The Start Predicts the Finish:

Factors Associated With Antidepressant Nonadherence Among Older Veterans During the Acute and Maintenance Treatment Phases

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ABSTRACT

Objective: To best prevent depression relapse and reduce recurrence, an understanding of the factors associated with continued maintenance treatment is needed. This study compared factors associated with antidepressant nonadherence during the acute (ie, during the first 4 months) and maintenance (ie, during 12 months) treatment phase among older veterans with depression.

Methods: In this prospective, observational study of 278 older veterans with depression (Patient Health Questionnaire-9 score ≥ 5), patients had been given a new antidepressant prescription between 2008 and 2011. Participants completed initial and follow-up interviews at 4 and 12 months. Medication adherence was assessed by the Brief Medication Questionnaire. A generalized estimating equation was used to determine patient factors associated with nonadherence at each time point.

Results: Nearly a third of veterans were nonadherent at 4- and 12-month follow-up. In adjusted analyses, nonadherence was significantly associated with African American race (adjusted odds ratio [AOR] = 2.69, 95% CI, 1.30–5.57; $P = .01$), being unmarried (AOR = 1.84; 95% CI, 1.16–2.92; $P = .049$), greater medical comorbidity (AOR = 1.30; 95% CI, 1.13–1.49; $P < .001$), functional impairment (AOR = 1.34; 95% CI, 1.10–1.63; $P = .01$), and self-reported side effects (AOR = 2.48; 95% CI, 1.57–3.94; $P < .001$) at both 4 and 12 months. Depression or anxiety severity did not predict antidepressant adherence at either time point.

Conclusions: Rates of and factors associated with antidepressant nonadherence were similar at 4 and 12 months. Further work is needed to develop tailored treatment programs to engage older veterans at higher risk of nonadherence in the early treatment period, which may ultimately help to both achieve remission and reduce relapse and recurrence.

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Depression is often an episodic and recurrent disorder, with studies suggesting that 50%–90% of patients with depression will have multiple episodes throughout their lifetime.[1] Recurrent episodes can lead to worsening depression severity, longer duration of illness, reduced quality of life, and increased morbidity.[2,3] Given the severity and negative impact of recurrent depression, clinicians often recommended continued maintenance antidepressant therapy to prevent illness relapse.[4] Guidelines on depression from professional organizations such as the American Psychiatric Association[5] and the National Institute for Health and Care Excellence[6] advise a minimum of 6 to 9 months of antidepressant treatment after a first depressive episode. For patients with a history of recurrent depression, longer treatment is recommended; for those with a history of suicidal behavior and treatment refractoriness, lifetime treatment is often warranted to prevent illness relapse.[6]

Despite improved recognition and diagnosis of later-life depression, adherence to antidepressant medication remains low,[7] with studies demonstrating that upwards of 40%–75% of older adults do not take antidepressants as prescribed or stop treatment early.[8] Studies of antidepressant medication adherence have largely focused only on the acute treatment phase (ie, first 4 months),[8,9] which often serves as a patient's first exposure to antidepressant medication. Studies have found that younger age, minority status, and higher medical comorbidity are associated with antidepressant nonadherence within the acute treatment phase.[9,10]

However, among older adults with depression, much less is known about the factors that impact antidepressant adherence in the maintenance phase of depression treatment (ie, during the first 12 months) and how these factors may vary from the acute treatment phase. For example, prior exposure to antidepressant treatment or concurrent treatment with a therapist may lead to greater adherence in the maintenance phase than in the acute treatment phase as common misperceptions about antidepressant treatment are addressed (eg, concern that medications are addictive or ineffective). Additionally, concerns regarding medication side effects may be more tolerable during the acute treatment phase, but as a patient's depression improves, the continued presence of side effects may become less tolerable in the maintenance phase. While there have been no studies directly comparing the acute and maintenance phases of depression treatment specifically for older adults, one study[11] evaluating antidepressant adherence among

Clinical Points

- To best prevent depression relapse and reduce recurrence, an understanding of the factors that predict antidepressant adherence in the acute (ie, first 4 months) and maintenance (ie, 12-month) treatment phases is needed.
- In this study, nearly a third of veterans were nonadherent to antidepressant treatment at both 4- and 12-month follow-up, with antidepressant nonadherence associated with African American race, being unmarried, greater medical comorbidity, functional impairment, and self-reported side effects at both time points.
- Identifying and engaging older veterans at higher risk of nonadherence early in treatment may ultimately help achieve remission and reduce relapse and recurrence.

adults during a 2-year follow-up period found that 69% of patients were nonadherent by the end of the study, with no measured patient demographic or clinical factors associated with medication nonadherence.

Older veterans represent a growing population in the United States; in 2017, 9.7 million veterans were over the age of 65 years.[12] Veterans have high burden of medical comorbidity and psychiatric diagnoses as compared to non-veteran samples, with the Veterans Health Study[13] finding that older veterans' rate of depression was nearly double that of non-veterans. The evidence shows that continued antidepressant maintenance treatment can reduce the odds of depression relapse by two-thirds,[4] in line with the adage "the dose that gets you well, keeps you well." Therefore, it is crucial to understand the factors that impact adherence during the maintenance phase of treatment in order to develop strategies to help prevent relapse of depressive symptoms among older veterans with depression, a period about which much less is known as compared to the acute treatment phase. In this study, we evaluated antidepressant adherence among older veterans with depression who were newly started on an antidepressant medication in a mental health or primary care clinic between 2008 and 2011. The goals of this study were to (1) identify the rate of antidepressant nonadherence during the acute (ie, first 4 months) and maintenance (ie, 12-month) treatment phases; (2) identify patient sociodemographic, clinical, and depression treatment characteristics that predict antidepressant nonadherence; and (3) assess how these factors may vary between the acute and maintenance treatment phases among older veterans with depression.

METHODS

Study participants were recruited from 3 Veterans Affairs (VA) medical centers (Ann Arbor, Detroit, and Battle Creek) in Michigan from 2008 to 2011 from both primary care and mental health clinics. Study inclusion criteria required participants to be ≥ 60 years old, have a depression diagnosis (ie, Patient Health Questionnaire-9 [PHQ-9] score ≥ 5[14]), and have received a new antidepressant prescription (ie, no use in the past 6 months) from a VA outpatient primary care or mental health clinic within the previous week. Participants were excluded if they suffered from another serious mental illness (ie, including psychosis or bipolar disorder), had cognitive impairment (ie, ≥3 errors on the Six-Item Screener[15]), had a legal guardian, or were actively suicidal. Participants were interviewed at baseline (mean [SD] time to baseline interview = 49 [11.6] days) and at 4 months and 12 months from the initial treatment recommendation. Interviews were conducted by trained research assistants, and all participants provided written informed consent prior to study participation. This study was approved by the VA Ann Arbor Healthcare System and Wayne State University Institutional Review Boards.

Research Assessments

A structured telephone interview included assessment of both modifiable and non-modifiable factors shown to potentially influence depression treatment adherence.[9] Demographic variables collected included age, race, sex, marital status, and education. Illness burden of depression was assessed by the PHQ-9 (scores range from 0 to 27 with a higher score indicating greater depression)[14] and a history of past antidepressant use. Anxiety was assessed with the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A; scores range from 0 to 21 with higher score indicating more anxiety symptoms)[16] and Anxiety Sensitivity Index-Revised (ASI-R; scores on subscales 1 and 4 range from 0 to 105 with a higher score indicating greater anxiety).[17] Medical illness burden was evaluated using the Charlson Comorbidity Index (CCI),[18] with score based on *ICD-9* codes listed in the participants' medical record during the 12 months prior to the initial interview. Functional status assessment was based on the Instrumental Activities of Daily Living scale (IADL; scores range from 0 to 8 with a higher score indicating greater function),[19] Short Form-12 (SF-12, which contains 2 weighted summary scales—the Mental Component Summary [MCS] and Physical Component Summary [PCS]—ranging from 0 to 100 with a higher score indicating a higher level of health),[20] and cognitive executive functioning as measured by the Wechsler Letter-Number Sequencing scale (LNS; scores range from 0 to 21 with a higher score indicating greater executive function).[21] Features of depression treatment were characterized including antidepressant class, concurrent use of psychotherapy, and patient self-rated side effects (using the UKU Side Effects Rating Scale,[22] a standardized scale specific for side effects of psychotropic medications, including tremor, gastrointestinal distress, weight gain, and sexual side effects, among others). Lastly, change in PHQ-9 score at 4 months and 12 months was assessed to determine potential improvement (ie, reduction in total PHQ-9 score from previous assessment) in depressive symptoms throughout the study period.

Medication Adherence

At 4- and 12-month follow-up, medication adherence was measured using a validated self-report adherence question

from the Brief Medication Questionnaire (BMQ)[23] that asks the patients how consistently they took medication in the week prior. Adherence of less than 80% was considered to be inadequate, with those missing 2 or more daily doses in a given week considered nonadherent as in previous studies.[8,23] For participants who were nonadherent to antidepressant medication at 4 or 12 months, their charts were reviewed to determine if their provider recommended medication discontinuation (eg, given depression remission or intolerable side effects). In such cases, participants were classified as adherent since they were following provider recommendations.

Statistical Analysis

Descriptive statistics were calculated for the total study sample using *t* tests and χ^2 tests for continuous and categorical variables, respectively. To address the concern that the time lag between treatment recommendation and initial interview might have affected the results, we examined the relationship between initial PHQ-9 score and length of time between treatment recommendation and initial interview. Among nonadherent participants, the most commonly reported side effects at 4 and 12 months were noted.

A generalized estimating equation (GEE) was used for longitudinal data analysis to (1) assess factors associated with antidepressant adherence at both the 4-month and 12-month time points and (2) compare differences across these time points, controlling for characteristics previously shown or thought to influence depression treatment adherence as found in our previous work.[8,9] The GEE was completed in lieu of logistic regression, as it takes into consideration the correlated structure of the data from repeated measures at baseline, and 4- and 12-month follow-up. Covariates included demographics (age, education, marital status, site of recruitment), illness burden (determined by any prior use of an antidepressant; scores on the PCS, MCS, PHQ-9, HADS-A, and ASI; change in PHQ-9 score; medication side effects; CCI score; substance abuse; posttraumatic stress disorder (PTSD); and anxiety disorders), cognitive function (IADL score, Wechsler LNS score), and treatment site (psychiatry vs primary care). Covariates were organized as sets of variables and entered hierarchically in a predefined order, with the potentially confounding contextual variables entered first in order to sequentially assess their influence on adherence. On the basis of this reasoning, demographic characteristics were entered first, followed by treatment and illness burden variables, then cognitive function variables, and finally, treatment site. Within each block, covariates were assessed for multicollinearity, and highly collinear variables were not included together. Among the study sample, 3.2% (n = 9) had missing data for at least 1 risk factor. A multiple imputation strategy using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina) was adopted to impute missing values per a multivariate model that included all covariates as well as medication adherence using the Rubin method.[24]

RESULTS

Sample Characteristics

A total of 834 veterans were found to be potentially eligible based on age and receipt of a new antidepressant prescription; of those potentially eligible, 448 were able to be contacted. Of those contacted, 379 veterans completed screening, with 285 participants found to be eligible for study participation. Of eligible veterans, 97.5% (n = 278) agreed to study participation, provided informed consent, and completed the baseline assessment. No participants were lost to follow-up in the 4-month study period; 12 participants were lost to follow-up at the 12-month assessment (n = 266 completed the 12-month assessment).

The demographic and clinical characteristics of the study sample are shown in Table 1. At baseline, most of the 278 older adults (mean ± SD age = 65 ± 6.3 years) who completed the initial assessment were male (n = 270, 97.1%), white (n = 237, 85.3%), and married (n = 164, 59.0%). A total of 62.2% had prior depression treatment, and 36.3% were currently seeing a therapist. Other comorbid psychiatric diagnoses included PTSD (n = 101, 36.3%), other anxiety disorder (n = 55, 19.8%), and substance abuse (n = 43, 15.5%). Mean scores on clinical assessments conducted at baseline are reported in Table 1. Initial PHQ-9 scores ranged from 5 to 26. There was no association between initial PHQ-9 score and time between treatment recommendation and initial interview. Additionally, time from treatment recommendation to enrollment in the study did not significantly differ by 4- or 12-month adherence. The most commonly prescribed antidepressants were citalopram (n = 125, 45.0%), bupropion (n = 44, 15.8%), and sertraline (n = 42, 15.1%).

Predictors of Antidepressant Nonadherence

Rates of antidepressant nonadherence were similar at both 4-month (n = 76/278, 27.3%) and 12-month (n = 76/266, 28.6%) follow-up. In unadjusted analyses, at 4 months, nonadherent participants were more likely to be African American ($\chi^2_2 = 10.98$, $P < .01$), be unmarried ($\chi^2_1 = 12.33$, $P < .01$), be seen in primary care ($\chi^2_1 = 5.42$, $P = .02$), report medication side effects ($\chi^2_2 = 20.7$, $P < .01$), and have increased medical comorbidity (ie, have a higher CCI score; $\chi^2_1 = 13.33$, $P < .01$; Table 1). At 12 months, in unadjusted analyses, participants with prior depression treatment ($\chi^2_1 = 4.22$, $P = .04$), medication side effects ($\chi^2_2 = 14.3$, $P < .01$), and a history of PTSD ($\chi^2_1 = 6.41$, $P = .01$) were more likely to be adherent (Table 1). While adherent participants were more likely to show improvement on the PHQ-9 at 4- and 12-month follow-up than nonadherent participants (4-month: 55% [n = 110] vs 46% [n = 35], $P = .17$; 12-month: 55% [n = 105] vs 51% [n = 39], $P = .54$), this difference was not statistically significant.

Among nonadherent participants, the most commonly reported side effects at each time point were dry mouth (25.0%), decreased libido (21.1%), and drowsiness (19.7%) at 4 months and dry mouth (19.7%), drowsiness (19.7%), and anxiety (18.4%) at 12 months.

Table 1. Participant Characteristics at Baseline for Total Sample and by 4- and 12-Month Adherence Status

			4 Months (N = 278)					12 Months (n = 266)				
	Baseline (N = 278)		Adherent (n = 202)		Nonadherent (n = 76)			Adherent (n = 190)		Nonadherent (n = 76)		
Characteristic	n	%	n	%	n	%	*P* Value	n	%	n	%	*P* Value
Site of Recruitment												
Ann Arbor	100	36.0	75	37.1	25	32.9	.71	66	34.7	30	39.5	.73
Battle Creek	96	34.5	70	34.7	26	34.2		68	35.8	24	31.6	
Detroit	82	29.5	57	28.2	25	32.9		56	29.5	22	28.9	
Primary care*	133	47.8	88	43.6	45	59.2	.02	85	44.7	43	56.6	.08
Mental health	145	52.2	114	56.4	31	40.8		105	55.3	33	43.4	
Patient Characteristics												
Female	8	2.9	5	2.5	3	3.9	.51	6	3.2	2	2.6	.82
Male	270	97.1	197	97.5	73	96.1		184	96.8	74	97.4	
Race												
African American**	31	11.2	16	7.9	15	19.7	< .01	19	10.0	10	13.2	.34
White	237	85.3	176	87.1	61	80.3		162	85.3	65	85.5	
Other[a]	10	3.6	10	5.0	0	0.0		9	4.7	1	1.3	
Age, y												
60–64	190	68.3	142	70.3	48	63.2	.19	138	72.6	44	57.9	.05
65–74	57	20.5	36	17.8	21	27.6		32	16.8	22	28.9	
75–90	31	11.2	24	11.9	7	9.2		20	10.5	10	13.2	
Education												
High school or below	113	40.6	77	38.1	36	47.4	.16	76	40.0	31	40.8	.91
Some college	165	59.4	125	61.9	40	52.6		114	60.0	45	59.2	
Marital status												
With spouse/partner**	164	59.0	132	65.3	32	42.1	< .01	120	63.2	40	52.6	.11
Single/no partner	114	41.0	70	34.7	44	57.9		70	36.8	36	47.4	
Depression Treatment Characteristics												
Citalopram or sertraline	167	60.1	119	58.9	48	63.2	.52	107	56.3	52	68.4	.07
Other antidepressant use	111	39.9	83	41.1	28	36.8		83	43.7	24	31.6	
Prior depression treatment*	173	62.2	127	62.9	46	60.5	.76	128	67.4	41	53.9	.04
Seeing a therapist	101	36.3	77	38.1	24	31.6	.48	75	39.5	22	28.9	.11
Any medication side effect**	83	29.9	51	25.2	32	42.1	< .01	55	28.9	28	36.8	< .01
Clinical Characteristics												
PTSD*	101	36.3	79	39.1	22	28.9	.12	79	41.6	19	25.0	.01
Substance abuse	43	15.5	28	13.9	15	19.7	.23	28	14.7	12	15.8	.83
Anxiety disorder	55	19.8	41	20.3	14	18.4	.73	40	21.1	14	18.4	.63
Charlson Comorbidity Index score**												
0	104	37.4	79	39.1	25	32.9	< .01	74	38.9	26	34.2	.05
1	76	27.3	64	31.7	12	15.8		57	30.0	15	19.7	
> 1	98	35.3	59	29.2	39	51.3		59	31.1	35	46.1	
Self-Report Scale Score	Mean ± SD		Mean ± SD		Mean ± SD		*P* Value	Mean ± SD		Mean ± SD		*P* Value
PCS score[b]	36.8 ± 11.7		36.9 ± 11.6		36.7 ± 12.0		.91	37.1 ± 11.6		37.0 ± 11.9		.94
MCS score[b]	38.1 ± 11.5		38.2 ± 11.6		37.9 ± 11.3		.81	37.7 ± 11.5		39.0 ± 11.5		.40
PHQ-9 score[c]	12.4 ± 6.3		12.3 ± 6.4		12.7 ± 5.9		.65	12.7 ± 6.5		11.9 ± 5.6		.40
HADS-A score[d]	8.7 ± 5.1		8.9 ± 5.0		8.1 ± 5.2		.21	9.1 ± 5.1		7.9 ± 5.0		.10
ASI-R score[e]	51.8 ± 26.1		52.2 ± 25.7		51.0 ± 27.1		.74	52.1 ± 25.6		52.5 ± 27.1		.91
IADL total score[f]	7.4 ± 1.4		7.4 ± 1.4		7.5 ± 1.4		.41	7.3 ± 1.5		7.6 ± 1.1		.13
Wechsler LNS score[g]	7.9 ± 3.5		7.9 ± 3.5		7.9 ± 3.5		.94	8.1 ± 3.4		7.8 ± 3.7		.45

[a]Other races include 5 Hispanic white individuals, 2 Pacific Islanders, 2 individuals of American Indian and white ancestry, and 1 individual with self-reported unknown race.
[b]SF-12 PCS and MCS scores range from 0 to 100 with a higher score indicating a higher level of health.
[c]PHQ-9 scores range from 0 to 27 with a higher score indicating greater depression.
[d]HADS-A scores range from 0 to 21 with higher score indicating more anxiety symptoms.
[e]ASI-R subscales 1 and 4 scores range from 0 to 105 with a higher score indicating greater anxiety.
[f]IADL total scores range from 0 to 8 with a higher score indicating greater function.
[g]Wechsler LNS subscale scores range from 0 to 21 with a higher score indicating greater executive function.
*$P < .05$ vs other groups in this category of characteristic.
**$P < .01$ vs other groups in this category of characteristic.
Abbreviations: ASI-R = Anxiety Sensitivity Index-Revised, HADS-A = anxiety subscale of Hospital Anxiety and Depression Scale, IADL = Instrumental Activities of Daily Living scale, LNS = Letter-Number Sequencing scale, MCS = Mental Component Summary of the Short Form-12 (SF-12), PCS = Physical Component Summary of the SF-12, PHQ-9 = Patient Health Questionnaire-9, PTSD = posttraumatic stress disorder.

Table 2. Factors Associated With Antidepressant Nonadherence at 4-Month and 12-Month Follow-Up

Characteristic	Adjusted Odds Ratio	95% CI	*P* Value
Site of Recruitment			
Ann Arbor	1.11	0.60–2.03	.74
Battle Creek	1.53	0.83–2.85	.18
Detroit (reference)	1.0	…	…
Primary care	1.24	0.76–2.03	.40
Patient Characteristics			
African American**	2.69	1.30–5.57	.008
Female	0.62	0.18–2.17	.45
Age category, y			
60–64 (reference)	1.0	…	…
65–74	1.35	0.78–2.31	.28
75–90	0.93	0.42–2.08	.87
Education: some college	0.91	0.58–1.42	.67
Marital status: without spouse/ partner*	1.84	1.16–2.92	.009
Depression Treatment Characteristics			
Citalopram or sertraline	1.16	0.72–1.87	.55
Prior depression treatment	0.85	0.53–1.36	.50
Seeing a therapist	0.98	0.59–1.64	.94
Any medication side effect**	2.48	1.57–3.94	<.001
Clinical Characteristics			
PTSD	0.62	0.35–1.10	.10
Substance abuse	1.27	0.70–2.31	.44
Anxiety disorder	1.18	0.68–2.05	.57
Charlson Comorbidity Index score**	1.30	1.13–1.49	<.001
PCS score	1.01	0.98–1.03	.65
MCS score	1.00	0.97–1.03	.97
PHQ-9 score	1.01	0.95–1.07	.83
Change in PHQ-9 score[a]	1.04	0.99–1.09	.13
HADS-A score	0.95	0.89–1.02	.16
ASI-R score	1.00	0.99–1.01	.66
IADL score**	1.34	1.10–1.63	.004
Wechsler LNS score	1.00	0.93–1.07	.98

[a]Change in PHQ-9 score from baseline or change from previous period.
*P < .05 vs other groups within this category of characteristic (see Table 1).
**P < .01 vs other groups within this category of characteristic (see Table 1).
Abbreviations: ASI-R = Anxiety Sensitivity Index-Revised, HADS-A = anxiety subscale of the Hospital Anxiety and Depression Scale, IADL = Instrumental Activities of Daily Living scale, LNS = Letter-Number Sequencing scale, MCS = Mental Component Summary of the Short Form-12 (SF-12), PCS = Physical Component Summary of the SF-12, PHQ-9 = Patient Health Questionnaire-9, PTSD = posttraumatic stress disorder.

GEE models were completed to determine factors associated with antidepressant adherence at both 4 and 12 months and compare potential differences across these time points, adjusted for other covariates. In adjusted analyses (Table 2), African American race (adjusted odds ratio [AOR] = 2.69; 95% CI, 1.30–5.57; P = .008), being unmarried (AOR = 1.84; 95% CI, 1.16–2.92; P = .009), increased medical comorbidity (AOR = 1.30; 95% CI, 1.13–1.49; P < .001), greater functional impairment (AOR = 1.34; 95% CI, 1.10–1.63; P = .004), and presence of self-reported side effects (AOR = 2.48; 95% CI, 1.57–3.94; P < .001) were associated with nonadherence at both 4 and 12 months, with no significant differences between the factors that predicted adherence during the acute and maintenance phases. Depression and anxiety severity scores did not predict antidepressant adherence at either time point. No other sociodemographic, clinical, or depression treatment characteristics were associated with antidepressant adherence at 4 or 12 months.

DISCUSSION

In this sample of older veterans newly prescribed an antidepressant within a primary care or mental health clinic, roughly a third of veterans were nonadherent to medication during both the acute and maintenance treatment phases. The majority of previous research evaluating antidepressant adherence has focused solely on the acute treatment phase, as this is often a patient's first exposure to antidepressant medication and a potentially high-risk period for suicide.[25] However, to best prevent depression relapse and reduce recurrence, an understanding of the factors associated with continued maintenance treatment is needed. Among the study sample, antidepressant discontinuation was strongly associated with nonclinical factors (eg, race and marital status). While depression and anxiety severity did not predict adherence at either time point, increased medical comorbidity, functional impairment, and self-reported side effects were associated with worse antidepressant adherence. There was no significant difference in factors associated with nonadherence at 4 and 12 months.

As was also demonstrated in previous work,[8,26] African American race and lack of spouse or partner were both associated with antidepressant medication nonadherence. Studies have consistently shown that African Americans are less likely to receive a diagnosis of depression compared to older white adults and have increased barriers to engaging in mental health treatment.[10] Qualitative studies suggest that African Americans may have greater concerns regarding the use of medications to treat depression, viewing antidepressant medications as non-efficacious or potentially addictive,[27] thus leading to lower rates of medication adherence.[28,29] In our previous work,[29] we demonstrated that after controlling for beliefs about the importance and efficacy of antidepressants, racial differences were no longer significant in impacting adherence. Additionally, marital status has been shown across several studies to positively impact antidepressant and depression treatment adherence.[10] Independent of marital status, higher perceived social support from family and friends may also help to buffer against negative depression symptom outcomes and can improve antidepressant medication adherence.[26,30]

The results of this study suggest that patients with increased medical comorbidity and greater functional impairment are at particularly high risk for antidepressant medication nonadherence. Medical comorbidity and functional limitations often accompany later-life depression[31]; further, untreated depression can lead to worsening control of comorbid medical conditions and subsequent functional decline, which are of particular concern in an aging veteran population.[32] Previous studies have shown that older adults may prioritize their physical health needs over mental health treatment, leading to less adherence to mental health treatment.[33] Further, addressing patient-reported side effects to antidepressants early in treatment is important, as overall baseline side effects predicted antidepressant adherence at both 4 and 12 months.

The current study has several limitations. Our study sample was drawn from outpatient clinics associated with 3 VA medical centers in southeastern Michigan with a high proportion of male patients. It is possible that the results of our study may have differed if conducted in another geographic area and that the findings may not fully generalize to other clinical or civilian populations. The rate of antidepressant nonadherence found in this study is lower than that found in previously published studies (eg, 45%–75%)[8,10]; this discrepancy may be due to our use of a self-reported adherence measure with the BMQ. In our previous work with this sample,[8,26] comparing the BMQ scores with the medication possession ratio (MPR) from VA pharmacy data demonstrated nonadherence rates closer to 50% during the acute treatment phase, suggesting our results may underestimate these rates. Additionally, we performed chart reviews to correctly classify patient nonadherence (eg, if the prescribing physician recommended discontinuation of treatment, patients were classified as adherent), which may have further decreased our nonadherence rates. Lastly, while the study excluded veterans with more severe cognitive impairment (≥ 3 errors on the Six-item Screener), other than executive functioning, other milder deficits in memory and attention were not assessed within this study and may be associated with medication adherence.

To help prevent depression recurrence, it is important to recognize and address factors that can impact adherence in both the acute and maintenance treatment phases. In this study, nonadherence was associated with race, marital status, medical comorbidity, and functional impairment, which appear to be equally important in both acute and maintenance treatment phases. Depression and anxiety severity were not predictive of medication adherence, suggesting that approaches to improve adherence that focus only on specific clinical diagnoses may have limited success. Instead, further work is needed to develop tailored treatment programs to identify and engage older veterans at higher risk of nonadherence early in treatment, including specifically addressing and supporting the needs of racial minorities and those without spouses or partners. At the start of antidepressant treatment, it is important for prescribers to directly address early side effects and debunk common misperceptions of antidepressant treatment, such as concerns that treatment is not effective and that medications are addictive. Further, for patients with multiple medical comorbidities and diminished functioning, it is important for prescribers to discuss the benefits and importance of depression treatment adherence not only in improving their depressive symptoms but also in improving management of comorbid medical issues and preserving functioning. Lastly, given that the majority of depression care for older adults is provided outside of specialty mental health care settings,[34] it is important for health systems to continue to provide financial support to services for primary care (eg, VA primary care–mental health integration and collaborative care programs) to support these frontline providers.

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