Treatment Persistence & Health Care Costs Of Adult MDD Patients Treated With Escitalopram Vs. Citalopram in a Medicaid Population

Escitalopram patients in a Florida Medicaid population had better treatment persistence and lower total health care costs than patients prescribed citalopram

Eric Q. Wu, PhD, managing principal; Rym Ben-Hamadi, MSc, manager; Mei Lu, MS, associate; Nicolas Beaulieu, MA, associate; and Andrew P. Yu, PhD, manager, all from the Analysis Group Inc., and M. Haim Erder, PhD, vice president for health economics and outcomes, Forest Research Institute

ABSTRACT

Objective: Compare treatment persistence and health care costs of major depressive disorder (MDD) Medicaid patients treated with escitalopram versus citalopram.

Design: Retrospective analysis of Medicaid administrative claims data.

Methodology: Analyzed administrative claims data from the Florida Medicaid program (07/2002–06/2006) for patients ages 18–64 years with ≥1 inpatient claim or 2 independent medical claims for MDD. Outcomes included discontinuation and switching rates and prescription drug, medical, and total health care costs, all-cause and related to mental disorder. Contingency table analysis and survival analysis were used to compare outcomes between treatment groups, using both unadjusted analysis and multivariate analysis adjusting for baseline characteristics.

Results: The study included 2,650 patients initiated on escitalopram and 630 patients initiated on citalopram. Patients treated with escitalopram were less likely to discontinue the index drug (63.7% vs. 68.9%, P=0.015) or to switch to another second-generation antidepressant (14.9% vs. 18.4%, P=0.029) over the six months post index date. Patients treated with escitalopram had $1,014 lower total health care costs (P=0.032) and $519 lower health care costs related to mental disorder (P=0.023). More than half of the total cost difference was attributable to savings in inpatient hospitalizations related to mental disorder ($571, P=0.003) and to outpatient costs ($53, P<0.001). Escitalopram therapy was also associated with $736 lower medical costs related to mental disorder (P=0.009).

Conclusion: In the Florida Medicaid program, compared to adult MDD patients initiated on citalopram, escitalopram patients have better treatment persistence and lower total health care costs due to any cause and due to mental disorder, mostly driven by lower hospitalization costs related to mental disorder.

Disclosure/Conflicts

This study was supported by funding from Forest Laboratories Inc., manufacturer of Lexapro (the brand name for escitalopram) and of Celexa (the brand name of citalopram).

Address for correspondence:
Eric Q. Wu, PhD
Analysis Group Inc.
111 Huntington Avenue, Tenth Floor
Boston, MA 02199
Tel: 617–425–8254
Fax: 617–425–8001
E-mail: ewu@analysisgroup.com

INTRODUCTION

Major depressive disorder (MDD) is a common, serious mental illness with a high economic and societal burden. In 2001, the lifetime prevalence of MDD in adults in the United States was 16.2%, with a 12-month incidence of 6.6% (Kessler 2003). MDD is twice as common in women as men, and is more prevalent in older persons and persons with lower socioeconomic status (Kessler 2003). Up to 60% of MDD sufferers never seek treatment, and many of those seeking help are likely to be undertreated (Davidson & Meltzer-Brody 1999).

MDD patients who do not receive adequate antidepressant treatment have higher rates of concurrent medical disorders, are less productive in the workplace, and use more health care resources than patients in remission (Bradvik 2008; Conner 1999; Hirschfeld 1997). Poor compliance with antidepressant therapy is associated with higher short-term disability (Burton 2007), medical costs (Cantrell 2006; Eaddy 2005; Sheehan 2005; Thompson 1996), and relapse rates (Claxton 2000). The overall economic burden of depression in the United States was estimated to be $83.1 billion in 2000 (Greenberg 2003).

Selective serotonin reuptake inhibitors (SSRIs) are a highly effective class of antidepressants that are more cost-effective in long-term MDD treatment than older antidepressants (Frank 2001; Panzarino & Nash 2001; Peveler 2005; Revicki 1998). Escitalopram is the therapeutically active S-enantiomer of the SSRI citalopram, which is a racemic mixture of both the S and R forms (Burke 2002). Both escitalopram and citalopram are efficient and well-tolerated in MDD

treatment (Burke 2002; Feighner & Overo 1999; Franchini 1999; Kornstein 2006; Lepola 2003; Murdoch & Keam 2006; Wade 2006). Escitalopram, however, has a faster onset, greater overall magnitude of therapeutic effect, and lower discontinuation rate than citalopram and the other SSRIs (Armstrong 2007; Baldwin 2002; Baldwin 2007; Gorman 2002; Lam & Andersen 2006; Lepola 2004; Moore 2005).

Multiple studies have found escitalopram to be more cost-effective in the treatment of MDD than citalopram and other SSRIs, such as fluoxetine, sertraline, and paroxetine, and the serotonin norepinephrine reuptake inhibitor (SNRI) venlafaxine (Armstrong 2007; Demyttenaere 2005; Fantino 2007; Fernandez 2005; François 2003; Hemels 2004; Llorca & Fernandez 2007; Sorensen 2007; Sullivan 2004; Wade 2005a).

SSRIs are frequently used as a first-line therapy for MDD (Kroenke 2001). Expenditures from the Medicaid program for antidepressants have grown rapidly in the past 15 years. From 1996 to 2002, antidepressants were one of the fastest-growing classes of drugs for Medicaid expenditures (Banthin & Miller 2006). The total number of antidepressant prescriptions for Medicaid enrollees increased from 6.8 million to 32.7 million from 1991 to 2005. Total expenditures on antidepressants increased from $159 million to almost $2 billion in the same period (Chen 2008), constituting approximately 5% of the total Medicaid pharmaceutical budget (National Pharmaceutical Council 2005). The growth in antidepressant use outpaced the growth in Medicaid enrollment (approximately 3.5% per year) during this time, indicating that increased enrollment does not fully account for the increased use (Chen 2008).

In the Texas Medicaid program, SSRIs accounted for 52% of all antidepressants dispensed to beneficiaries in 2000 and for 71% of all antidepressant costs over the same year because of their higher unit costs compared to older agents (Johnsrud & Crismon 2002). Citalopram had a significantly lower calculated cost per day compared to sertraline, fluoxetine, paroxetine, and venlafaxine in this adult Medicaid cohort, which did not include an escitalopram treatment group (Johnsrud & Crismon 2002).

Because the use of SSRIs and total expenditures associated with it continue to increase within the Medicaid program, it is important to analyze the economic impact of individual drugs in this class. The objective of this study is to retrospectively compare antidepressant treatment persistence and health care costs for the 6-month period following therapy initiation for a sample of Florida Medicaid adult beneficiaries with MDD who were initiated on escitalopram versus citalopram.

METHODS

Data source

This study used Medicaid medical and prescription drug claims data, as well as enrollment records, for the state of Florida from July 2002 to June 2006. This database contains complete medical and pharmaceutical claims (both fee-for-service and managed care organizations) from Medicaid records, as well as information on Medicare/Medicaid dual eligibility, for 5.6 million eligible people during the covered years. Each record in the database contains information on the amount paid for the procedure/medical visit. That amount was used in the calculation of costs.

Study population

To be selected for the study, patients were required to meet all of these criteria: (1) have had at least 1 claim with an inpatient place of service or 2 independent medical claims of another type with different dates of service associated with MDD diagnosis (ICD-9-CM=296.2x, 296.3x), from Jan. 1, 2003 to Dec. 31, 2005; (2) have been initiated on citalopram or escitalopram by filling at least 1 prescription (index date) during the same period; (3) have been continuously enrolled for at least 12 months, including 6 months before the index date (baseline period) and 6 months after (study period); (4) be between 18 and 64 years old on the index date; (5) have had no second-generation antidepressant use during the 6 months before the date (washout period); (6) have had no other second-generation antidepressant use within 2 weeks after the index date, to exclude cases on combination therapies; and (7) have not been eligible for Medicare (i.e., no Medicare/Medicaid crossovers or dual eligibility allowed) during the baseline and study periods.

Second-generation antidepressants included SSRIs (i.e., citalopram, escitalopram, fluoxetine, sertraline, paroxetine, and fluvoxamine), SNRIs (i.e., venlafaxine and duloxetine), bupropion, nefazodone, trazodone, fluoxetine-olanzapine, and mirtazapine. Table 1 summarizes the sample selection criteria and corresponding sample sizes.

Patient baseline characteristics were measured over the 6-month pre-index period, including patient demographics (gender and age at index date); Charlson Comorbidity Index (CCI) and profile for various comorbidities (mental disorders and other chronic illnesses); and baseline health care resource utilization (emergency room visits, psychiatry institution visits, regular inpatient visits, and outpatient visits) and costs (prescription drug, medical services, total).

All outcomes were measured over the 6-month study period and compared patients on escitalopram with those on citalopram. Treatment persistence was measured using discontinuation and switching rates. Patients were considered to discontinue the index therapy if they did not re-

fill the index drug within 45 days after the end of the most recent index drug supply.

Patients who discontinued were further classified into two groups, depending on whether they switched to a new second-generation antidepressant therapy: discontinuation with switching vs. outright discontinuation (without switching). Patients were considered to have switched to another therapy if they filled a prescription for a second-generation antidepressant other than the index drug within 45 days after the end of the most recent index drug supply and had discontinued the index therapy.

Study design

Time from index therapy initiation to discontinuation or switching was estimated using Kaplan-Meier (K-M) survival curves, and the difference was determined using log-rank tests. Unadjusted analysis compared the observed 6-month discontinuation and switching rates for the two treatment groups using the chi-square test. Cox Proportional Hazards Models were then used to compare the rates of the treatment groups, adjusting for differences in patient baseline characteristics. Discontinuation with and without switching were modeled as competing risks using the Cox model.

The costs of medical services (e.g., psychiatry visit, hospital inpatient and outpatient care, professional services) and prescription drugs were analyzed from Florida Medicaid's perspective. Mental-disorder-related costs were identified using ICD-9-CM codes for the following psychiatric conditions: schizophrenia, other psychotic disorders, dementia and Alzheimer's disease, generalized anxiety disorder, phobia, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, sleeping disorder, and substance abuse. The 6-month all-cause costs and costs related to mental disorder were compared using the Wilcoxon test.

To control for differences in patient baseline characteristics, we used a multivariate generalized linear model (GLM) with log link function and a gamma distribution. Two-part models were adjusted for occurrence of zero costs. The first part was a logistic regression predicting whether any costs were incurred, and the second part was a GLM model with log link and gamma distribution to determine the cost amount. These two parts generated the predictive models for costs for all patients.

TABLE 1
Sample counts of patients in Florida Medicaid by selection criteria

Selection criteria	N
Claimants with ≥2 claims of MDD one of which was after 1/1/2003, or ≥1 inpatient claim with MDD diagnosis that occurred after 1/1/2003.	74,325
Claimants who also have ≥1 fill of SSRI or SNRI after 1/1/2003	53,569
No use of 2nd generation antidepressants in 6 months before the potential index date	33,801
6 months continuous eligibility before and after potential index date, exclude patients eligible to Medicare	16,597
Claimants with monotherapy within 14 days of index date	14,875
Claimants between 18 and 64 years of age taking escitalopram or citalopram as index drug	3,280
Claimants with escitalopram as index drug	2,650
Claimants with citalopram as index drug	630

RESULTS

Baseline characteristics

At baseline, 2,650 patients were initiated on escitalopram and 630 on citalopram. Table 2 summarizes patients' baseline characteristics. There were no significant differences between the two groups in average age, gender distribution, CCI, and mental or other disease prevalence. Although patients from the escitalopram group had significantly more psychiatry institution visits than patients in the citalopram group (21.0% vs. 17.5%, P=0.048), both groups had similar emergency room and office visits, hospitalization rates, prescription drug use, and health care costs in the 6 months pre-index date (Table 2).

Treatment persistence

Results of the unadjusted analysis indicate that patients treated with escitalopram were less likely to discontinue their treatment than were patients treated with citalopram (63.7% vs. 68.9%, P=0.015, Table 3). Escitalopram patients were also less likely to switch to another second-generation antidepressant (14.9% vs. 18.4%, P=0.029). The rate of outright discontinuation of the index drug was comparable between escitalopram and citalopram (48.8% vs. 50.5%, P=0.458). Results of the Cox Proportional Hazards Model confirmed these findings: Escitalopram patients had a lower probability of discontinuing the index treatment (Hazard Ratio=0.85, 95% CI 0.77–0.95) and of switching to another antidepressant (HR=0.75, 95% CI 0.61–0.93). Although escitalopram patients had a lower rate of outright discontinuation, the difference was not statistically significant (HR=0.89, 95% CI 0.78–1.01) (Table 4).

TABLE 2
Baseline characteristics of adult MDD patients in Florida Medicaid by index therapy
Escitalopram vs. citalopram

Baseline characteristics [1]	Escitalopram [A]		Citalopram [B]		Difference [2] [A]–[B] or [A]/[B]	P-value [3] [A] vs. [B]
Study sample (N)	2,650		630			
Demographic characteristics						
Age on index date (Mean, SD)	42.7	(12.9)	43.4	(12.6)	–0.7	0.2501
Female (%)	71.0		70.8		1.0	0.9110
Year of index date (%)<None>						<.0001
Year 2003	35.7		50.8		0.7	
Year 2004	34.2		26.5		1.3	
Year 2005	30.2		22.7		1.3	
Deyo Charlson comorbidity index (Mean, SD)	0.8	(1.7)	0.9	(1.8)	–0.1	0.9406
Comorbidity profile (%)						
Mental diseases						
Schizophrenia	10.9		9.7		1.1	0.3860
Other psychotic disorders	3.9		4.6		0.8	0.3850
Dementia and Alzheimer's disease	0.6		0.5		1.3	0.7040
Generalized anxiety disorder	1.0		0.8		1.3	0.6050
Phobia	0.0		0.0			
Panic disorder	0.8		0.5		1.6	0.4510
Obsessive-compulsive disorder	0.1		0.2		0.7	0.7690
Posttraumatic stress disorder	0.9		0.3		2.8	0.1350
Sleeping disorder	1.3		1.0		1.3	0.4970
Substance abuse	10.9		9.2		1.2	0.2030
Other comorbidities						
Cancer	2.5		2.7		0.9	0.8080
Renal disease	2.5		2.7		0.9	0.7650
Cardiovascular disease	15.7		14.8		1.1	0.5750
Hypertension	19.9		20.6		1.0	0.6890
Diabetes	10.9		12.7		0.9	0.2010
Epilepsy	1.9		2.5		0.7	0.2640
Hyperlipidemia	12.2		10.6		1.2	0.2680
Chronic obstructive pulmonary disease	15.2		14.0		1.1	0.4470
Irritable bowel syndrome	0.6		0.6		0.9	0.8380
Stroke	2.8		1.6		1.7	0.0940
Rheumatoid arthritis and osteoarthritis	4.9		4.6		1.1	0.7220
Number of prescription drugs used (Mean, SD)	9.1	(8.6)	9.1	(9.5)	0.0	0.3990
Health care service utilization (%)						
ER visits	31.5		31.8		1.0	0.9090
Psychiatry institution visits	21.0		17.5		1.2	0.0480*
Regular hospital visits	22.8		23.0		1.0	0.9210
Outpatients hospital/office visits	40.9		38.6		1.1	0.2760
Health care costs, $ (Mean, SD)						
Prescription drug	1,967	(3,616)	1,973	(3,358)	–6	0.7770
Medical service	5,535	(12,223)	6,183	(15,413)	–649	0.3282
Total health care costs	7502	(13,307)	8,156	(16,008)	–654	0.8556

Notes:
[1]Baseline characteristics are measured over the 6-month pre-index period.
[2]Relative risk is calculated for proportions; difference is calculated for continuous variables.
[3]Wilcoxon test is used for comparing continuous variables; Chi-square test is used for comparing categorical variables.
* Significant at 95 percent confidence level.

TABLE 3
Treatment pattern of adult MDD patients in Florida Medicaid by index therapy
Escitalopram vs. citalopram

Treatment pattern [1]	Escitalopram (N=2,650) 6-month rate (%)	Citalopram (N=630) 6-month rate (%)	P-value [2]
Discontinuation [3]	63.7	68.9	0.0150*
With switching [4]	14.9	18.4	0.0290*
Without switching [5]	48.8	50.5	0.4580

Notes:
[1]Observed over the 6-month post-index period.
[2]Chi-square test is used to compare discontinuation rates between therapy groups.
[3]Discontinuation is defined as having at least one 45-day gap between any adjacent index drug supplies.
[4]Discontinuation with switching is defined as having no refill of index drug but at least one prescription of another 2nd generation antidepressant within 45 days from the end of last index drug supply.
[5]Discontinuation without switching is defined as having no refill of index drug as well as any other 2nd generation antidepressant within 45 days from the end of last index drug supply.
* Significant at 95 percent level.

Kaplan-Meier analyses show that escitalopram patients had a significantly longer time to treatment discontinuation than patients treated with citalopram within 6 months post index date (median time 84 days vs. 66 days, P=0.003, Figure 1). Patients in the escitalopram group also had a significantly longer time before switching to a different antidepressant (P=0.004) over the same period (Figure 2). Of patients who discontinued the index drug outright, escitalopram patients stayed 22 days longer on their medication than citalopram patients, although the difference was not statistically significant (median time 120 days vs. 98 days, P=0.073; Figure 3).

TABLE 4
Cox Proportional Hazard Model for therapy compliance of adult MDD patients in Florida Medicaid
Escitalopram vs. Citalopram

Treatment pattern [1]	Coefficient [2]	Hazard ratio	95% Confidence interval	P-value
Discontinuation [3]	–0.161	0.851	(0.765, 0.947)	0.0031*
With switching [4]	–0.284	0.753	(0.610, 0.928)	0.0078*
Without switching [5]	–0.119	0.888	(0.784, 1.005)	0.0605

Notes:
[1]Observed over the 6-month post-index period.
[2]Negative coefficient indicates lower risk of discontinuation for escitalopram patients. Cox regression model is used to control for confounding factors.
[3]Discontinuation is defined as having at least one 45-day gap between any adjacent index drug supplies.
[4]Discontinuation with switching is defined as having no refill of index drug but at least one prescription of another 2nd generation antidepressant within 45 days from the end of last index drug supply.
[5]Discontinuation without switching is defined as having no refill of index drug as well as any other 2nd generation antidepressant within 45 days from the end of last index drug supply.
* Significant at 95 percent level.

Health care costs

In unadjusted analyses of health care costs within 6 months post index date, total prescription drug costs were $347 higher for escitalopram patients than for citalopram patients, although this difference was not statistically significant (P=0.246). However, antidepressant costs were $22 (P=0.004) higher for patients treated with escitalopram than for those treated with citalopram. In terms of medical costs, compared to patients initiated on citalopram, patients initiated on escitalopram had $274 (P=0.782) lower all-cause medical service costs and $333 (P=0.190) lower mental-disorder-related medical service costs (Table 5).

There were no statistically significant differences in these costs by place of service, except for outpatient visits, which were $33 lower for escitalopram patients than for citalopram patients (Table 5). Overall, patients treated with escitalopram had lower all-cause total health care costs (–$621, P=0.070) and mental-disorder-related total health care costs (–$348, P=0.913, Table 5).

After controlling for differences in patient baseline characteristics, over the 6-month post-index time frame, escitalopram patients had $736 lower mental-disorder-related total medical services costs (P=0.009) than citalopram patients (Table 5). Total medical service costs were also numerically lower in the escitalopram cohort (–$467, P=0.251) (Table 5). The majority of the difference in total health care cost appears to be attributable to savings in inpatient hospitalizations related to mental disorder (–$571, P=0.003) and, to a lesser extent, in outpatient visit costs related to mental disorder (–$53, P<0.001) (Table 5). These factors outweighed the higher antidepressant costs ($32, P<0.0001) in the escitalopram group.

On the whole, escitalopram patients had $1,014 lower all-cause total health care costs (P=0.032) and $519 lower total costs related to mental dis-

TABLE 5
6-month health care costs of adult MDD patients in Florida Medicaid by index therapy

	Unadjusted analysis (Wilcoxon test)						Multivariate analysis[4]			
6-month health care costs ($) [1]	Escitalopram (N=2,650) [A]		Citalopram (N=630) [B]		Difference [A]–[B]	P-value [2] [A] vs. [B]	Escitalopram (N=2,650) [C]	Citalopram (N=630) [D]	Difference [C]–[D]	P-value [5] [C] vs. [D]
Prescription drug (mean, SD)										
Total prescription drug cost	3,224	(4,145)	3,571	(4,423)	–347	0.2456	3,426	3,621	–195	0.1582
Total antidepressant cost	310	(208)	288	(230)	22	0.0037*	312	280	32	<.0001*
Total antipsychotics cost	704	(1,324)	742	(1,380)	–38	0.3109	707	727	–19	0.6100
Other drug cost	2,210	(3,799)	2,541	(4,074)	–331	0.2348	2,562	2,817	–255	0.0921
Medical service (mean, SD)										
Psychiatry visit	211	(1,328)	216	(1,533)	–4	0.0656	210	234	–24	0.4342
Psychiatry visit, MD-related[3]	176	(697)	157	(556)	19	0.0678	171	178	–7	0.6941
Inpatient visit	2,389	(8,372)	2,591	(8,130)	–202	0.2674	2,388	2,658	–270	0.2549
Inpatient visit, MD-related[3]	1,479	(6,474)	1,805	(6,276)	–326	0.1961	1,452	2,023	–571	0.0027*
Outpatient / Office visit	434	(1,055)	489	(1,274)	–55	0.5664	431	499	–69	0.0548
Outpatient / Office visit, MD-related[3]	92	(441)	125	(462)	–33	0.0481*	89	142	–53	0.0006*
Professional service	810	(1,756)	794	(1,435)	17	0.4888	822	804	19	0.7629
Professional service, MD-related[3]	126	(381)	128	(391)	–2	0.1942	125	129	–4	0.6602
Total medical service cost	5,534	(12,174)	5,808	(12,272)	–274	0.7821	5,601	6,068	–467	0.2506
Total medical service cost, MD- related[3]	1,935	7067.34	2,268	(6,926)	–333	0.1900	2,058	2,794	–736	0.0092*
Total health care cost (mean, SD)										
Total health care cost	8,758	(13,353)	9,379	(13,315)	–621	0.0696	9,289	10,302	–1,014	0.0320*
Total health care cost, MD-related[3]	2,950	(7,465)	3,298	(7,293)	–348	0.9129	3,076	3,595	–519	0.0234*

MD = mental disorder
Notes:
[1]Costs are measured over 6 months post-index date.
[2]Wilcoxon test is used to compare the costs between therapy groups.
[3]Mental disorder includes major depressive disorder, anxiety, adjusted reaction, bipolar disorder, schizophrenia, other depressive disorders, other psychotic disorder, dementia, Alzheimer's disease, substance abuse, sleeping disorder, and eating disorder
[4]Two-part model is used to estimate the costs for patients on escitalopram or citalopram; GLM model is used for other cost categories.
[5]Bootstrap is used to estimate p-value for the cost difference between patients on escitalopram and patients on citalopram.
* Significant at 95 percent level.

order than citalopram patients (P=0.023) (Table 5).

DISCUSSION

In this analysis of Florida Medicaid claims data, we compared antidepressant treatment persistence, health care resource utilization, and health care costs over 6 months after the initiation of the index SSRI therapy in adult MDD patients treated with citalopram vs. escitalopram. This time frame is critical because 6 months is the minimum duration of successful treatment for an acute depressive episode (i.e., an acute treatment phase plus a continuation phase to prevent relapse) (Conner 1999; Crismon 1999).

Compared to citalopram, treatment with escitalopram was associated with a significantly longer time to discontinuation (84 days vs. 66 days) and longer time to switching to a different second-generation antidepressant. Because patients who have better treatment persistence typically achieve more positive clinical outcomes than patients who are not compliant, the lower discontinuation rate for escitalopram suggests an advantage over citalopram in this specific patient population. While switching to a different SSRI or an SNRI is often effective in MDD patients who do not respond to the initial SSRI therapy (Fava 2003; Nurnberg 1999; Papakostas 2008; Perahia 2008; Ruhe 2006; Rush 2004; Wohlreich 2005), switching to a different SSRI for maintenance therapy can be associated with an increased likeli-

FIGURE 1
K-M estimate of time to index therapy discontinuation

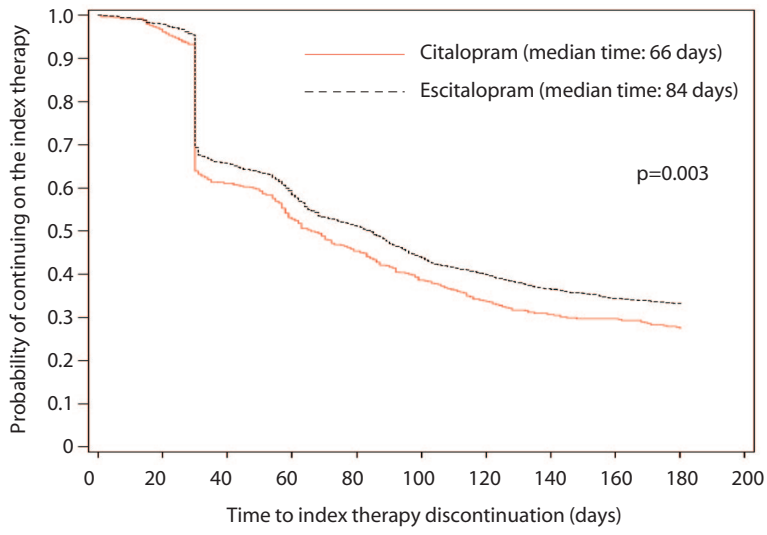
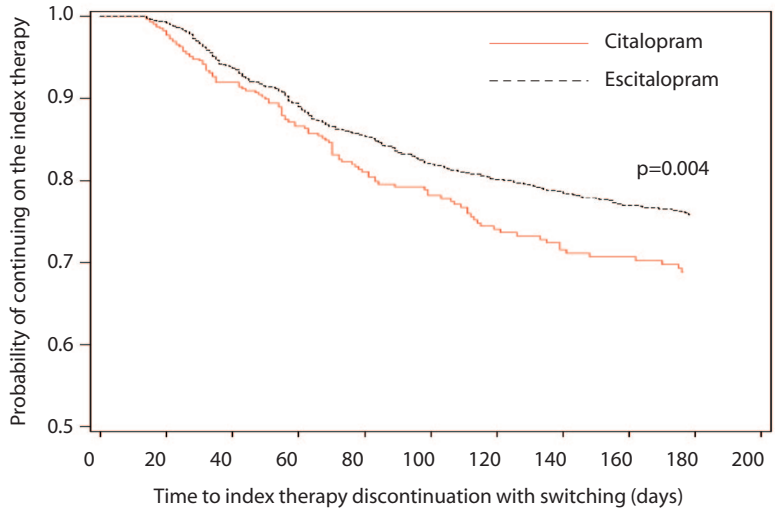


FIGURE 2
K-M estimate of time to index therapy discontinuation with switching



hood of discontinuation because of adverse side effects (Miner 2002).

In addition, early discontinuation of antidepressant treatment and switching to alternate antidepressants have been associated with increased direct medical costs (McCombs 1990; Thompson 1996). It is possible, therefore, that the higher switching rate among citalopram patients contributes to their higher total health care costs compared to escitalopram patients.

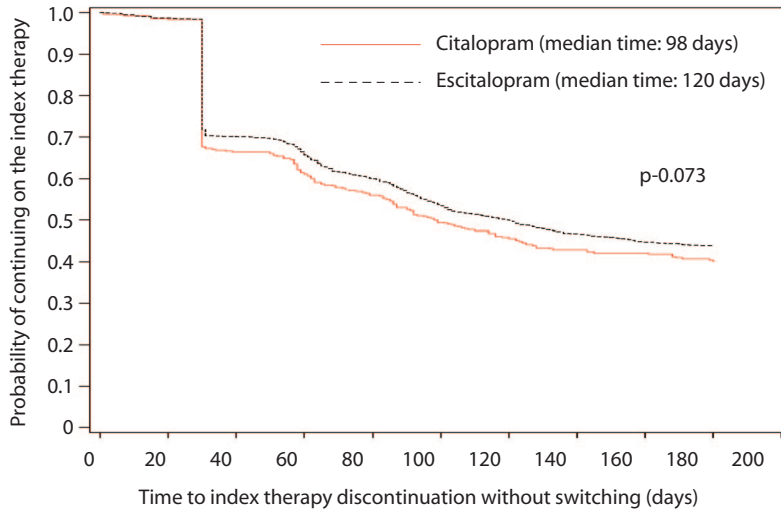
After controlling for differences in patient baseline characteristics, total health care costs in patients treated with escitalopram were lower than for patients treated with citalopram. In the 6 months after therapy initiation, escitalopram patients incurred $1,014 lower all-cause total health care costs and $519 lower mental-disorder-related health care costs (both $P<0.05$). Escitalopram patients also incurred $736 lower total medical costs related to mental disorders compared to citalopram patients.

The biggest contributors to the total cost difference were lower mental-disorder-related hospitalization costs ($571) and lower mental-disorder-related outpatient visit costs ($53) in escitalopram patients vs. citalopram patients, significantly outweighing the higher pharmacy costs for escitalopram. Although in general practice MDD is often not the primary reason for hospitalization, and patients frequently have multiple health conditions in addition to MDD, better treatment for MDD may help patients achieve improved compliance with treatment for other conditions and, therefore, may help reduce overall costs of treatment.

The findings of this study are consistent with a recent comparison of managed care MDD patients ages ≥65 treated with either escitalopram or citalopram, in which escitalopram patients had lower discontinuation and switching rates and lower total health care costs than patients treated with citalopram (Wu 2008). Similar to the findings of the present study, the majority of the total cost reduction was attributable to significantly lower inpatient rates and total medical costs (Wu 2008).

Similarly, a Danish study that compared escitalopram, citalopram, and venlafaxine in the treatment of primary-care MDD patients found escitalopram to be more cost-effective than citalopram, from both health care system and societal perspectives (Sorensen 2007). A prospective double-blind study recently conducted a head-to-head cost comparison between escitalopram and citalopram as a first-line MDD treatment and found that escitalopram was associ-

FIGURE 3
K-M estimate of time to index therapy discontinuation without switching



ated with significantly lower health care costs over the 2-month study period, with most of the difference attributable to fewer hospitalizations (Fantino 2007). Escitalopram was also found to be more cost-effective than citalopram in the treatment of depression in Austria (Hemels 2004), Belgium (Demyttenaere 2005), Norway (François 2003), and the UK (Wade 2005a; Wade et al. 2005b).

Evidence from the present study suggests that escitalopram is associated with better persistence than citalopram in real-world settings; however, additional research is warranted to examine reasons for observed differences in treatment patterns between the two therapies. Persistence results may reflect differences in the clinical efficacy and safety profiles of either therapy, although clinical data signaling efficacy and adverse events could not be obtained from claims data. Many other factors may influence patients' level of persistence to their index antidepressant therapy, including copayment level, availability of coupons for partial copayment reimbursement, other postmarketing promotions, and enrollment in adherence-monitoring programs to encourage long-term persistence.

Although limited data are available in claims to ascertain reasons for observed medication-taking behavior, future studies based on physician chart review/survey or patient registry data may provide insight into the persistence results from the present analysis.

STUDY LIMITATIONS

The present study has several limitations. First, as with all other claims-data studies, it does not permit assessment of direct measures of disease severity or clinical outcomes; thus, outcomes of clinical efficacy could not be compared. Moreover, for a variety of misclassification reasons, not all patients treated for depression are identifiable by ICD-9 code classification.

Second, although administrative claims provide a rich data source for measuring real-world treatment persistence, reasons for discontinuation or switching cannot be determined from the database. This data limitation prevented further investigation of the reasons for differences in persistence between the treatment groups.

Third, patient selection bias may exist if patients in one of the treatment groups had significantly more severe or less severe depression, or if prescribing physicians' characteristics were different between the treatment groups. Although data on patient baseline clinical severity and characteristics of the treating physician (e.g., physician specialty type) were not available, every effort was taken to control for a comprehensive set of patient baseline characteristics observable in claims, including multiple comorbidities and baseline health care usage. Results showed no significant differences between treatment groups in the 6-month baseline period.

Fourth, because patients who augmented treatment with another second-generation antidepressant (i.e., had refills of the index drug as well as other second-generation antidepressants within 45 days after the end of most recent index drug supply) were excluded from the analysis, discontinuation rates for both escitalopram and citalopram could be underestimated.

Fifth, this study focused on a relatively short-term period (6 months) of MDD treatment. Thus, no conclusions about long-term impact can be inferred. None of these factors, however, would be expected a priori to introduce a bias in favor of either escitalopram or citalopram in the present study.

CONCLUSION

This analysis of Florida Medicaid administrative claims data showed that, compared to adult MDD patients initiated on citalopram, escitalopram patients have better treatment persistence and lower total health care costs for any cause and for mental disorders. Most of this is due to lower mental-disorder-related hospitalization costs.

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