Selective Contracting and Patient Outcomes: A Case Study of Formulary Restrictions for Selective Serotonin Reuptake Inhibitor Antidepressants

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Abstract

Objectives: **Many health maintenance organizations (HMOs) have selected 1 or 2 selective serotonin reuptake inhibitors (SSRIs) as their preferred drug for treating depression. This study investigated the effect of "single-drug" formulary restrictions on the likelihood of drug therapy completion for new patients, controlling for initial SSRIs used and other factors.**

Methods: **Prescription drug and medical record data for 187 patients who were newly prescribed SSRIs were retrieved from a single California group practice consisting of 22 board-certified primary care physicians. The group practice contracted with 2 independent practice association-model HMOs with different SSRI formulary restrictions. A multivariate analysis of drug therapy completion was conducted and 2 sensitivity analyses were performed. Completed therapy was based on the patient having achieved 6 months of uninterrupted therapy at a minimum therapeutic dose.**

Results: **Patients from the HMO with a single preferred SSRI (paroxetine) were 80% less likely to complete therapy than were patients from the HMO with 2 preferred SSRIs (fluoxetine and paroxetine) (odds ratio [OR] = 0.200, 95% confidence interval [CI] = 0.083-0.430). This formulary effect was independent of the initial drug used to treat the patient. Drug selection was also found to affect completion rates. Patients treated with sertraline were significantly less likely to complete therapy than were patients treated with fluoxetine (OR = 0.319, 95% CI = 0.105-0.968). Similar results were found for patients taking paroxetine relative to fluoxetine (OR = 0.357, 95% CI = 0.149-0.853).**

Conclusion: **These results suggest that the use of single-product formularies may have unintended consequences on patient completion rates, independent of whether or not the most effective product is selected for preferred formulary status.**

(Am J Manag Care 1999;5:1133-1142)

For editorial comment, please see page 1202.

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Selective contracting is a widely accepted tool in the managed care environment for obtaining price discounts from such diverse medical care providers as hospitals and prescription drug manufacturers. Most clinicians and healthcare executives agree, in principle, that care must be taken to balance price with quality of care, and to provide clinicians with a sufficient range of alternatives with which to tailor treatment to the risk characteristics

of the individual patient. Reliable data on quality of care based on patient outcomes are limited, while data on the potential adverse patient outcomes associated with "single-provider" contracts are nonexistent.

The purpose of this research is to investigate if "single-provider" contracts adversely affect patient outcomes within the context of drug formularies. Horn and colleagues found that restrictive formularies in managed care were associated with higher per capita healthcare costs.[1] The causal relationship between the restrictiveness of the formulary and cost in this study, however, was tentative because of the aggregate level of the data. In contrast, our study focused on a single disease state, depression, for which several alternative selective serotonin reuptake inhibitor (SSRI) antidepressants were competing for market share.

Two specific research questions are posed for analysis. First, do formulary restrictions that limit patient access to a single preferred SSRI adversely affect the likelihood that a patient will complete an adequate course of antidepressant therapy in terms of dose and duration? Second, is there any evidence that the likelihood that a patient will complete therapy differs significantly across the alternative SSRIs? Our focus on therapy completion assumes that an adequate course of antidepressant therapy in terms of dose and duration is a valid measure of treatment effectiveness. McCombs et al[2] estimated that completed antidepressant therapy was associated with a reduction in total posttreatment cost of nearly $1500 per patient in the first year. Thompson et al[3] found that depressed patients who discontinued therapy early had higher costs than patients with 3 months of continuous use. Completion of therapy has also been found to reduce the likelihood of relapse or recurrence of the depressive episode.[4-6]

The correlation between completed drug therapy and reductions in future healthcare costs and relapse and recurrence rates is not unexpected. Depression is a common and debilitating illness in the noninstitutionalized population. The 6-month and lifetime prevalences of current depressive disorders were estimated at 1% to 3% and 5.8% in the general population, respectively, based on data from the Epidemiologic Catchment Area Study.[7,8] The total annual cost of depression has been estimated at $43 billion in 1990 dollars, of which $12.4 billion is devoted to direct medical care costs.[9] Depression is a serious disorder, which interferes more with social and physical functioning than do common chronic physical illnesses, such as hypertension, diabetes, arthritis, and back pain.[10-13] It is associated with significant morbidity and a high mortality rate from suicide.[14,15]

Nearly 74% of Americans who seek help for depression or symptoms of depression get that care from primary care physicians rather than from a mental health professional.[16] The treatment of depression in the primary care setting has been shown to be ineffective because of either missed diagnosis or failure by patients to complete an adequate course of drug therapy. More importantly, ineffective treatment has been found to result in high levels of healthcare use.[2,3,12,16,17] With appropriate treatment, about two thirds of patients with major depression respond dramatically to acute antidepressant therapy.[18] Moreover, completion of an appropriate course of antidepressant drug therapy has been found to result in significant cost savings in direct healthcare costs.[2]

Serotonin reuptake inhibitors offer clinicians a therapeutic alternative to the traditional tricyclic and heterocyclic antidepressants in the treatment of depression.[19] The advent of SSRIs, however, has resulted in rapidly increasing cost of drug therapy for depression. SSRIs have become the single most expensive drug class for many pharmacy benefit management companies.[20] Johnson, McFarland, and Nichols[21] report an 8-fold increase in the use of antidepressants and a 10-fold increase in costs for this class of medications in the Northwest Region of Kaiser Permanente during the 8-year period following the introduction of the SSRIs in 1987.

These rapidly increasing costs have tempted health maintenance organizations (HMOs) and other managed care organizations to reduce drug costs for the SSRIs through selective contracting that, in some plans, has resulted in the selection of a single "preferred" SSRI. Unfortunately, the selection of a preferred product is often based on drug costs alone, without taking other clinical and economic factors into account.

···METHODS ···

Study Site

The site for this study was the Community Medical Group (CMG) of the West Valley (California), a group practice that consisted of 22 primary care physicians (PCPs). Each physician was board certified in either family medicine or internal medicine and was responsible for providing primary mental health services. CMG contracted with 2 independent practice association (IPA)-model HMOs to provide care for the

HMOs' members. These contracts included shared risk provisions for the patients' pharmacy costs.

Each HMO specified its own drug formulary with regard to SSRI antidepressants. The preferred SSRI for the "single-product" plan (denoted as Plan A) was paroxetine, while the preferred SSRIs for the "multiple-product" plan (Plan B) were paroxetine and fluoxetine. A nonformulary SSRI, such as sertraline, could be used if a prior-authorization form was filled out by the prescribing physician and approved by the plan.

CMG physicians were aware that the SSRIs were a major factor in determining total drug expenditures for plan members enrolled with the medical group. In an effort to minimize its risk of exceeding contractual drug expenditure limits, CMG instructed its physicians to prescribe paroxetine whenever possible due to its lower acquisition costs relative to fluoxetine and sertraline.

Patients in both HMOs had variable copayments for prescription drugs, PCP visits, and specialty physician visits, including psychiatric visits, depending on the benefits package specified in their group policy. However, CMG physicians had no financial barriers to referring patients to a psychiatrist or for psychological counseling under the benefit package options offered by either plan.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were designed to identify patients experiencing a new treatment episode for depression. Specifically, patient records were selected from the medical group computerized pharmacy database if:

- The patient maintained continuous membership in 1 of the 2 study HMOs from 1/1/96 to 7/1/97.
- The patient received at least one prescription of fluoxetine, paroxetine, or sertraline for the treatment of depression between 1/1/96 and 12/31/96. This window for selecting patients ensures that a minimum of 6 months of posttreatment data are available with which to measure the dose and duration of therapy. Patients beginning drug therapy early in the selection window could have up to 18 months of posttreatment data available.
- The patient had never taken fluoxetine, paroxetine, sertraline, or another antidepressant prior to 1996 and had no prior history of depression.

The patient was excluded from the study if the patient's medical chart review indicated:

- The patient had a history of other serious mental disorders, such as bipolar disorder, schizophrenia, or dementia.
- The patient was receiving antidepressant drug therapy for obsessive-compulsive disorder, bulimia, or other disorders for which SSRI antidepressants are indicated.

Patient Data

Patient-specific data were collected from 2 sources: CMG's computerized pharmacy database and from chart review in the physician's office. Pharmacy data included detailed data on each prescription dispensed (date dispensed, quantity, and strength) and were used to identify those SSRI patients who used an anxiolytic agent before or during the drug treatment episode. Medical charts were reviewed by trained abstractors who retrieved data for the following items:

- patients' demographic information (age, gender, HMO enrollment)
- prescriber's specialty (PCP or consultant psychiatrist)
- use of other mental health services (psychotherapy), or presence of other disease states or health conditions:
  - mental health symptoms prior to diagnosis of depression, as indicated by clinical notes in the patient's chart (eg, anxious, moody, stressed, sad, angry, etc)
  - elevated cardiovascular risk (documented atherosclerosis, diabetes mellitus, hypertension, or hyperlipidemia)
  - insomnia
  - anxiety
  - recently diagnosed conditions generating patients' concerns about quality or duration of life
  - obesity either noted by physician or perceived by patient
  - chronic pain
  - social factors:
    - —relationship problems experienced at home or at work
    - —substance abuse (past or present)
    - —current cigarette smoking
    - —disability preventing employment at the time of the diagnosis

If the patient discontinued taking the prescribed antidepressant before completing the 6-month treatment period, the abstractor assessed if the primary care physician documented the discontinuation in the chart.

Definition of Adequate Dose and Duration of Therapy

The guidelines for the treatment of depression developed by the Agency for Health Care Policy and

Research[22] were used to define adequate dose and duration of therapy. These guidelines specified that antidepressant drug therapy should continue for between 4 and 9 months. For this analysis, the duration of therapy required for "completed therapy" was set at 180 days or 6 months. The minimum therapeutic dose requirements for fluoxetine and paroxetine were 20 mg daily, and for sertraline 50 mg daily.

Adequate dose and duration were established as follows. Average daily dose for a specified course of therapy was calculated by dividing the total milligrams of medication dispensed by the total days covered by all prescriptions for the medication as long as breaks in prescription drug purchases did not exceed 45 days (30-day supply + 15-day grace period). Next, the average daily dose was divided by the minimum daily therapeutic dose for the drug to derive the relative effective dose achieved. If this value exceeded 0.9, then the entire period covered by the prescription(s) was defined as being therapeutic.

Similar calculations were undertaken for any secondary antidepressant used by the patient. An ade-

Table 1. Descriptive Statistics by HMO Enrollment Status

Description	Plan A (%)*	Plan B (%)†	*P*
Sample size	82 (43.9)	105 (56.1)	
Female gender	53 (64.6)	83 (79.1)	.028‡
Age (years ± SD)	55.5 ± 18.5	46.0 ± 14.8	.0002§
Antidepressant drug use patterns			
Initial antidepressant			
Fluoxetine	20 (24.4)	42 (40.0)	
Paroxetine	46 (56.1)	39 (37.1)	.026‡
Sertraline	16 (19.5)	24 (22.9)	
Augment antidepressant	2 (2.4)	2 (1.9)	1.000
Switch antidepressant	2 (2.4)	0 (0.0)	.191
Concomitant psychotherapy	3 (3.7)	16 (15.2)	.009§
SSRI initiated by			
Primary care physicians	73 (89.0)	80 (76.2)	.024‡
Psychiatrists	9 (11.0)	25 (23.8)	
History or presence of			
Mental illness (exclude depression)	29 (35.4)	39 (37.1)	.802
Cardiovascular problems	38 (46.3)	29 (27.6)	.008§
Insomnia	9 (11.0)	6 (5.7)	.189
Anxiety	21 (25.6)	40 (38.1)	.071
Life-threatening diseases	4 (4.9)	5 (4.8)	1.000
Weight problems	8 (9.8)	20 (19.1)	.077
Chronic pain	15 (18.3)	23 (21.9)	.542
Relationship problems	14 (17.1)	27 (25.7)	.156
Substance abuse	6 (7.3)	4 (3.8)	.290
Smoking	8 (9.8)	21 (20.0)	.055
Working disability	5 (6.1)	12 (11.4)	.208

HMO = health maintenance organization; SSRI = selective serotonin reuptake inhibitor; SD = standard deviation.
*Preferred SSRI = paroxetine.
†Preferred SSRI = paroxetine & fluoxetine.
‡Significant at 5%.
§Significant at 1%.

quate course of therapy (treatment completion) was defined as the patient having achieved 180 consecutive days of minimum therapeutic dosing, whether or not these days were achieved on the initial medication prescribed or on an added antidepressant medication. The inclusion of a secondary antidepressant medication into the calculation of total therapeutic days was done to facilitate a comprehensive intent-to-treat comparison across the alternative SSRI antidepressants.

Statistical Methods

Descriptive statistics were calculated that compared the demographic and clinical characteristics of the study population across the 2 HMOs studied (Table 1) and across patients who completed or failed to complete an adequate course of antidepressant therapy (Table 2). Drug profile data by initial SSRI selected, including completion rates, are presented in Table 3. Univariate statistical comparisons in all 3 tables employed χ^2 test and Student's *t* test for categorical and continuous data, respectively.

Logistic regression models were estimated to investigate if drug formulary restrictions and the selection of an initial SSRI antidepressant affected the likelihood of completion of antidepressant therapy. In order to control for possible baseline differences across alternative antidepressants, all models

Table 2. Descriptive Statistics by Antidepressant Therapy Completion Status

Description	Adequate Antidepressant Therapy Complete (%)	Incomplete (%)	*P*
Sample size	57 (30.5)	130 (60.5)	
Female gender	42 (73.7)	94 (72.3)	.846
Age (years ± SD)	49.6 ± 16.4	50.4 ± 17.5	.788
Antidepressant drug use patterns			
Plan A (1 SSRI)	13 (15.9)	69 (84.1)	.001*
Plan B (2 SSRIs)	44 (41.9)	61 (58.1)	
Augment antidepressant	3 (5.3)	1 (0.8)	.085
Switch antidepressant	1 (1.8)	1 (0.8)	.518
Concomitant psychotherapy	7 (12.3)	12 (9.3)	.525
SSRI initiated by			
Primary care physicians	43 (75.4)	110 (84.6)	.134
Psychiatrists	14 (24.6)	20 (15.4)	
History or presence of			
Mental illness (exclude depression)	15 (26.3)	53 (40.8)	.059
Cardiovascular problems	22 (38.6)	45 (34.6)	.601
Insomnia	3 (5.3)	12 (9.2)	.559
Anxiety	23 (40.4)	38 (29.2)	.135
Life-threatening diseases	3 (5.3)	6 (4.6)	1.000
Weight problems	9 (15.8)	19 (14.6)	.836
Chronic pain	12 (21.1)	26 (20.0)	.869
Relationship problems	8 (14.0)	33 (25.3)	.084
Substance abuse	3 (5.3)	7 (5.4)	1.000
Smoking	10 (17.5)	19 (14.6)	.611
Working disability	1 (1.8)	16 (12.3)	.021†

SD = standard deviation; SSRI = selective serotonin reuptake inhibitor.
*Significant at 1%.
†Significant at 5%.

contained independent variables for patient demographic characteristics, concomitant diagnoses, and health status.

The primary logistic regression specification was designed to differentiate between the direct effect on completion rates of restricting choice to a single SSRI and any effects that may be attributed to the specific initial medication selected to treat the patient. This was accomplished by including dichotomous variables identifying the HMO plan that covered the patient and the initial antidepressant used. The results of this model are provided in Table 4. The standards of comparisons (left-out groups) are patients treated subject to the 2-drug formulary and fluoxetine as initial therapy.

Two sensitivity analyses were also performed to test the robustness of the estimated effects of a single-product formulary and initial drug selection on completion rates. The first sensitivity analysis investigated the one-drug formulary effect by removing the dichotomous variables identifying the initial SSRI used by the patient from the model. This model estimated the "global" effect of the one-drug formulary without controlling for the specific initial antidepressant used by the patient. The second sensitivity analysis removed the dichotomous variable for the HMO formulary from the primary analysis. As before, fluoxetine was the standard of comparison in this model.

···RESULTS ···

Descriptive Statistics

A total of 479 patients received 1 or more of the 3 SSRIs during 1996, of which 187 (39.0%) were identified to be new episodes of therapy based on 6 months of data without any prior antidepressant use. Descriptive statistics are provided in Table 1 for study patients according to HMO plan membership. Eighty-two (43.9%) patients belonged to Plan A, which specified a single product (paroxetine) as its preferred SSRI. The remaining 105 patients (56.1%) belonged to Plan B, which specified 2 preferred SSRIs (paroxetine and fluoxetine).

Some significant differences exist across the 2 HMOs that could affect the likelihood of treatment completion. SSRI patients from Plan A (single-SSRI formulary) were more likely to be male, had higher average age and higher cardiovascular risk when compared to Plan B patients. Enrollees of Plan A were also less likely to undergo concomitant psychotherapy (3.7%) and their SSRI therapy was more likely to be initiated by PCPs (89%) than were patients in Plan B (15.2% and 76.2%, respectively). There were no differences between the 2 study HMOs in the rate of sertraline use as initial therapy or in other disease states and social factors. However, patients in Plan B had unrestricted access

Table 3. Pattern of Antidepressant Use by Initial Antidepressant

Description	Fluoxetine (%)	Paroxetine (%)	Sertraline (%)	*P*
	n = 62	n = 85	n = 40	
Completed antidepressant therapy	28 (45.1)	19 (22.3)	10 (25.0)	.009*
Completed therapy: Plan A (1 preferred SSRI)	5 / 15 (25.0)	6 / 40 (13.0)	2 / 14 (12.5	.423
Completed therapy: Plan B (2 preferred SSRIs)	23 / 42 (54.8)	13 / 39 (33.3)	8 / 16 (33.3)	.093
Used as second antidepressant (from switching or augmenting)	3	2	1	
Completers second antidepressant†	1 (33.3)	1 (50.0)	1 (100.0)	1.000

SSRI = selective serotonin reuptake inhibitor.
*Significant at 1%.
†These patients completed both initial antidepressant and second antidepressant.

to fluoxetine and were more likely to use this medication (40%) than were patients from the paroxetine-only plan (24.4%).

The descriptive statistics comparing patients who completed 6 months of antidepressant therapy to "noncompleters" are provided in Table 2. There were 57 new patients who achieved 6 months of uninterrupted therapeutic antidepressant dosing (30.5%). The rate of completed therapy was lower in Plan A (15.9%), which specified a single preferred SSRI, than in Plan B (41.9%) ($P < .001$). Data from Table 2 help clarify the issue of whether these differences are due to formulary differences or differences in the populations studied from both plans. Factors such as age, gender, cardiovascular risk, rate of concomitant psychotherapy, and prescriber's specialty were not found to be significantly associated with completion rates using univariate statistical comparisons. Moreover, the rates of switching or augmentation with a second antidepressant were below 4% in the total population and were not associated with therapy completion. Therefore, any differences across plans among these factors are unlikely to explain the differences in completion rates across plans. A significant association did exist between working disability at the time of diagnosis and noncompletion of the therapeutic course. However, there was not a statistically significant difference between plans in terms of disability status of SSRI patients. To more fully account for possible effects of population differences across plans on the likelihood of completion, patient characteristics, psychiatric prescribing, psychotherapy use, and selection of an initial SSRI were accounted for in the logistic regression models of completion reported below.

Additional descriptive data on the patterns of antidepressant drug use by initial SSRI used are presented in Table 3. Overall, the completion rate for fluoxetine as initial agent (45.1%) was nearly twice that of paroxetine (22.3%) or sertraline (25%). The completion rates were lower across all 3 alternative SSRIs in Plan A, which specified paroxetine as its only preferred agent, suggesting that a formulary effect may exist.

Multivariate Results

The descriptive data presented in Table 3 suggest that selecting a single SSRI as the preferred antidepressant adversely affected overall completion rates across all alternative SSRIs. This descriptive analysis, however, does not clarify if this apparent 1-product effect is real or is related to SSRI choice as the single preferred antidepressant in Plan A. Multivariate logistic regression analysis is required to differentiate between the effects of specifying a

Table 4. Factors Affecting Completion Rates for Antidepressant Therapy: Results from the Primary Logistic Regression Model

Description	Odds Ratio (CI)*	*P*
Demographic characteristics		
Age (years)	0.997	.8424
Gender (male = 1)	0.940	.8966
Antidepressant drug use patterns		
Member of Plan A (1 preferred SSRI)	0.200 (0.083-0.485)	.0004
Paroxetine as initial SSRI (fluoxetine as comparison)	0.357 (0.149-0.853)	.0205
Sertraline as initial SSRI (fluoxetine as comparison)	0.319 (0.105-0.968)	.0437
Augmented therapy	11.554	.0668
Switched therapy	13.332	.1233
Concurrent psychotherapy	1.960	.2815
SSRI prescribed by PCP	1.063	.9090
History or presence of		
Concomitant mental illness	0.489	.1107
Cardiovascular problems	1.651	.2683
Insomnia	0.770	.7429
Anxiety	1.864	.1286
Life-threatening diseases	0.618	.6120
Weight problems	0.920	.8773
Chronic pain	1.012	.9798
Relationship problems	0.339 (0.118-0.976)	.0451
Substance abuse	1.530	.6581
Smoking	1.137	.8063
Working disability	0.111 (0.013-0.969)	.0467

SSRI = selective serotonin reuptake inhibitor; PCP = primary care physician.
*Confidence intervals (CI) reported for statistically significant factors only. Model $\chi^2 = 48.8$, (20 DF) $P = .0003$.

single-product formulary from the effects of which drug is selected as the plan's preferred agent.

The primary logistic regression model specified for this study is summarized in Table 4. These results document that patients subject to the single-SSRI formulary were 80% less likely to complete an adequate course of antidepressant therapy than patients subject to a 2-drug formulary (odds ratio [OR] = 0.200, 95% confidence interval [CI] = 0.083-0.485). This result is independent of the effects of initial drug selection, which is captured by the dichotomous variables identifying the drug used by the patient as initial therapy. These latter intent-to-treat results indicate that patients treated with paroxetine were 64% less likely than patients treated with fluoxetine to complete therapy (OR = 0.357, 95% CI = 0.149-0.853). Similarly, patients treated with sertraline were also less likely than those given fluoxetine to complete therapy (OR = 0.319, 95% CI = 0.105-0.968).

Several other factors related to the patient's use of an antidepressant are of interest. Augmenting or switching of initial antidepressant therapy was not found to affect the likelihood of completed therapy, although the number of patients in these categories was low and estimates are unreliable. Patients whose SSRI was prescribed by a psychiatrist or who received psychotherapy were also found not to have higher therapy completion rates.

Very few patient demographic or clinical characteristics were found to affect the likelihood of completed therapy. Specifically, only those patients with reported problems with relationships or functional disabilities exhibited significantly lower completion rates. Age, gender, health status, mental health symptoms, substance abuse, insomnia, anxiety, weight problem, cardiovascular risk, chronic pain, smoking behavior, and the presence of a life-threatening illness were not found to affect completion rates.

Sensitivity Analyses

The results for the sensitivity analyses are reported in Table 5. Model 1 used a single dichotomous variable to identify the HMO in which the patient was enrolled. The results from this analysis are virtually identical to results from the primary model. Patients enrolled in the HMO plan with only one preferred SSRI were more than 5 times less likely to complete antidepressant therapy compared to patients from the HMO with 2 preferred agents (OR = 0.180, 95% CI =0.075-0.430).

Model 2 considers the effects of the physician's choice of initial antidepressant therapy on completion rates without considering any HMO formulary effects investigated in Model 1. Again, these results are virtually identical to those reported in the primary analysis (Table 4). Patients who initiated therapy on either paroxetine or sertraline were approximately 70% less likely to complete therapy relative to patients who initiated therapy with fluoxetine.

Table 5. Factors Affecting Completion Rates for Antidepressant Therapy: Results from Alternative Logistic Regression Models

Description	Odds Ratio (CI)	*P*
Sensitivity model 1: Formulary effect only		
Belonged to Plan A (1 preferred SSRI)	0.180 (0.075 - 0.430)	<.0001
Sensitivity model 2: Intent-to-treat effects only		
Paroxetine as initial SSRI (fluoxetine as comparison)	0.303 (0.132 - 0.694)	.0047
Sertraline as initial SSRI (fluoxetine as comparison)	0.289 (0.100 - 0.830)	.0212
Primary model		
Belonged to Plan A (1 preferred SSRI)	0.200 (0.083-0.485)	.0004
Paroxetine as initial SSRI (fluoxetine as comparison)	0.357 (0.149-0.853)	.0205
Sertraline as initial SSRI (fluoxetine as comparison)	0.319 (0.105-0.968)	.0437

CI = confidence interval; SSRI = selective serotonin reuptake inhibitor.

···DISCUSSION ···

Our results suggest that depressed patients who were treated under a single-product formulary for SSRIs were 80% less likely to complete antidepressant drug therapy than were patients who were provided access to 2 pre-

ferred SSRIs. Our results also found significant differences in the likelihood of completing drug therapy depending on the SSRI antidepressant used as initial therapy. Specifically, patients treated with sertraline or paroxetine were 70% less likely to complete therapy than were patients treated initially with fluoxetine. Finally, our results indicate that the single-product formulary effect is independent of which SSRI was selected for preferred status.

Several factors support the internal validity of these results. First, all patients were treated by the same group of primary care physicians, which eliminates possible provider effects on completion rates. Second, few differences were found across plans in the characteristics of the patients treated, and those differences were not found to affect the likelihood of completing therapy. Third, multivariate statistical techniques were used to control any effects of these factors on the likelihood of completing therapy. Finally, the estimated single-product formulary effect was highly significant and was found to be robust across alternative specifications of the model.

Our results are also consistent with other research. Horn et al[1] found that HMO formulary restrictions affecting drug selection for 5 common disease states (arthritis, asthma, epigastric pain/ulcer, hypertension, and otitis media) were associated with increased direct healthcare costs for all chronic conditions investigated. Specifically, formulary limitations were significantly related to higher rates of emergency department visits and hospital admissions. Increases in drug cost, drug count, and office visits were also observed but were not consistently statistically significant. However, Horn and colleagues did not investigate drug therapy completion specifically.

Several studies using data from real-world practice settings have also found differences in treatment completion rates that favor the SSRI relative to older antidepressants. However, completion rate comparisons across SSRIs are limited in number. For example, McCombs et al[2] found significant differences in completion rates across fluoxetine (55%), sertraline (25.4%), and paroxetine (14.4%) using data for Medicaid patients in California. However, the California Medicaid study was based on a limited sample of SSRI users (n = 367).

Limited sample size is a major factor that calls into question the internal validity of the results presented here. Further research is needed to confirm the single-product formulary effect found in this analysis, using data from a larger sample of patients and for disease states in addition to depression.

Several factors limit the external validity of this study. First, the study population was drawn from one group practice in California. Therefore, the patients studied do not reflect the population as a whole. Second, the standard of practice for treating depression within the study site may also vary significantly from practice norms in other locations.

This study was restricted to an analysis of the medication completion rates and did not report on either the total cost of the healthcare consumed by depressed patients or their functional status. The impact of completion of antidepressant therapy on cost and patient function can only be extrapolated from other studies. For example, depression has been shown in previous research to significantly affect both function and healthcare costs. In an analysis of 2980 participants in the Epidemiologic Catchment Area Study, researchers found that participants with major depression had a 4.8 times greater risk of disability than did those who did not have depression.[23] A similar relationship between depression and disability was also observed in high utilizers of healthcare services enrolled in a health maintenance organization.[12] The Medi-Cal SSRI study found that depressed patients each consumed more than $500 per month in direct healthcare services prior to initiation of antidepressant therapy and that completed therapy reduced the total direct healthcare cost per patient in the posttreatment year by $1487 ($P$ = .0479).[2]

···CONCLUSION ···

The possibility that limiting drugs within a class to a single agent has a negative impact on completion rates and, therefore, on a patient's function and healthcare costs should be considered. Furthermore, HMOs should be careful in selecting drugs for preferred formulary status to ensure that products with better clinical outcomes and drug therapy completion rates are not replaced by less effective drugs that offer significantly higher rebates to the HMO. When this is the case, physician group practices that contract with the HMO on a capitated basis should be aware that the selection of a single preferred agent based solely on the rebates paid to the HMO could have a significant detrimental effect on the treatment outcomes achieved by the group practice and, thus, on practice operating costs.

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