Article

The Effects of Antidepressant Step Therapy Protocols on Pharmaceutical and Medical Utilization and Expenditures

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Objective: This study examined the effects of step therapy for antidepressants on prescription drug and other medical utilization and spending. Step therapy is a type of pharmaceutical benefit design that requires that patients try certain specified medications (typically generic medications) prior to using alternative, more expensive medications within the same medication class. Step therapy is not the same as generic substitution.

Method: Using the 2003–2006 Thomson Reuters MarketScan claims databases, antidepressant users enrolled in employer plans that implemented antidepressant step therapy were compared with antidepressant users enrolled in employer plans that had not implemented step therapy. Multivariate generalized estimating equation models were used to analyze the relationship between step therapy for antidepressants and 1) pharmacy and medical utilization and 2) spending.

Results: Antidepressant days supplied and medication costs decreased after step therapy was implemented, relative to the comparison group. However, overall and mental health-specific inpatient and emergency room utilization and costs increased.

Conclusions: Step therapy may have the unintended effect of reducing overall antidepressant use and increasing medical use and costs.

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Managed care organizations and insurance plans are increasingly adopting step therapy in an effort to contain costs by steering patients away from more costly pharmacotherapies (1). Step therapy requires a member to try a first-line medication within a drug class, usually a generic alternative, prior to receiving coverage for a second-line agent, usually a branded product (2). However, step therapy is not the same as generic substitution, since it may require different types of medications to be tried other than just generic substitutes for the same medication in brand form. Currently, most pharmacy benefit managers that implement step therapy allow patients to use a second-line agent if insurance claims are found in the recent past for the first-line agent or if members obtained a prescription for the second-line drug in the recent past (2). If a prescription for a second-line agent is rejected, members may have their healthcare provider change the prescription to the first-line agent or submit a request for coverage of the second-line agent through a prior authorization (2).

Although step therapy plans for antidepressant medications have become prevalent, there has been little research examining their effects (1). Prior research has focused on the effects of step therapy on prescription drug utilization and spending (3, 4). In contrast, the present study focuses on the effects of step therapy on medication and nonmedication medical care utilization and spending. Specifically, this study aims to provide understanding of the association between step therapy implementation and changes in prescription drug, outpatient, inpatient, and emergency room utilization and spending.

Method

The data source for the study was the Thomson Reuters MarketScan Research Database, which represents the healthcare experience of enrollees in employer-sponsored health plans in the United States. The database, in its entirety, represents more than 60 employers. Thomson Reuters account managers were surveyed to determine whether any of their employer clients either had recently implemented step therapy (i.e., in 2003 and 2004) or did not have step therapy and would be willing to participate anonymously in the study. As an additional requirement, the step therapy program had to be implemented equally across all benefit plans available to an enrollee. Step therapy could not be selected or deselected by the individual enrollee, in order to reduce the likelihood of selection bias. Two firms had recently implemented step therapy programs and were identified as the treatment group. Two employers that did not have a program in effect during the same time were identified as the comparison group. No other employer groups that might have been eligible to participate in the study were identified.

A step therapy program was implemented at the beginning of 2003 in one plan and on April 1, 2004, in the other plan. Both step therapy programs were administered by the same pharmacy benefit manager. The present analysis focuses on step therapy programs for antidepressant medications because these are among the most commonly used medications (5).

The sample was limited to employees, and their dependents, of the selected employers (step therapy and comparison groups) who were continuously enrolled from 2003 through the third quarter of 2006, were under 65 years of age, and were not Medicare eligible. An analytic file was created using a panel data (repeated-

This article is featured in this month's AJP Audio and is discussed in an editorial by Dr. Greden (p. 1148).

TABLE 1. Characteristics of Individuals Treated With Antidepressant Medications in Step Therapy Plans Relative to Comparison Plans

Characteristic	Step Therapy Plan Subjects (N=15,552)		Comparison Plan Subjects (N=45,244)		Analysis
	N	%	N	%	p
Age group (years)					
0–17	1,464	9.4	4,584	10.1	<0.001
18–34	3,093	19.9	8,878	19.6	0.138
35–44	3,734	24.0	9,030	20.0	<0.001
45–54	5,033	32.4	16,356	36.2	<0.001
55–64	2,228	14.3	6,396	14.1	0.685
Gender					
Female	11,200	72.0	30,030	66.4	<0.001
Male	4,352	28.0	15,214	33.6	<0.001
Relationship to Employee					
Employee	11,621	74.7	22,661	50.1	<0.001
Spouse	2,276	14.6	15,432	34.1	<0.001
Child/other	1,655	10.7	7,151	15.8	<0.001
	Mean	SD	Mean	SD	p
Age (years)	40.62	13.40	40.58	13.96	0.764
Median household income in residential zip code (U.S. dollars)[a]	39,143.00	12,598.00	47,861.00	13,984.00	<0.001
College graduates in residential zip code (%)[a]	0.21	0.13	0.23	0.13	<0.001
Deyo-Charlson Comorbidity Index rating	0.29	0.78	0.27	0.74	0.005
Chronic Disease Score rating	2.85	3.00	2.44	2.80	<0.001
ICD-9 count	6.90	5.18	6.98	5.58	0.263

[a] Data taken from the U.S. Census.

TABLE 2. Unadjusted Average Health Care Utilization and Expenditures After Implementation of Step Therapy Plans (in 2006) Relative to Comparison Plans

	Step Therapy Plan Subjects		Comparison Plan Subjects		Analysis
Variable	Mean	SD	Mean	SD	p
Enrollees receiving antidepressant medication[a]					
Utilization					
Days antidepressant medication supplied[b]	35.3	38.6	39.5	39.5	<0.0001
Antidepressant discontinuation rate[b]	0.03	0.018	0.03	0.18	0.6864
All prescriptions filled[b]	6.58	6.62	7.05	7.15	<0.0001
Emergency room visits[b]	0.11	0.42	0.09	0.37	<0.0001
Outpatient office visits[b]	1.39	1.71	1.25	1.76	<0.0001
Inpatient admissions[b]	0.034	0.21	0.028	0.19	<0.0001
Expenditures (U.S. dollars)					
Prescription drugs	498.00	943.00	629.00	1,008.00	<0.0001
Emergency room visits	115.00	1,864.00	70.00	436.00	<0.0001
Inpatient admissions	409.00	4,615.00	363.00	3,769.00	0.0502
Outpatient medical visits	948.00	3,788.00	1,053.00	3,171.00	<0.0001
All enrollees[c]					
Antidepressant initiation rate (per enrollee per year)	0.007	0.08	0.006	0.08	0.0082
Days antidepressant medication supplied (per enrollee)	8.27	23.91	8.78	24.84	<0.0001

[a] Step therapy plan participants receiving antidepressants: N=15,552; comparison plan participants receiving antidepressants: N=45,224.

[b] Data represent the average per participant receiving antidepressant treatment.

[c] Enrollees in the step therapy plan: N=66,308; enrollees in the comparison plan: N=203,253.

measures) framework with one observation each quarter for each individual. Each enrollee in the analytic file had 15 observations (i.e., quarters of data). The total sample consisted of 269,561 enrollees. Of these, 66,308 were enrolled in step therapy plans and 203,253 were enrolled in comparison plans. We also focused on the subset of enrollees in each plan who were being treated with any antidepressant medication (N=60,796). Of these, 15,552 were in step therapy plans and 45,244 were in comparison plans.

The dependent variables were prescription drug and medical costs and utilization. The following quarterly utilization measures were examined for individuals being treated with antidepressant medication: the number of antidepressant days supplied (within the time period covered by the quarter), the number of prescriptions filled, the number of all disease- (i.e., somatic and mental health conditions combined) and mental health-related outpatient office visits, the number of all disease- and mental health-related emergency room visits, and the number of all disease- and mental health-related inpatient admissions. Mental health-related utilization was defined as services used for a primary psychiatric diagnosis (ICD-9-CM, 290–319). Four spending measures for antidepressant users were examined: outpatient prescription drug costs, emergency room costs, inpatient medical

TABLE 3. Multivariate Results of the Effects of Step Therapy on Prescription Drug Utilization

	Enrollees Receiving Antidepressant Medication[a]					
	Antidepressant Days			Generic Antidepressant Days		
Variable	Coefficient	SD	p	Coefficient	SD	p
Step therapy plan/non-step therapy plan (reference=non-step therapy plan)	–0.103	0.010	<0.001	0.020	0.027	0.455
After step therapy plan implementation (reference=before implementation/non-step therapy plan)	–0.054	0.009	<0.001	0.052	0.024	0.030
Time after step therapy plan implementation	0.015	0.002	<0.001	0.032	0.005	<0.001
Quarter	0.067	0.001	<0.001	0.195	0.004	<0.001
Quarter^2	–0.003	0.000	<0.001	–0.008	0.000	<0.001
Age (years)	0.015	0.000	<0.001	0.018	0.001	<0.001
Female	0.122	0.008	<0.001	0.181	0.021	<0.001
Deyo-Charlson Comorbidity Index rating	–0.003	0.002	0.210	–0.002	0.006	0.800
Diagnoses	0.017	0.000	<0.001	0.008	0.001	<0.001
College graduates in residential zip code (%)[c]	0.273	0.039	<0.001	0.040	0.097	<0.001
Median income in residential zip code[c]	0.000	0.000	0.895	–0.002	0.001	0.100
Constant	2.851	0.017	<0.001	0.773	0.045	<0.001

[a] Days supplied and the number of prescriptions were estimated using a negative binomial generalized estimating equation with a log link. Coefficients in these models are partial elasticities. Step therapy plan participants receiving antidepressants: N=15,552; comparison plan participants receiving antidepressants: N=45,224.

[b] Step therapy plan participants among all enrollees: N=66,308.

[c] Data taken from the U.S. Census.

TABLE 4. Multivariate Results of the Effects of Step Therapy on Medical Care Utilization[a]

	Outpatient Visits for All Diagnoses			Outpatient Mental Health-Related Visits		
Variable	Coefficient	SD	p	Coefficient	SD	p
Step therapy plan (reference=non-step therapy plan)	0.099	0.007	<0.001	–0.964	0.031	<0.001
After step therapy plan implementation (reference=before implementation/non-step therapy plan)	0.045	0.008	<0.001	0.166	0.037	0.000
Quarter after step therapy plan implementation	0.001	0.002	0.387	0.010	0.007	0.158
Quarter	0.014	0.001	<0.001	0.031	0.004	<0.001
Quarter^2	–0.001	0.000	<0.001	–0.001	0.000	<0.001
Age (years)	0.003	0.000	<0.001	–0.024	0.001	<0.001
Female	0.148	0.007	<0.001	–0.070	0.020	<0.001
Deyo-Charlson Comorbidity Index rating	0.043	0.003	<0.001	–0.044	0.007	<0.001
Diagnoses	0.029	0.000	<0.001	0.034	0.001	<0.001
College graduates in residential zip code (%)[b]	0.203	0.028	<0.001	1.409	0.098	<0.001
Median income in residential zip code[b]	0.001	0.000	<0.001	0.001	0.001	0.319
Constant	–0.432	0.013	<0.001	–0.897	0.039	<0.001

[a] Models were estimated using a negative binomial generalized estimating equation model with a log link. Coefficients represent partial elasticities.

[b] Data taken from the U.S. Census.

(admissions) costs, and outpatient medical (nondrug) costs. Expenditures were defined as the total amount reimbursed to providers from all sources of payment, including the health plan, the patient, and any third party (coordination of benefits amount). One utilization measure was examined for all enrollees: antidepressant days supplied.

Statistics were performed using UNIX SAS, Version 9.01 (SAS Institute, Inc., Cary, N.C.), and Stata 9.0 for Windows (StataCorp, LP, College Station, Tex.). Chi-square and Student's t tests were computed to compare demographic and clinical characteristics as well as outcome variables between the step therapy and comparison groups after step therapy had been implemented.

The general model specification equation was as follows (where "i" represents person and "t" represents time in quarters): $Y=g(a_0+\beta_1 Step_{it}+\beta_2 AfterStep_{it}+b_3 TimeStep_{it}+\beta_4 Quarter_t+\beta_5 Quarter^2_t+\beta 6 Dem_{it}+\beta_7 * Clinical_{it})$

The explanatory variables were defined as follows: Y=medical care utilization or expenditure measure; Step=a 0/1 dummy variable that equals 1 if the employer instituted step therapy at any time during the study period and equals 0 otherwise; AfterStep=a 0/1 dummy variable that equals 1 after the employer instituted step therapy and equals 0 otherwise; TimeStep=a numeric counter measuring the number of quarters since the step therapy program began (i.e., 1, 2, 3); Quarter=a "time trend" variable to capture the linear utilization and spending trends common to both the step therapy and comparison groups, with the first quarter of 2003 coded as 1 and the third quarter of 2006 coded as 15. Quadratic trends were captured in the Quarter^2 variable; Dem=demographic characteristics, including age, gender, median income in the patient's residential zip code, and percent of college graduates in the patient's residential zip code (from the U.S. Census); Clinical=clinical characteristics, including the

Enrollees Receiving Antidepressant Medication[a]						All Enrollees		
Brand Antidepressant Days			Number of Prescriptions			Antidepressant Days[b]		
Coefficient	SD	p	Coefficient	SD	p	Coefficient	SD	p
–0.155	0.015	<0.001	–0.074	0.008	<0.001	–0.080	0.015	<0.001
–0.189	0.018	<0.001	–0.011	0.006	0.055	–0.048	0.011	<0.001
–0.002	0.004	0.682	0.007	0.001	<0.001	0.012	0.002	<0.001
0.035	0.002	<0.001	0.016	0.001	<0.001	0.059	0.002	<0.001
–0.002	0.000	<0.001	–0.001	0.000	<0.001	–0.003	0.000	<0.001
0.012	0.000	<0.001	0.024	0.000	<0.001	0.041	0.000	<0.001
0.188	0.013	<0.001	0.084	0.007	<0.001	0.626	0.013	<0.001
0.003	0.004	0.434	0.020	0.002	<0.001	–0.009	0.004	0.016
0.020	0.001	<0.001	0.014	0.000	<0.001	0.029	0.001	<0.001
0.250	0.059	<0.001	–0.043	0.030	0.158	0.384	0..060	<0.001
0.001	0.001	0.304	0.000	0.000	0.130	–0.001	0.001	0.018
2.415	0.025	<0.001	1.377	0.013	<0.001	0.964	0.024	<0.001

Inpatient Admissions for All Diagnoses			Inpatient Mental Health-Related Admissions			Emergency Room Visits for All Diagnoses			Emergency Room Visits for Mental Health-Related Diagnoses		
Coefficient	SD	p	Coefficient	SD	p	Coefficient	SD	p	Coefficient	SD	p
0.063	0.026	0.017	–0.329	0.099	<0.001	–0.642	0.024	<0.001	0.001	0.080	0.994
0.150	0.041	<0.001	0.184	0.129	0.15	0.267	0.025	<0.001	0.185	0.121	0.127
0.009	0.008	0.264	0.010	0.023	0.68	0.050	0.004	<0.001	–0.020	0.021	0.344
0.041	0.008	<0.001	0.188	0.028	<0.001	0.120	0.006	<0.001	0.070	0.022	0.002
–0.003	0.000	<0.001	–0.010	0.002	<0.001	–0.010	0.000	<0.001	–0.003	0.001	0.052
–0.002	0.001	0.007	–0.045	0.003	<0.001	0.001	0.001	0.466	–0.044	0.003	<0.001
–0.135	0.021	<0.001	–0.637	0.082	<0.001	–0.008	0.024	0.732	–0.551	0.068	<0.001
0.086	0.008	<0.001	–0.116	0.050	0.02	0.005	0.010	0.617	–0.077	0.036	0.031
0.069	0.001	<0.001	0.071	0.005	<0.001	0.041	0.002	<0.001	0.072	0.005	<0.001
–0.641	0.092	<0.001	0.401	0.332	0.23	–0.153	0.114	0.181	0.023	0.261	0.931
–0.002	0.001	0.047	–0.006	0.003	0.06	–0.003	0.001	<0.001	0.000	0.003	0.907
–4.130	0.045	<0.001	–6.196	0.154	<0.001	–2.334	0.045	<0.001	–6.074	0.148	<0.001

number of ICD-9-CM codes and Deyo-Charlson Comorbidity Index ratings, which were measured as lagged variables over a 1-year period prior to the time the outcome was measured.

Multivariate generalized estimating equation models were used to determine the effects of step therapy on spending and utilization while controlling for important covariates. Generalized estimating equation models were used because they adjust the standard errors for the effect of repeated measures by patient and are flexible enough to allow for different distributions of the dependent variables, such as skewed and binary distributions and distributions with a concentration of zero values (6). Utilization variables, representing counts of each type of service, were estimated with a negative binomial distribution and a log link. Expenditures were estimated using a gamma distribution with a log link.

The effects of step therapy are captured in the coefficients of the AfterStep and TimeStep variables. The first variable (AfterStep) captures the immediate and static effects of step therapy, and the second (TimeStep) captures the time varying effects in each quarter after the plan was implemented. In order to estimate the full magnitude of the effects of step therapy on the outcome measures (as expressed in these two coefficients), we calculated a nonlinear prediction (predictnl in Stata) at the mean of each control variable (7).

Results

Sample Description

Table 1 compares the characteristics of enrollees who used antidepressant medications at any time during the study period in both step therapy and comparison plans.

The two populations had relatively similar mean ages. There was a greater percentage of women in the step therapy group than the comparison group, and a greater percentage of the step therapy beneficiaries represented employees. The step therapy participants had a lower median income and percentage of college graduates in their residential zip codes. The samples were relatively comparable in terms of comorbidity measures. There was no statistically significant difference in the count of three-digit ICD-9-CM diagnostic categories. The mean Deyo-Charlson Comorbidity Index rating was slightly higher in the step therapy group. The mean Chronic Disease Score rating was slightly lower in the step therapy group.

Table 2 describes the utilization and spending outcome measures in 2006, after the step therapy programs had been implemented in both employer plans. Average days supplied per antidepressant user and per enrollee was lower in the step therapy plans relative to the comparison plans. The number of prescriptions of all types as well as prescription drug costs were also lower in the step therapy plans. In contrast, emergency room and inpatient admission costs were higher in the step therapy plan.

Multivariate Model

The results of the multivariate models indicate that after implementation of step therapy, antidepressant days supplied in the step therapy plans was 3.9% lower than the nonstep plans (Table 3). However, this effect declined with time, and at four quarters after implementation of step therapy, the number of antidepressant days supplied in step therapy plans began to exceed the days supplied in comparison plans. Similarly, the number of antidepressant days supplied over all enrollees was 3.6% lower in the quarter after step therapy was initiated but then grew to equal that of nonstep therapy plans. In contrast, essentially, there was no effect of step therapy on prescriptions of all types (a decrease of only 0.4% in the first quarter and then an increase of 0.3% in the second quarter).

Also shown in Table 3 is the shift from generic medication to brand in the step therapy plans relative to the comparison plans. The step therapy plan had 8.8% higher generic antidepressant days supplied in the quarter after step therapy was implemented, increasing to 23.6% in the fifth quarter after the plan was implemented. Conversely, step therapy plans had 17.4% less use of brand medications in the first quarter after plans were implemented, an effect that remained relatively unchanged over time.

For antidepressant users, step therapy was associated with an increase in outpatient office visits of 4.7% in the quarter following step therapy implementation, which remained relatively constant over time. Inpatient admissions were 17% higher in the quarter following step therapy implementation, relative to the comparison plans, and the increase grew over time. Step therapy was associated with a 37% increase in the number of emergency room visits in the quarter immediately following implementation, and the increase in emergency room visits grew with the amount of time elapsed since step therapy was implemented.

Mental health-related utilization also increased. Specifically, in the quarter immediately following step therapy implementation, the number of mental health-related outpatient visits was 19% higher, the number of mental health-related inpatient admissions was 21% higher, and the number of mental health-related emergency room visits was 18% higher (Table 4).

Table 5 displays the coefficients of the spending models for antidepressant users. Step therapy was associated with 17% higher inpatient spending, and the difference grew larger over time. Step therapy was also associated with 8.4% higher outpatient spending. Emergency room spending was 28% higher in the quarter after implementation of step therapy, and the effects increased with time. In contrast, prescription drug spending experienced a decline of 1.7% after implementation of step therapy.

Figure 1 shows the difference in the predicted results of the inpatient, emergency room, and prescription drug spending models, the three expenditure categories significantly affected by implementation of a step therapy program. In the first quarter after step therapy was implemented, inpatient costs were slightly lower in the step therapy plan ($0.33), although in the second quarter, the inverse was true and step therapy inpatient costs grew relatively more expensive, reaching a $51.63 difference by the eighth quarter. Additionally, emergency room spending in the step therapy plans consistently exceeded the spending levels of the comparison group. Conversely, step therapy prescription drug expenditures were consistently lower than those of the comparison group, although the difference diminished over time.

Discussion

Prior studies have found that antidepressant step therapy increases the use of generic medications and reduces pharmaceutical expenditures (3). This study expands the research on step therapy by examining its impact on medical care utilization and expenditures in addition to pharmaceutical utilization and expenditures. We found that while step therapy led to some medication cost savings in the short run, the number of antidepressant days supplied declined after step therapy was implemented and inpatient and emergency room admissions and costs increased postimplementation, relative to the comparison plans. Drug savings were offset by higher medical spending, resulting in no net change in total spending.

Step therapy has become a common aspect of private health insurance plans. In theory, if step 1 (preferred) medications were perfect substitutes for step 2 medications and selecting the preferred drug was administratively seamless, then one would anticipate that step therapy would lower medication costs with no negative effects on drug use patterns, outcomes, or expenditures.

TABLE 5. Effects of Step Therapy Plans on Expenditures[a]

Variable	Outpatient Expenditures			Inpatient Expenditures			Emergency Room Expenditures			Prescription Drug Expenditures		
	Coefficient	SD	p	Coefficient	SD	p	Coefficient	SD	p	Coefficient	SD	p
Step therapy plan (reference=non-step therapy plan)	–0.206	0.012	<0.001	–0.180	0.062	0.004	–0.135	0.033	<0.001	–0.219	0.014	<0.001
After step therapy plan implementation (reference=before implementation/non-step therapy plan)	0.074	0.018	<0.001	0.129	0.086	0.131	0.205	0.051	<0.001	–0.022	0.010	0.039
Quarter after step therapy plan implementation	0.007	0.003	0.032	0.031	0.013	0.013	0.044	0.010	<0.001	0.005	0.002	0.033
Quarter	0.034	0.003	<0.001	0.096	0.016	<0.001	0.078	0.008	<0.001	0.044	0.001	<0.001
Quarter^2	–0.001	0.000	<0.001	–0.005	0.001	<0.001	–0.003	0.001	<0.001	–0.002	0.000	<0.001
Age (years)	0.014	0.000	<0.001	0.011	0.002	<0.001	–0.008	0.001	<0.001	0.024	0.000	<0.001
Female	0.022	0.010	0.023	–0.352	0.038	<0.001	–0.250	0.023	<0.001	–0.064	0.012	<0.001
Deyo-Charlson Comorbidity Index rating	0.134	0.007	<0.001	0.171	0.013	<0.001	0.071	0.012	<0.001	0.045	0.005	<0.001
Diagnoses	0.060	0.001	<0.001	0.092	0.003	<0.001	0.070	0.002	<0.001	0.017	0.001	<0.001
College graduates in residential zip code (%)[b]	0.101	0.042	0.015	–0.508	0.178	0.004	–0.315	0.089	<0.001	0.093	0.051	0.069
Median income in residential zip code[b]	–0.001	0.000	<0.001	–0.003	0.002	0.072	–0.002	0.001	0.008	0.001	0.001	0.033
Constant	5.827	0.020	<0.001	4.708	0.077	<0.001	3.387	0.051	<0.001	5.630	0.023	<0.001

[a] Models were estimated using a generalized estimating equation model with a gamma distribution and log link. Coefficients represent partial elasticities.

[b] Data taken from the U.S. Census.

However, step therapy may have unintended consequences. Rather than shifting patients to generic or other preferred medications, step therapy may deter patients from filling prescriptions all together. This may happen for several reasons. Physicians may generally not know that patients only have coverage for step 1 medications and may still be prescribing step 2 medications. Patients may only find out about their limited coverage for step 2 medications once they try to obtain a prescription from a pharmacy and might be deterred by the time and administrative constraints of obtaining a prescription for a step 1 medication or an exemption for a step 2 medication. As a result, patients might decide not to fill the prescription at all.

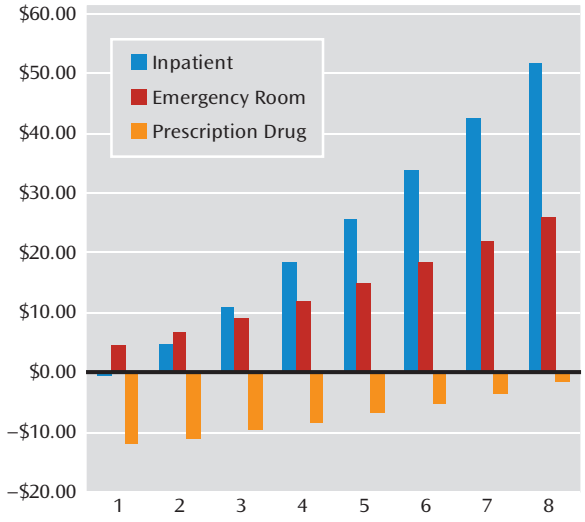
Some prior studies support this scenario. During the first 4 months of the Medicare prescription drug benefit, a study of dual-eligible psychiatric patients found that among patients with "fail first" or step therapy policies, 78% reported an access problem, a much greater percentage of access problems relative to those without step therapy policy (8). A study of Medicaid prior authorization and step therapy plans for antipsychotic medications found that the programs resulted in greater medication discontinuation (9).

In another study, Motheral et al. (4) surveyed plan members who had been subject to step therapy edits (i.e., denied prescriptions for a step 2 medication) for proton pump inhibitors, selective serotonin reuptake inhibitors, and nonsteroidal antiinflammatory drugs. They found that nearly 17% received no medication and another 10% only received a sample or an over-the-counter alternative. Finally, a study using the same employers we utilized in the present study, but focused on antihypertensives versus antidepressants, found that step therapy resulted in a decline in the number of antihypertensive medications supplied and an increase in inpatient and emergency room utilization (10).

A clear direction for future research is to understand in more depth the nature of the potential administrative barriers that step therapy and fail first policies are creating that may be preventing people from filling needed prescriptions. For example, private and public third-party payers may need to understand how quickly and easily patients can obtain provider authorization for step 2 medications. Additionally, there is a need to understand how well "step edits," which rely on claims history to determine prior use of step 1 and 2 medications, are accurately capturing prior use or might be missing claims, for example, because a patient recently switched plans. Finally, research and perhaps more education is needed to explain to patients the direction that they can take when they are denied a step 2 medication.

Another possible hypothesis as to why step therapy participants experienced lower days supplied and more hospitalizations and emergency room visits is that the step 1 medications were less efficacious or were associated with more side effects than the step 2 medications. The research to support efficacy differences among antidepressants is limited, although most clinical trials are not conducted with the power to test noninferiority and may not capture modest differences in efficacy (11). Moreover, comprehensive reviews find that antidepressants cannot

FIGURE 1. Predicted Values for Inpatient, Emergency Room, and Prescription Drug Spending Models in Step Therapy Plans Relative to Comparison Plans



Quarters Since Step Therapy Implementation	Inpatient	Emergency Room	Prescription Drug
1	–$0.33	$4.44	–$12.02
2	$4.89	$6.59	–$10.93
3	$10.98	$9.05	–$9.71
4	$18.46	$11.83	–$8.34
5	$25.58	$14.94	–$6.86
6	$33.86	$18.37	–$5.24
7	$42.61	$22.09	–$3.51
8	$51.63	$26.10	–$1.69

be considered identical drugs, and evidence supports differences with respect to onset of action, side effects, and effects on health-related quality of life (e.g., sexual functioning) (11). It may be true that despite limited differences in average efficacy, when physicians are provided with a range of treatment options, they select antidepressants for particular patients while taking into account the patient's treatment history as well as side effect concerns, which in turn promotes adherence and hence efficacy.

One policy implication of this line of research is that programs that are structured to only address pharmaceutical utilization in isolation from medical utilization may be operating at cross purposes. For example, pharmaceutical benefits that are managed by pharmaceutical benefit managers who are operating under incentives to reduce pharmaceutical costs and only view pharmaceutical claims may not have the motivation or information necessary to consider the impact of their policies on medical care expenditures. In the areas of copayment design, recognition of this type of misalignment because of silos in benefit management has led to the idea of a value-based insurance design, where copayments are adjusted to encourage appropriate use of medications, such as better adherence for patients with diabetes (12).

Our study should be understood in light of its strengths and limitations. Step therapy is implemented in various ways by different pharmacy benefit managers and health plans. By its nature, it must be examined through a natural experiment, which was done in this study. Although we employed a strong pre/post design, estimating the common effects of step therapy plans instituted at two different points in time relative to a contemporaneous comparison group, it is possible that studies of other step therapy systems would yield different results. In particular, it may be that the comparison and step therapy plans were starting at different baselines, which influenced the relative change after step therapy. Additionally, this study examined utilization and cost outcomes, and other outcome measures, such as psychiatric symptoms and functioning, are not captured in insurance claims but are important to evaluate. Finally, while the study examined differences in expenditures and utilization, it did not decompose changes in expenditures into changes in price and changes in utilization. Such an analysis would further inform the effect of step therapy. Clearly, there is a need for additional research to understand both the strengths and limitations of step therapy as a cost saving tool.

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Thomson Reuters worked under contract to Pfizer, Inc. to conduct this study. The study was a collaborative effort with Thomson Reuters and Pfizer employees. The analytic file was derived from the Thomson Reuters MarketScan data set. All authors had the ability to query the analytic file. Drs. Mark, Gibson, and McGuigan designed the questions addressed in this study. The analytical approach was developed by Drs. Mark and Gibson. The approach was reviewed by Dr. McGuigan. The statistical analyses were carried out by Dr. Chu. Dr. Mark wrote the first draft of the article, and all authors reviewed each version of the article.

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