RESEARCH

Initial Results of the Use of Prescription Order Change Forms to Achieve Dose Form Optimization (Consolidation and Tablet Splitting) of SSRI Antidepressants in a State Medicaid Program

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ABSTRACT

BACKGROUND: One method to reduce drug costs is to promote dose form optimization strategies that take advantage of the flat pricing of some drugs, i.e., the same or nearly the same price for a 100 mg tablet and a 50 mg tablet of the same drug. Dose form optimization includes tablet splitting; taking half of a higher-strength tablet; and dose form consolidation, using 1 higher-strength tablet instead of 2 lower-strength tablets. Dose form optimization can reduce the direct cost of therapy by up to 50% while continuing the same daily dose of the same drug molecule.

OBJECTIVE: To determine if voluntary prescription change forms for antidepressant drugs could induce dosing changes and reduce the cost of antidepressant therapy in a Medicaid population.

METHODS: Specific regimens of 4 selective serotonin reuptake inhibitors (SSRIs)—citalopram, escitalopram, paroxetine, and sertraline—were identified for conversion to half tablets or dose optimization. Change forms, which served as valid prescriptions, were faxed to Oregon prescribers in October 2004. The results from both the returned forms and subsequent drug claims data were evaluated using a segmented linear regression. Citalopram claims were excluded from the cost analysis because the drug became available in generic form in October 2004.

RESULTS: A total of 1,582 change forms were sent to 556 unique prescribers; 9.2% of the change forms were for dose consolidation and 90.8% were for tablet splitting. Of the 1,118 change forms (70.7%) that were returned, 956 (60.4% of those sent and 85.5% of those returned) authorized a prescription change to a lower-cost dose regimen. The average drug cost per day declined by 14.2%, from $2.26 to $1.94 in the intervention group, versus a 1.6% increase, from $2.52 to $2.56, in the group without dose consolidation or tablet splitting of the 3 SSRIs (sertraline, escitalopram, and immediate-release paroxetine). Total drug cost for the 3 SSRIs declined by 35.6%, from $333,567 to $214,794, as a result of a 24.8% decline in the total days of SSRI drug therapy and the 14.2% decline in average SSRI drug cost per day. The estimated monthly cost avoidance from this intervention, based on pharmacy claims data, was approximately $35,285, about 2% of the entire spending on SSRI drugs each month, or about $0.09 per member per month. Program administration costs, excluding costs incurred by prescribers and pharmacy providers, were about 2% of SSRI drug cost savings.

CONCLUSIONS: Voluntary prescription change forms appear to be an effective and well-accepted tool for obtaining dose form optimization through dose form consolidation and tablet splitting, resulting in reduction in the direct costs of SSRI antidepressant drug therapy with minimal additional program administration costs.

KEYWORDS: Selective serotonin reuptake inhibitors, Dose optimization, Tablet splitting, Prescription change forms

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The clinical impact from many drug cost control policies remains largely unknown, and some policies may have adverse health consequences.[1] Dose optimization is one strategy to reduce prescription drug costs while maintaining nearly identical therapy. Flat-pricing of prescription drugs (i.e., all strengths priced the same) presents an opportunity to save up to 50% of the original prescription cost by using half of a higher-strength tablet (tablet splitting) or by using 1 higher-strength tablet instead of 2 lower-strength tablets (dose consolidation).

The selective serotonin reuptake inhibitor (SSRI) antidepressants are ideal drugs for dose optimization. SSRIs have relatively flat pricing, are manufactured in forms that can be easily split, have a long half-life (with the effect that they are generally taken once daily), and their clinical actions depend on long-term alterations of receptors and neurotransmitter production. Minor variations in dose from the split SSRI tablets are not likely to have significant clinical consequences.[2,3] In addition, SSRIs have a large therapeutic index, so if the dose is inadvertently doubled, the consequences are not typically toxic.[4] Still, not all drugs and not all patients are candidates for dose optimization. For tablet splitting, patients should be physically and cognitively capable of cutting tablets.

The potential cost avoidance of dose optimization programs can be significant.[2,5-7] According to Cohen and Cohen, U.S. taxpayers could have avoided in excess of $1.7 billion dollars in 2000 if all new antidepressant medication prescriptions that

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TABLE 1 *Targeted Tablet Splitting and Dose Consolidation Options*

Target Drug and Regimen		Recommended Drug Regimen(s)	
Tablet-Splitting Targets			
Citalopram 10 mg	1 per day/qty. 30	Citalopram 20 mg	1/2 per day/qty. 15
Citalopram 20 mg	1 per day/qty. 30	Citalopram 40 mg	1/2 per day/qty. 15
Escitalopram 10 mg	1 per day/qty. 30	Escitalopram 20mg	1/2 per day/qty. 15
Escitalopram 5 mg	1 per day/qty. 30	Escitalopram 10 mg	1/2 per day/qty. 15
Paroxetine 10 mg	1 per day/qty. 30	Paroxetine 20 mg	1/2 per day/qty. 15
Paroxetine 20 mg	1 per day/qty. 30	Paroxetine 40 mg	1/2 per day/qty. 15
Sertraline 25 mg	1 per day/qty. 30	Sertraline 50 mg	1/2 per day/qty. 15
Sertraline 50 mg	1 per day/qty. 30	Sertraline 100 mg	1/2 per day/qty. 15
Dose Consolidation Targets			
Citalopram 10 mg	2 per day/qty. 60	Citalopram 20 mg	1 per day/qty. 30
		Citalopram 40 mg	1/2 per day/qty. 15
Citalopram 20 mg	2 per day/qty. 60	Citalopram 40 mg	1 per day/qty. 30
Escitalopram 10 mg	2 per day/qty. 60	Escitalopram 20 mg	1 per day/qty. 30
Paroxetine 10 mg	2 per day/qty. 60	Paroxetine 20 mg	1 per day/qty. 30
		Paroxetine 40 mg	1/2 per day/qty. 15
Paroxetine 10 mg	3 per day/qty. 90	Paroxetine 30 mg	1 per day/qty. 30
Paroxetine 20 mg	1.5 per day/qty. 45	Paroxetine 30 mg	1 per day/qty. 30
Paroxetine 20 mg	2 per day/qty. 60	Paroxetine 40 mg	1 per day/qty. 30
Sertraline 25 mg	2 per day/qty. 60	Sertraline 50 mg	1 per day/qty. 30
		Sertraline 100 mg	1/2 per day/qty. 15
Sertraline 50 mg	2 per day/qty. 60	Sertraline 100 mg	1 per day/qty. 30
Sertraline 50 mg	4 per day/qty. 120	Sertraline 100 mg	2 per day/qty. 60

qty. = quantity.

could be split used pill-splitting regimens.[2] The Portland, Oregon VA described a tablet-splitting program focusing on the SSRIs where clinical pharmacists reviewed refill records for regimens amenable to tablet splitting and substituted higher-dose tablet-splitting regimens when appropriate.[5] The savings attributable to the tablet-splitting program were estimated to be $175,000 over 35 months of follow-up.

The Oregon Health Plan (OHP), Oregon's Medicaid program, covers approximately 400,000 recipients in either contracted capitated managed care plans or in a traditional fee-for-service (FFS) plan. Most psychiatric medications, including antidepressants and antipsychotics, are carved out of managed care contracts and paid directly by the state. The state is prohibited by Oregon statute (ORS 414.325) from engaging in traditional cost-reduction efforts, such as prior authorization, prospective quantity limits, and enforced preferred drug lists, for any of the carved-out psychiatric medications. In 2004, approximately $120 million, 49% of total outpatient drug expenditures (excluding managed care drug payments), was spent on mental health carve-out drugs. Due to the high expenditures and limited options to contain costs, the Oregon State University College of Pharmacy, in conjunction with the Oregon Department of Human Services, initiated a voluntary antidepressant dose optimization program for Medicaid clients. This paper describes the implementation of this program and evaluates its impact on prescription drug utilization and costs.

Methods

Description of the Program

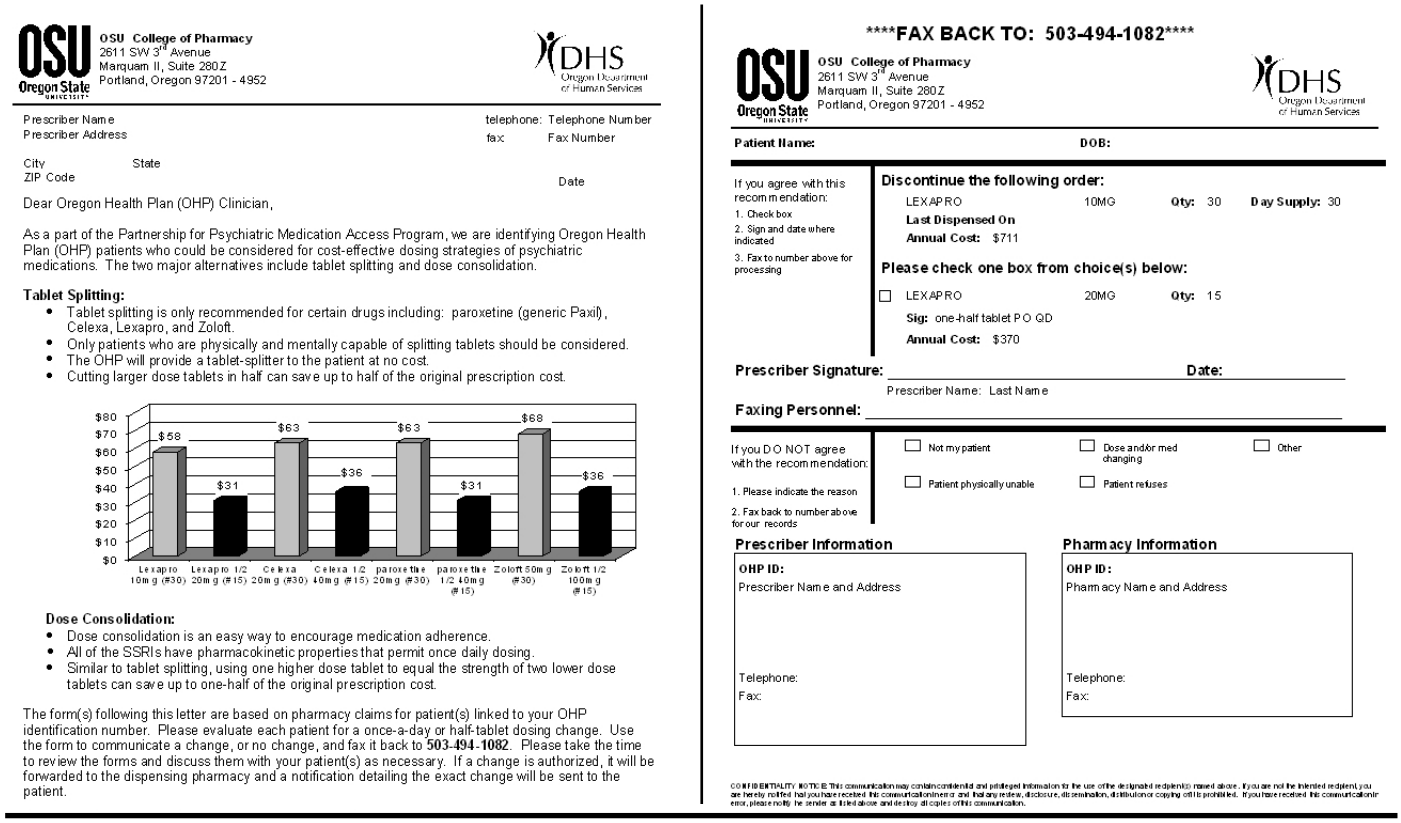
Daily consumption rates from the OHP pharmacy claims data from August and September 2004 were used to identify patients who were receiving 1 of the 4 targeted SSRIs in a dosing regimen listed in Table 1. Because antidepressant medication adherence in a population of patients begins to decline after the initial 2 months of therapy,[8] patients were excluded if they had less than a 60-day SSRI treatment history. Other exclusion criteria were: residence in a long-term care facility and age greater than 74 years. Children were not excluded from this intervention. The intervention also required a valid and identifiable individual prescriber identification number, which was used to determine the prescriber's contact information, including fax number.

Beginning in October 2004, Medicaid prescribers were contacted by fax, using patient-specific forms that identified drug regimens acceptable for dose consolidation (e.g., changing from citalopram 10 mg one tablet twice daily to citalopram 20 mg one tablet daily) or tablet splitting (e.g., changing from sertraline 50 mg one tablet daily to sertraline 100 mg one-half tablet daily) (Table 1). The change forms listed the patient's current therapy (drug, strength, quantity, and estimated annual cost), the suggested alternative regimen(s), and the resulting estimated annual cost (Figure 1 shows an example of a dose optimization change form faxed to a prescriber). Prescribing providers were asked to indicate their desire to discontinue the current dosing regimen in favor of the lower-cost dosing regimen and sign the form, which served as a new prescription. The program was completely voluntary, but prescribing providers were asked to provide reasons why they did not agree with the suggested changes. Authorized prescription forms were forwarded to the patient's pharmacy of record for the original SSRI claim. Notification letters and a brochure describing the program were sent to patients to inform them of the treatment change. Each patient was provided up to 2 tablet splitters per year as part of the program. This intervention program and processes were approved by the Oregon Board of Pharmacy, and evaluation of the program was approved by the Oregon State University Institutional Review Board.

Analysis of the Intervention

The impact of the intervention was evaluated using estimates from returned forms and actual findings from pharmacy claims

FIGURE 1 *Example Dose Optimization Change Form*



OSU College of Pharmacy
2611 SW 3rd Avenue
Marquam II, Suite 280Z
Portland, Oregon 97201 - 4952

DHS Oregon Department of Human Services

Prescriber Name
Prescriber Address
City State
ZIP Code

telephone: Telephone Number
fax: Fax Number

Date

Dear Oregon Health Plan (OHP) Clinician,

As a part of the Partnership for Psychiatric Medication Access Program, we are identifying Oregon Health Plan (OHP) patients who could be considered for cost-effective dosing strategies of psychiatric medications. The two major alternatives include tablet splitting and dose consolidation.

Tablet Splitting:

- Tablet splitting is only recommended for certain drugs including: paroxetine (generic Paxil), Celexa, Lexapro, and Zoloft.
- Only patients who are physically and mentally capable of splitting tablets should be considered.
- The OHP will provide a tablet-splitter to the patient at no cost.
- Cutting larger dose tablets in half can save up to half of the original prescription cost.

Dose Consolidation:

- Dose consolidation is an easy way to encourage medication adherence.
- All of the SSRIs have pharmacokinetic properties that permit once daily dosing.
- Similar to tablet splitting, using one higher dose tablet to equal the strength of two lower dose tablets can save up to one-half of the original prescription cost.

The form(s) following this letter are based on pharmacy claims for patient(s) linked to your OHP identification number. Please evaluate each patient for a once-a-day or half-tablet dosing change. Use the form to communicate a change, or no change, and fax it back to **503-494-1082**. Please take the time to review the forms and discuss them with your patient(s) as necessary. If a change is authorized, it will be forwarded to the dispensing pharmacy and a notification detailing the exact change will be sent to the patient.

****FAX BACK TO: 503-494-1082****

OSU College of Pharmacy
2611 SW 3rd Avenue
Marquam II, Suite 280Z
Portland, Oregon 97201 - 4952

DHS Oregon Department of Human Services

Patient Name: **DOB:**

If you agree with this recommendation:
1. Check box
2. Sign and date where indicated
3. Fax to number above for processing

Discontinue the following order:
LEXAPRO 10MG **Qty:** 30 **Day Supply:** 30
Last Dispensed On
Annual Cost: $711

Please check one box from choice(s) below:
☐ LEXAPRO 20MG **Qty:** 15
Sig: one-half tablet PO QD
Annual Cost: $370

Prescriber Signature: **Date:**
Prescriber Name: Last Name

Faxing Personnel:

If you DO NOT agree with the recommendation:
1. Please indicate the reason
2. Fax back to number above for our records

☐ Not my patient ☐ Dose and/or med changing ☐ Other
☐ Patient physically unable ☐ Patient refuses

Prescriber Information
OHP ID:
Prescriber Name and Address
Telephone:
Fax:

Pharmacy Information
OHP ID:
Pharmacy Name and Address
Telephone:
Fax:

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data. The proportion of suggested changes that were accepted or denied was calculated from returned forms. If denied and returned, the reason for denial was also tabulated. Pharmacy claims data were used to estimate the overall program effectiveness and drug costs avoided. Drug costs were defined as ingredient cost, which included the cost of medication and excluded any cost sharing, professional dispensing fee, or third-party contribution (e.g., Champus, Veterans Administration, workers' compensation, etc.). The changes in average drug cost per pharmacy claim were quantified for the 4-month period prior to the intervention (i.e., June through September 2004) and for the 4-month period following the intervention (i.e., November 2004 through February 2005). Additionally, changes in the average units and days supply dispensed for targeted patients were evaluated to quantify the impact of this program. "Daily units consumed" was calculated by dividing total quantity dispensed by the total days supply as entered by dispensing pharmacists. Daily units consumed was used as one of the primary indicators of program effectiveness because the overall goal of the intervention was to reduce the number of tablets taken per day (i.e., converting a patient from one 50 mg sertraline tablet per day to one half 100 mg sertraline tablet per day). In order to quantify cost avoidance attributable to the program and to verify the estimates made from returned forms, a linear extrapolation of total drug costs for targeted patients based on data from the previous 6 months was conducted and compared with the costs observed. Cost avoidance was estimated as the difference between costs predicted by the linear model and actual observed costs and differs from the immediate reduction in cost estimated from the segmented regression model.

Statistical significance of categorical data was tested with chi-square tests. Monthly trends before and after the intervention were compared using a segmented (piece-wise) ordinary linear squares regression model. The regression model has the general structure:

$$y = \beta_0 + \beta_1 x_1 + \beta_2 z_2 + \beta_3 (x_1 - 4)\, z_2 + \varepsilon$$

where y is the monthly utilization or cost; x_1 is the month number starting with 0 in June; Z_2 is a period indicator variable (0 = preperiod, 1 = postperiod); β_0 estimates the intercept (mean utilization for first month); β_1 estimates the preperiod trend (slope); β_2 estimates the level change in the monthly utilization after the intervention month (November 2004); and β_3 estimates the change in trend (slope change) in the postperiod. This model was applied using the dependent variables total cost and daily units consumed as described by Wagner et al.[9]

TABLE 2 Patient Characteristics

Characteristic	Overall SSRI Population (n = 27,458)	Tablet Splitting (n = 1,436)	Dose Consolidation (n = 146)
Age (SD)	48.5 (21.2)	43.6 (18.3)	44.8 (14.0)
Gender			
Female (%)	19,682 (71.7)	975 (67.9)	107 (73.9)
Race (%)			
White	24,844 (90.5)	1,301 (90.6)	136 (93.2)
Native American	578 (2.1)	42 (2.9)	0 (0)
Hispanic	747 (2.7)	33 (2.3)	5 (3.4)
African American	668 (2.4)	31 (2.2)	2 (1.4)
Asian	421 (1.5)	20 (1.4)	2 (1.4)
Other	200 (0.7)	9 (0.6)	1 (0.7)

SSRI = selective serotonin reuptake inhibitor.

TABLE 3 Change Form Responses From Prescribers

Drug Types	Sent	Returned	% of Sent*	Accepted	% of Sent†	% of Returned Not Accepted
Citalopram	242	171	70.7	145	59.9	15.2
Escitalopram	499	365	73.2	311	62.3	14.8
Paroxetine	448	322	71.9	272	60.7	15.5
Sertraline	393	260	66.2	228	58.0	12.3
Dosing Suggestions	**Sent**	**Returned**	**% of Sent‡**	**Accepted**	**% of Sent§**	**% of Returned Not Accepted**
Dose consolidation	146	87	59.6	72	49.3	17.2
Tablet splitting	1,436	1,031	71.8	884	61.6	14.3
Total	1,582	1,118	70.7	956	60.4	14.5

Chi-square test results:
** P = 0.13 for differences in response between drug type.*
† P = 0.61 for differences in recommendation acceptance between drug type.
‡ P = 0.002 for differences in response between recommendation type.
§ P = 0.004 for differences in recommendation acceptance between recommendation type.

Because the intervention was rolled out during the month of October, that month was omitted from the analysis, resulting in analytical periods of 4 months before and 4 months after October 2004. Statistical significance was set at $P < 0.05$. All statistical analyses were performed with SAS version 8 (SAS Institute, Cary, NC).

Results

In October 2004, 1,582 change forms were faxed to 556 unique prescribing providers. Table 2 shows the general demographic characteristics of patients who were targeted for this intervention and all SSRI users at the time. Compared with the general Oregon Medicaid population of SSRI users, the targeted group was younger, due to the exclusion from the intervention patients residing in long-term care facilities. On average, 2.8 forms were faxed to each prescribing provider (range: 1-22 change forms per prescriber).

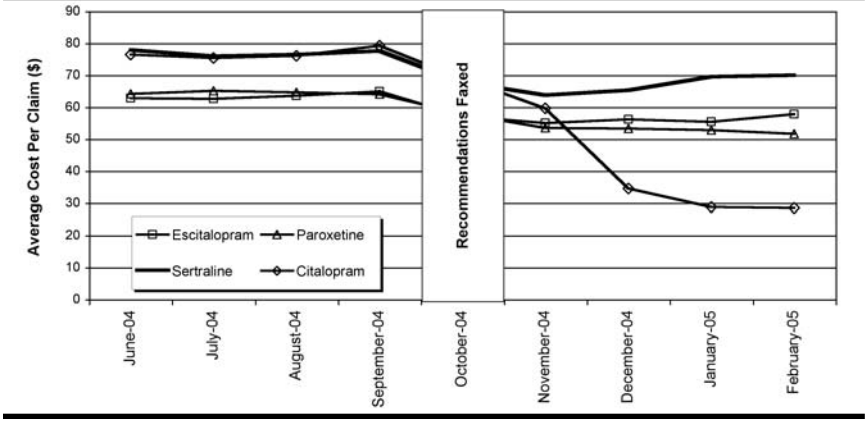
Overall, a total of 1,118 forms (70.7%) were returned, and authorization was provided to change the dosing regimen for 956 patients (60.4% of all forms sent out and 85.5% of returned forms, Table 3). The rate of return was statistically similar between drugs ($P = 0.13$). Forms recommending tablet splitting were significantly more likely ($P = 0.002$) to have been returned (1,031/1,436, 71.8%) than forms suggesting dose consolidation (87/146, 59.6%). However, the rates of acceptance on returned forms were statistically similar between specific drug types and dosing suggestions.

Of those change forms returned and not approved, 96 (8.6%) indicated that the patient was unknown to them, 18 (1.6 %) stated that the patient's dose was changing, 8 (0.7%) indicated that the patient was physically unable to split tablets, 3 (0.3 %) stated that the patient refused, and 37 (3.3 %) did not indicate a reason for denial. Patients for whom a change was authorized were similar to those whose forms were not returned or not authorized with respect to age and gender (data not shown). There were differences in the racial demographics of those patients who received approval for a dosing change compared with those who did not (e.g., 61% of white patients were approved for a change versus 32% of African American patients).

Cost Savings Analysis

Figure 2 shows the average cost per pharmacy claim among patients who were targeted for either of the 2 dose-optimization interventions 4 months before and after recommendations were faxed to prescribers. Reductions in the cost per claim were observed for all 4 target drugs. The average cost per claim for citalopram was reduced by 50%, from $76 in the preperiod (June 2004-September 2004) to $38 in the period after the intervention (November 2004-February 2005). The coincident availability of citalopram in generic form on October 28, 2004,[10] contributed to the reduction in average cost, and citalopram was excluded from the cost savings analysis. Unlike citalopram, by October 2004, only 1 % of all paroxetine immediate-release claims were filled for brand-name Paxil, so the preperiod and postperiod comparisons represent generic paroxetine immediate-release claims. The average drug cost per escitalopram claim was reduced by 12%, from $64 to $56, the average paroxetine drug cost per claim was reduced by 18%, from $64 to $53, and the average sertraline drug cost per claim was reduced by 13%, from $77 to $67 (Figure 2).

FIGURE 2 Average Cost per Claim Among Patients Approved for Dose Optimization



Of the total 26,934 patients who received these 3 SSRIs in June-September 2004, 1,340 (5.0%) were found to be candidates for intervention according to the inclusion/inclusion criteria and the availability of the prescriber's fax number (Table 4). The average units per day declined by 16.4% in the intervention group, from 1.089 in the preperiod to 0.91 in the postperiod, while the average units per day for the nonintervention group was unchanged at 1.149 in the preperiod and 1.148 in the post-period. The average drug cost per day dropped by 14.2%, from $2.26 in the preperiod to $1.94 in the postperiod, compared with a 1.6% increase in the nonintervention group, from $2.52 to $2.56.

Table 5 shows the results of the segmented regression model of the trends for total cost and average units consumed per day for each dosing target. The model demonstrates a statistically significant ($P = 0.05$) reduction in total costs of approximately $24,326 in the month immediately following distributions of our recommendations. The trend (slope) in costs per month did not change significantly ($P = 0.23$). Among patients targeted for dose consolidation, the average units consumed per day was reduced by 0.57 ($P < 0.001$) and the rate decreased by 0.06 units per day per month ($P = 0.03$). Among patients targeted for tablet splitting, a significant -0.30 units per day ($P < 0.001$) decline was observed after October 2004. The rate among those targeted for tablet splitting was also reduced by 0.03 units per day per month ($P < 0.001$).

Based on an extrapolated linear model, we estimate an average monthly cost avoidance of approximately $35,285 for the 4 months from November 2004 through February 2005. This estimate is derived by taking the average of the difference between the projected costs and observed costs for the targeted patients over the study period, as shown in Figure 3. The average monthly enrollment over the study period was 386,312, yielding an average monthly cost per member per month (PMPM) reduction of around $0.09. This estimate does not include the cost avoidance from the dose optimization of citalopram.

Discussion

The intervention using prescription change forms to encourage the dose form optimization of SSRIs appears to be an effective method that resulted in significant cost avoidance. Other studies have demonstrated drug cost savings from interventions designed to affect dose consolidation.[6,11] Calabrese and Baldinger[6] reported an estimated annualized drug cost savings of $390,662 for 454 approved dosage optimization changes, or $1.67 per member per year (PMPY; $0.14 PMPM). Their study was not limited to the SSRI drug class (sertraline, fluoxetine, and immediate-release paroxetine); it also included venlafaxine XR, 3 HMG CoA reductase inhibitors, 2 angiotensin-converting enzyme inhibitors, 2 proton pump inhibitors, and 2 calcium channel blockers.

Later, Delate et al., in a randomized study design, found that administrative costs incurred by the dose form consolidation program and accounting for dose changes and discontinued therapy that occurred regardless of the dose consolidation intervention resulted in net estimated savings of only $0.02 to $0.03 PMPM across 68 dosage strengths of 37 single-source maintenance drugs.[11] This compares with our $0.09 PMPM in the present study for 3 SSRI drugs and $0.14 PMPM in the Calabrese and Baldinger analysis, also across a much wider array of drugs and drug classes. The intervention program described by Delate et al. did not use preprinted change forms. The use of preprinted forms that serve as valid prescriptions for specific patients, with specific dose regimen changes and pharmacy contact information, may facilitate change by making the process more readily useable, with less administrative cost for prescribers. Our intervention was also 2-fold: dose optimization composed of both dose consolidation and tablet splitting.

Because approximately 60% of the dose change requests were accepted shows that the intervention in the present study was well received by prescribers. Our 60% success rate was higher than the 49% rate reported by Calabrese and Baldinger,[6] but our rate of 71% of requests that were returned is similar to the 68% reported by Calabrese and Baldinger. While we experienced a rejection (denied) rate of 15% of returned forms, Calabrese and Baldinger reported that 19% of change requests were denied by prescribers.

Although no formal analysis of physician or pharmacist time was performed, suggestions about the efficiency of the intervention process were solicited from pharmacists who attended the state-wide meeting of the Oregon State Pharmacist Association in May 2005.

The voluntary nature of this program maintained the

TABLE 4 Drug Cost and Utilization Outcomes

All SSRI Medicaid Except Intervention Patients	Preintervention Jun.-Sep. 2004	Postintervention Nov.-Feb. 2005	% Change
Total SSRI drug cost*	$5,545,600	$5,471,042	-1.3
Total number of SSRI claims	74,603	72,145	-16.7
Total number of SSRI days	2,200,389	2,137,522	-2.9
Total number of SSRI units	2,528,905	2,454,804	-2.9
Total number of SSRI patients	25,594	24,334	-4.9
Average days per patient	86.0	87.8	2.1
Average units per day	1.149	1.148	<0.1
Average drug cost per day	$2.52	$2.56	1.6
Intervention Patients Only			
Total SSRI drug cost	$333,567	$214,794	-35.6
Total number of SSRI claims	4,927	3,697	-25.0
Total number of SSRI days	147,284	110,712	-24.8
Total number of SSRI units	160,412	100,772	-37.2
Total number of SSRI patients	1,340	1,340	0.0
Average days per patient	109.9	82.6	-24.8
Average units per day	1.089	0.910	-16.4
Average drug cost per day	$2.26	$1.94	-14.2

** Drug cost is the ingredient cost (total amount paid + patient copays + third-party contribution – pharmacy professional fee).*
SSRI = selective serotonin reuptake inhibitor. The SSRIs in this analysis include escitalopram, paroxetine, and sertraline.

TABLE 5 Segmented Linear Regression Models

Dependent Variable	Immediate Change After Intervention Period	*P* Value†	Slope Change (Per Month)	*P* Value†
Total costs*	-$24,326	0.05	-$4,309	0.23
Units per day dose consolidation	-0.57	<0.001	-0.06	0.03
Units per day tablet splitting	-0.30	<0.001	0.029	<0.001

** Excludes citalopram drug costs.*
† P values from segmented linear regression model beta coefficients.

prescriber's autonomy while providing a convenient mechanism for prescription changes. The segmented linear regression model showed significant reductions in SSRI expenditures and units consumed for both recommendations. Using data from pharmacy claims, we estimate the drug cost savings attributable to this program to be approximately $35,285 per month, or approximately $141,000 over the 4-month study period. Due to the chronic nature of the use of antidepressant medications, the savings from this intervention would be expected to accrue beyond the 4-month measurement period.

During the intervention period, approximately $1.8 million per month was spent for the SSRI drug class among about 27,000 unique users; thus, a 2% savings was realized from the limited target population. Estimated startup costs for this intervention, including the cost of program development, programming, and dissemination, were approximately $7,000. This estimate includes 60 hours of pharmacist time and 30 hours of data programming time. The pharmacist time was used in the development and approval process of the intervention. The data programmer was responsible for automating the prescription change form. The annual administrative costs for this program are estimated to be an additional $7,000, including 20 hours per year of pharmacist time, 60 hours per year of administrative time, and 60 hours per year of data programming time. On an ongoing basis, the pharmacist promotes the intervention in public meetings and modifies the intervention as necessary with the help of the data programmer. The administrative time is used in answering questions and gathering missing data. Overall, the cost of the program is estimated to be less than 2% of the annual cost avoidance.

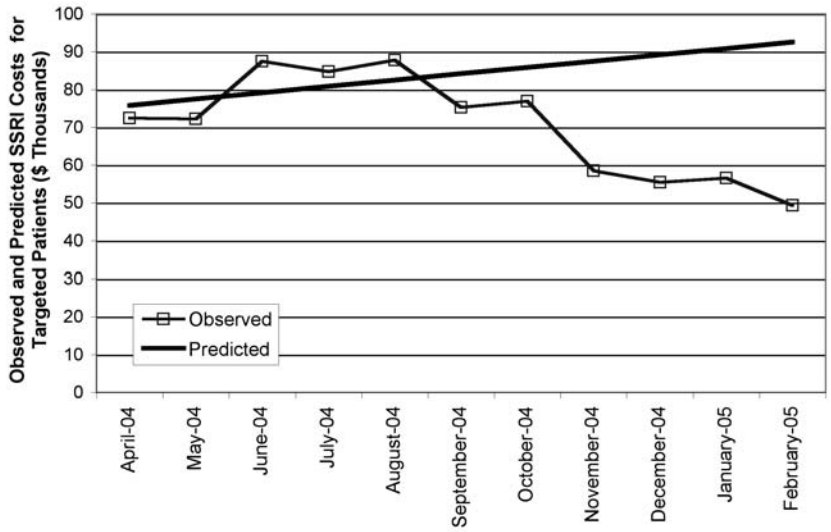
The pharmacological properties (e.g., long half-life and relative safety in overdose) and relatively flat pricing of SSRI doses make this an ideal drug class to test the use of prescription change forms. As more of the brand-name SSRIs become generic, there will be less cost savings available from a dose optimization intervention. The principles of prescription change forms, however, can be used with a variety of other mediation classes (e.g., angiotensin receptor blockers [ARBs], duloxetine, venlafaxine XR, atypical antipsychotics, etc.).[6,11,12] Specific drug interventions should be selected carefully, however, because of the potential risk of patients doubling the intended dose of their medications.

Another process to promote the cost-effective dosing of SSRIs would be to use quantity limits in the benefit coding, which would require the use of half tablets or dose consolidation prior to claim payment. While this approach may be effective, it would create the need for override criteria to deal with claim denial when the clinician believes half tablets or dose consolidation is not appropriate for the patient, potentially leading to a delay in therapy for some patients and additional administrative cost for prescribers and pharmacy providers.

Limitations

There are a number of limitations associated with this intervention and its analysis that should be noted. First, the coincident introduction of generic citalopram made it difficult to differentiate the proportion of costs that were produced from the dose optimization intervention compared with the market shift from brand to generic citalopram. To avoid an overestimate, we excluded those patients and the costs of citalopram from the overall cost analyses. Based on our analysis of returned forms, converting a citalopram prescription to a dose optimized

FIGURE 3 Average Cost per Claim Among Patients Approved for Dose Optimization



regimen was no less likely than any other drug type. Therefore, the exclusion of citalopram from the cost analysis most likely contributed somewhat to an underestimate of the actual drug cost savings from this intervention program.

A second important limitation is the absence of a thorough analysis of the administrative cost of this intervention. While we estimated departmental administrative cost, we did not determine or estimate the time spent by physicians and their office staff and pharmacists and pharmacy personnel in making the dose changes for these Medicaid recipients. However, the program was believed to be well received by most pharmacists and clinic staff who interacted with us during administration of this intervention.

Third, based on prior experience with similar interventions, it was determined that tablet splitters should be made available at no cost to patients, and OHP administrators agreed to reimburse the cost of 2 tablet splitters per patient per year. However, most tablet splitters do not have a National Drug Code (NDC) number, which is necessary for point-of-sale billing. The absence of NDC numbers makes pharmacy reimbursement through electronic pharmacy claims difficult. To help alleviate this problem, pharmacies were routinely sent lists of billable tablet splitters and their NDC numbers.

Fourth, this type of intervention requires a prescriber file with the fax numbers of the medical offices. In Oregon, pharmacy claims are linked to a unique OHP identification number that is issued to each OHP prescriber and group practice. Linking pharmacy claims to the prescriber file obviously requires that pharmacies transmit accurate prescriber identification numbers. Pharmacies have the ability to use an override code when the prescriber identification number is unknown to them. Approximately one third of pharmacy claims are processed with the unknown prescriber override code. Therefore, this intervention was limited to the two thirds of SSRI claims for which the prescriber could be identified.

Fifth, drug manufacturer rebates were not considered in the cost impact analysis, although this omission would have a negligible effect since we measured the cost difference between 2 periods of time for the same drug. More important, we made no attempt to estimate total potential cost avoidance in future claims from the effect of educating prescribers of the opportunity for dose optimization through dose consolidation or table splitting. The latter omission could contribute to significant understatement of the actual drug cost savings associated with this intervention.

Finally, we did not evaluate the impact of the order change forms on medication adherence or other potential indicators of clinical outcomes. A substantial decline in the average days supply dispensed per patient was observed among targeted patients (Table 4). This observation could be due to a break or stop in therapy as a result of the transition from the old to a new regimen. Alternatively, it could have been an artifact of pharmacists entering a reduced day supply for a targeted patient regimen change (i.e., 15 tablets for 15 days instead of 30 days). Although prescribers and dispensing pharmacists were strongly encouraged to speak with patients about potential medication changes, and patients received a letter describing the exact medication change, there is the potential that patients could misunderstand the dosage change and inadvertently take a dose other than the dose intended.

Conclusion

The utilization of a voluntary prescription change form process appears to be an effective mechanism to promote dose form optimization and reduction in the direct costs of SSRIs. The 71% prescriber response rate and overall 60% success rate suggests that the program was well received by prescribing providers. We estimate that this program saved the state approximately $35,285 per month, or 2% of the total SSRI-related pharmacy costs.

DISCLOSURES

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thors. Drafting of the manuscript and its revision were primarily the work of Hamer, Hartung, and Haxby, with input from the coauthors.

REFERENCES

1. Soumerai S. Unintended outcomes of medicaid drug cost-containment policies on the chronically mentally ill. *J Clin Psychiatry.* 2003;64(suppl 17):19-22.

2. Cohen CI, Cohen SI. Potential savings from splitting newer antidepressant medications. *CNS Drugs*. 2002;16(5):353-58.

3. Polli JE, Kim S, Martin BR. Weight uniformity of split tablets required by a Veterans Affairs policy. *J Manag Care Pharm*. 2003;9(5):401-07.

4. Isbister GK, Bowe SJ, Dawson A, Whyte IM. Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose. *J Toxicol Clin Toxicol*. 2004;42(3):277-85.

5. Dobscha SK, Anderson TA, Hoffman WF et al. Strategies to decrease costs of prescribing selective serotonin reuptake inhibitors at a VA Medical Center. *Psychiatry Serv.* 2003;54(2):195-200.

6. Calabrese DC, Baldinger SL. Dose-optimization intervention yields significant drug cost savings. *J Manag Care Pharm*. 2002;8(2):146-51.

7. Curtiss FR, Dose optimization: an opportunity for pharmacy administrative services. *J Manag Care Pharm*. 2002;8(2):81-82.

8. Curtiss FR, Evidence-based medicine: are SSRIs more effective than placebo and what length of therapy is enough? *J Manag Care Pharm*. 2005;11(2):172-76, 77-78.

9. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther.* 2002;27(4):299-309.

10. U.S. Food and Drug Administration. Center for Drug Evaluation and Research First-time Generics—October 2004. October 28, 2004, Available at: http://www.fda.gov/cder/ogd/approvals/1stgen1004.htm. Accessed March 6, 2006.

11. Delate T, Fairman KA, Carey SM, Motheral BR. Randomized controlled trial of a dose consolidation program. *J Manag Care Pharm*. 2004;10(5):396-403.

12. Gee M, Hasson NK, Hahn T, Ryono R. Effects of a tablet-splitting program in patients taking HMG-CoA reductase inhibitors: analysis of clinical effects, patient satisfaction, compliance, and cost avoidance. *J Manag Care Pharm*. 2002;8(6):453-58.