Disparities in Antidepressant Adherence in Primary Care: Report From Israel

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Objectives: To evaluate patient and physician characteristics associated with the purchase of antidepressant medication for at least 6 months.

Study Design and Methods: Clalit Health Services is the largest managed care health fund in Israel, a country that uses a universal healthcare system. We randomly sampled 30,000 primary care patients over the age of 22 years. Our analytic sample consisted of those 949 patients who did not purchase antidepressant medication during the last quarter of 2005 and purchased antidepressant medication at least once in 2006. We used multilevel analysis, with whether or not medication was purchased for at least 6 months as an indicator of adherence. Patient and physician characteristics were evaluated as potential predictors.

Results: Only 23% of the sample was classified as adherent. Physician characteristics explained only a small portion of the variance in adherence and, as a result, were not included in multivariate analysis. Patients who did not have a somatic diagnosis, had a depression diagnosis, and were of higher socioeconomic status were more likely to be classified as adherent. Patients who purchased tricyclic antidepressants were less likely to be classified as adherent.

Conclusions: The findings suggest that in a managed care setting, there is high uniformity among physicians. Although physician characteristics explain little of the variability associated with adherence, certain patient characteristics as determined by their physicians (eg, antidepressant drug class, psychiatric diagnosis) do play a role in adherence.

(Am J Manag Care. 2011;17(9):e340-e347)

For author information and disclosures, see end of text.

The public health costs associated with untreated or undertreated depression or anxiety are substantial.[1-4] Primary care providers serve as the main gatekeepers for mental health problems in Israel as in other countries,[5] with both depression and anxiety being most often managed in primary care clinics by primary care providers.[6-8] Fortunately, the past few decades have seen a tremendous improvement in the management of depression and anxiety.[9,10] According to current clinical guidelines, the first line of treatment for the management of either depression or anxiety should be an antidepressant such as a serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor. Older antidepressant medications, such as tricyclic antidepressants (TCAs) or monoamine oxidase inhibitors, may also be indicated for specific populations or as augmentation therapy.[11] Clinical guidelines recommend the use of these agents for a minimum of 6 consecutive months in order to achieve adequate efficacy and stabilize the psychiatric condition.[11-14]

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Despite the documented efficacy of these pharmacologic agents in the management of depression and anxiety, reports of nonadherence are staggering.[15-17] Studies have shown that more than 30% of the patients discontinue their medications within the first 4 weeks of treatment[15,18] and more than 60% discontinue within the first 6 months.[16]

Reasons for nonadherence vary and may relate to patient, drug, and provider characteristics. Studies that have focused primarily on patient characteristics found that individuals of ethnic minority background, younger or older adults,[19] individuals of lower socioeconomic status (SES),[17,18] and those with a personality, substance use,[19] somatization, depression, or anxiety diagnosis[20] are less likely to adhere to their regime. In contrast, others found that carrying a dual depression and anxiety diagnosis results in better adherence.[21] Beliefs concerning psychotropic medications,[22,23] the stigma of mental illness,[24] or a mismatch between patients' preferred and assigned treatment[25] have also been shown to be barriers to adherence. In addition, the side effect profile of a particular drug[26] is of importance, with certain psychotropic drugs resulting in lower adherence than others.[17,18,27]

It has been argued that physicians' knowledge about appropriate treatments, and their ability to establish rapport, assess patients' attitudes, and

In this article
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Published as a Web exclusive
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provide appropriate consultation and information are all essential for establishing appropriate adherence.[28] Hence, as expected, physician characteristics have also shown to be associated with adherence to antidepressant medication. Whereas some found that receiving services from providers with a mental health specialty results in better adherence to psychotropic medication,[21,29] others noted that simply providing patients with educational messages concerning the importance of the medication improves adherence.[30] Using a guideline-concordant follow-up[13] or concurrent psychotherapy[31] was also associated with improved adherence. Nevertheless, several different interventions specifically geared toward increasing adherence to psychotropic medication were found to be largely ineffective,[32] leading researchers to argue for a need for a substantial shift in services at the organizational level in order to improve adherence.[33] Thus, questions have arisen about the provider role in improving adherence to psychotropic medications.

Although informative, the majority of research to date focused either on patient characteristics or on provider characteristics as facilitators of adherence, but did not take both into account simultaneously. In addition, results are still equivocal with regard to the role of primary care physicians as facilitators of adherence to antidepressant medications. Moreover, the majority of research was conducted in countries that do not use a universal healthcare system. Thus, although we know that the prohibitive costs of psychotropic medications may be a potential barrier for some patients,[34] we do not know whether disparities in adherence continue in the absence of financial constraints to the patient.

The present study provided a unique opportunity to evaluate patient and provider characteristics associated with adherence to antidepressant medications in primary care clinics in Israel, a country that uses a universal healthcare system, providing a comprehensive, uniform basket of services that includes psychotropic medications, but not psychotherapy.[35] We used a comprehensive computerized medical registry of Clalit Health Services, the largest healthcare fund in Israel, which insures 53% of the Israeli population and operates as a managed care organization. Under the Israeli system, the primary care provider is considered responsible for all patient healthcare needs. The provider is responsible for the care of a defined number of patients and refers patients for consults as needed. Based on expert recommendations, the primary care provider determines patients' treatment. The database includes information on patient characteristics as well as primary care provider characteristics, thus allowing a distinctive analysis of the actual purchasing behavior of patients instead of relying on self-reports, which have known limitations, in particular regarding sensitive issues.[36]

Based on past research concerning nonadherence to psychotropic medications, we expected both patient and physician characteristics to be associated with nonadherence. Specifically, we expected older and younger individuals as well as ethnic minorities to show higher levels of nonadherence. We also expected those who did not carry a psychiatric diagnosis to have lower levels of adherence. We expected physician specialty to be associated with adherence (ie, patients of physicians who specialize in family medicine would demonstrate higher levels of adherence). This expectation was based on past research, which has shown that family medicine physicians are more likely than internal medicine physicians to manage depression by themselves.[37]

Take-Away Points

Characteristics of patients and physicians at Israel's largest HMO were evaluated as potential predictors of antidepressant adherence (ie, the medication was purchased for 6 months or longer).

- Only 23% of the patient sample was classified as adherent.
- Although physician characteristics explain little of the variability in adherence, certain patient characteristics as determined by their physicians (eg, antidepressant drug class, psychiatric diagnosis) do play a major role in adherence.
- Even in a country that has universal healthcare, population group differences exist and are associated with socioeconomic status.

METHODS

We randomly sampled 30,000 primary care patients over the age of 22 years as of January 2006 from Clalit Health Services' computerized medical registry. Of these patients, 591 died in 2006 and 4446 had incomplete physician data. Thus, the source sample consisted of 25,086 primary care patients. (These are not mutually exclusive; one can have missing values and be dead at same time.) Of these, 1219 had a documented purchase of antidepressant medication in the last quarter of 2005 and were excluded from analysis. Our study group consisted of the 949 patients who did not purchase antidepressant medication during the last quarter of 2005, but did purchase antidepressant medications at least once in 2006.

Measures

Clalit Health Services uses a computerized medical registry that contains both patient and physician data. All physician visits are recorded in this registry and are matched with

pharmacy data using patient and physician unique IDs. For the purpose of the study, data were deidentified to prevent patients' breach of confidentiality.

Adherence to Antidepressant Medications. We extracted data regarding antidepressant (eg, SSRIs, TCAs, other) purchase. Adherence to a new antidepressant regime was defined as no purchases of antidepressant medication in the last quarter of 2005, followed by at least 6 months of purchase starting in 2006. Although purchasing is not necessarily synonymous with adherence as indicated by actual usage of the medication, it does indicate an active decision on the part of the patient and involves a financial investment. In addition, once antidepressants are purchased for 3 months or longer, they are considered a chronic medication by Clalit Health Services. As such, they are listed in all patient-related correspondence. According to the clinical guidelines of Clalit Health Services, discontinuation of a chronic medication is not automatic, but instead requires a discussion between patient and provider.

Patient-Level Predictors

Demographic Information. Age, sex, birth country, and number of years in Israel are listed in the registry based on patients' self-report during their first visit.

The Charlson Comorbidity Index. The Charlson Comorbidity Index (CCI) score uses both the number and seriousness of medical conditions to predict mortality. The CCI includes 19 medical conditions that are weighted on a scale of 1 to 6 based on their 12-month relative mortality risk, with total scores ranging from 0 to 37. Because age was found to be an independent risk factor for mortality, one score is added to the CCI total score for each decade of life over the age of 50 years.[38] Past research has recommended the use of the CCI as a continuous measure rather than a categorical one, in order to refine its ability to distinguish between patients.[39] This score is calculated by Clalit Health Services' medical division for all primary care patients, adjusted for their age.

Somatic Diagnosis. A list of common nonpsychiatric somatic conditions that may indicate a psychiatric condition was constructed by the authors based on the medical literature.[40-44] These conditions include the various types of arthritis pain, head and back pain, abdominal pain, and insomnia. The presence of any of these diagnoses was classified as a somatic diagnosis.

Psychiatric Diagnosis. Mood disorders, anxiety disorders, adjustment disorders, and somatoform disorders were included under this category, using the *International Classification of Diseases, 10th Edition,* codes. We excluded post-traumatic stress disorder, obsessive compulsive disorder, bipolar disorder, and body dysmorphic disorder, as our aim was to focus on psychiatric conditions that are within the mandate of Clalit's primary care physicians,[11,45] rather than psychiatrists.

Medication Type. Medications were classified into 4 groups: SSRIs, TCAs, other, or a combination of at least 2 of these classes.[11]

Socioeconomic Status. Socioeconomic status (low, medium, high) was based on the Israeli Central Bureau of Statistics classification.[46] Although these data are available at the primary care clinic level and not at the patient level, they are considered a good proxy of patient SES.[47,48] The vast majority of patients are registered in neighborhood clinics; thus, the SES of clinics reflects that of the patients' place of residence.

Population Group. Individuals were classified as Arabs or Jews based on Clalit Health Services' classification of primary care clinics into locations that serve at least 70% Israeli Jews versus Israeli Arabs. Although these data are available at the primary care clinic level, they are considered a good proxy of patients' ethnicity, given Israel's highly segregated nature.[49]

Physician-Level Predictors

Physician age, sex, place of birth, number of years in the country, number of years of experience, and specialty (none, family, other) were available from employee records.

Analysis

We first conducted univariate and bivariate analyses. Next, we conducted multilevel analysis, with patient-level data representing the first level of predictors (eg, patient age, sex, SES) and physician-level data (eg, physician age, sex, number of years in the country) representing the second level of predictors. The outcome variable was whether or not antidepressant medications were purchased for at least 6 months starting in 2006 with no purchases in the last quarter of 2005.

The first step of a multilevel analysis used an empty model with physician random effect. This model estimated the outcome per physician rather than per patient. This analysis yielded an intraclass correlation (ICC) score, which ranged between 0% and 100%. The ICC reflected the degree to which patients of the same physician were more similar to one another than to patients of other physicians. Thus, it reflected the proportion of the total variance that was due to differences between physicians. If the ICC is relatively large, a multilevel analysis is justified. On the other hand, if the ICC is relatively low, a multilevel analysis is unjustified, and analysis should take into consideration only patient-level variables (ie, level 1). As a rule of thumb, ICCs of .05, .10, and .15 represent small, medium, and large effect sizes, respectively.[50]

Given the binary nature of the outcome, we used the linear threshold model to obtain an ICC.[51] Following the calculation of ICC (which was less than 1%), logistic analysis was conducted with the purchase of antidepressant medica-

tions for at least 6 months as an outcome. Only significant predictors identified in bivariate analyses were entered into the model.

RESULTS

The final sample consisted primarily of women (63%); most patients were over the age of 46 years (72%). The sample consisted primarily of Jews born in Israel (34.8%) or in East Europe (24%). Most of the sample had no psychiatric diagnosis (69.3%) and most purchased SSRIs (57%). The majority of physicians were female (54.8%) and were born in East Europe or the former Soviet Union (54.8%). Most had a specialty in family medicine (51.4%). See **Table 1**.

Only 23% of the sample was classified as adherent. In bivariate analysis, those purchasing for 6 months or longer were less likely to have a somatic diagnosis, more likely to have a psychiatric diagnosis, and more likely to purchase SSRIs or combined psychotropics. They also were more likely to be of higher SES. See Table 1.

Results of logistic regression analysis revealed that those who did not have a somatic diagnosis, had a diagnosis of depression, and were of higher SES were more likely to be classified as adherent. In addition, compared with those purchasing SSRIs, those purchasing TCAs were less likely to be classified as adherent. See **Table 2**.

DISCUSSION

The present study evaluates patient and provider characteristics associated with adherence to antidepressant medications. This study is unique for several reasons. First, we evaluated patient and provider characteristics simultaneously in an attempt to identify their exclusive roles in adherence. Second, we used a representative sample of patients of the largest managed care organization in Israel, a country that uses a universal healthcare system, thus eliminating financial barriers to patients. As a result, we could evaluate disparities, which may stem from reasons other than patients' financial status. Third, we evaluated purchasing data rather than self-report data concerning nonadherence, and thus were more likely to get an accurate estimation of nonadherence. Finally, the focus on all patients who purchased antidepressant medications rather than only on those diagnosed with depression or anxiety was valuable, given the tendency to underdocument mental illness in primary care.[7]

The most notable finding of the present study is that only 23% of patients purchasing antidepressant medications were classified as adherent. This figure likely represents an underestimate of nonadherence, given the fact that patients who were prescribed antidepressant medications, but for some reason did not purchase the medications even once, were not included in our analysis. Findings suggest that even in a country that uses a universal healthcare system, nonadherence is substantial.

Our findings show that those patients who had a documented depression diagnosis were more likely to adhere to their medication regime, whereas those with a somatic diagnosis were less likely to adhere. Possibly, when a psychiatric diagnosis such as depression is documented in a patient's medical record, the patient tends to agree with the psychiatric diagnosis and thus is also more likely to agree with psychiatric treatment. On the other hand, a somatic diagnosis likely is assigned to patients who are less accepting or are less willing to view their problems as psychiatric in nature and thus also are less accepting of psychotropic medications.

An important finding of the present study is the fact that physician characteristics play only a minor role in patients' adherence. Whereas this study contradicts some research that argued for the important role of the provider,[29,30] it does support other studies that found the provider's role to be of lesser importance.[33] This finding may be explained in several ways. First, we focused on purchasing behaviors and not on prescription patterns. Thus, most of the variability associated with purchasing was expected to be associated with patient characteristics rather than provider characteristics. In addition, some patient characteristics that have shown to be associated with adherence are actually determined by the provider (eg, chart diagnosis, class of medication purchased). Hence, providers likely do play an indirect role in patients' purchasing patterns. Finally, lack of variance between physicians may be accounted for by the organizational setting—all worked in a managed care organization that uses specific guidelines for the management of mental illness.

A striking finding of this study is the fact that individuals of higher SES were more likely to purchase their medications for at least 6 months. Although SES may serve as a proxy of education as well as of more accepting attitudes toward mental health treatment, it is still possible that financial constraints limit adherence to antidepressant medications in individuals of lower SES. This finding is particularly surprising given the fact that the healthcare system in Israel is designed to ensure universal access to services, including antidepressant medications.

Finally, our study showed that patients were less likely to purchase TCAs than SSRIs for a period of 6 months or longer. This finding could be explained by the side effect profile of the TCAs and is consistent with findings demonstrating a

Table 1. Characteristics of Patients Who Purchased Antidepressant Medications

Characteristics	Total (n = 949)	Purchased for Fewer Than 6 Consecutive Months (n = 722)	Purchased for at Least 6 Consecutive Months (n = 219)	*P*
Patient				
Female	600 (63.2%)	459 (63.0%)	141 (64.1%)	.41
Age, y				.31
22-45	265 (27.9%)	212 (29.1%)	53 (24.1%)	
46-65	346 (36.5%)	264 (36.2%)	82 (37.3%)	
>65	338 (35.6%)	253 (34.7%)	85 (38.6%)	
Population group				.07
Jews born in Israel	330 (34.8%)	253 (35.4%)	77 (35.2%)	
Arabs	79 (8.3%)	65 (9.1%)	14 (6.4%)	
Jews born in Eastern Europe or the Former Soviet Union	228 (24.0%)	173 (24.2%)	55 (25.1%)	
Jews born in Europe or America	52 (5.5%)	32 (4.5%)	20 (9.2%)	
Jews born in Asia or Africa	244 (25.7%)	191 (26.8%)	53 (24.2%)	
Years in Israel				.35
>10	910 (95.9%)	696 (96.4%)	214 (97.3%)	
Charlson Comorbidity Index score, mean (SD)	2.8 (2.6)	2.85 (2.5)	2.98 (2.6)	.51
Somatic diagnosis	555 (58.5%)	446 (61.2%)	109 (49.5%)	<.01
Psychiatric diagnosis				<.001
None	658 (69.3%)	534 (73.3%)	124 (56.4%)	
Other	9 (.9%)	6 (.8%)	3 (1.4%)	
Depression	157 (16.5%)	102 (14.0%)	55 (25.0%)	
Anxiety	48 (5.1%)	34 (4.7%)	14 (6.4%)	
Combined	77 (8.1%)	53 (7.3%)	24 (10.9%)	
Type of drug				<.001
Combined	83 (8.7%)	56 (7.7%)	27 (12.3%)	
TCA	270 (28.5%)	243 (33.3%)	27 (12.3%)	
SSRI	542 (57.1%)	389 (53.4%)	153 (69.5%)	
Other	54 (5.7%)	41 (5.6%)	13 (5.9%)	
Socioeconomic status				.002
Low	379 (39.9%)	313 (43.4%)	66 (30.1%)	
Medium	396 (41.7%)	291 (40.3%)	105 (47.9%)	
High	166 (17.5%)	118 (16.3%)	48 (21.9%)	
Physician (n = 640)				
Female	351 (54.8%)			
Age, mean (SD)	49.3 (7.3)			
Birth country				
Israel	214 (33.4%)			
Eastern Europe or the Former Soviet Union	351 (54.8%)			
Europe or America	50 (7.8%)			
Asia or Africa	21 (3.3%)			
No. of years in Israel, mean (SD)	30.6 (15.7)			
No. of years of experience, mean (SD)	15.7 (7.)			
Specialty				
None	267 (41.7%)			
Family	329 (51.4%)			
Other	44 (6.9%)			

SSRI indicates selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

tendency to use SSRIs in preference to these drugs.[52] It may also be due to the fact that TCAs are also used for the management of other conditions such as pain which may justify a shorter period of use.[53]

The present study has some limitations that should be noted. First, we evaluated purchasing data, but not actual use. Although our method is likely more reliable than solely relying on self-report, purchasing data may still represent an underestimation of adherence as our data did not include patients who may have been prescribed medication but never filled the prescription or patients who purchased medication but failed to take it as prescribed. It is, however, important to note that the purchase of antidepressant medications does indicate an active decision on the part of the patient and involves a financial investment. In addition, once antidepressants have been purchased for 3 months or longer, they are considered a chronic medication. As such, they are listed in all patient-related correspondence. Discontinuation of a chronic medication is not automatic, but instead requires a discussion between patient and provider. In addition, we were unable to distinguish between continuous purchase and sporadic purchase over the study period, because under the current system, patients are allowed to purchase medications for a period of several months in advance. Second, we did not specifically focus on patients diagnosed with depression and/or anxiety, as was the case in the majority of past research. Thus, it is possible that some patients purchased these medications for reasons other than mental illness, such as pain or smoking cessation. Nevertheless, regardless of indication, antidepressant medications should be used for at least 6 months in order to ensure efficacy.[11] Third, we did not evaluate reasons for discontinuation. Hence, it is likely that some patients discontinued treatment because of medication side effects, whereas others discontinued treatment because of the stigma associated with the medication. Finally, this is a cross-sectional study that did not allow assumptions about cause and effect.

Nevertheless, this study has multiple strengths that outweigh its limitations. Our findings suggest that only 23% of all new patients who purchased antidepressant medications in 2006 did so according to clinical guidelines. Our findings further demonstrate that although physician characteristics explain little in terms of the variability associated with adherence, patient characteristics that were determined by their physicians (eg, presence or absence of a chart diagnosis) do play a major role in adherence. Finally, the findings suggest high uniformity among physicians. This may be the result of Clalit's attempt to direct clinical decisions by disseminating clinical guidelines as well as other administrative measures to ensure adequate care of mental health conditions, which are expected to result in reduced healthcare costs.

Table 2. Results of Logistic Regression Analysis to Predict Medication Purchase for at Least 6 Months[a]

Patient Characteristics	OR	95% CI
Somatic diagnosis		
None	—	—
Yes	0.68	0.49-0.95
Psychiatric diagnosis		
None	—	—
Other	1.52	0.36-6.38
Depression	1.59	1.19-2.67
Anxiety	1.55	0.79-3.05
Combined	1.69	0.98-2.90
Type of drug		
SSRI	—	—
TCA	0.36	0.22-0.57
Combined	1.29	0.77-2.16
Other	0.70	0.35-1.39
Socioeconomic status		
Low	—	—
Medium	1.68	1.17-2.40
High	1.80	1.15-2.81

CI indicates confidence interval; OR, odds ratio; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.
[a]Logistic regression χ^2 (10) = 68.2, P <.001.

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Funding Source: This study was funded by Clalit Health Services.

Author Disclosures: The authors (LA, RG, AY, EF, RDB, MG) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (LA, RG, AY, RDB, MG); acquisition of data (AY, EF, RDB, MG); analysis and interpretation of data (LA, RG, EF, MG); drafting of the manuscript (LA, MG); critical revision of the manuscript for important intellectual content (LA, RG, AY, MG); statistical analysis (LA); provision of study materials or patients (MG); obtaining funding (LA, RG, AY, MG); administrative, technical, or logistic support (EF, RDB, MG); and supervision (MG).

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