTUMS electronic record reviews using a standard assessment tool (125). Cost data will be estimated for each inpatient, ER, and outpatient visit using Current Procedural Terminology (CPT) codes. A relative value unit (RVU) weight will allow for the use of the Medicare Fee Schedule to calculate a standardized cost for each service. Costs incurred in different years will be discounted at an annual rate of 3% and adjusted for inflation and discounted to the baseline (first) year of the study. Other costs incurred by the participants including medications, visit co-pays, transportation, and time involved in the CCM will be ascertained from the

patient survey. CCM cost data will be estimated using a time-motion survey developed by study investigators (R01 MH 79994) administered monthly to the CMs and quarterly to providers over a 2-year period, which ascertains time spent on CCM activities, including self-management, phone contacts, and documentation.

C.5.g. Analyses. General approach: The principal analyses will be for the primary hypotheses. An intent-to-treat analysis will be performed for all analyses. Bivariate baseline analyses will first be conducted to see if randomization was successful by comparing patient demographics and clinical characteristics (e.g., mental health diagnoses) between randomization groups. If there is a lack of equal distribution across groups, these variables will be added as covariates to analyses or propensity scoring will be used. Baseline characteristics will be compared among those enrolled but dropped out over time to those who remained in the study. Our unit of analysis for patient-level outcomes will be patients nested within practices with an indicator for non-solo practice provider sites (126, 127) and an indicator for patients diagnosis (bipolar vs. unipolar depression).

Missing Data: We attained subject retention of 80% over a three-year follow-up in one study (50, 51), and recent 1-year data (MH0745409) indicate 90% retention. Extent and pattern of missingness will be examined for outcome variables as well as for baseline covariates. We expect missingness to be completely at random or at random, in which case the proposed analytical methods will give unbiased estimates of treatment comparison. We will examine how sensitive our conclusions are to potential non-ignorable missingness using a pattern mixture model that will allow us to either model the observed pattern of missingness or change the imputations to represent the likely differences in conditional distributions between observed and missing data (128, 129). For the latter, we will combine the results from each imputed data using Rubin's rules (130).

Aim 1 primary outcomes (**H1a: symptoms, quality of life**): Primary outcomes are continuous, and based on pilot data, are expected to be normally distributed. If a continuous outcome exhibits a significant lack of normality, other options will be considered including data transformation, categorization, and non-parametric analyses. Four linear mixed-effects models accounting for clustering will be run to assess the CCM effects compared to EC on changes in PHQ-9, ISS, and SF-12 PCS and MCS scores over 12-months, adding baseline values of the outcome measure, the effect of CCM, time, and CCM X time interaction.

Aim 1 secondary analyses: For guideline concordance and hospitalization, we will compare the likelihood of receiving the guideline-concordant treatment over 12 months (Table 5) as well as the likelihood of an ambulatory care sensitive admission using a generalized linear mixed-effects model (GLM) with logit link. Similar to our primary hypotheses, linear mixed-effects models will be conducted to determine the effect of CCM vs. EC on changes in the Work and Social Adjustment Scale.

Aim 2 analyses are considered exploratory but will be used to gain insight into the mechanisms by which CCM impacts patient outcomes. We will first explore the strength and direction of the association between patient-level CCM engagement (API-D scores- see section **C.5.f**) (119) on changes in outcomes (SF-12, PHQ-9 and ISS scores) by adding patient-level API-D scores to the aforementioned linear mixed-effects models from Aim 1. We will also be run exploratory analyses in which we add key organizational factors (e.g., non-solo practice, practice type-primary care vs. behavioral health, presence of non-MD clinical staff, EMR use, ownership), and other patient factors (e.g., demographics, comorbidities) in the models specified in Aim 1. In secondary analyses we will also incorporate the number of additional optional sessions covering supplemental modules completed by the patient (Section C.5.d).

Aim 3: Both a payer and societal-based cost-effectiveness analysis (CEA) will be conducted. A CEA from the payer perspective will involve comparison of utilization costs of health service providers including CM's time ascertained from time-motion survey. A societal perspective will add non-health care costs incurred by patients including time and transportation. Generalized Linear Models with log link functions will be used to correct for heteroscedasticity and reduce the impact of outliers (131). The incremental effectiveness of CCM compared to EC will be measured by changes in health utilities, assessed using a method described by Zivin (132) and Brazier (133) which translates six of the SF-12 items to changes in health utility (SF-6) based on responses to standard gamble questions given by community members regarding all combinations of possible health states. Cost-effectiveness ratios will be calculated based on the difference in per patient costs and effectiveness of CCM versus EC. To quantify uncertainty around these ratios, a standard nonparametric

bootstrapping approach will be employed. For the business case, additional analyses will be conducted in which changes over time in utilization and costs of inpatient, ER, and outpatient services (medical, psychiatric) will be compared between patients in the CCM or EC arms over a 2-year period, in order to determine the time dynamics by which the CCM led to changes in health care costs. Additional cost analyses will take into consideration the return-on-investment of the CCM and changes in enrollee turnover (134).

C.5.h. Business plan development (Aim 3). The business case development plan is based on our Enhanced REP framework (73) and informed by the work by Leatherman and colleagues (also see Appendix for submitted paper on business case). In brief, a business case for the CCM exists if the Aetna realizes a financial return on investment or other positive impact on organizational function or sustainability within a "reasonable" time frame (134). Other positive impacts beyond the potential cost savings from implementing CCM include revenue-based from the payer perspective (i.e., value added to payers when the health plan offers CCMs in terms of improved enrollee health and access to care). We chose 2 years as the time frame for outcomes in this study because prior research on CCMs has not found a return-on-investment within one year (3), and 2 years is below the average tenure of an Aetna enrollee. From a business case standpoint, attrition from the health plan may attenuate savings from the initial investment, and our analysis will implicitly account for this by only counting within-plan utilization costs. Enhanced REP addresses organizational and financial incentives (Table 6) designed to inform the CCM return-on-investment (73) and will lead to the development of a reimbursement model for CCMs. Preliminary stages for business case development (134), including (a) the implementation of a program (CCM) shown to improve patient health (135), (b) establishment of quality and cost indicators aligned with existing national initiatives (e.g., ACOs), and (c) identification of a health plan champion and consultant team have been completed. The remaining years (3-5) will be devoted to refining and marketing the business plan, which will include a CCM reimbursement strategy.

Table 6: Enhanced REP Framework Business Case Development Steps by Year and Study Aim

Enhanced REP Phase	Incentives Components Informing Business Case
Pre-conditions (Years 1-2)	Identify health plan's current priorities, and organizational barriers and facilitators to implementing CCM (Aim 2). Establish, publicize measureable CCM outcomes (Aim 1), aligned with existing measures (e.g., ACO quality, measures: cardiometabolic, mood stabilizer use, and hospitalizations (111))
Pre-Implementation (Years 1-5)	Identify health plan, provider champions who mobilize support for CCM (Aetna, consultant team) Identify successfully implemented CCM components across plan (e.g., existing health IT-eTUMS)
Implementation (Years 3-5)	Consultant team reviews EBP business case, holds regular calls to develop business plan based on study findings (Aim 3- CEA). Propose reimbursement strategies (e.g., billing codes, bundled payments through ACOs- See Appendix) and highlight trade-offs with initial investment, long-term ROI
Maintenance and Evolution (Years 4-5)	Market business plan to sustain CCM beyond health plan to other national leaders in public, private sector (Dissemination plan). Leverage CCM with existing federal programs that are reimbursable (ACOs, health home models); continue publicizing CCM, find consumer stories re: CCM benefits

Generalizability of CCM business plan: A manuscript describing a generic CCM business plan/reimbursement strategy by study investigators is currently under review. An external consultant team (Bao, Bauer, Fortney, Simon, Van Deusen Lukas) was also established to advise on the updated business plan based on study findings, and to ensure generalizability to other health plans and national organizations beyond Aetna. They will also advise on the financial impact of the CCM on the patient, practice, as well as the health plan, and the trade-offs between quality improvement and the business case in order to inform the future implementation of CCMs in other health care settings. The consultant team will work with study investigators and Aetna leadership particularly in Years 3-5 via regular conference calls to review the business case. Based on these calls in Year 5 we will produce a series of papers, presentations, and conference workshops on the CCM business case with an eye towards other health plans and state and federal government entities including the Centers for Medicare and Medicaid Services and AHRQ. These products will present and critique the results

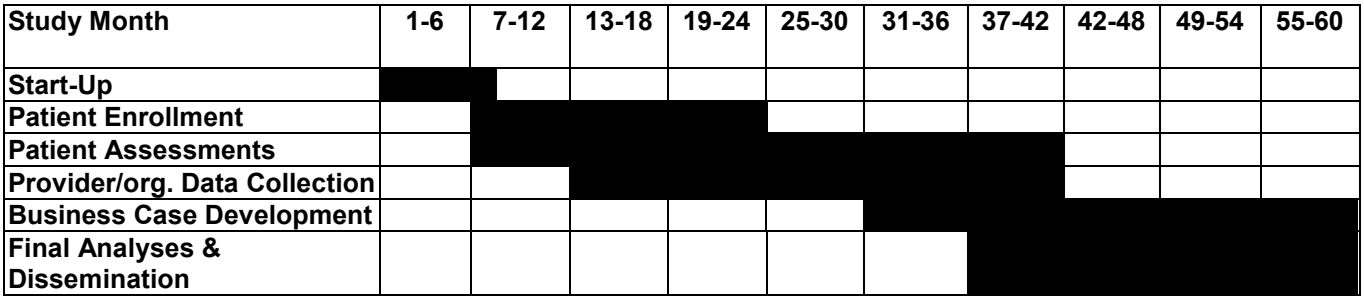
and business case in order to support movement toward wider adaptation and dissemination of the CCM for other mental health conditions.

C.5.i. Sample Size and Power. Sample size is estimated based on our primary aim and informed by our updated CCM pilot studies that estimate effects on changes in depressive symptoms and well-being across mood disorders (e.g., Cohen's D=.36). Assuming 90% power based on a 0.05 level two-sided test and a conservatively assumed ICC of 0.05 at the practice level and an average of 2 patients per practice, a total of 86 practices for each intervention arm (solo or small group providers) would be required. Assuming 20% dropout by 12 months, a projected 172 patients per arm (344 patients total) should give us adequate power to detect the expected between-group difference in mean outcome scores. For discrete outcomes including guideline concordance, using similar assumptions, the proposed sample size provides >90% power to detect a difference in guideline concordance of 46.5% (CCM) vs. 27.1% (EC) (98).

C5.j. Potential Study Limitations. This study involves a number of strengths, including a groundbreaking health plan- academic partnership, comprehensive data sources, and emphasis on smaller and solo practices. Nonetheless, there are key limitations of this proposed design to consider. The focus on mood disorders potentially limits the immediate reach of this novel approach to implement CCMs for other chronic conditions. However, mood disorders have been identified by Aetna as priority conditions, and represent the most common and costly mental disorders in routine practice (136). In addition, while many persons with mood disorders are privately insured under network-model HMOs such as Aetna (137), the potential generalizability of this study is restricted to insured individuals. This study nonetheless complements a number of initiatives in the public sector that are currently being implemented to increase the uptake of CCMs for mental disorders such as health homes (10). Site providers will not be blinded to treatment assignment because CCM management and guideline supports require care manager-provider communication. Guideline concordance based on CM-provider coordination was found to be a key factor to the improvement of outcomes in the CCM (98). Finally, the cost effectiveness analysis is exploratory and not fully powered, but will nonetheless, provide valuable information for organizations considering its further adoption.

C.5.k. Timeline and Organization. The first 6 months of the study will involve staff training and finalization of recruitment procedures (Figure 3). Once recruitment and enrollment begin in month 6, the CCM will be implemented throughout all study locations. Based on pilot studies recruitment is anticipated to last 18 months, hence allowing for ample time to recruit patients with either bipolar disorder or depression. Years 3-5 will be devoted to follow up data, business case, as well as other dissemination and implementation activities.

Figure 3: Study Timeline



Organizational relationship between investigator team and Aetna group (also see letter from Dr. Un): Aetna is providing support for the study organization through in kind contribution of effort by thee key personnel (Dr. Gillis, Ms. Stevens, and Ms. Keating) and the establishment of a Joint Operating Committee to facilitate project operations, care management infrastructure, and the informatics system. Aetna has used joint operating committees successfully in past clinical trials involving academic partnerships (e.g., 1R01DA029716; 1R01DA026414). Specifically, Dr. Kilbourne and Dr. Un will serve as Co-Chairs of the Joint Operating Committee which will include both Aetna leaders and study investigators of the project, and will have oversight of all aspects of the project. The Committee will employ three function-oriented subcommittees with one co-chair from Michigan or Harvard and one from Aetna who will oversee: CCM Implementation (Co-chairs: Kilbourne, Gillis), Patient Enrollment and Data Collection (Co-chairs Kilbourne, Eisenberg, and Stevens), and

Data Management and Analysis (Co-chairs Kilbourne, Kim and Keating). The Aetna co-leaders from each subcommittee have oversight over the Aetna personnel responsible for the respective functions. All Aetna data will be available for audit by the Committee, and additionally we will utilize a Data Safety and Monitoring Board comprised of scientists separate from this project who will have similar access. Thus our joint operating structure provides both the data monitoring oversight and the line authority control required to ensure the successful implantation of this project. Dr. William Gillis, Clinical Specialty Programs Head for the Aetna Behavioral Health, will oversee and manage the clinical operations and fidelity of the CCM implementation, including care manager and research associate supervision. This will include weekly meetings with the care managers' supervisors to review the pilot's key operational performance and fidelity metrics to ensure adherence to pilot workflows and protocols. He will coordinate with leadership to support overall implementation. Ms. Stevens will support Dr. Gillis and have responsibility for planning, execution and finalization of the project according to identified timelines and within budget. Ms. Keating, Head of Aetna Behavioral Health Clinical Program Informatics, will be responsible for managing and aggregating the necessary outcome measures defined for the study (See Budget Justification).

C.5.I. Dissemination and Generalizability. A dissemination strategy that ensures awareness and knowledge of research findings among clinicians, consumers, and policymakers, is an initial step to realizing the promise of this project, and fostering the potential generalizability of the findings. Once the intervention is completed and if proven effective, the Enhanced REP Framework will be applied to train other Aetna care managers in CCM. There are three stages of REP (packaging, training, and technical assistance). The CCM package will consist of a web-based therapist manual, administrator overview, and consumer handouts. Care managers as part of this study as well as providers with a high uptake score will be encouraged to become mentor-trainers who can provide training for other providers in the CCM. A refined technical assistance program based on study findings will be incorporated into the business plan for sustaining CCMs across Aetna and elsewhere. Study findings as well as the business plan will be disseminated through web sites, press releases, national conferences, policy briefs, as well as traditional forms of academic scholarship. If proven effective, the telephonic mood disorders CCM program may also potentially be scaled up to larger practices, notably through the use of technologies such as telemedicine or web-based portals independent of the care manager's physical location. At least five manuscripts will be produced based on study aims including: 1) description of the Aetna CCM, and 2) CCM main outcomes, 3) mechanisms of CCM effects, 4) cost and utilization of CCM, and 5) the updated CCM business plan. A policy brief based on study findings will be disseminated to consumer and policy groups (e.g., AHRQ, CMS, Depression and Bipolar Support Alliance, National Alliance for the Mentally Ill, Primary Care Associations, National Council for Community Behavioral Healthcare), as well as to policymakers who have an interest in mental health.

References

1. U.S. Department of Health and Human Services. U.S. Department of Health and Human Services (HHS) Inventory of Programs, Activities and Initiatives Focused on Improving the Health of Individuals with Multiple Chronic Conditions (MCC): Compiled by the HHS Interagency Workgroup on Multiple Chronic Conditions under the direction of Anand Parekh, MD, MPH, Deputy Assistant for Health (Science and Medicine), Office of the Assistant Secretary for Health; September 2011 Contract No.: Document Number|.
2. Miller BF, Kessler R, Peek CJ. A National Agenda for Research in Collaborative Care: Papers from the Collaborative Care Research Network Research Development Conference. Rockville, MD: Agency for Healthcare Research and Quality, June 2011. Report No.: 11-0067 Contract No.: Document Number|.
3. Woltmann E, Grogan-Kaylor A, Perron B, Georges H, Kilbourne AM, Bauer MS. Comparative effectiveness of collaborative chronic care models for mental health conditions across primary, specialty, and behavioral health care settings: systematic review and meta-analysis. Am J Psychiatry. 2012;169(8):790-804.
4. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness: the chronic care model, Part 2. JAMA. 2002;288(15):1909-14.
5. Wagner EH, Austin BT, Von Korff M. Organizing care for patients with chronic illness. Milbank Q. 1996;74(4):511-44.
6. Coleman K, Austin BT, Brach C, Wagner EH. Evidence on the Chronic Care Model in the new millenium. Health Affairs. 2009;28:75 - 135.
7. Bauer MS. The collaborative practice model for bipolar disorder: design and implementation in a multi-site randomized controlled trial. Bipolar Disord. 2001;3(5):233-44.
8. Bauer MS, Williford WO, Dawson EE, Akiskal HS, Altshuler L, Fye C, et al. Principles of effectiveness trials and their implementation in VA Cooperative Study #430: 'Reducing the efficacy-effectiveness gap in bipolar disorder'. J Affect Disord. 2001;67(1-3):61-78.
9. Coleman K, Mattke S, Perrault PJ, Wagner EH. Untangling practice redesign from disease management: how do we best care for the chronically ill? Annu Rev Public Health. 2009;30:385-408.
10. Collins C, Hewson DL, Munger R, Wade T. Evolving models of behavioral health integration in primary care. 2010: Available from: www.milbank.org/reports/10430EvolvingCare/EvolvingCare.pdf.
11. Findlay S. Managed behavioral health care in 1999: an industry at a crossroads. Health Aff (Millwood). 1999;18(5):116-24.
12. Bauer MS, Leader D, Un H, Lai Z, Kilbourne AM. Primary Care and Behavioral Health Practice Size: The Challenge for Health Care Reform. Med Care. 2012.
13. Rittenhouse DR, Casalino LP, Shortell SM, McClellan SR, Gillies RR, Alexander JA, et al. Small and medium-size physician practices use few patient-centered medical home processes. Health Aff (Millwood). 2011;30(8):1575-84.
14. Fisher ES, McClellan MB, Bertko J, Lieberman SM, Lee JJ, Lewis JL, et al. Fostering accountable health care: moving forward in medicare. Health Aff (Millwood). 2009;28(2):w219-31. PMCID: PMC2656392.
15. Shortell SM, Casalino LP. Implementing qualifications criteria and technical assistance for accountable care organizations. JAMA. 2010;303(17):1747-8.
16. Nutting PA, Miller WL, Crabtree BF, Jaen CR, Stewart EE, Stange KC. Initial lessons from the first national demonstration project on practice transformation to a patient-centered medical home. Ann Fam Med. 2009;7(3):254-60. PMCID: 2682981.
17. Carrier E, Gourevitch MN, Shah NR. Medical homes: challenges in translating theory into practice. Med Care. 2009;47(7):714-22. PMCID: 2790523.
18. Rittenhouse DR, Casalino LP, Gillies RR, Shortell SM, Lau B. Measuring the medical home infrastructure in large medical groups. Health Aff (Millwood). 2008;27:1246-58

19. Rittenhouse DR, Shortell SM, Gillies RR, Casalino LP, Robinson JC, McCurdy RK, et al. Improving chronic illness care: findings from a national study of care management processes in large physician practices. Med Care Res Rev. 2010;67(3):301-20.
20. Casalino L, Gillies RR, Shortell SM, Schmittdiel JA, Bodenheimer T, Robinson JC, et al. External incentives, information technology, and organized processes to improve health care quality for patients with chronic diseases. JAMA. 2003;289(4):434-41.

21. Druss BG, von Esenwein SA, Compton MT, Rask KJ, Zhao L, Parker RM. A randomized trial of medical care management for community mental health settings: the Primary Care Access, Referral, and Evaluation (PCARE) study. Am J Psychiatry. 2010;167(2):151-9.
22. Katon WJ, Lin EH, Von Korff M, Ciechanowski P, Ludman EJ, Young B, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med. 2010;363(27):2611-20.
23. Bauer MS. Bipolar (manic-depressive) disorder. In: Tasman A, Kay J, Lieberman J, Maj M, First MB, editors. Psychiatry. 3rd ed. London: Wiley-Blackwell; 2008.
24. Lopez AD, Murray CC. The global burden of disease, 1990-2020. Nat Med. 1998;4(11):1241-3.
25. Judd LL, Akiskal HS. The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. J Affect Disord. 2003;73(1-2):123-31.
26. Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, et al. Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. Arch Gen Psychiatry. 2007;64(5):543-52.
27. Kessler RC, Wang PS. The descriptive epidemiology of commonly occurring mental disorders in the United States. Annu Rev Public Health. 2008;29:115-29.
28. Goodwin RD, Davidson KW, Keyes K. Mental disorders and cardiovascular disease among adults in the United States. J Psychiatr Res. 2009;43(3):239-46.
29. Katon W, Lin EH, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. Gen Hosp Psychiatry. 2007;29:147-55.
30. Goldstein BI, Fagiolini A, Houck P, Kupfer D. Cardiovascular disease and hypertension among adults with bipolar I disorder in the United States. Bipolar Disord. 2009;11:657-62.
31. Osby U, Brandt L, Correia N, Ekbom A, Sparen P. Excess mortality in bipolar and unipolar disorder in Sweden Arch Gen Psychiatry. 2001;58(9):844-50.
32. Angst F, Stassen HH, Clayton PJ, Angst J. Mortality of patients with mood disorders: follow-up over 34-38 years. J Affect Disord. 2002;68(2-3):167-81.
33. Institute of Medicine, Committee on Quality of Health Care in America. Crossing the quality chasm: A new health system for the 21st century. Washington, D.C.: National Academy Press; 2003.
34. Boardman JB. Health access and integration for adults with serious and persistent mental illness. Families, Systems, & Health. 2006;21(1):3-18.
35. Busch S, Leslie D, Rosenheck R. Comparing the quality of antidepressant pharmacotherapy in the Department of Veterans Affairs and the private sector. Psych Serv. 2004;55:1386 - 91.
36. Druss BG, Bradford DW, Rosenheck RA, Radford MJ, Krumholz HM. Mental disorders and use of cardiovascular procedures after myocardial infarction [see comments] 1 31. JAMA. 2000;283(4):506-11.
37. Druss BG, Rosenheck RA, Desai MM, Perlin JB. Quality of preventive medical care for patients with mental disorders. Med Care. 2002;40(2):129-36.
38. Hogan MF. The President's New Freedom Commission: recommendations to transform mental health care in America. PsychiatrServ. 2003;54(11):1467-74.
39. Leslie DL, Rosenheck RA. Adherence of schizophrenia pharmacotherapy to published treatment recommendations: patient, facility, and provider predictors. Schizophr Bull. 2004;30(3):649-58.
40. Leslie DL, Rosenheck RA. Benchmarking the quality of schizophrenia pharmacotherapy: a comparison of the Department of Veterans Affairs and the private sector. J Ment Health Policy Econ. 2003;6(3):113-21.
41. Sernyak MJ, Dausey D, Desai R, Rosenheck R. Prescribers' nonadherence to treatment guidelines for schizophrenia when prescribing neuroleptics. Psychiatr Serv. 2003;54(2):246-8.
42. Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research. Washington, D.C.: The National Academies Press; 2009.
43. Peele PB, Xu Y, Kupfer DJ. Insurance expenditures on bipolar disorder: clinical and parity implications. Am J Psychiatry. 2003;160(7):1286-90.
44. Bryant-Comstock L, Stender M, Devercelli G. Health care utilization and costs among privately insured patients with bipolar I disorder. Bipolar Disord. 2002;4:398-405.
45. Simon GE, Unutzer J. Health care utilization and costs among patients treated for bipolar disorder in an insured population. Psych Serv. 1999;50:1303-8.

46. Dilsaver SC. An estimate of the minimum economic burden of bipolar I and II disorders in the United States: 2009. J Affect Disord. 2011;129(1-3):79-83.
47. Gilbody S, Bower P, Fletcher J, Richards D, Sutton AJ. Collaborative care for depression: a cumulative meta-analysis and review of longer-term outcomes. Arch Int Med. 2006;166(21):2314-21.
48. Badamgarav E, Weingarten SR, Henning JM, Knight K, Hasselblad V, Gano A, Jr., et al. Effectiveness of disease management programs in depression: a systematic review. Am J Psychiatry. 2003;160(12):2080-90.
49. Unutzer J, Katon WJ, Fan MY, Schoenbaum MC, Lin EH, Della Penna RD, et al. Long-term cost effects of collaborative care for late-life depression. Am J Managed Care. 2008;14(2):95-100.
50. Bauer MS, McBride L, Williford WO, Glick H, Kinosian B, Altshuler L, et al. Collaborative care for bipolar disorder: Part I. Intervention and implementation in a randomized effectiveness trial. Psychiatr Serv. 2006;57(7):927-36.
51. Bauer MS, McBride L, Williford WO, Glick H, Kinosian B, Altshuler L, et al. Collaborative care for bipolar disorder: Part II. Impact on clinical outcome, function, and costs. Psychiatr Serv. 2006;57(7):937-45.
52. Kilbourne AM, Post EP, Nossek A, Drill L, Cooley S, Bauer MS. Improving medical and psychiatric outcomes among individuals with bipolar disorder: a randomized controlled trial. Psychiatr Serv. 2008;59(7):760-8.
53. Simon GE, Ludman EJ, Bauer MS, Unutzer J, Operskalski B. Long-term effectiveness and cost of a systematic care program for bipolar disorder. Arch Gen Psychiatry. 2006;63(5):500-8.
54. American Psychiaric Association. Practice guideline for the treatment of patients with bipolar disorder (revision). Am J Psychiatry. 2002;159(4 Suppl):1-50.
55. Yatham LN, Kennedy SH, Schaffer A, Parikh SV, Beaulieu S, O'Donovan C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2009. Bipolar Disord. 2009;11(3):225-55.
56. Kilbourne AM, Biswas K, Pirraglia PA, Sajatovic M, Williford WO, Bauer MS. Is the collaborative chronic care model effective for patients with bipolar disorder and co-occurring conditions? J Affect Disord. 2009;112(1-3):256-61.
57. Datto CJ, Thompson R, Horowitz D, Disbot M, Oslin DW. The pilot study of a telephone disease management program for depression. Gen Hosp Psychiatry. 2003;25(3):169-77.
58. Hunkeler EM, Meresman JF, Hargreaves WA, Fireman B, Berman WH, Kirsch AJ, et al. Efficacy of nurse telehealth care and peer support in augmenting treatment of depression in primary care. Arch Fam Med. 2000;9(8):700-8.
59. Ludman EJ, Simon GE, Grothaus LC, Luce C, Markley DK, Schaefer J. A pilot study of telephone care management and structured disease self-management groups for chronic depression. Psychiatr Serv. 2007;58(8):1065-72.
60. Lynch D, Tamburrino M, Nagel R, Smith MK. Telephone-based treatment for family practice patients with mild depression. Psychol Rep. 2004;94(3 Pt 1):785-92.
61. Mohr DC, Hart SL, Julian L, Catledge C, Honos-Webb L, Vella L, et al. Telephone-administered psychotherapy for depression. Arch Gen Psychiatry. 2005;62(9):1007-14.
62. Oslin DW, Sayers S, Ross J, Kane V, Ten Have T, Conigliaro J, et al. Disease management for depression and at-risk drinking via telephone in an older population of veterans. Psychosom Med. 2003;65(6):931-7.
63. Ransom D, Heckman TG, Anderson T, Garske J, Holroyd K, Basta T. Telephone-delivered, interpersonal psychotherapy for HIV-infected rural persons with depression: a pilot trial. Psychiatr Serv. 2008;59(8):871-7.
64. Simon GE, VonKorff M, Rutter C, Wagner E. Randomised trial of monitoring, feedback, and management of care by telephone to improve treatment of depression in primary care. BMJ. 2000;320(7234):550-4. PMCID: 27299.
65. Simon GE, Ludman EJ, Rutter CM. Incremental benefit and cost of telephone care management and telephone psychotherapy for depression in primary care. Arch Gen Psychiatry. 2009;66(10):1081-9.

66. Stein MD, Herman DS, Bishop D, Anderson BJ, Trisvan E, Lopez R, et al. A telephone-based intervention for depression in HIV patients: negative results from a randomized clinical trial. AIDS Behav. 2007;11(1):15-23.
67. Tutty S, Ludman EJ, Simon G. Feasibility and acceptability of a telephone psychotherapy program for depressed adults treated in primary care. Gen Hosp Psychiatry. 2005;27(6):400-10.
68. Lynch DJ, Tamburrino MB, Nagel R. Telephone counseling for patients with minor depression: preliminary findings in a family practice setting. J Fam Pract. 1997;44(3):293-8.
69. Pariser D, O'Hanlon A. Effects of telephone intervention on arthritis self-efficacy, depression, pain, and fatigue in older adults with arthritis. J Geriatr Phys Ther. 2005;28(3):67-73.
70. Davis CL, Kilbourne AM, Pierce JR, Langberg R, Blow FC, Winkel BM, et al. Reduced mortality among VA patients with schizophrenia or bipolar disorder lost to follow-up and engaged in active outreach to return to care. Am J Public Health. 2012;102:S74-S9.
71. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. Health Aff (Millwood). 2008;27(3):759-69.
72. Kilbourne AM, Goodrich DE, Clogston J, Bauer MS, Waxmonsky JA, VanDeusen Lukas C, et al. Randomized controlled trial of the Replicating Effective Programs implementation framework: the Recovery-Oriented Collaborative Care Study. Implement Sci. 2012;In review.
73. Kilbourne AM, Neumann MS, Waxmonsky J, Bauer MS, Kim HM, Pincus HA, et al. Public-academic partnerships: evidence-based implementation: the role of sustained community-based practice and research partnerships. Psychiatr Serv. 2012;63(3):205-7.
74. Green LW, Kreuter MW, Deeds SG, Partridge KB. Health Education Planning: A Diagnostic Approach. 1st ed. Mountain View, CA: Mayfield Publishing Co.; 1980.
75. Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O. Diffusion of innovations in service organizations: systematic review and recommendations. Milbank Q. 2004;82:581-629.
76. Kilbourne AM, Neumann MS, Pincus HA, Bauer MS, Stall R. Implementing evidence-based interventions in health care: application of the replicating effective programs framework. Implement Sci. 2007;2:42.
77. Neumann MS, Sogolow ED. Replicating effective programs: HIV/AIDS prevention technology transfer. AIDS Educ Prev. 2000;12(5 Suppl):35-48.
78. Stetler CB. Role of the organization in translating research into evidence-based practice. Outcomes Manag. 2003;7(3):97-103.
79. Kelly JA, Somlai AM, DiFranceisco WJ, Otto-Salaj LL, McAuliffe TL, Hackl KL, et al. Bridging the gap between the science and service of HIV prevention: transferring effective research-based HIV prevention interventions to community AIDS service providers. Am J Public Health. 2000;90(7):1082-8. PMCID: 1446305.
80. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977;84(2):191-215.
81. Rogers E. Diffusion of Innovations. 5th ed. New York, NY: Free Press; 2003.
82. Fleuren M, Wiefferink K, Paulussen T. Determinants of innovation within health care organizations: literature review and Delphi study. Int J Qual Health Care. 2004;16(2):107-23.
83. Kirsh SR, Lawrence RH, Aron DC. Tailoring an intervention to the context and system redesign related to the intervention: a case study of implementing shared medical appointments for diabetes. Implement Sci. 2008;3:34. PMCID: 2442606.
84. Shaw B, Cheater F, Baker R, Gillies C, Hearnshaw H, Flottorp S, et al. Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes. Cochrane Database Syst Rev. 2005(3):CD005470.
85. Stetler C, Legro M, Wallace C, Bowman C, Guihan M, Hagedorn H, et al. The role of formative evaluation in implementation research and the QUERI experience. J Gen Intern Med. 2006;21:S1 - 8.
86. Wensing M, Wollersheim H, Grol R. Organizational interventions to implement improvements in patient care: a structured review of reviews. Implement Sci. 2006;1:2. PMCID: 1436010.
87. Yano EM. The role of organizational research in implementing evidence-based practice: QUERI Series. Implement Sci. 2008;3:29. PMCID: 2481253.

88. Lukas CV, Holmes SK, Cohen AB, Restuccia J, Cramer IE, Shwartz M, et al. Transformational change in health care systems: an organizational model. Health Care Manage Rev. 2007;32(4):309-20.
89. VanDeusen Lukas C, Engle RL, Holmes SK, Parker VA, Petzel RA, Nealon Seibert M, et al. Strengthening organizations to implement evidence-based clinical practices. Health Care Manage Rev. 2010;35:235-45.
90. Gold M, Taylor E. Moving research into practice: Lessons from the Agency for Healthcare Research and Quality's IDSRN program. Implement Sci. 2007;2:9.
91. Post EP, Kilbourne AM, Bremer RW, Solano FX, Jr., Pincus HA, Reynolds CF, 3rd. Organizational factors and depression management in community-based primary care settings. Implement Sci. 2009;4(1):84.
92. Wang PS, Simon GE, Avorn J, Azocar F, Ludman EJ, McCulloch J, et al. Telephone screening, outreach, and care management for depressed workers and impact on clinical and work productivity outcomes: a randomized controlled trial. JAMA. 2007;298(12):1401-11. PMCID: 2859667.
93. Wennberg DE, Marr A, Lang L, O'Malley S, Bennett G. A randomized trial of a telephone care-management strategy. N Engl J Med. 2010;363(13):1245-55.
94. Bruce ML, Ten Have TR, Reynolds CF, III, Katz II, Schulberg HC, Mulsant BH, et al. Reducing suicidal ideation and depressive symptoms in depressed older primary care patients: a randomized controlled trial. JAMA. 2004;291(9):1081-91.
95. Bauer MS, Kilbourne AM, Greenwald DE, Ludman EJ, McBride L. Overcoming Bipolar Disorder: A Comprehensive Workbook for Managing Your Symptoms & Achieving Your Life Goals. Oakland, CA: New Harbinger Publications, Inc.; 2008.
96. Dennehy EB, Bauer MS, Perlis RH, Kogan JN, Sachs GS. Concordance with treatment guidelines for bipolar disorder: data from the systematic treatment enhancement program for bipolar disorder. Psychopharmacol Bull. 2007;40(3):72-84.
97. Depression Guideline Panel. Depression in Primary Care: Volume 1. Dectection and Diagnosis. Clinical Practice Guideline, Number 5. Rockville, MD: U.S. Department of Health and Human Services; 1993. Report No.: AHCPR Publication No. 93-0550 Contract No.: Document Number|.
98. Bauer MS, Biswas K, Kilbourne AM. Enhancing multiyear guideline concordance for bipolar disorder through collaborative care. Am J Psychiatry. 2009;166(11):1244-50.
99. Kilbourne AM, Post EP, Nossek A, Sonel E, Drill LJ, Cooley S, et al. Service delivery in older patients with bipolar disorder: a review and development of a medical care model. Bipolar Disord. 2008;10(6):672-83.
100. Ludman EJ, Simon GE, Tutty S, Von Korff M. A randomized trial of telephone psychotherapy and pharmacotherapy for depression: continuation and durability of effects. J Consult Clin Psychol. 2007;75(2):257-66.
101. Insel TR. Translating scientific opportunity into public health impact: a strategic plan for research on mental illness. Arch Gen Psychiatry. 2009;66(2):128-33.
102. Saarelainen S, Rytkonen-Nissinen M, Rouvinen J, Taivainen A, Auriola S, Kauppinen A, et al. Animal-derived lipocalin allergens exhibit immunoglobulin E cross-reactivity. Clinical and Experimental Allergy. 2008;38(2):374-81.
103. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med. 2001;16:606-13.
104. Bauer MS, Crits-Christoph P, Ball WA, Dewees E, McAllister T, Alahi P, et al. Independent assessment of manic and depressive symptoms by self-rating. Scale characteristics and implications for the study of mania. Arch Gen Psychiatry. 1991;48(9):807-12.
105. Bauer MS, Vojta C, Kinosian B, Altshuler L, Glick H. The Internal State Scale: replication of its discriminating abilities in a multisite, public sector sample. Bipolar Disord. 2000;2(4):340-6.
106. Cooke RG, Kruger S, Shugar G. Comparative evaluation of two self-report Mania Rating Scales. Biol Psychiatry. 1996;40(4):279-83.
107. Sajatovic M, Bauer MS, Kilbourne AM, Vertrees JE, Williford W. Self-reported medication treatment adherence among veterans with bipolar disorder. Psychiatr Serv. 2006;57(1):56-62.
108. Bauer MS, McBride L, Shea N, Gavin C, Holden F, Kendall S. Impact of an easy-access VA clinic-based program for patients with bipolar disorder. Psychiatric Services. 1997;48(4):491-6.

109. Work Group on Major Depressive Disorder. Practice Guideline for the Treatment of Patients with Major Depressive Disorder Third Edition. Washington, D.C.: American Psychiatric Association; 2010 Contract No.: Document Number|.
110. Disorder WGftToPwB. Clinical Practice Guideline for Bipolar Disorder, Third Edition. Washington, D.C.: American Psychiatric Association; 2010 Contract No.: Document Number|.
111. Department of Health & Human Services, Centers for Medicare & Medicaid Services. 42 CFR Part 425. Medicare Program; Medicare Shared Savings Program; Accountable Care Organizations. Washington, D.C.: Federal Register; November 2, 2011 [updated November 2, 2011; cited 2012 May 1, 2012]; Available from: http://www.gpo.gov/fdsys/pkg/FR-2011-11-02/pdf/2011-27461.pdf.
112. The STABLE National Coordinating Council. STABLE: STAndards for BipoLar Excellence. A performance measurement and quality improvement program. Center for Quality Assessment and Improvement in Health; 2006 [updated 2006; cited]; Available from: http://www.cqaimh.org/pdf/measures_summary.pdf.
113. Kilbourne AM, Lai Z, Bowersox N, Pirraglia P, Bauer MS. Does colocated care improve access to cardiometabolic screening for patients with serious mental illness? Gen Hosp Psychiatry. 2011.
114. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care. 2004;27:596-601.
115. Prevention Quality Indicators Overview: AHRQ Quality Indicators. Rockville, MD: Agency for Healthcare Research and Quality, July, 2004 Contract No.: Document Number|.
116. Mundt JC, Marks IM, Shear MK, Greist JH. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry. 2002;180:461-4.
117. Hill SA, Laugharne R. Decision making and information seeking preferences among psychiatric patients. Journal of Mental Health. 2006;15:75-84.
118. Hamann J, Cohen R, Leucht S, Busch R, Kissling W. Do patients with schizophrenia wish to be involved in decisions about their medical treatment? Am J Psychiatry. 2005;162(12):2382-4.
119. Ludman EJ, Simon GE, Rutter CM, Bauer MS, Unutzer J. A measure for assessing patient perception of provider support for self-management of bipolar disorder. Bipolar Disord. 2002;4(4):249-53.
120. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092-7.
121. Gordon AJ, Maisto SA, McNeil M, Kraemer KL, Conigliaro RL, Kelley ME, et al. Three questions can detect hazardous drinkers. J Fam Pract. 2001;50(4):313-20.
122. Kessler RC, Andrews G, Mroczek D, Üstün TB, Wittchen HU. The World Health Organization Composite International Diagnostic Interview Short Form (CIDI-SF) Int J Methods Psychiatr Res. 1998;7:171-85.
123. Rehm J, Ustun TB, Saxena S, Nelson CB, Chatterji S, Ivis F, et al. On the Development and Psychometric Testing of the WHO Screening Instrument to Assess Disablement in the General Population. Int J Methods Psychiatr Res. 1999;8 (2):110-22.
124. Ustun TB, Chisholm D. Global "burden of disease"-study for psychiatric disorders. Psychiatrische Praxis. 2001;28 Suppl 1:S7-11.
125. Kilbourne AM, Farmer Teh C, Welsh D, Pincus HA, Lasky E, Perron B, et al. Implementing composite quality metrics for bipolar disorder: towards a more comprehensive approach to quality measurement. Gen Hosp Psychiatry. 2010;32:636-43. PMCID: PMC3086005.
126. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika. 1986;73:13-22.
127. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics. 1986;42(1):121-30.
128. Diggle PJ, Kenward MG. Informative dropout in longitudinal data analysis (with discussion). J Royal Stat Soc, Series C (applied statistics). 1994;43:49-94.
129. Little RJA, Rubin DB. Satatistical analysis with missing data. New York, NY: Wiley; 1987.
130. Rubin D. Multiple imputation for non-response in surveys. New York, NY: Wiley; 1987.

131. Manning WG, Mullahy J. Estimating log models: to transform or not to transform? J Health Econ. 2001;20(4):461-94.
132. Zivin K, McCarthy JF, McCammon RJ, Valenstein M, Post EP, Welsh DE, et al. Health-related quality of life and utilities among patients with depression in the Department of Veterans Affairs. Psychiatr Serv. 2008;59(11):1331-4.
133. Brazier J, Akehurst R, Brennan A, Dolan P, Claxton K, McCabe C, et al. Should patients have a greater role in valuing health states? Appl Health Econ Health Policy. 2005;4(4):201-8.
134. Leatherman S, Berwick D, Iles D, Lewin LS, Davidoff F, Nolan T, et al. The business case for quality: case studies and an analysis. Health Aff (Millwood). 2003;22(2):17-30.
135. Woltmann E, Grogan-Taylor A, Perron B, Georges H, Kilbourne AM, Bauer MS. Comparative effectiveness of collaborative chronic care models for mental health. Am J Psychiatry. 2012;In Press.
136. Simon GE, Katon WJ, VonKorff M, Unutzer J, Lin EH, Walker EA, et al. Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. Am J Psychiatry. 2001;158(10):1638-44.
137. Frank RG, Huskamp HA, Pincus HA. Aligning incentives in the treatment of depression in primary care with evidence-based practice. Psychiatr Serv. 2003;54(5):682-7.