Does Patient Adherence to Antidepressant Medication Actually Vary Between Physicians?

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ABSTRACT

Objective: Previous research and improvement efforts have presumed that patients' nonadherence to antidepressant medication reflects physicians' quality of care. We used population-based health records to examine whether adherence to antidepressant medication actually varies between prescribing physicians.

Methods: Electronic health records and insurance claims data from 5 integrated health systems in Washington, Idaho, Minnesota, Colorado, Hawaii, and California were used to identify 150,318 adults starting new episodes of antidepressant treatment for depression between January 1, 2010, and December 31, 2012. Early adherence was defined as any refill or dispensing of antidepressant medication in the 180 days following an initial antidepressant prescription. Patient-level demographic and clinical characteristics potentially associated with adherence were identified from health system records.

Results: Average probability of early adherence was 82% for psychiatrists and 74% for primary care physicians. Among individual physicians, the range of raw or unadjusted early adherence rates (5th to 95th percentiles) was from 33% to 100% for psychiatrists and from 0% to 100% for primary care physicians. After accounting for sampling variation and case mix differences, the range of adjusted early adherence rates (5th to 95th percentiles) was from 72% to 78% for psychiatrists and from 64% to 69% for primary care physicians.

Conclusions: After accounting for sampling variation and case mix differences, early adherence to antidepressant medication varies minimally among prescribing physicians. Early discontinuation of antidepressant treatment is not an appropriate measure of individual physician performance, and efforts to improve adherence should emphasize system-level interventions rather than the performance of individual physicians.

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Premature discontinuation of antidepressant medication has long been identified as an important gap in depression treatment.[1–3] More than one-third of outpatients starting antidepressant medication treatment for depression do not refill the initial prescription,[4,5] and fewer than half continue medication for the recommended minimum 4 to 6 months.[6] Despite repeated identification of this gap, rates of premature antidepressant discontinuation have improved only slightly over the last 15 years.[6]

Early adherence to antidepressant treatment has also been identified as a priority area for quality assessment and quality improvement. Receipt of adequate acute-phase medication treatment is one of the 3 National Committee for Quality Assurance/Healthcare Effectiveness Data and Information Set (NCQA/HEDIS) measures for comparing quality of care across health plans.[6] Using that measure, early adherence rates are typically 65%–70% for patients insured by commercial or Medicare health plans and 50% for patients insured by Medicaid plans.[6]

Previous research and practice guidelines have presumed that early adherence to antidepressant medication reflects quality of care provided by the prescribing physician.[1,7–14] For example, previous research has found associations between patients' antidepressant adherence and specific aspects of the physician-patient relationship, including patients' perception of the treatment relationship,[11,12] physicians' communication of positive outcome expectations,[15] and physicians' provision of appropriate education regarding expected side effects and delayed therapeutic effect of antidepressants.[1,10,13,14]

Prior to accepting that a patient's antidepressant adherence accurately reflects an individual physician's performance, we must consider alternative explanations. A simple patient-level correlation between patients' adherence and patients' reported experience of care does not necessarily imply a causal relationship. A first step in evaluating a potential causal relationship is to determine whether patients' adherence actually varies among prescribing physicians. Apparent differences in physician performance could reflect either random variation due to small numbers of patients per physician (sampling variance) or bias due to differences in patient populations (case mix).

With regard to sampling variation, most previous research examining physicians' influence on antidepressant adherence has not examined whether variation among physicians in average adherence actually exceeds that expected by chance. Nearly all previous studies[1,7–10,12–14] lacked the sample size (in numbers of physicians and/or number of patients per physician) to address

Clinical Points

- Early discontinuation of antidepressant medication is an important and persistent gap in care for depression.
- After accounting for differences in patient characteristics, rates of early medication differ only minimally between individual physicians—both psychiatrists and primary care physicians.
- Patients' adherence to antidepressant medication is not a valid measure of individual physician performance. Efforts to improve antidepressant adherence should focus more on system-level interventions (such as collaborative care) than on targeting "low-performing" physicians.

this question. The limited data available regarding this question[16] suggest that most observed variation among physicians is likely random.

With regard to case mix differences, we have previously reported that early adherence to antidepressant medication is strongly related to patient race/ethnicity (highest in non-Hispanic whites) and increases moderately with patient age.[5] Apparent differences between health systems in rates of antidepressant adherence are largely explained by differences in patient characteristics.[4] Accounting for differences in racial and ethnic distribution of patient populations largely eliminated observed differences between health systems. No previous research has examined this case mix bias question regarding differences in antidepressant adherence rates among physicians.

Here, we used data from 5 large health systems to examine variation among physicians in patients' early adherence to antidepressant treatment. We examined the degree to which initially observed differences among physicians in patients' early antidepressant adherence rates are or are not explained by either sampling variation (ie, small sample sizes per physician) or case mix bias (demographic or preexisting clinical differences in patient panels served by different physicians). We estimated the true variation among physicians as the variability remaining after accounting for sampling variation and case mix differences.

METHODS

Data are drawn from the Mental Health Research Network (MHRN), a consortium of public-domain research centers affiliated with large not-for-profit integrated health care systems. Each of these systems provides comprehensive care (including general medical and specialty mental health care) to a defined population of members or patients. Five MHRN health care systems contributing data to this study include Group Health Cooperative, HealthPartners, Kaiser Permanente Colorado, Kaiser Permanente Hawaii, and Kaiser Permanente Southern California. These 5 systems serve a combined population of approximately 5 million members/patients in the states of Washington, Idaho, Minnesota, Colorado, Hawaii, and California. Members are enrolled through employer-sponsored insurance, individual insurance plans, and capitated Medicare and Medicaid programs and are generally representative of each system's service area population.[4,17,18] In 2011, 10.2% of all adult members of these health care systems filled 1 or more antidepressant prescriptions, similar to national rates.[19] Using NCQA/HEDIS measures of adherence to acute-phase antidepressant treatment, average adherence in these health systems is modestly higher than in other insured populations.[20] Across these systems, electronic medical records, insurance claims, and other administrative data systems have been organized in a Virtual Data Warehouse to facilitate population-based research.[21] Responsible institutional review boards and privacy boards for each health system approved all study procedures and granted waivers of consent for this research use of deidentified health records data.

The sample included all adult members filling a new outpatient antidepressant prescription between January 1, 2010, and December 31, 2012. Eligible antidepressant medications included all drugs approved by the US Food and Drug Administration for treatment of major depression, excluding trazodone (more often prescribed for insomnia). A list of included medications and corresponding National Drug Codes is available at https://github.com/mhresearchnetwork. A new episode of antidepressant treatment was defined as a filled antidepressant prescription preceded by an interval of at least 270 days with no antidepressant dispensing. While this interval is longer than the "washout period" used to define new antidepressant treatment episodes in NCQA/HEDIS measures[3] and in some of our previous research,[22,23] it is supported by findings in these health systems regarding timing of refills for patients receiving ongoing antidepressant treatment.[24] The study sample was limited to those with a recorded diagnosis of any depressive disorder (*ICD-9* diagnosis 296.2, 296.3, 300.4, or 311) in the interval starting 90 days before the index prescription and ending 15 days after. In these health care systems, approximately 60% of adults receiving antidepressant treatment have a recorded diagnosis of depressive disorder,[25] with approximately 15% receiving some other mental health diagnosis and 25% having no recorded mental health diagnosis. Patients with any diagnosis of bipolar disorder or psychotic disorder prior to the index prescription were excluded. To ensure availability of records data to assess inclusion and exclusion criteria, the sample was limited to those continuously enrolled in the participating health care systems for at least 270 days prior to the index prescription. Among patients contributing multiple episodes of treatment during the study period, a single episode was selected at random. To ensure adequate capture of refill prescriptions, the analytic sample only included those enrolled in each health system for at least 180 days following the initial prescription.

Electronic medical records and health care system administrative databases were used to identify the specialty of the prescribing physician and the following patient characteristics: sex, age at time of the eligible first prescription, race/ethnicity, neighborhood income, neighborhood educational attainment, prior history of antidepressant

treatment, concomitant receipt of psychotherapy, and co-occurring general medical diagnoses included in the Charlson Comorbidity Index.[26]

Medical records and insurance claims data were used to identify all filled antidepressant prescriptions (for the originally prescribed medication or any other antidepressant) following the index prescription. We defined early antidepressant nonadherence as failure to fill any subsequent antidepressant prescription within 180 days of the index prescription. This differs from the NCQA/HEDIS definition of "adequate acute-phase treatment." The NCQA/HEDIS measure requires receipt of at least 84 days' supply of antidepressant medication over 90 days, including the index prescription and any refills. The increasing use of 90- or 100-day initial antidepressant prescriptions, however, creates problems with use of the NCQA/HEDIS 84-day standard.[27] A patient receiving an initial 90-day prescription would be classified by the NCQA/HEDIS measure as receiving adequate treatment even if that initial prescription was never refilled. Such a patient would be classified as nonadherent by our measure unless the patient refilled that initial prescription.

Descriptive analyses examined the distribution of patient characteristics, the number of new antidepressant treatment episodes per physician during the study period, and the proportion of episodes for each physician in which patients were classified as adherent (ie, the observed physician-level average adherence rate).

To evaluate variability among physicians in probability of adherence, a logistic random effects model[28] was used to model probability of adherence at the patient level, including 2 random effects at the physician level (1 for primary care physicians and 1 for psychiatrists). Random effects terms presumed a Gaussian distribution. An initial model (not accounting for case mix differences) included physician specialty as a fixed effect and the 2 random effects distributions. A subsequent model (accounting for case mix differences) included fixed effect adjustment for baseline patient-level characteristics (age, sex, race/ethnicity, neighborhood income, neighborhood educational attainment, and Charlson Comorbidity Index score, prior use of antidepressant medication, and concurrent receipt of psychotherapy). The marginal log-odds ratio of adherence was calculated for physicians, conditional on physician specialty. Model-based estimates were transformed via an inverse logit link to produce a distribution of physician level random effects expressed as physician level adherence rates. This 2-step approach allows for shrinkage of physician-level adherence probabilities due to small sample sizes of patients per physician and adjustment of those estimated probabilities for differences in patient characteristics between physician panels.

RESULTS

Health care system records identified 172,015 new episodes of antidepressant treatment for depression during the study period. Restriction to patients enrolled in the participating health system for at least 180 days following the index prescription reduced this sample to 156,283. Restriction to a single randomly selected episode per patient further reduced this sample to 150,318. In this sample of treatment episodes, initial prescriptions were from psychiatrists in 36,615 cases and primary care physicians in 113,703 cases. Baseline demographic and clinical characteristics for psychiatry and primary care treatment episodes are shown in Table 1. As previously reported regarding this sample,[5] probability of early adherence was much higher in non-Hispanic whites, moderately higher among patients treated by psychiatrists than by general medical physicians, and slightly higher among older patients.

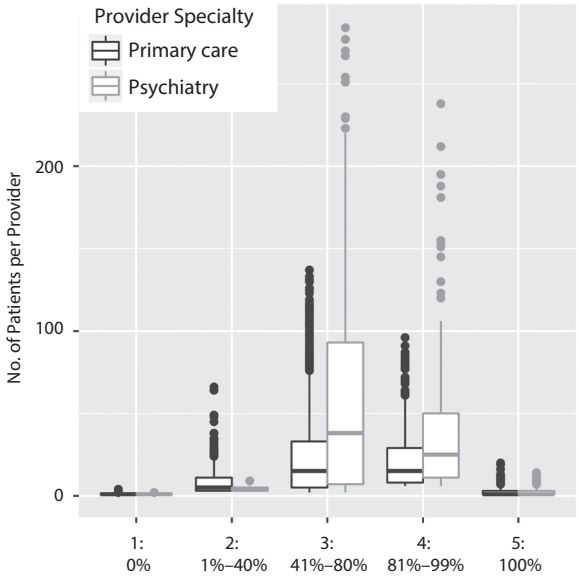
Overall rates of early antidepressant adherence (ie, refill or dispensing of an antidepressant prescription within 180 days of the index prescription) were 82% for psychiatrists and 74% for primary care physicians. For individual physicians, adherence rates ranged from 0% to 100% among both psychiatrists and primary care physicians.

The number of patients per physician ranged from 1 to 294 for psychiatrists and from 1 to 119 for primary care

Table 1. Characteristics of Patients Starting Episodes of Antidepressant Treatment With Psychiatrists and Primary Care Physicians

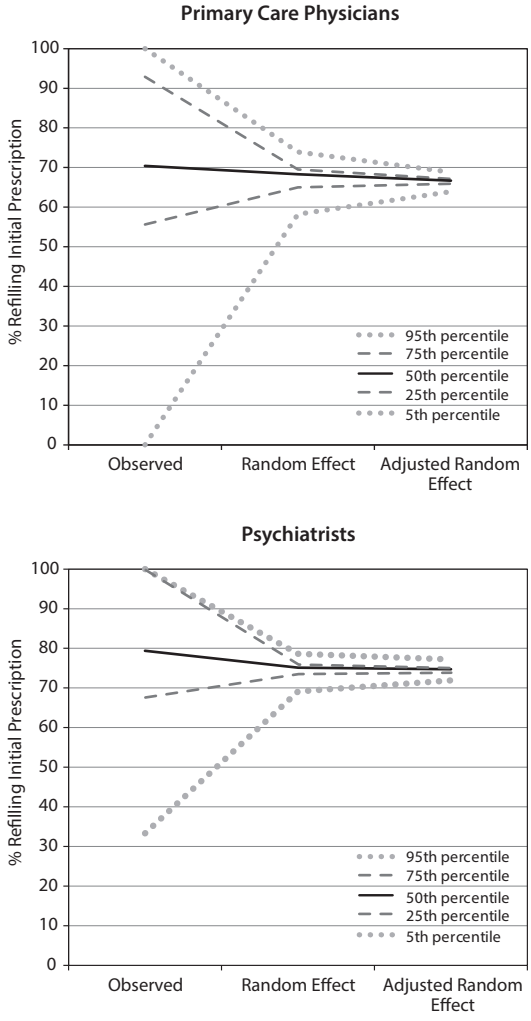
Characteristic	Psychiatry, n (%)	Primary Care, n (%)
Age		
18–29 y	9,527 (26)	15,857 (14)
30–44 y	11,775 (32)	27,965 (25)
45–59 y	10,184 (28)	34,950 (31)
60–74 y	4,171 (11)	21,983 (19)
75+ y	987 (3)	12,919 (11)
Gender		
Female	23,984 (65)	79,296 (70)
Male	12,660 (35)	34,378 (30)
Race/ethnicity		
Non-Hispanic white	17,539 (48)	58,404 (51)
Asian	2,052 (6)	5,274 (5)
Non-Hispanic black	3,780 (10)	7,213 (6)
Hispanic	9,909 (27)	28,137 (25)
Native Hawaiian/Pacific Islander	441 (1)	1,133 (1)
Native American/Alaskan native	221 (1)	739 (1)
Mixed race, other or unknown	2,702 (7)	12,774 (11)
Neighborhood annual income		
≥ $25,000	24,921 (68)	85,131 (75)
< $25,000	11,723 (32)	28,543 (25)
Neighborhood education		
≥ 25% college graduates	11,774 (32)	41,561 (37)
< 25% college graduates	24,870 (68)	72,113 (63)
Charlson Comorbidity Index		
0	31,140 (85)	90,344 (79)
1	3,519 (10)	11,619 (10)
≥ 2	1,985 (5)	11,711 (10)
Prior antidepressant use		
No	22,280 (61)	71,619 (63)
Yes	14,364 (39)	42,055 (37)
Also receiving psychotherapy		
No	19,568 (53)	98,955 (87)
Yes	17,076 (47)	14,719 (13)
Initial antidepressant prescribed		
Citalopram	8,723 (24)	34,443 (30)
Fluoxetine	9,766 (27)	36,038 (32)
Sertraline	7,825 (21)	14,513 (13)
Bupropion	4,785 (13)	9,942 (9)
Other	5,545 (15)	18,738 (16)

Figure 1. Distribution of Number of Patients per Provider, Stratified by Provider-Level Rate of Initial Prescription Refill and Provider Specialty[a]



[a]Boxes show range from range from 25th to 75th percentiles (with bar for median). Lines show range from 5th to 95th percentiles.

Figure 2. Variation Among Physicians in Refill Rates Before and After Accounting for Sample Size and Differences in Patient Characteristics



physicians, with respective means of 36 and 18 patients per physician. Figure 1 shows the distribution of the number of episodes for each physician, stratified by physician-level adherence rate and physician specialty. Physicians with extremely low (0%) or extremely high (100%) adherence rates typically prescribed for fewer than 10 treatment episodes. Physicians with moderately low (1%–40%) or moderately high (80%–99%) adherence rates typically prescribed for fewer than 20 episodes. In contrast, physicians with more typical or modal adherence rates (40%–80%) typically prescribed to more than 25 patients, and often more than 50.

Figure 2 displays percentiles from the distribution of physician-level adherence rates, accounting for both sampling variation (small number of patients per physician) and potential biases due to case mix differences (differences in baseline patient characteristics between physicians). As illustrated by the left portion of each graph, the observed raw physician-level adherence rates vary widely—with the range between the 5th and 95th percentile physicians equaling approximately 67% for psychiatrists and 100% for primary care physicians. As shown in the middle portion of each graph, the physician-level random effect estimates from the unadjusted model (accounting for sampling variation but not for case mix differences) had a much smaller variance. The range between 5th and 95th percentiles was approximately 9% for psychiatrists and 16% for primary care physicians. Added adjustment for differences in patient characteristics (shown at the right of each graph) further reduced this variation, with the range between 5th and 95th percentiles equaling approximately 5% for both psychiatrists and primary care physicians.

Sensitivity analyses examined variation in adherence using the HEDIS standard for adequate acute-phase treatment (ie, receiving at least 84 days of medication). After excluding 25,871 (17%) episodes with initial prescriptions covering 84 days or more, the range between 5th and 95th percentiles on this measure was approximately 8% for psychiatrists and 7% for primary care physicians.

DISCUSSION

Among patients starting antidepressant treatment in large integrated health systems, true variation between physicians in probability of patients' early adherence is quite small. While initially observed adherence rates varied widely among physicians, an exceptionally high or exceptionally low physician-level adherence rate was typically associated with an exceptionally small number of patients treated for depression in a physician's caseload. Appropriately accounting for these small sample sizes and

for differences in patient characteristics across physicians indicated that the "true" variability in adherence among physicians was actually quite small for both psychiatrists and primary care physicians. Initial observations of exceptionally good or exceptionally poor performance by individual physicians were largely due to sampling variation, with a smaller additional contribution due to case mix bias.

We should acknowledge some limitations of these data. Records were drawn from large integrated health systems, and most physicians practiced in group-model clinics supported by electronic health records and evidence-based treatment guidelines. Participating systems also facilitated refill ordering via online patient portals and automated telephone ordering systems. We might observe lower average adherence rates and greater variability in adherence among physicians practicing in less homogeneous or less structured settings, especially those outside the United States or those serving the most disadvantaged patients. These findings should be replicated in less structured practice settings before assuming generalizability. Our data reflect medication refills rather than actual medication use, so they may not accurately reflect partial adherence such as intermittent use or use at a dose less than prescribed. Nevertheless, refill-based measures are widely used as indicators of depression treatment quality[6] and show good agreement with adherence measured by anonymous measurement of serum levels.[29] In some cases, patients may have discontinued medication treatment on the advice of the prescribing physician, but our data do not allow us to distinguish planned or recommended discontinuation from unplanned discontinuation. Records available for this study did not include data regarding patients' reasons for discontinuing medication, but previous research indicates that adverse effects are the most commonly reported reason for discontinuation.

Physician caseloads did differ in characteristics related to antidepressant adherence, such as age and race/ethnicity. Adjusting for these differences did reduce initially observed differences between physicians in patient adherence rates. Our data, however, included only relatively simple measures readily available from electronic health records. Adjusting for additional patient characteristics not included in our data might further reduce our estimates of true variability among physicians in patients' adherence to antidepressants. We lack data regarding physician characteristics (training, age, time in practice) that might further account for initially observed differences between physicians.

Our data do not exclude the possibility that physician-patient interactions may have important effects on the likelihood that patients will continue using antidepressant medication. These findings do, however, suggest that any stable or consistent differences between physicians in ability to promote antidepressant adherence are quite small—at least within large integrated health systems. This result has important implications for both quality measurement and quality improvement.

With regard to quality measurement, these data suggest that early adherence to antidepressant treatment is not an appropriate measure of individual physician performance within large health systems. Observed differences likely reflect sampling variation and differences between physicians in patient characteristics (such as age or race/ethnicity) that are associated with antidepressant adherence. After accounting for these factors, estimated true differences between physicians performing at the highest and lowest extremes of performance are quite small. While pay-for-performance has potential for improving quality of depression care,[30] incentives should be tied to specific physician behaviors (such as systematic follow-up) shown to improve outcomes.[31]

With regard to quality improvement, these findings should not be interpreted as evidence that early discontinuation of antidepressant medication is not an important clinical and public health problem. Outcomes of antidepressant treatment in community practice fall far short of those seen in controlled trials,[23] and early discontinuation of medication is a major contributor to that gap. Our findings do indicate that true differences in physicians' ability to encourage or promote antidepressant adherence are quite small. This finding is consistent with previous research finding that educational or training interventions intended to improve practices of "low performing" physicians do not appear to improve quality or patient outcomes.[32,33] Other research, however, has demonstrated that system-level approaches can significantly improve both antidepressant adherence and outcomes of depression treatment.[34–36] Key elements of those effective system-level or collaborative care interventions include systematic monitoring of adherence and clinical outcomes, measurement-based adjustment of treatment, and systematic outreach to those who discontinue treatment prematurely. This distinction between provider-focused and system-level interventions is consistent with the broader recognition that important gaps in quality of care for chronic illness more often reflect poorly designed systems of care than failures of individual providers.[37]

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