

Controlling Prescription Drug Expenditures: A Report of Success

David P. Miller, MD; Curt D. Furberg, MD, PhD; Ronald H. Small, MBA;
Franklyn M. Millman, MD; Walter T. Ambrosius, PhD;
Julia S. Harshbarger, PharmD; and Christopher A. Ohl, MD

The United States spends more than \$700 per capita on prescription drugs yearly, a figure nearly twice as high as that in any other country.^{1,2} Since the year 2000, national spending on prescription drugs has increased between 8% and 15% annually, representing the fastest-growing segment of healthcare spending.^{1,3} Current yearly spending on prescription drugs exceeds \$200 billion.

Faced with these rising costs, employers and health benefit plans have attempted to control drug expenditures by restricting access to expensive medications and encouraging cost-effective prescribing. Specific strategies have included imposing quantity limits, requiring prior approval for select medications, establishing restrictive formularies, and introducing cost sharing.⁴ Studies examining the impact of these strategies on cost containment and quality of care have yielded mixed results. Some studies have reported harmful effects of quantity limits and cost sharing, including patients discontinuing their use of essential medications, higher rates of hospitalizations, and increased numbers of emergency department visits.⁵⁻¹² When changes to cost sharing are small, others have found no effect on health outcomes.^{7,13}

Although prior studies have focused on the short-term effects of single interventions, most health plans use a combination of strategies to control costs. Whether combining strategies can yield additional cost savings (and whether cost savings can be sustained over time) is unknown. The lack of comparative studies also makes it difficult to determine which strategies are most effective. In addition, the impact of cost sharing on health outcomes and the use of essential medications in diverse populations remains unclear. Many prior studies focused on the adverse effects in vulnerable populations, who may be more cost sensitive.^{5,6,8,9} Higher-income individuals may respond to cost sharing differently.

We report on the 3-year experience of a health plan in North Carolina that implemented a series of evidence-based interventions to control prescription drug expenditures in a varied population. To examine the impact of the program on cost and access to medications, we used a quasi-experimental pre-post design.

Objective: To determine whether a multi-interventional program can limit increases in prescription drug expenditures while maintaining utilization of needed medications.

Study Design: Quasi-experimental, pre-post design.

Methods: The program included formulary changes, quantity limits, and mandatory pill splitting for select drugs implemented in phases. We assessed the short-term effects of each intervention by comparing class-specific drug spending and generic medication use before and after benefit changes. Long-term effects were determined by comparing overall spending with projected spending estimates, and by examining changes in the planwide use of generic medications over time. Effects on medication utilization were assessed by examining members' use of selected classes of chronic medications before and after the policy changes.

Results: Over 3 years, the plan and members saved \$6.6 million attributed to the interventions. Most of the savings were due to the reclassification of select brand-name drugs to nonpreferred status (estimated annual savings, \$941 000), followed by the removal of nonsedating antihistamines from the formulary (annual savings, \$565 000), and the introduction of pill splitting (annual savings, \$342 000). Limiting quantities of select medications had the smallest impact (annual savings, \$135 000). Members' use of generic medications steadily increased from 40% to 57%. Although 17.5% of members stopped using at least 1 class of selected medications, members' total use of chronic medications remained constant.

Conclusions: A combination of interventions can successfully manage prescription drug spending while preserving utilization of chronic medications. Additional studies are needed to determine the effect of these cost-control interventions on other health outcomes.

(*Am J Manag Care.* 2007;13:473-480)

METHODS

Study Health Plan

Wake Forest University Baptist Medical Center is comprised of Wake Forest University Health Sciences and

In this issue

Take-away Points / p479

www.ajmc.com

Full text and PDF

Web exclusive

eFigures A and B

**For author information and disclosures,
see end of text.**

Table 1. Demographic Characteristics of Study Plan Members (Employees Only)

Employee Characteristic	Employer	
	Health Sciences	Hospital
Compensation type, n (%)		
Hourly	1645 (45.5)	5077 (71.4)
Salaried	1970 (54.5)	2036 (28.6)
Total	3615 (100)	7113 (100)
Age, mean (SD)	43.6 y (10.8 y)	40.4 y (11.0 y)
Annual income, mean (SD)	\$50 143 (\$47 869)	\$49 167 (\$36 995)
Female sex, n (%)	2421 (67.0)	5484 (77.1)
Race/ethnicity, n (%)		
White	3094 (85.6)	5029 (70.7)
Black	288 (8.0)	1794 (25.2)
Asian	161 (4.5)	206 (2.9)
Hispanic/Latino	50 (1.4)	69 (1.0)
Other	22 (0.6)	15 (0.2)

SD indicates standard deviation.

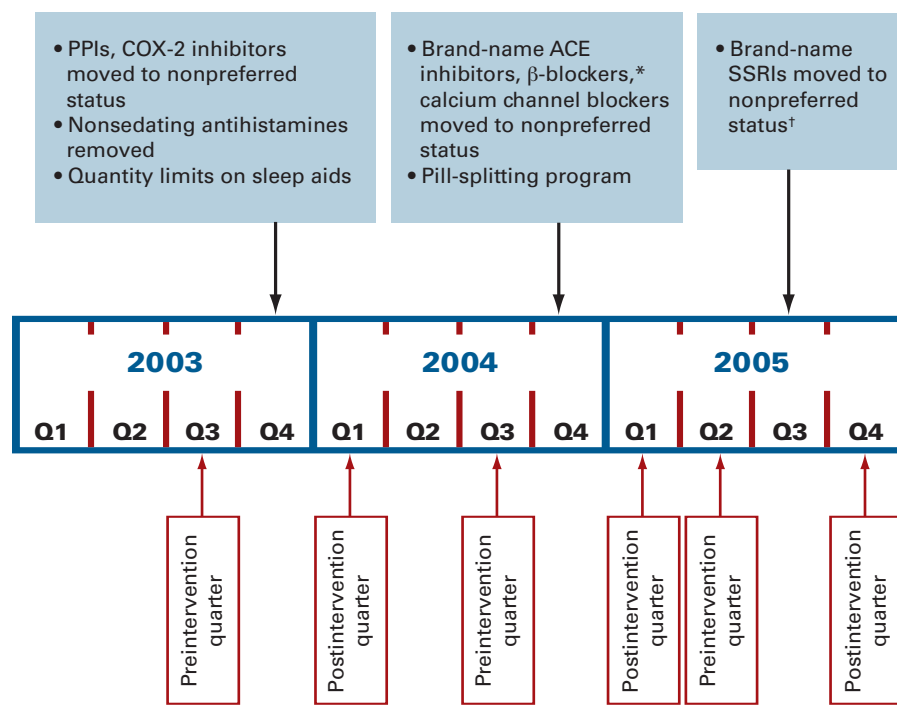
the North Carolina Baptist Hospital, an 821-bed licensed teaching hospital. With more than 11 000 employees, this medical center ranks among the top 15 largest employers in North Carolina. The institution manages its own health benefit plan that covers more than 22 000 lives comprised of hourly and salaried workers and their dependents (Table 1). All plan members have prescription drug coverage with a 3-tiered copayment structure (current copayments for 30-day supplies are \$10 for generics, \$25 for preferred brand-name products, and \$50 for nonpreferred brand-name products). Because the plan has retail pharmacies on site, it does not offer a mail-order pharmacy. Over-the-counter (OTC) medications are not covered.

Cost-control Interventions

The health plan’s goal was to control prescription drug spending while preserving high-quality medical care through a variety of approaches. To best implement this goal, the health plan first sought to learn from the experiences of local and regional experts. A local advisory committee of clinical leaders, pharmacists, and administrators was formed. The advisory committee reviewed the literature examining the effectiveness of interventions designed to control drug spending and considered any proposed strategy’s potential impact on healthcare quality. A statewide workshop attended by the leadership of North Carolina’s major health plans, the Department of Veterans Affairs, and other experts also was convened to share experiences with controlling drug expenditures.

Through this evolving process, the committee identified 4 interventions to encourage cost-effective prescribing. These 4 interventions were launched in 3 phases between the fourth quarter of 2003 and the third quarter of 2005 (Figure). First,

Figure. Time Line of Interventions and Study Time Periods



*Sustained-release metoprolol (Toprol XL) and carvedilol (Coreg) were retained as preferred drugs because of cost and quality concerns.
 †Sertraline (Zoloft) was retained as a preferred drug because of quality concerns.
 PPI indicates proton pump inhibitor; COX-2, cyclooxygenase enzyme type 2;
 ACE, angiotensin-converting enzyme; SSRI, selective serotonin reuptake inhibitor.

Controlling Prescription Drug Expenditures: A Report of Success

for classes of medications with similarly effective or potentially safer generic substitutions, the plan shifted all brand-name drugs from preferred to nonpreferred status, eliminating the preferred brand-name tier. Second, classes of medications with similarly effective OTC substitutions were removed from the formulary. In these cases, the OTC medication was less expensive than the prior required copayment. Third, the plan introduced quantity limits for medications not indicated for daily use. Fourth, a program of mandatory pill splitting for select drugs in the institution's outpatient pharmacies was begun. The pill-splitting program, which was based on a similar policy of the Department of Veterans Affairs Mid-Atlantic Healthcare Network, applied to 6 brand-name antidepressants and 3 brand-name 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins).

Data Collection

The Wake Forest University Health Sciences Institutional Review Board approved the study protocol. We obtained all prescription data and cost information from the firm that manages the plan's pharmaceutical benefits (Catalyst Rx®, Rockville, Md). We examined the ability of each intervention to control short-term costs by comparing class-specific spending for all prescription drugs during the quarter after the cost-containing strategy was implemented with the class-specific spending in the quarter before it was implemented (Figure 1). The quarter in which each change was made was excluded from analysis to account for the variable amount of time it may take patients to respond to benefit changes. Plan cost was defined as the actual amount spent by the plan (total prescription cost less member copayments). Member cost was defined as the total spending on copayments. Member expenditure on OTC medications was not measured. To determine specific strategies' ability to encourage the use of cheaper alternatives, we also tracked class-specific use of generic medications.

We assessed the long-term combined effects of the interventions by examining the plan's use of generic medications in aggregate and total spending on prescription drugs over time. To determine total savings, we compared combined plan and member spending with expected spending based on national figures reported by the Centers for Medicare and Medicaid Services.³ We also examined changes in the use of generic medications over time.

To determine effects on healthcare quality, we assessed members' use of selected classes of long-term medications before and after changes in the benefit plan. Selected classes included angiotensin-converting enzyme (ACE) inhibitors, β -blockers, calcium channel blockers, and selective serotonin reuptake inhibitors (SSRIs). We chose med-

ication utilization as the quality outcome of interest because it is the most proximate to changes in benefit design. We hypothesized that if members' use of needed medications remained constant, then other health outcomes should remain unchanged.

Statistical Analysis

As described above, we focused on claims in the quarters immediately before and after the interventions. The total costs were calculated by summing all claims during the preintervention and postintervention quarters. Significance of savings (Table 2) was assessed using a Wilcoxon signed rank test (a paired analysis) using the participant-specific costs in both quarters. Participants with claims in only 1 quarter were assigned a cost of zero in the other quarter, which is consistent with the fact that the plan did not incur charges for those participants at those times. Significance of generic utilization (Table 3) also was assessed using a Wilcoxon signed rank test, with the proportion of generic utilization per quarter as the participant-specific outcome variable.

RESULTS

At baseline in 2003, 36% of the plan's members used the prescription drug benefit. There was an average of 2.8 drug claims per member per quarter. The majority of claims (60%) were for brand-name-only drugs. Total plan costs for prescription drugs in 2003 totaled \$10.1 million or \$35.57 per member per month, and drug expenditures had doubled over the prior 5 years. In comparison, similar hospital-based health plans reported an average of 1.9 claims per member per quarter at a plan cost of \$27.73 per member per month (Catalyst Rx® data).

Short-term Effects

Table 2 summarizes the quarterly changes in plan and member spending attributed to each of the 4 interventions and the overall total. Comparing the preintervention quarters with the postintervention quarters, plan and member spending on prescription medications fell by \$496 000 (or approximately \$2 million annualized). This amount equates to a quarterly savings of \$39.34 per utilizing member. Approximately half of these savings is attributable to reclassifying select brand-name drugs as nonpreferred agents.

Reclassifying all brand-name proton pump inhibitors as nonpreferred resulted in the largest quarterly savings to the plan (~\$156 000). The remaining 3 interventions also decreased total spending, although to a lesser extent (Table 2). Removing nonsedating antihistamines from the formulary

■ **Table 2.** Savings by Specific Interventions in US Dollars

Intervention	No. of Utilizing Members	Plan Spending (US \$)			Member Spending (US \$)			Total Difference (US \$)	Annualized Savings [†] (US \$)
		Pre-intervention Quarter	Post-intervention Quarter	Difference* (Post - Pre)	Pre-intervention Quarter	Post-intervention Quarter	Difference* (Post - Pre)		
Move brand-name drugs to nonpreferred status									
β-blockers	1098	7354	4849	-2504	23 577	24 657	1080 (NS)	-1424	5697
Calcium channel blockers	631	31 113	20 370	-10 743	22 689	27 507	4818	-5925	23 699
ACE inhibitors	980	16 892	8825	-8068	26 947	26 277	-670 [‡]	-8738	34 952
COX-2 inhibitors or NSAIDs	2114	91 960	47 139	-44 821	39 224	51 939	12 715	-32 107	128 427
Proton pump inhibitors	1621	310 015	153 768	-156 247	72 336	66 286	-6050	-162 298	649 190
SSRIs	2016	131 853	92 766	-39 087	63 728	78 044	14 316	-24 771	99 084
Total for status change	8460 [§]	589 187	327 717	-261 470	248 502	274 710	26 207 (NS)	-235 262	941 050
Remove items from formulary									
Nonsedating antihistamines	1329	83 344	271	-83 074	58 312	150 [§]	-58 162	-141 236	564 942
Limit drug quantities									
Sedative sleep aids	632	35 019	6438	-28 581	18 998	13 848	-5149	-33 731	134 922
Mandate pill splitting	2181	221 063	147 035	-74 028	109 674	98 142	-11 532	-85 560	342 239
Total	12 602[§]			-447 153			-48 636	-495 789	1 983 153

**P* < .001 unless otherwise noted.
[†]Estimated annualized savings were calculated by multiplying the combined quarterly plan and member savings by 4.
[‡]*P* < .05.
[§]Because some members used more than 1 class of drugs, members may be counted more than once.
NS indicates not significant (*P* > .05); ACE, angiotensin-converting enzyme; COX-2, cyclooxygenase enzyme type 2; NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitor.
^{||}Due to technical issues, a few prescriptions for nonsedating antihistamines were filled after the date they were removed from the formulary.

resulted in plan quarterly cost savings of approximately \$83 000; mandatory pill splitting resulted in plan quarterly savings of approximately \$74 000. Limiting quantities of sedating sleep aids had the smallest impact, with plan quarterly savings of approximately \$29 000.

Member spending on prescription drugs also decreased, with total quarterly savings of approximately \$49 000. Removal of nonsedating antihistamines yielded the largest spending decrease (~\$58 000). This spending decrease did not reflect possible member purchases of OTC antihistamines. Pill splitting decreased members' quarterly spending by approxi-

mately \$12 000, and quantity limits on sleep aids lowered spending by approximately \$5000. In contrast, member spending on drugs reclassified as nonpreferred agents increased by approximately \$26 000 per quarter. Most of the increased spending can be attributed to use of SSRIs and cyclooxygenase enzyme type 2 inhibitors.

Within specific classes, the use of generic medications increased after brand-name drugs were reclassified as nonpreferred agents (Table 3). On average, generic utilization increased from 44.8% to 53.7% in the first quarter after the changes were made. Generic utilization increased the least

■ **Table 3.** Generic Utilization for Select Drug Classes, Preintervention vs Postintervention

Drug Class	Preintervention Quarter		Postintervention Quarter		% Change	P
	Total No. of Scripts	% Generic	Total No. of Scripts	% Generic		
ACE inhibitors	1959	68.8	1925	82.1	13.3	<.0001
β-blockers	1998	65.9	2007	66.4	0.5	.03
Calcium channel blockers	1191	47.9	1138	61.9	13.9	<.0001
COX-2 inhibitors or NSAIDs	2289	46.2	1954	54.0	7.8	.05
Proton pump inhibitors	3025	15.9	1870	18.3	2.4	.25
SSRIs	3357	42.0	3391	46.6	4.6	<.0001
Total	13 819	44.8	12 285	53.7	8.9	<.0001

ACE indicates angiotensin-converting enzyme; COX-2, cyclooxygenase enzyme type 2; NSAID, nonsteroidal anti-inflammatory drug; SSRI, selective serotonin reuptake inhibitor.

for β-blockers, which had a high baseline rate of generic utilization at 65.9%. For all other classes of medications, use of generic agents increased by 2.4% to 13.9%.

Long-term Effects

Since implementing these strategies, combined plan and member spending for prescription drugs has remained constant over 3 years. During this same time period, national spending rose by 7.9% to 8.3% annually.³ At this rate of increase, calculated savings during 2006 was \$3.4 million or approximately \$156 per member (eFigure A; see www.ajmc.com). Over the past 3 years, total estimated cost avoidance has exceeded \$6.6 million. Coincident with these savings, members' use of generic medications has progressively increased from 40% during the third quarter in 2003 to 57% in the third quarter of 2006 (eFigure B; see www.ajmc.com). Members' share of total drug expenditures also has remained constant, with copayments accounting for 30% to 32% of total spending.

Utilization of Long-term Medications

Approximately 3800 members used at least 1 ACE inhibitor, β-blocker, calcium channel blocker, or SSRI in the quarter before and after the interventions (Table 4). Although 17.5% of members ceased their use of at least 1 of these classes within 6 months of the interventions, an equal number of members started taking at least 1 of these medications. Individual member discontinuation rates were highest for SSRIs (21.9%) and lowest for ACE inhibitors (11.7%). Total member utilization of these classes was unchanged over time.

DISCUSSION

In summary, we found that a series of easy-to-implement interventions successfully controlled prescription drug spending while maintaining utilization of selected classes of long-term medications. Following the implementation of the interventions, total spending on prescription drugs by the health plan and by its members has remained constant over 3 years, compared with a nationally observed average 8% annual increase in prescription drug spending. The resulting cumulative cost avoidance has exceeded \$6.6 million. Of note, this is a conservative estimate as surveys of major insurers projected prescription spending increases of 14% to 18% over the same time frame.¹⁴

Similar to prior studies, we found that reclassifying drugs within a tiered copayment system can reduce drug expenditures by encouraging the use of more cost-effective medications.¹⁵ However, we also examined the effectiveness of interventions other than cost sharing such as pill splitting and quantity limits. In our analysis, eliminating the preferred brand-name tier by moving all brand-name drugs to nonpreferred status when similarly effective generic agents were available was responsible for approximately half the yielded savings. Removing medications from the formulary when similarly effective OTC therapies existed yielded the next greatest savings. In all cases in which drugs were removed from or shifted within the formulary, members' out-of-pocket spending would have remained constant or decreased if they changed to the generic or OTC alternatives.

Previous studies have documented the potential for pill splitting to save costs, but they have not reported significant

■ **Table 4.** Members' Use of Select Medications Before and After Interventions

Drug Class	Preintervention	Postintervention	
	No. of Utilizing Members	No. of Utilizing Members	% Discontinuing Class of Drug*
ACE inhibitors	829	839	11.7
β-blockers	902	928	14.5
Calcium channel blockers	501	509	19.1
SSRIs	1580	1569	21.9
Total	3812	3845	17.5

*"Percent discontinuing class of drug" is the percentage of members with at least 1 claim in the preintervention quarter who had no claim in the postintervention quarter. Members who exited the health plan before the end of the postintervention quarter were excluded from this analysis.
ACE indicates angiotensin-converting enzyme; SSRI, selective serotonin reuptake inhibitor.

savings in actual practice.^{16,17} Many medications are priced the same, regardless of the medication dose. Therefore, significant cost savings may be achieved by splitting tablets. In our study, the limited pill-splitting program accounted for approximately 17% of the total savings.

Some national organizations have raised concerns about the safety of splitting tablets.¹⁸ Tablet splitting requires some dexterity, and not all split tablets result in similarly weighted halves.¹⁹ Despite these limitations, prior studies have demonstrated similar outcomes for blood pressure and lipid control in patients taking split-tablet medications.²⁰ A second concern is the additional pharmacist time that tablet splitting requires. Even if patients are given tablet-splitting devices, pharmacists must instruct patients on the proper technique and assess their capability.

The final intervention of introducing quantity limits for select drugs yielded the least amount of savings. The impetus for this intervention was to discourage the daily use of medications that are indicated for intermittent use only. Although calculated savings were less than those resulting from the other interventions, they still approached \$135 000 yearly.

Others have found that patients' use of long-term medications may decrease when cost sharing is introduced or increased.^{10-12,15} Total member use of our selected classes of long-term medications did not change. However, there was a turnover of individual users, with 12% to 22% of members discontinuing therapy within 6 months of the interventions and a similar percentage starting therapy. Others have found similar rates of patients discontinuing medications even in the

absence of a benefit change. For example, prior studies have reported discontinuation rates of 11% to 16% for antihypertensives and 20% for SSRIs.^{7,13,21} For new users of antidepressants, discontinuation rates at 3 months may be as high as 44%.²² Determination of whether individual members stopped taking medications for appropriate reasons such as adverse reactions or a change to a more effective agent would require a resource-intensive chart review and was outside the scope of this study. Nonetheless, the constant aggregate use of medications and the fact that the discontinuation rates we observed are within expected ranges suggest that members' access to needed medications remained intact.

One possible explanation for the constant aggregate use of medications is that member spending on prescription drugs did not increase significantly following the implementation of the cost-control strategies. Alternatively, our studied population may have more financial resources, decreasing this population's price sensitivity. However, given the observed rise in the use of generic medications, it appears the members responded to the incentives by switching to more cost-effective alternatives. Recent data on the safety of generic drugs with narrow therapeutic windows suggest that patients may safely switch from brand-name to generic agents.²³

One challenge for benefit administrators is ensuring that new policies are acceptable to clinicians. The use of an advisory committee that included clinical leaders from the parent institution helped the health plan accomplish this goal. The plan also consulted in advance with physicians in specialties that might be affected by a proposed benefit change. In addition, the plan consciously avoided any policies that might substantially increase clinician workloads, such as requiring prior approvals for costly therapies. Although clinician satisfaction was not measured, there were very few formal or informal negative comments or complaints brought to committee members by their medical staff colleagues.

Preventing prescription drug costs from rising has allowed the health plan to invest in new initiatives to improve the health outcomes of patients with chronic disease. For example, the plan recently moved all brand-name formulations of insulin and diabetic testing supplies to the generic copayment tier (\$10 per month) to encourage medication adherence and monitoring. The plan also moved all formulations of warfarin to the generic copayment level to facilitate adequate anticoagulation therapy.

Controlling Prescription Drug Expenditures: A Report of Success

The prescription drug market is in constant flux, with changes in the availability of generic agents and an expanding evidence base for both the benefits and harms of individual therapies. Therefore, the process of controlling drug expenditures requires constant vigilance. Copayment structures must be continually reevaluated to ensure that the most cost-effective care is being encouraged. In addition, new strategies for controlling costs must be explored. The study health plan is continuing to monitor and update its formulary to reflect this changing landscape. Recent changes not reflected in this analysis include a reclassification of all brand-name statins and all brand-name SSRIs to nonpreferred status given the recent new generic availability of additional medications within these classes.

Limitations

As with any single-site study, our findings may not be applicable to other settings. Observational studies also are unable to control for every factor. One factor that changed during our retrospective review was a modest increase in the copayment amounts for preferred and nonpreferred drugs of \$5 and \$10, respectively. The effect of small increases in copayments on medication continuance rates is unclear. Several prior studies have reported no change,^{13,24-26} whereas others have reported small decreases in utilization in response to modest copayment increases.^{11,12} In our analysis, members' total use of medications remained unchanged, but it is possible that these modest copayment increases contributed to the observed use of less-expensive medications.

Historical control groups can be susceptible to confounding if other factors change over time. However, aside from the interventions studied, there were no significant changes in the health plan or its membership during the study period. Specifically, there were no other targeted interventions or campaigns, and the size and demographics of the membership remained similar over the 3 years (data not shown). To further guard against confounding, we calculated long-term savings compared with conservative national averages and projections to account for any possible societal trends toward the use of more cost-effective medications, such as the natural increased availability of generic medications as patents expire.

Additional limitations include the constraints of the claims database, which does not capture members' payments for OTC medications. However, medications were only removed from the formulary if the cost for the OTC substitute was similar to or less than the prior required copayments. For example, a 30-day supply of OTC loratadine costed \$26.60,

Take-away Points

Carefully selecting cost-control interventions that avoid increasing plan members' out-of-pocket costs may avert increases in prescription drug spending while preserving long-term medication use.

- Encouraging the use of cost-effective alternatives to brand-name drugs through formulary changes may yield the most savings.
- Pill splitting for select medications can yield substantial cost savings.
- The ever-changing landscape of the prescription drug market requires health plans to continually reevaluate and adjust benefit designs.
- Controlling prescription drug spending can allow health plans to encourage better health outcomes by reducing price barriers for the treatment of chronic diseases.

whereas the relevant copayments for brand-name non-sedating antihistamines were \$25 or \$50. Therefore, we would expect members' out-of-pocket costs to remain the same or decrease after the benefit changes, making it unlikely that OTC spending would substantially change our results.

Our database also did not include information on health outcomes other than medication utilization. Additional studies are needed to determine whether health outcomes such as disease control or hospitalization are similarly unaffected by the benefit changes.

CONCLUSION

By carefully selecting cost-control interventions that offer the potential for plan members to reduce their out-of-pocket costs, health plans may control their prescription drug spending while preserving access to needed medications. Additional studies are needed to determine the effect of these cost-control interventions on other health outcomes. Given the ever-changing landscape of the prescription drug market and the constant addition of new medical knowledge, the process of encouraging cost-effective medical care requires continued reevaluation and adjustment.

Acknowledgments

The Wake Forest University Baptist Medical Center Outpatient Prescription Drug Subcommittee formulated the interventions studied. Ron Hoth, BSBA, Henry Russ, BA, and Marc Sears, MS, provided the baseline data for the study health plan.

Author Affiliations: From the Department of Internal Medicine (DPM, FMM, CAO) and the Division of Public Health Sciences (CDF, WTA), Wake Forest University School of Medicine, Winston-Salem, NC; North Carolina Baptist Hospital, Winston-Salem, NC (RHS); and Catalyst Rx®, Rockville, Md (JSH).

Author Disclosure: Five of the authors (DPM, CDF, FMM, RHS, CAO) serve on the Outpatient Prescription Drug Subcommittee for the study's health plan. One author (JSH) is an employee of Catalyst Rx®, the pharmacy benefit management company for the health plan.

The authors (DPM, CDF, RHS, FMM, WTA, JSH, CAO) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter discussed in this manuscript.

Authorship Information: Concept and design (DPM, CDF, FMM, CAO); acquisition of data (DPM, RHS, JSH); analysis and interpretation of data (DPM, CDF, RHS, WTA, JSH, FMM, CAO); drafting of the manuscript (DPM, WTA, CAO); critical revision of the manuscript for important intellectual content (DPM, CDF, RHS, FMM, WTA, CAO); statistical analysis (DPM, WTA); administrative, technical, or logistic support (CDF); supervision (CDF).

Address correspondence to: David P. Miller, MD, General Internal Medicine, Wake Forest University Health Sciences, Medical Center Blvd, Winston-Salem, NC 27157. E-mail: dmiller@wfubmc.edu.

REFERENCES

1. **Heffler S, Smith S, Keehan S, Borger C, Clemens MK, Truffer C.** U.S. health spending projections for 2004-2014. *Health Aff (Millwood)*. 2005 Jan-Jun;Suppl Web Exclusives:W5-74-W5-85.
2. **Organization for Economic Cooperation and Development.** *OECD Health Data 2004*. 1st ed. June 2004. Available at: <http://www.oecd.org/dataoecd/3/62/31938359.pdf>. Accessed January 14, 2005.
3. **Centers for Medicare & Medicaid Services.** *National Health Care Expenditures Projections: 2005-2015*. 2006. Available at: http://www.cms.hhs.gov/NationalHealthExpendData/03_NationalHealthAccountsProjected.asp#TopOfPage. Accessed July 19, 2007.
4. **Olson BM.** Approaches to pharmacy benefit management and the impact of consumer cost sharing. *Clin Ther*. 2003;25:250-272.
5. **Tamblyn R, Laprise R, Hanley JA, et al.** Adverse events associated with prescription drug cost-sharing among poor and elderly persons. *JAMA*. 2001;285:421-429.
6. **Goldman DP, Joyce GF, Escarce JJ, et al.** Pharmacy benefits and the use of drugs by the chronically ill. *JAMA*. 2004;291:2344-2350.
7. **Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG.** The effect of incentive-based formularies on prescription-drug utilization and spending. *N Engl J Med*. 2003;349:2224-2232.
8. **Soumerai SB, Ross-Degnan D, Avorn J, McLaughlin T, Chodnovskiy I.** Effects of Medicaid drug-payment limits on admission to hospitals and nursing homes. *N Engl J Med*. 1991;325:1072-1077.
9. **Blais L, Couture J, Rahme E, LeLorier J.** Impact of a cost sharing drug insurance plan on drug utilization among individuals receiving social assistance. *Health Policy*. 2003;64:163-172.
10. **Gibson TB, Mark TL, McGuigan KA, Axelsen K, Wang S.** The effects of prescription drug copayments on statin adherence. *Am J Manag Care*. 2006;12:509-517.
11. **Goldman DP, Joyce GF, Karaca-Mandic P.** Varying pharmacy benefits with clinical status: the case of cholesterol-lowering therapy. *Am J Manag Care*. 2006;12:21-28.
12. **Schultz JS, O'Donnell JC, McDonough KL, Sasane R, Meyer J.** Determinants of compliance with statin therapy and low-density lipoprotein cholesterol goal attainment in a managed care population. *Am J Manag Care*. 2005;11:306-312.
13. **Fairman KA, Motheral BR, Henderson RR.** Retrospective, long-term follow-up study of the effect of a three-tier prescription drug copayment system on pharmaceutical and other medical utilization and costs. *Clin Ther*. 2003;25:3147-3161.
14. **The Segal Company.** 2007 Segal health plan cost trend survey. 2006. Available at: <http://www.segalco.com/publications/surveysandstudies/2007trendsurvey.pdf>. Accessed March 23, 2007.
15. **Gibson TB, Ozminkowski RJ, Goetzel RZ.** The effects of prescription drug cost sharing: a review of the evidence. *Am J Manag Care*. 2005;11:730-740.
16. **Stafford RS, Radley DC.** The potential of pill splitting to achieve cost savings. *Am J Manag Care*. 2002;8:706-712.
17. **Vuchetich PJ, Garis RI, Jorgensen AM.** Evaluation of cost savings to a state Medicaid program following a sertraline tablet-splitting program. *J Am Pharm Assoc*. 2003;43:497-502.
18. **Tablet splitting: evaluating appropriateness for patients.** *J Am Pharm Assoc (2003)*. 2004;44:324-325.
19. **Polli JE, Kim S, Martin BR.** Weight uniformity of split tablets required by a Veterans Affairs policy. *J Manag Care Pharm*. 2003;9:401-407.
20. **Noviasky J, Lo V, Luft DD, Saseen J.** Clinical inquiries. Which medications can be split without compromising efficacy and safety? *J Fam Pract*. 2006;55:707-708.
21. **Bull SA, Hu XH, Hunkeler EM, et al.** Discontinuation of use and switching of antidepressants: influence of patient-physician communication. *JAMA*. 2002;288:1403-1409.
22. **Lin EH, Von Korff M, Katon W, et al.** The role of the primary care physician in patients' adherence to antidepressant therapy. *Med Care*. 1995;33:67-74.
23. **Paterson JM, Mamdani M, Juurlink DN, Naglie G, Laupacis A, Stukel TA.** Clinical consequences of generic warfarin substitution: an ecological study. *JAMA*. 2006;296:1969-1972.
24. **Motheral B, Fairman KA.** Effect of a three-tier prescription copayment on pharmaceutical and other medical utilization. *Med Care*. 2001;39:1293-1304.
25. **Johnson RE, Goodman MJ, Hornbrook MC, Eldredge MB.** The impact of increasing patient prescription drug cost sharing on therapeutic classes of drugs received and on the health status of elderly HMO members. *Health Serv Res*. 1997;32:103-122.
26. **Motheral BR, Henderson R.** The effect of a copayment increase on pharmaceutical utilization, expenditures, and treatment continuation. *Am J Manag Care*. 1999;5:1383-1394. ■