HHS Public Access

Author manuscript

Psychiatr Serv. Author manuscript; available in PMC 2018 May 01.

Published in final edited form as:

Psychiatr Serv. 2017 May 01; 68(5): 449–455. doi:10.1176/appi.ps.201600197.

Antidepressant Prescribing in Primary Care to Older Adults without Major Depression

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Abstract

Objective—To determine whether older adults newly prescribed an antidepressant for depression by their primary care physician but found to not have MDD have similar levels of distress compared to those prescribed an antidepressant with MDD.

Methods—This analysis uses a convenience sample of participants (n=231) newly prescribed an antidepressant in the Treatment Initiation and Participation (TIP) program, a randomized controlled trial to improve antidepressant adherence and depression outcomes in older adults (≥55). After determining the proportion with and without MDD (using Structured Clinical Interview for DSM-IV [SCID]), we compared groups on demographic, clinical, and psychosocial characteristics, including SF-12 physical and mental component summaries (PCS and MCS). We used logistic regression to test the association of these characteristics and antidepressant use without MDD.

Results—57% (n=131) of participants did not have MDD. Compared to the MDD group, the non-MDD group was older (69.4 years [standard deviation 9.1] v. 64.7 [6.5], p<.001) and a larger proportion was white (82% v. 56%, p<.001). The non-MDD group reported better physical and emotional well-being (PCS 43.4 v. 39.9, p=.03; MCS 40.2 v. 30.5, p<.001). In the final regression model, white race (adjusted odds ratio [AOR]=3.11, 95% CI=1.15–8.43, p=.03) and better mental well-being on the MCS (AOR=1.16, CI=1.10–1.22, p<.001) were associated with antidepressant use without MDD.

Conclusions—Older adults prescribed antidepressants without MDD do not report distress similar to those with MDD who receive antidepressants. Given the continued emphasis on screening for depression in primary care, it is important to consider the potential for over-treatment.

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Disclosures

The authors have no conflicts to disclose.

INTRODUCTION

Depression among older adults has been the subject of a significant amount of research and education over the past twenty years. Initially, work highlighted that depression often went unrecognized in typical care settings and, when diagnosed, was often undertreated (1). Significant subsequent efforts went into improving detection and treatment of depression in primary care (2, 3), since few older adults have access to specialty mental health care. While a variety of models have been studied, collaborative care has been particularly effective (4). However, implementation of these models has lagged far behind their evidence base, largely due to the lack of sustainable reimbursement models (5). While the most effective models of depression care go unimplemented, use of antidepressants continues to increase (6), with use pervasive among older adults seen in outpatient care (7).

Recent analyses of nationally-representative surveys have suggested extensive use of antidepressants without a diagnosis of major depressive disorder (MDD) or significant depressive symptoms (8, 9). In addition, analyses of national claims data from the Veterans Affairs system (10) and a private insurance claims database (11) have also suggested that a significant proportion of antidepressant use occurs without a psychiatric diagnosis. However, these survey and administrative data do not contain information about a patient's clinical status at the time of the prescription. What appears to be antidepressant use without a psychiatric indication could be due to the survey format (e.g., limited space to list diagnoses) or clinician oversight (e.g., not adding MDD as a billing diagnosis although the provider recognized it as present). However, in another study where patients were contacted by telephone shortly after a new antidepressant was prescribed, the majority had depressive symptoms below what would suggest the presence of MDD (12). Finally, a recent analysis of participants in the Baltimore Epidemiologic Catchment Area Study followed for 4 survey waves from 1981–2005 found that, among antidepressant users in the final wave, 69% did not currently and had never met criteria for MDD based on their survey assessments over the preceding 2 decades. Even a recent analysis arguing that antidepressant use without MDD is *not* a significant problem found that, among those ≥65 and newly-prescribed an antidepressant, 26% had symptoms below the threshold that suggests MDD (13).

Taken together, these analyses suggest that, conservatively, at least one quarter of antidepressant use occurs in the absence of significant depressive symptoms. These patients lack the condition for which an antidepressant might benefit them, yet they are still subject to the side effects and adverse events (14–16) along with the unnecessary cost and risks of polypharmacy. However, a key limitation of each study is the lack of information about the prescriber's rationale. It may be that providers are responding to some other psychological or emotional distress that is not being captured by a standard inventory of depressive symptoms. In addition, some amount of antidepressant use may have been off-label for reasons such as insomnia or neuropathic pain, which is not uncommon (17) and is arguably appropriate.

In this analysis, we use data from the Treatment Initiation and Participation Program (TIP) study, an NIH-sponsored, randomized controlled trial of an intervention to improve antidepressant adherence and depression outcomes in older adults. This study recruited older

adults from primary care practices in New York and Michigan that had been newly-prescribed an antidepressant that, based on chart review, was prescribed by the provider for the purpose of treating depression. However, based on the baseline study assessment, a significant proportion was found to not have MDD. We hypothesized that a similar burden of both medical illness and psychosocial distress would be associated with antidepressant receipt without a diagnosis of MDD, suggesting that providers are prescribing an antidepressant in response to patient distress that may not precisely fit the constellation of symptoms required for a diagnosis of MDD. In addition, based on prior work demonstrating an association between demographic characteristics and antidepressant use absent a diagnosis (8, 11, 18), we hypothesized that prescribing without MDD would be associated with female gender, older age, and white race.

METHODS

Sample

The study population were participants in the Treatment Initiation and Participation Program (TIP) study, an NIH-sponsored randomized controlled trial (R01 MH087562 [PI: Dr. Y] & R01 MH087557 [PI: Dr. Z]). The study was completed at three primary care practice sites: one in New York City and two in southeastern Michigan. Adults ≥55 who received a new antidepressant prescription for depression (e.g., had not been on an antidepressant during the previous 6 months) were eligible. Participants were identified by physician referral as well as chart review, with chart review completed for all patients to confirm that the antidepressant was prescribed for depression rather than another reason (e.g., neuropathy or insomnia; patients prescribed an antidepressant for both depression and a comorbid condition were eligible). Older adults meeting any of the following criteria were excluded: 1) presence/history of psychotic or bipolar disorder; 2) suicidal intent or plan in the immediate future; 3) MMSE<24; 4) alcohol or substance dependence (see Consort diagram in eFigure 1). The study was approved by the Institutional Review Boards of Weill Cornell Medical College and the University of Michigan Medical School. Participants were randomized to the TIP intervention or treatment as usual, with research assessments conducted at study entry and multiple time periods out to 24 weeks. This analysis uses only baseline data collected at study entry and includes data from all participants, regardless of whether randomized to the intervention or treatment as usual.

Baseline evaluations with study participants were conducted by research assistants from March 6, 2011 to January 9, 2015 and were conducted within 10 days of their being prescribed an antidepressant by their primary care provider. The Structured Clinical Interview for DSM-IV (SCID) was conducted by research staff to establish the presence of a depressive disorder and to screen for the exclusion criteria. The SCID data were reviewed by a clinical psychologist to establish the final diagnosis of major, minor, or no depressive disorder. Minor depression, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*), is two to four symptoms of depression for ≥2 weeks of duration, at least one of which is depressed mood or anhedonia. To assess the burden of depressive symptoms, each participant completed the Patient Health Questionnaire depression scale (PHQ-9; range 0–27 with higher score indicating more depressive

symptoms) (19) and the 24-item Hamilton Depression Rating Scale (HDRS; range 0–75 with higher scores indicating more depressive symptoms) (20).

Participant Characteristics

This analysis uses demographic and clinical covariates from the baseline assessment shown to influence clinicians' assessment of MDD (e.g., race, gender, and comorbidity (21, 22)). The primary intervention study, given its goal of improving antidepressant treatment initiation and participation, included a variety of other measures to assess psychosocial features that may influence perceived need for or engagement in treatment. From among these additional measures, we selected those measures that might capture distress as perceived by a clinician.

Demographic variables included age, gender, race/ethnicity, living alone or with others, and education.

Clinical variables included: the Chronic Disease Score, a measure of medical comorbidity derived from prescription medications (23); the SF-12 physical component score (PCS), a measure of the participant's perception of overall physical well-being (range 0–100, population mean 50 with lower score indicating worse perceived well-being) (24); the Cornell Services Index, which captures service utilization (specifically acute care [emergency department and inpatient admission], outpatient medical care, and other support services [e.g., home health aide, home meal delivery]) over the prior 90 days (25); self-reported history of prior antidepressant use; and time the participant reported they spent in discussion with provider about the newly-prescribed antidepressant.

Psychosocial variables included*:* the Inventory of Interpersonal Problems (IIP), which measures distress arising from interpersonal problems (10 items, total range 0–40; higher score indicating more difficulty relating to others) (26); Anxiety Sensitivity Index-Revised (ASI-R), specifically the subscales pertaining to beliefs and fears about somatic sensations, as these beliefs would possibly influence antidepressant adherence (16 of 36 items, total range 0–80; higher score indicating more fear about anxiety symptoms) (27); perceived need, while was the response to: "In the past month have you had severe enough personal, emotional, behavior, or mental problems that you needed help with?" (28); Duke Social Support Index, to measure perceived support and understanding from family and friends (8 items, total range 7–21; lower score indicates less perceived support) (29); Beck Hopelessness Scale (10 items, total range 0–10; higher score suggests more hopelessness) (30); General Self-Efficacy Scale, a measure of perceived ability to cope with problems in life (10 items, total range 10–40; lower score indicates lower rating of self-efficacy) (31); and SF-12 mental component score (MCS), a measure of the participant's perception of overall emotional well-being (range 0–100, population mean 50) (24).

Statistical Methods

A total of 231 participants completed the baseline assessment. For this analysis, patients diagnosed with MDD (n=100) were compared to those without MDD (n=131; 63 with minor depression, 68 with symptoms below the threshold for minor depression). The patients without MDD were grouped together as the evidence of efficacy for antidepressants in minor

depression is limited (32, 33). Groups were initially compared on the characteristics described above using a t-test for continuous variables and chi-square test for categorical variables. Then, we used multivariable logistic regression to test the association of patient characteristics with the outcome of interest (0=antidepressant with diagnosis of MDD v. 1=antidepressant without diagnosis of MDD). This model adjusted for all demographic characteristics and site, as well as the clinical and psychosocial characteristics significant at $p<0.10$ in bivariate analysis. As a sensitivity analysis of our decision to group all patients without MDD together, we performed a multinomial regression comparing the outcomes of no depression, minor depression, and MDD. For final results, a p-value of <0.05 was used as the level of statistical significance.

RESULTS

Baseline participant characteristics are in Table 1 (characteristics by site are presented in eTable 1); 131 of 231 (57%) did not have MDD, while 100 (43%) did. Those without MDD had significantly lower mean scores on the PHQ-9 and HDRS than counterparts with MDD. Among those prescribed an antidepressant but without a diagnosis of MDD, participants were older and disproportionately white; there was no association with gender.

While participants did not vary by burden of chronic disease, the non-MDD group reported slightly better perceived physical well-being. They also reported having fewer outpatient medical visits as well as fewer support services. Those prescribed antidepressants but without MDD had better scores on every psychosocial measure except the Perceived Need item.

Prior to performing the regression model, a correlation matrix was performed using the psychosocial variables, given their strong association with the presence of MDD. As the single psychosocial variable most closely correlated with the others, the SF-12 MCS was chosen for the regression. In the final model (Table 2), the only characteristics significantly associated with antidepressant prescribing without an MDD diagnosis were being white (OR=3.11, CI=1.15–8.43, p=.03) and reporting better emotional well-being (OR=1.16, CI=1.10–1.22, p<.001). In the sensitivity model, patients with minor depression most closely resembled those patients with no depressive symptoms, confirming our *a priori* grouping decision.

DISCUSSION

In this study of older adults newly prescribed an antidepressant to treat depression, the majority of patients did not meet criteria for MDD; 29% did not even meet criteria for minor depression. Those prescribed an antidepressant in the absence of MDD were older and more likely to be white. However, rather than reporting equivalent distress to the MDD group, those without MDD generally reported better health and well-being on all measures. Other than race, the one significant factor in the final regression was emotional well-being—those prescribed antidepressants without a MDD diagnosis reported better well-being, contrary to our hypothesis.

The proportion of prescribing without a depression diagnosis was less than the 72.7% described by Mojtabai and Olfson in their NAMCS analysis (8), yet higher than the 26% found by Simon et al. (13), which is likely a function of the respective data sources. NAMCS limits the number of visit diagnoses reported to just 3, so there may be visits for MDD occurring that do not get captured in NAMCS because MDD is in a lower position on the problem list. In contrast, the Simon et al. analysis uses data from health systems participating in the Mental Health Research Network, limited to patients that received a baseline PHQ-9. It would be expected that the sensitivity and specificity of depression treatment in such settings might be better than average. Our results are consistent with Wiechers et al.'s analysis of a commercial claims database, which found that 52% of antidepressant use was absent a psychiatric diagnosis (11).

We hypothesized that the non-MDD group would be high utilizers and report levels of psychosocial distress similar to those with MDD. This would be consistent with literature suggesting that older adults experience depression differently than younger counterparts—reporting feelings of hopelessness and social isolation rather than sadness (34–36)—in which case providers in this study were perhaps appropriately responding by prescribing antidepressants. However, this appears to not have been the case: based on the SF-12 MCS, which was included as the representative psychosocial variable in the final model, the group without MDD reported significantly *better* well-being.

While age was associated with the presence of MDD in the initial analysis, it was not significant in the final model. It may be that, while age influences recognition of MDD when comparing younger to older adults, this age effect is attenuated specifically within an older population. There was no association with gender, contrary to our hypothesis. The association of white race with antidepressant treatment without MDD may be the unanticipated but logical consequence of white older adults being both more likely to receive care for depression (37) and more likely to find antidepressants acceptable than other racial and ethnic groups (38).

What exactly is driving this antidepressant use? It is possible that providers (correctly) did not believe MDD was present, but chose to prescribe the antidepressant for subsyndromal symptoms. There is substantial evidence that such symptoms in older adults have a significant impact on function, mortality, and cost (39–41). There is not, however, evidence that antidepressants are beneficial for these symptoms (32, 33, 42). Perhaps this is a case of the "worried well", where antidepressant use is prompted more by concern about depression rather than the actual presence of the disorder. The threshold for prescribing may also be getting lower, as changing public attitudes toward antidepressant use and mental illness as well as direct to consumer advertising may mean that older patients are more open to trying an antidepressant (43, 44). Lastly, it may simply be a case of incorrect diagnosis, given the difficulty of accurately diagnosing late-life depression in primary care settings (45). While the PHQ-9 scores of those without MDD were not insignificant (mean 8.9 among the group without MDD), comorbid conditions in older adults may lead to elevated PHQ-9 scores for somatic symptoms such as low energy or poor sleep, while the cardinal features of anhedonia or depressed mood are absent.

Our analysis has several limitations. First, the generalizability may be limited as the study was conducted in just 3 primary care practices. However, as noted above, the proportion of antidepressant use without MDD is consistent with other analyses of national data and the clinical sites serve a diverse population of patients. Second, there is no information as to the provider's thought process at the time of prescription, though it was established by chart review that it was meant to treat depression. Third, the baseline assessment may have been completed as many as 10 days after the prescription, and thus the patient may have changed clinically since seen by the provider. However, given the timespan over which antidepressants work, it is unlikely that there would have been a significant reduction in the burden of depressive symptoms within, at most, 10 days.

This analysis of older adults prescribed antidepressants for depression confirms what other data sources have suggested: a significant amount of antidepressant use meant to treat depression is occurring without the MDD diagnosis that warrants pharmacotherapy. The extent of inappropriate use is especially concerning given the emphasis on screening for depression in primary care, which is reimbursed by Medicare and required as a quality measure for Medicare accountable care organizations (46). In a meta-analysis of identification of depression in primary care, based on the prevalence of depression in primary care and the sensitivity and specificity of providers' ability to diagnose MDD, Mitchell et al. found that misidentification of depression outnumbers missed cases (45). Therefore, while screening may be critical to detect undiagnosed MDD, the potential for increased overdiagnosis and overtreatment must be acknowledged. Older patients misidentified as having MDD lack the condition for which an antidepressant might benefit them, though they are still subject to the potential side effects, adverse events, and risks of polypharmacy (14–16), along with the unnecessary cost.

CONCLUSIONS

Depression has a significant adverse impact on older adults and magnifies the morbidity associated with other chronic medical illness. While improving the recognition and treatment of depression in primary care has been an important focus of research and policy, it is important to recognize the potential for over-treatment. While providers and the public increasingly recognize depression as a medical problem meriting treatment, they should be aware that, whereas antidepressants are beneficial for MDD, they are not helpful for lower levels of depressive symptoms, while the potential side effects and costs remain. Primary care continues to be both the *de facto* and preferred mental health treatment setting for older adults (7, 47), while collaborative care continues to be the standard for addressing depression in primary care (48). It is critical to consider how such a model might support primary care providers to reduce both undertreatment and overtreatment of depression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Dr. Maust was supported by the Beeson Career Development Award Program (NIA K08AG048321, AFAR, The John A. Hartford Foundation, and The Atlantic Philanthropies). The Treatment Initiation and Participation Program study was funded by R01 MH087562 (PI: Dr. Sirey) & R01 MH087557 (PI: Dr. Kales).

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Psychiatr Serv. Author manuscript; available in PMC 2018 May 01.

Table 1

Comparison of baseline characteristics of Treatment Initiation and Participation Program study participants by presence or absence of major depressive disorder (MDD).

Characteristics	Total (N=231)		Patients without MDD (N=131)		Patients with MDD (n=100)		P value
	N	%	N	%	N	%	
Patient Health Questionnaire (PHQ-9)[a] (M±SD)	12.4± 6.3		8.9± 4.8		17.1± 4.8		<.001
Hamilton Depression Rating Scale[b] (M±SD)	17.8± 9.5		12.8± 7.4		24.5± 7.6		<.001
DEMOGRAPHIC							
Age (M±SD)	67.3± 8.4		69.4± 9.1		64.7± 6.5		<.001
55–64	98	42	47	36	51	51	.001
65–74	85	37	46	35	39	39	
>=75	48	21	38	29	10	10	
Gender							
Female	167	72	91	69	76	76	.27
Male	64	28	40	31	24	24	
Race							
White	163	71	107	82	56	56	<.001
Black	46	20	16	12	30	30	
Other	22	10	8	6	14	14	
Living alone	77	33	39	30	38	38	.19
Education							
< 12 years	18	8	7	5	11	11	.35
= 12 years	51	22	29	22	22	22	
> 12 years	161	70	94	72	67	67	
CLINICAL							
Chronic disease score[c] (M±SD)	3.6± 2.8		3.4± 2.8		3.8± 2.9		.29
Physical component summary of SF-12 (PCS)[d] (M±SD)	41.9±12.2		43.4±11.6		39.9±12.6		.03

Characteristics	Total (N=231)		Patients without MDD (N=131)		Patients with MDD (n=100)		P value
	N	%	N	%	N	%	
Prior antidepressant use	126	55	72	55	54	54	.52
Number of inpatient admissions and ED visits[e] (M±SD)	.8± 6.1		.7± 5.4		1.0± 7.0		.78
Number of outpatient medical visits[e] (M±SD)	3.7± 7.2		2.5± 2.6		5.4±10.4		.01
Number of support services[e] (M±SD)	4.5±16.1		1.9± 9.5		7.9±21.5		.01
Number of minutes provider spent on discussion/education of antidepressant use (M±SD)	6.8± 8.9		6.1± 7.6		7.6±10.3		.25
PSYCHOSOCIAL							
Inventory of Interpersonal Problems[f] (M±SD)	12.9± 8.0		11.4± 7.8		15.0± 8.0		<.001
Anxiety Sensitivity Index-Revised[g] (M±SD)	30.8±19.0		24.8±16.5		38.5±19.4		<.001
Perceived need	125	54	67	51	58	58	.38
Duke Social Support Index[h] (M±SD)	17.4± 3.3		18.2± 2.7		16.2± 3.7		<.001
Beck Hopelessness[i] (M±SD)	2.5± 2.6		2.0± 2.2		3.2± 3.0		<.001
General Self-Efficacy[j] (M±SD)	28.8± 6.0		30.0± 4.3		27.1± 7.4		<.001
Mental Component Summary of SF-12 (MCS)[d] (M±SD)	36.0±10.1		40.2± 9.8		30.5± 7.5		<.001

[a] Possible scores on the 9-item PHQ-9 range from 0 to 27, with higher scores indicating greater depression.

[b] Possible scores on the Hamilton Depression Rating Scale range from 0 to 30, with higher scores indicating greater depression.

[c] Possible scores on the revised Chronic disease score range from 0 to 13, with higher scores indicating more chronic diseases.

[d] Possible component summary scores on the 12-item Short-Form Health Survey (SF-12) range from 0 to 100, with a population mean of 50 and higher scores indicating a greater health.

[e] Refers to number of encounters/services used in past 90 days; support services includes nursing service, personal home aide, home meal service, physical/occupational therapy, transportation assistance.

[f] Possible scores on the Inventory of Interpersonal Problems range from 0 to 40, with higher scores indicating greater interpersonal problems.

[g] Possible scores on the Anxiety Sensitivity Index–Revised (ASI-R) range from 0 to 80, with higher scores indicating greater fear about somatic anxiety symptoms.

[h] Possible scores on the Duke social support index range from 7 to 21, with higher scores indicating greater social support.

[i] Possible scores on the Beck homelessness scale range from 0 to 10, with higher scores indicating greater sense of hopelessness.

[j] Possible scores on the General self-efficacy range from 10 to 40, with higher scores indicating better self-efficacy

Table 2

Logistic regression models of the association of patient demographic, clinical, and psychosocial characteristics with antidepressant use without Major Depressive Disorder (MDD).[a]

Characteristic	Adjusted odds ratio	95% CI[b]	P value
Demographic			
Age	1.04	.99– 1.09	.09
Gender			
Male (ref.)	1.0		
Female	1.30	.56– 2.98	.54
Race			
Black (ref.)	1.0		
White	3.11	1.15– 8.43	.03
Other races	1.87	.46– 7.54	.38
Living alone			
No (ref.)	1.0		
Yes	.78	.35– 1.76	.55
Education			
< 12 years	1.0		
= 12 years	1.31	.25– 7.01	.75
> 12 years	1.04	.21– 5.10	.96
Clinical[c]			
SF-12, physical component summary (PCS)	1.02	.99– 1.05	.26
Number of outpatient medical visits	.96	.88– 1.06	.44
Number of support services	.99	.96– 1.01	.38
Psychosocial[c]			
SF-12, Mental Component Summary (MCS)	1.16	1.10– 1.22	<.001

[a] n=231; dependent variable: 0=antidepressant with diagnosis of MDD v. 1=antidepressant without diagnosis of MDD.

[b] CI: confidence interval; model adjusted for site of recruitment.

[c] All clinical and psychosocial variables are continuous. For example, 1 additional point on the MCS was associated with higher odds (1.16) of antidepressant use without MDD present.