The Management of Depression and Anxiety in Primary Care: Examining Predictors of Adherence to a Psychopharmacological Collaborative Care Management Program for Veterans

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Abstract

Collaborative care management (CoCM) is an evidenced based approach to psychiatric treatment in primary care, yet literature examining factors associated with program adherence is lacking. This study analyzed predictors of adherence to a CoCM model of psychopharmacological treatment of depression and anxiety in primary care by conducting a retrospective cohort analysis on Veterans referred to a large VA Medical Center's CoCM program over an 18-month period. Baseline characteristics, symptomatic assessments, and covariates of interest were collected. For the primary outcome, the association between covariates and programmatic completion were analyzed. Secondary analyses assessed improvements in psychiatric symptoms. A total of 757 Veterans with depressive or anxiety disorders were included, and 256 completed the CoCM program. Baseline covariates associated with differences in completion rates included the following: age, contact with psychology prior to referral, baseline PHQ-9, baseline GAD-7, and a number of comorbid psychiatric/substance abuse covariates. After controlling for baseline differences, age remained a significant positive predictor of completion (OR 1.019, 95% CI 1.008−1.030) and cannabis use a significant negative predictor (OR 0.507, 95% CI 0.275−0.934). Both early improvement in PHQ-9 (OR 1.864, 95% CI 1.210−2.872) and GAD-7 (OR 1.762, 95% CI 1.154−2.691) scores were positive predictors. Secondary analyses showed that programmatic completion was associated with greater reductions in psychiatric symptoms. Results identified a number of modifiable parameters associated with differences in completion rates and greater symptomatic reduction for those who complete the program. Additional studies should be conducted examining interventions to optimize CoCM programs by supporting positive predictors while minimizing negative predictors.

Introduction

Depression and anxiety are two of the most common mental health disorders, with approximately 21 million American adults experiencing major depression and an additional 48 million living with anxiety disorders.[1] Studies have shown that prevalence rates for these conditions are even higher within the Veteran population treated by the Department of Veteran's Affairs (VA).[2] Research has consistently demonstrated that the majority of individuals receive treatment for mental health disorders, including mild to moderate depression and anxiety in a primary care setting as opposed to a specialty mental health setting.[3] Therefore, it is important to implement programs in the primary care setting to adequately address depressive and anxiety disorders. This is particularly true within VA, and the VA system has responded by embedding mental health resources within primary care teams.[4]

One strategy for addressing the mental health needs of patients with depression and anxiety disorders in the primary care setting is through the prescription of antidepressant medications. Over half of individuals who are prescribed an antidepressant are receiving them from a primary care physician.[5] However, while antidepressants can be effective treatments for anxiety and depressive disorders, patient adherence to mental health medications is suboptimal—with an estimated 68% of patients discontinuing their medications within three months.[6,7] Collaborative care management

(CoCM) is one clinical approach utilized to improve patient adherence to mental health treatment. CoCM refers to evidence-based protocols for the treatment of common mental health problems that present in primary care. One such iteration of CoCM is antidepressant monitoring (ADM), which consists of collaboration between primary care physicians (PCPs), consulting psychiatrists, and collaborative care managers. ADM is a protocol-driven treatment model consisting of frequent, regularly scheduled, telephonic follow-up contacts to monitor medication efficacy, tolerability, and adherence and to reinforce patient symptom self-management skills. CoCM programs have been shown to be more effective at reducing symptoms of depression and anxiety when compared to treatment as usual.[8–10] In addition to symptom reduction, care management leads to improvements in patient functioning, engagement, adherence, and all-cause mortality.[8–10]

Despite the benefits of CoCM, patient adherence to CoCM programs remains a concern. Since adherence to treatment is associated with improved outcomes, optimizing adherence to, and completion of, a CoCM program treatment course is essential to achieve the most benefit from this model of care. While factors associated with medication adherence in a traditional outpatient treatment model have been reported, including age, severity of depressive symptoms, comorbid conditions such as PTSD, beliefs about treatment, concerns related to medication side effects, and number of prescribed medications,[11–13] there is a paucity of research examining factors influencing adherence specifically to CoCM programs. Therefore, the purpose of this study was to analyze factors which may act as predictors of adherence to a CoCM model of psychopharmacological treatment in the primary care setting within a large VA medical center. Secondary aims include analyzing patient outcome measures for individuals in the program, including comparing response and remission rates for depression and anxiety in individuals who complete the ADM program compared to those who enroll but do not complete.

Methods

A retrospective cohort analysis was conducted on all individuals who were referred for enrollment in the Tampa VA's Antidepressant Monitoring Program from June 4, 2018, to December 4, 2019. Data was obtained from the facility's electronic health record (EHR) and from a pre-existing clinical database which was utilized for patient monitoring while receiving clinical care through the ADM program. This study was approved by the local VA Research and Development Committee and the affiliated university Institutional Review Board. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for the reporting of observational cohort studies were followed.

The ADM program is a clinical program for the management of Veterans with depression or anxiety disorders receiving treatment exclusively in primary care clinics as opposed to specialty mental health clinics. In our cohort, co-occurring mental health disorders were allowed for program enrollment; however, individuals with bipolar affective disorder or with psychosis (including depression with psychotic features and psychotic spectrum disorders such as schizophrenia) were excluded as they require a higher level of service than is offered in primary care and thus are excluded from receiving clinical care in the ADM program. This was a clinical cohort, as such there were no additional pre-defined inclusionary or exclusionary criteria specific to the study. Further programmatic details are as follows: Individuals with depression or anxiety were referred to the ADM program either from primary care physicians (PCPs) or from Primary Care Mental Health Integration (PCMHI) clinical psychologists who are embedded in the PCP clinics. Baseline depression and anxiety symptomatology was collected either by the referring PCMHI psychologist or, if absent at the time of referral, from a protocol-based comprehensive baseline assessment obtained by an RN CoCM. Consulting psychiatrists then utilized information in the medical record including information obtained from PCPs, PCMHI psychologists, and RN CoCMs to inform medication decisions

related to initiating antidepressant medications. There were no pre-determined pharmacological treatment algorithms, and the specific medication was selected by the consulting psychiatrist on an individual basis based on clinical patient level factors. Patients were then contacted telephonically by RN CoCMs in every 3 to 4-week intervals where information related to symptomatology (Patient Health Questionnare-9 Item (PHQ-9)[14] and the Generalized Anxiety Disorder Scale- 7 Item (GAD-7)[15]), medication adherence, and tolerability were collected. This information was utilized by the consulting psychiatrist to inform ongoing treatment decisions in collaboration with the patients' PCP, such as changes to medication regimens including dose adjustments and/or medication agent changes. Patients were followed in the program for a goal minimum of 6 months, although follow-up for a period of greater than 6 months was possible if medication changes or other indications for additional monitoring were present. Program completion being defined as completion of 6 months of follow-up on a stabilized pharmacological regimen. Concurrent psychotherapy was allowed but not a requirement nor a specific component of the ADM program.

This study examined predictors of adherence to this clinical treatment model. Data collected for the study was obtained from both a clinical dataset utilized for patient monitoring in the ADM program, as well as from the EHR, and included baseline information, covariates of interest, and longitudinal symptomatic monitoring assessments. Baseline data included the following: sociodemographic information, baseline depression and anxiety symptomatology as defined by scores on the PHQ-9 and the GAD-7, co-occurring psychiatric disorders, and co-occurring substance use disorders. Co-occurring disorders were obtained from EHR sources including problem lists, individual notes, and if applicable, from previously obtained mental health assessment scales. For PTSD and substance use disorders, co-occurring symptomatology was subdivided into those with "current" symptoms at time of enrollment (defined as PCL-5 $\geq$ 33, drinking above recommended limits, or actively using cannabis or other recreational substances of abuse, respectively), "historical" (defined as a prior diagnosis of PTSD or substance use disorder), and "anytime" (defined as one or both of "current" and "historical"). Covariates were collected which, based on a review of the literature as well as anecdotal clinical reports, were hypothesized to be either predictive of program adherence (lower baseline symptomatology, early response to treatment defined as 20% reduction in PHQ-9 or GAD-7 score from baseline to week 3 follow-up, clinical contact with a psychologist within 4 weeks prior to ADM program enrollment) and those hypothesized to be negative predictors of adherence (psychiatric polypharmacy at the time of program enrollment, suicidal thoughts at the time of program enrollment as defined by the suicidal ideation item on the PHQ-9 assessment scale; sleep impairments at the time of program enrollment as defined by the sleep item on the PHQ-9 assessment scale; and presence of comorbid mental health conditions/substance use disorders). Additionally, longitudinal tracking of PHQ-9 and GAD-7 was included in every 3–4-week intervals as per the clinical ADM program protocol to track symptomatic improvements. Response and remission were defined as per standards of the respective assessment scales (response being $\geq$ 50% reduction in total scores for PHQ-9 and GAD-7; remission being $\leq$ 4 for PHQ-9 and GAD-7 total scores). Program adherence was defined as programmatic completion with participation in the last scheduled ADM interval follow-up call. Reasons for non-completion were recorded.

Demographic and baseline characteristics were summarized as median and interquartile range for continuous variables and as frequencies and percentages for categorical variables. Characteristics were compared between participants that completed the program and those that did not using Mann–Whitney *U* tests for continuous variables and Chi-square tests for categorical variables. Significance was set to 0.05.

Primary analysis was carried out using logistic regression models. For each baseline characteristic, a univariable logistic regression model was used to evaluate the association between that variable and adherence to the program. Results were summarized as odds ratios (OR) accompanied by 95% confidence intervals (CI). Variables that were significantly associated with program adherence were

then included in a multivariable logistic regression model to control for all baseline characteristics associated with program adherence. Results in this model were also summarized as OR with 95% CI. Following this model, univariable models for both early improvement in PHQ-9 scores and early improvement in GAD-7 scores (as defined above) were conducted. Another multivariable logistic regression including early improvement variables as well as the variables with significant differences from the first set of univariable modeling was created to identify if early improvement variables remained significantly associated with program adherence when adjusting for baseline characteristics.

Secondary analysis was performed to assess outcome measures for individuals in the program, focusing on differences between program completers vs. non-completers. Reduction in PHQ-9 and GAD-7 scores between participants that completed the program and those that did not were summarized as median and interquartile range for each group and compared using Mann–Whitney *U* tests. For categorical variables, including response and remission for anxiety and depression based on PHQ and GAD scores, chi-square tests were used to compare proportions between completers and non-completers. These variables were summarized as frequencies and percentages. Significance was set at 0.05. All analysis was performed using IBM SPSS Statistics.[16]

Results

A total of 791 individuals were referred to the ADM program in the first 18 months following programmatic initiation. After excluding individuals who were referred but never reached by the ADM treatment team, 757 Veterans were included in analyses. The majority of the Veterans included in the cohort were male (77.01%) and White/Caucasian (53.24%); consistent with VA-wide population demographics. Veterans who were black/African American accounted for 28.27% of the cohort, and 14.3% were Hispanic/Latino. Mean age at the time of program enrollment was 50.36 years (SD 15.34); age range was 21–93 years old.

All individuals in the cohort were experiencing symptoms consistent with a depressive or anxiety disorder as defined by scores on mental health assessment scales (PHQ-9 $\geq$ 5; GAD-7 $\geq$ 5) obtained either prior to referral from a clinical psychologist or during a baseline assessment conducted by an RN CoCM. Baseline symptomatology reflects a cohort experiencing symptoms of depression and anxiety in the moderate ranges, with mean PHQ-9 = 13.57 (SD 5.65) and GAD-7 = 12.85 (SD 5.38). Co-occurring psychiatric and substance use disorders were common with 68.93% of Veterans having at least one co-occurring disorder. PTSD was the most common psychiatric comorbidity, with 31.44% of the cohort either meeting active PTSD symptomatic criteria (PCL-5 $\geq$ 33) or with a prior diagnosis of PTSD. Substance use was not uncommon, with 27.74% of individuals having current or past diagnoses of alcohol use disorder, 19.42% were drinking alcohol above recommended limits at time of ADM program enrollment, and 8.19% were using cannabis at time of enrollment, as self-reported during baseline assessments. Individual assessment scale items were not available for all Veterans in our dataset. However, of those with available individual items on the PHQ-9, a substantial majority (87.22%) endorsed sleep difficulties (PHQ-9 item #3 $\geq$ 1) and suicidal ideations at time of program enrollment were not uncommon as it was endorsed by 15.97% of Veterans in the cohort (PHQ-9 item #9 $\geq$ 1).

As the primary aim of the study was to examine associations between covariates of interest and programmatic adherence (defined as program completion as above), baseline characteristics are reported when separating program completers vs. non-completers. These results are summarized in Table 1. Of the Veterans referred, 158 either declined enrollment or did not answer contact attempts for enrollment, and an additional 18 agreed to enrollment but declined to start a mental health medication so were not enrolled, resulting in 615 Veterans beginning the program. Early drop out was

Table 1

Demographics and baseline characteristics

Characteristics	Completers ($n=256$)	Non-completers ($n=501$)
Gender		
Male	201 (78.5%)	382 (76.7%)
Female	55 (21.5%)	116 (23.2%)
Age	54.0 (41.0, 66.0)	47.0 (36.0, 61.0)
Race/Ethnicity		
White	133 (52.0%)	270 (54.2%)
Black/African-American	79 (30.9%)	135 (27.1%)
Hispanic/Latino	35 (13.7%)	72 (14.5%)
Asian	3 (1.2%)	8 (1.6%)
American Indian/Alaskan Native	1 (0.4%)	1 (0.2%)
Native Hawaiian/Pacific Islander	1 (0.4%)	8 (1.6%)
Decline to answer	4 (1.6%)	4 (0.8%)
Baseline PHQ-9	13.0 (9.0, 17.0)	14.0 (10.0, 18.0)
Baseline GAD-7	12.0 (8.0, 16.0)	14.0 (10.0, 18.0)
Suicidal thoughts	23 (14.2%)	53 (16.9%)
Sleep impairments	110 (85.3%)	197 (88.3%)
Any comorbid MH Dx	160 (62.5%)	357 (71.3%)
PTSD, current	51 (19.9%)	106 (21.2%)
PTSD, historical	46 (18.0%)	132 (26.3%)
PTSD, anytime	69 (27.0%)	169 (33.7%)
Alcohol use above recommended limits, current	40 (15.6%)	107 (21.4%)
Alcohol UD, historical	35 (13.7%)	99 (19.8%)
Alcohol UD, anytime	55 (21.5%)	155 (30.9%)
Cannabis Use, current	9 (3.5%)	53 (10.6%)
Cannabis UD, historical	14 (5.5%)	51 (10.2%)
Cannabis UD, anytime	15 (5.9%)	66 (13.2%)
Other SUD, current	5 (2.0%)	9 (1.8%)
Other SUD, historical	7 (2.7%)	28 (5.6%)
Other SUD, anytime	9 (3.5%)	32 (6.4%)

Summary results showing demographic information and baseline clinical characteristics when separating the cohort into those that completed the ADM program and those that enrolled but did not complete. For PTSD and substance use disorders, the cohort was subdivided into those with "current" symptoms at time of enrollment (defined as PCL-5 $\geq$ 33, drinking above recommended limits, or actively using cannabis or other recreational substances of abuse, respectively), "historical" (defined as a prior diagnosis of PTSD or substance use disorder) and "anytime" (defined as one or both of "current" and "historical"). Categorical variables are summarized as count (%). Continuous variables are summarized as median (IQR). *PHQ-9* Patient Health Questionnaire 9 Item, *MH Dx* mental health diagnoses, *GAD-7* Generalized Anxiety Disorder Scale 7 Item, *PTSD* post-traumatic stress disorder, *UD* use disorder, *SUD* substance use disorder (tobacco/nicotine use disorders not included)

not uncommon, with 131 participants failing to complete week 3 follow-up. However, the frequency of dropouts decreased as the Veterans progressed further in the program, with 67.56% of Veterans who participated in week 3 follow-up remaining active in the program at the 12 week/midpoint of the program. Contacts with RN Care Managers consisted of two introductory calls, followed by every 3-week contacts from program entry through week 12, resulting in a minimum of 6 contacts with program RNs for all Veterans who reached the program midpoint.

A total of 256 Veterans completed the entire ADM program (32.36% of those referred). The most common reasons for program non-completion were declining the program or not answering contact attempts for enrollment ($N = 158$, 31.54% of non-completers), partial participation before no longer responding to contact attempts ($N = 133$, 26.55%), referral to specialty mental health clinics ($N = 109$, 21.76%), self-discontinuing medications prior to program completion ($N = 60$, 11.98%), and agreeing to program enrollment but then declining to start psychiatric medications ($N = 18$, 3.59%). An additional 21 participants (4.19%) enrolled but did not complete the program for other reasons including two participants who passed away due to causes unrelated to their participation in the program nor to mental health conditions.

When analyzing covariates for predictors of completion utilizing univariable regression models, a number of baseline covariates were associated with differences in completion rates, including the following: age (OR 1.021, 95% CI 1.011–1.031), contact with a psychologist prior to program enrollment (OR 0.684, 95% CI 0.472–0.991), baseline PHQ-9 total score (OR 0.962, 95% CI 0.936–0.989), baseline GAD-7 total score (OR 9.50, 95% CI 0.922–0.977), any comorbid psychiatric disorder (which was inclusive of PTSD and also included other psychiatric diagnoses obtained from the EHR; OR 0.651, 95% CI 0.472–0.897), previous diagnosis of PTSD (OR 0.605, 95% CI 0.415–0.882), active alcohol use above the recommended limit (OR 0.653, 95% CI 0.437–0.978), anytime alcohol use above recommended limits or past alcohol use disorder (OR 0.611, 95% CI 0.429–0.870), active cannabis use (OR 0.283, 95% CI 0.137–0.584), previous diagnosis of cannabis use disorder (OR 0.501, 95% CI 0.272–0.924), and anytime cannabis use or past cannabis use disorder (OR 0.410 95% CI 0.229–0.734).

Next, a multivariable logistic regression model was run to identify if associations with program completion remained after controlling for significant baseline variables identified in the univariable model. Multivariable modeling showed that age remained a significant predictor of ADM program completion, with increased odds of programmatic completion with each unit increase in age (OR 1.019, 95% CI 1.008–1.030). Conversely, cannabis use/cannabis use disorder was associated with decreased rates of programmatic completion (OR 0.507, 95% CI 0.275–0.934). Of note, for covariates of psychiatric and substance use comorbidities, only the "anytime" variables (i.e., either or both "current" and "historical") were included in the multivariable model to prevent issues with multicollinearity. The remaining covariates which were statistically significant in the univariable model did not remain significant in the multivariable model after controlling for baseline differences. Results are summarized in Table 2.

Next, the association of early symptomatic improvements on program completion was examined. With univariable modeling, both early improvement in PHQ-9 total score (OR 2.308, 95% CI 1.602–3.326) and early improvement in GAD-7 total score (OR 2.258, 95% CI 1.571–3.245) were significantly associated with ADM program completion. Multivariable logistic regression was then used to examine this association when controlling for baseline differences. Both early improvement in PHQ-9 (OR 1.864, 95% CI 1.210–2.872) and GAD-7 (OR 1.762, 95% CI 1.154–2.691) remained statistically significant predictors of program completion when controlling for differences in other covariates. Results are summarized in Table 3 and Table 4.

Additional analyses were conducted to examine symptomatic outcome measures comparing those who completed the program compared to those who enrolled but do not complete. Individuals who completed the program had greater reductions in depression symptoms as evidenced by reductions in PHQ-9 total scores (median reduction of 68.18% [IQR 47.61, 88.89] for completers vs. 26.09% [-6.46, 57.52] for non-completers, $p \leq 0.001$), and greater reductions in anxiety symptoms as evidenced by changes in GAD-7 total scores (66.67% [43.75, 90.00] for completers vs. 26.67% [SD 0.00, 63.40] for non-completers, $p \leq 0.001$). Similarly, both depression response and depression remission rates were higher in program completers compared to non-completers (75.0% vs. 32.4%, $p \leq 0.001$; and 59.4% vs. 21.4%, $p \leq 0.001$, respectively). This was also observed for anxiety

Table 2

Association of covariates of interest with ADM program completion

	Univariable model			Multivariable model		
Variable	*n*	OR	95% CI	*n*	OR	95% CI
Age	752	1.021	(1.011, 1.031)*	691	1.019	(1.008, 1.030)*
Gender	754	-	-	-	-	-
Male		-[a]	-	-	-	-
Female		0.901	(0.626, 1.296)	-	-	-
Race/ethnicity	754	-	-	-	-	-
White		-[a]	-	-	-	-
Black/African-American		1.188	(0.840, 1.680)	-	-	-
Hispanic/Latino		0.987	(0.627, 1.554)	-	-	-
Asian		0.761	(0.199, 2.916)	-	-	-
American Indian/Alaskan Native		2.030	(0.126, 32.709)	-	-	-
Native Hawaiian/Pacific Islander		0.254	(0.031, 2.050)	-	-	-
Decline to answer		2.030	(0.500, 8.244)	-	-	-
Baseline PHQ-9	704	0.962	(0.936, 0.989)*	691	0.993	(0.959, 1.029)
Baseline GAD-7	699	0.950	(0.922, 0.977)*	691	0.970	(0.934, 1.007)
Suicidal thoughts	476	0.815	(0.479, 1.386)	-	-	-
Psychology contact pre-enroll	754	0.684	(0.472, 0.991)*	691	0.764	(0.505,1.158)
Sleep impairments	352	0.764	(0.405, 1.443)	-	-	-
Multiple medications	757	1.210	(0.892, 1.642)	-	-	-
Medication type	750	-	-	-	-	-
SSRI		-[a]	-	-	-	-
SNRI		1.003	(0.691, 1.456)	-	-	-
Non-antidepressant anxiolytics		0.801	(0.358, 1.789)	-	-	-
Other		0.824	(0.515, 1.320)	-	-	-
Any comorbid MH Dx	750	0.651	(0.472, 0.897)*	691	0.858	(0.596, 1.235)
PTSD, anytime	757	0.725	(0.520, 1.011)	-	-	-
PTSD, current	459	0.877	(0.583, 1.320)	-	-	-
PTSD, historical	750	0.605	(0.415, 0.882)*	-	-	-
Alcohol UD, anytime	757	0.611	(0.429, 0.870)*	691	0.774	(0.519, 1.156)
Alcohol use above recommended limits, current	691	0.653	(0.437, 0.978)*	-	-	-
Alcohol UD, historical	748	0.633	(0.416, 0.963)*	-	-	-
Cannabis UD, anytime	757	0.410	(0.229, 0.734)*	691	0.507	(0.275, 0.934)*
Cannabis Use, current	672	0.283	(0.137, 0.584)*	-	-	-
Cannabis UD, historical	746	0.501	(0.272, 0.924)*	-	-	-
Other SUD, anytime	757	0.534	(0.251, 1.137)	-	-	-
Other SUD, current	667	1.001	(0.332, 3.023)	-	-	-
Other SUD, historical	746	0.467	(0.201, 1.084)	-	-	-

Table 2
(continued)

Baseline covariates in relation to ADM program completion. Univariable modeling shows a significant association between a number of baseline variables and ADM program completion rates. For PTSD and substance use disorders, the cohort was subdivided into those with "current" symptoms at time of enrollment (defined as PCL-5 $\geq$ 33, drinking above recommended limits, or actively using cannabis or other recreational substances of abuse, respectively), "historical" (defined as a prior diagnosis of PTSD or substance use disorder), and "anytime" (defined as one or both of current and historical). Statistical significance is identified with an asterisk (*). A multivariable logistic regression model was then run to control for differences in baseline characteristics, and holding all else fixed, age remained a significant predictor of program completion, and "anytime" cannabis use disorder remained a significant predictor of program non-completion. For covariates of psychiatric and substance use comorbidities, only the "anytime" variable (i.e., either or both "current" and "historical") was included in the multivariable model to prevent issues with multicollinearity. Significance level is set to 0.05

PHQ-9 Patient Health Questionnaire 9 Item, *MH Dx* mental health diagnoses, *GAD-7* Generalized Anxiety Disorder Scale 7 Item, *PTSD* post-traumatic stress disorder, *UD* use disorder, *SUD* substance use disorder (tobacco/nicotine use disorders not included)

Table 3
Association of early symptomatic improvements and ADM program completion

Variable	*n*	OR	95% CI
Early improvement in PHQ	536	2.308	(1.602, 3.326)*
Early improvement in GAD	534	2.258	(1.571, 3.245)*

Univariable modeling showing the association of early improvement in PHQ-9 and GAD-7 total scores with ADM program completion. Reported as odds ratios and 95% confidence intervals. Both PHQ-9 and GAD-7 early improvements were statistically significant predictors of ADM program completion

PHQ-9 Patient Health Questionnaire 9 Item, *GAD-7* Generalized Anxiety Disorder Scale 7 Item

response and remission rates (69.4% vs. 34.1%, $p \leq 0.001$; and 57.0% vs 28.4%, $p \leq 0.001$). These results are summarized in Table 5.

Discussion

Study findings show that a number of covariates were associated with differences in psychopharmacological CoCM program completion rates. With initial univariable modeling, age, early improvement in anxiety symptoms, and early improvement in depression symptoms were all significantly associated with higher rates of program completion. Higher baseline depressive symptoms (PHQ-9 scores), higher baseline anxiety symptoms (GAD-7 scores), contact with a clinical psychologist prior to program enrollment, any history of concurrent mental health diagnoses, and several categories of substance use/abuse were associated with lower program completion rates. After statistical modeling controlling for univariable significant differences, age, early improvements in PHQ-9, and early improvements in GAD-7 all remained significant predictors of ADM program completion. Only cannabis use remained a significant negative predictor of program completion.

One finding of interest is the finding of reduced likelihood of program completion for those participants who had prior contact with a psychologist for assessment/evaluation purposes prior

Table 4
Association of early improvements with program completion, adjusted for significant covariates

Early improvements and program completion, adjusted for significant covariates ($n = 527$)

Variable	OR	95% CI
Age	1.019	(1.007, 1.032)*
Baseline PHQ-9	0.974	(0.933, 1.016)
Baseline GAD-7	0.978	(0.936, 1.023)
Early improvement in PHQ-9	1.864	(1.210, 2.872)*
Early improvement in GAD-7	1.762	(1.154, 2.691)*
Any comorbid MH Dx	0.875	(0.571, 1.342)
Alcohol UD, anytime	0.737	(0.470, 1.154)
Cannabis UD, anytime	0.497	(0.257, 0.960)*

Multivariable modeling was conducted to examine if early symptomatic improvements (defined as ≥ 20% reduction in total PHQ-9 or GAD-7 scores from baseline to 3-week follow-up) were associated with ADM program completion after controlling for baseline characteristics that were significantly different. Both early improvements in PHQ-9 and early improvements in GAD-7 remained statistically significant predictors of program completion. Significance level is set to 0.05 and significance is marked with an asterisk (*)

PHQ-9 Patient Health Questionnaire 9 Item, *GAD-7* Generalized Anxiety Disorder Scale 7 Item, *MH Dx* mental health diagnoses, *UD* use disorder

Table 5
Symptomatic improvements in ADM program completers vs. non-completers

Characteristics	Completers	Non-completers	*p* Value
Depression remission	152 (59.4%)	66 (21.4%)	< 0.001*
Depression response	192 (75.0%)	100 (32.4%)	< 0.001*
Anxiety remission	146 (57.0%)	88 (28.4%)	< 0.001*
Anxiety response	177 (69.4%)	105 (34.1%)	< 0.001*
Improvement in PHQ-9	68.18 (47.61, 88.89)	26.09 (− 6.46, 57.52)	< 0.001*
Improvement in GAD-7	66.67 (43.75, 90.00)	26.67 (0.00, 63.40)	< 0.001*

Symptomatic improvements in depression and anxiety in ADM program completers vs. non-completers. Program completers had prominent improvements in depression and anxiety symptoms as noted by greater than 66% reduction in both PHQ-9 and GAD-7 total scores. Similarly, high rates of depression response and remission were reported among ADM program completers, with 75% achieving response and 59.4% achieving remission. Additionally, high rates of anxiety response (69.4%) and remission (57.0%) were also observed among program completers. Statistically significant differences in symptomatic improvements were noted between ADM program completers vs. non-completers on all symptomatic outcome measures. Scores obtained during last ADM contact were used for both groups. Chi-square analyses were used to analyze differences in proportion of remission and response rates and are summarized as *n* (%). Mann–Whitney *U* tests were utilized for continuous variables with differences in improvement percentage summarized as median (IQR)

PHQ-9 Patient Health Questionnaire 9 Item, *GAD-7* Generalized Anxiety Disorder Scale 7 Item

to enrollment in the program. Data from the Center for Integrated Healthcare suggests that contact with Primary Care Integrated Mental Health, broadly-speaking, improves show-rates to higher levels of mental health care,[17] but there is little data on the interaction between psychotherapy and Collaborative Care Management as co-treatment approaches in terms of adherence. In fact, seminal trials of the CoCM method generally put medication management as the primary treatment approach, with referral for psychotherapy as a later stage in the algorithm (e.g., the IMPACT model). A possible interpretation of these results is that patients who obtain sufficient psychotherapy support prior to referral to CoCM may self-discontinue from the CoCM/ADM program due to lack of need. Alternatively, it could suggest that in the scope of the program under investigation, patients being referred to a CoCM program from a psychotherapist in primary care may benefit from more thorough or evidence-based discussion of CoCM and medication-management-based options prior to, or throughout, the CoCM treatment process.

The study also reiterated previous reports that psychopharmacological CoCM/ADM programs are effective interventions to support symptom reduction and, further, highlight the importance of programmatic completion in maximizing benefits gained in this treatment model. A notable difference in symptomatic outcomes was observed in program completers versus non-completers, with completers achieving impressively high rates of symptomatic response and remission. These findings, coupled with the modest programmatic completion rate (33.82%) highlights the importance of this study as the first step towards optimizing CM programs through increasing adherence to the treatment model and emphasizes the need to develop interventions that will improve programmatic adherence.

One area of potential intervention could be efforts to optimize early symptomatic improvements due to the strong associations observed between early improvements and program completion. Efforts to increase early improvement rates could include more aggressive medication regimens and dosing strategies, or more proactive concurrent treatment with time-limited psychotherapeutic interventions early in the course of treatment. Additionally, CoCMs could be advised to emphasize the importance of concurrent use of self-management strategies at each early contact to increase the likelihood of early improvement in symptoms. Conversely, due to the negative association observed between cannabis use and program completion, efforts to encourage cessation of substances of abuse, particularly cannabis, may be beneficial to increase program adherence and completion. Future iterations of the psychopharmacological CoCM/ADM program may benefit from the inclusion of treatment foci related to minimizing substance use and abuse.

Results of the study also suggests that age plays a role in program adherence, specifically that older patients were more adherent to the program. This finding is consistent with the fact that early iterations of CM were developed for use in geriatric populations.[10] Future research should focus on engaging younger populations into the program, perhaps through the use of modern tools such as text messaging and video chat technology. While this is an emerging literature base, there is preliminary evidence to suggest that technology can be leveraged to impact adherence to psychiatric medication recommendations within specific populations.[18]

In addition to the observations related to statistically significant predictors, several variables which were found to not be associated with differences in program completion are notable. Among these includes variables typically observed to be associated with higher levels of psychiatric complexity including comorbid psychiatric diagnoses, suicidal ideations, sleep disturbances, and baseline symptom severity. Although many of these variables have previously been reported as negative predictors of medication adherence in traditional psychiatric outpatient care models, none of these were significant predictors of ADM program non-completion in the final, controlled model. This is of particular interest as it suggests that the ADM program, which is a highly proactive intervention with frequent telephonic contacts, may be protective against these covariates that are historically associated with non-adherence and drop out. For example,

previous literature has suggested that higher baseline symptoms as measured by the PHQ-9 and GAD-7 may be a predictor of treatment non-adherence, however, that was not observed in this study cohort. This suggests a potential advantage of the ADM program as scheduled calls to patients may contribute to increased treatment adherence and serve as a protective factor regardless of symptom severity.

Limitations of the study include the retrospective nature of the work, including relying on the accuracy of the written medical record, the reliability of the EHR in reporting historical diagnoses, and difficulty in controlling for confounders. Another limitation in retrospective research is the potential for missing data. However, in our study, data is missing at random and not due to study design or implementation, thus reducing potential bias that could be introduced due to missing data. Additional limitations include a limited number of mental health assessment scales for symptomatic monitoring and a wholly Veteran cohort which may make the findings less generalizable. It is also of note that some findings in the study may be bidirectional or may be viewed as a confound or as not being fully independent, for example, the finding that early reductions in PHQ-9 and GAD-7 scores were associated with program completion. However, these early improvements may also impact the differences observed in final symptomatic improvement outcome measures between program completers and non-completers. Further, utilization of individual items of the PHQ-9 for both sleep disturbances (PHQ-9 item #3) and suicidal ideations (PHQ-9 item #9) is a limitation as these are often considered proxy measures which are less thorough than dedicated full sleep assessments (such as the Pittsburgh Sleep Quality Index [PSQI]) or assessments specific to suicidal thoughts and behaviors (such as the Columbia Suicide Severity Rating Scale [C-SSRS]). Specific strengths of the study include the large sample size, longitudinal patient monitoring, broad inclusion criteria, and pragmatic design utilizing a clinical population and clinical interventions which makes the findings directly relevant to clinical practice.

Implications for Behavioral Health

The authors' results examining a psychopharmacological collaborative care management treatment model for the management of depression and anxiety in the primary care setting identified a number of modifiable parameters associated with differences in ADM program completion rates including a positive association with early improvement in symptoms of depression and anxiety, and a negative association with cannabis use. Further, results showing greater symptomatic improvement in individuals who complete the CoCM program, coupled with the modest program completion rates, emphasize the importance of utilizing results of this work to develop interventions to increase program adherence. Additional studies should be conducted examining ways to optimize collaborative care management programs through interventions which support factors associated with positive predictors while minimizing identified negative predictors.

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Declarations

Conflict of Interest The authors declare no competing interests.

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Reporting Guidelines Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for the reporting of observational cohort studies were followed.