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RESEARCH STUDIES

Express Scripts Drug Trend Report 2004

Express Scripts Research Studies: 2002 to 2005

PHARMACY BENEFIT DESIGN

Cox ER, Mager DE. Geographic variation in generic fill rate. 2003. The purpose of this study was to evaluate the geographic variation in generic fill rate by state. Data were extracted from a 2003 database containing ambulatory administrative pharmacy-claims and eligibility information for a random sample of approximately 3 million commercially-insured members. The generic fill rate was adjusted for age and gender using a generalized linear model. The generic fill rate ranged from a low of 39.5% in New Jersey to a high of 51.3% in Massachusetts. Possible explanations for the variations include differences in prescribing patterns, state regulations and disease prevalence, and varying use of drug-benefit designs that encourage generic use. These findings suggest that opportunities exist to achieve greater savings through adoption of programs designed to increase generic use in states where the generic fill rates are lower.

Cox ER, Svirnovskiy Y, Mager DE, Fairman KA. Trends in the prevalence of antidepressant use in children: 2003-2004. In a study published by Express Scripts in 2004, the use of antidepressants among children 18 years old and younger increased 9.2% each year from 1998 to 2002. In 2003, the FDA issued a Public Health Advisory warning of increased suicidal thoughts and behavior in children taking certain antidepressants. To determine whether the warning affected the use of antidepressants in children, Express Scripts researchers evaluated prescription-claims data for 2003 and the first half of 2004. The study sampled more than 5 million commercially-insured children ranging in age from birth to 19 years old. Results indicate that antidepressant use in children continued to rise through the first half of 2004. The overall rate of antidepressant use in children grew from 1.47% in the first quarter of 2003 to 1.61% in first quarter 2004 — a 9.4% increase in the prevalence of use. While overall growth continued, rates of use appeared to moderate for teens and decrease for children under 9 years old in second quarter 2004. It is unclear whether the decrease in use among children 9 years old and under was due to the FDA Advisory, because the studies documenting increased risk were in children no younger than 7 years old (the youngest group studied ranged from 7 years old to 9 years old). Physicians can be anticipated to use greater caution when prescribing antidepressants for children, but a dramatic drop in antidepressant use is unlikely to be seen, due to the use of antidepressants for other mental health conditions in children and to the limited availability of therapeutically-equivalent alternatives.

Delate T, Mager DE, Sheth J, Motheral BR. Clinical and financial outcomes associated with a proton pump inhibitor prior-authorization program in a Medicaid population. *American Journal of Managed Care*. 2005;11(1):131-139.

The purpose of this study was to examine the outcomes associated with a proton pump inhibitor (PPI) prior-authorization (PA) policy. Using a time-series analysis, a six-month pre- and post-design was used to estimate clinical and financial effects of the policy. Results indicated that expenditures per member per month (PMPM) decreased 91% for PPIs and increased 223% for histamine 2-receptor antagonists (H2As) in the month immediately following the policy implementation. Analysis showed that enrollees who received an H2A or no antisecretory drugs were no more likely to have incurred greater total medical expenditures than enrollees who received a PPI. The use of PA for PPIs encouraged the use of lower-cost H2As and reduced the use of high-cost PPIs without evidence of adverse medical consequences.

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

The purpose of this study was to evaluate the effectiveness and financial impact of a drug dose-consolidation program using a letter-based communication intervention. Using a randomized, controlled research design, three study arms were evaluated: a letter-based intervention with both physicians and members, a letter-based intervention with physicians only, and a control group with no intervention to members or physicians. The letters, which were personalized to the member or physician, contained information about the inefficiency of prescribed regimens and suggested dose-consolidation options. A review of pharmacy-claims data was performed for three consecutive months. Data identified inefficient regimens for any one of 68 dosage strengths of 37 single-source maintenance drugs, which all have once-daily dosing recommendations.

Study results found that the rate of consolidation to a suggested dose was higher for both intervention groups compared with the control group; however, the rate was higher for the physician/member intervention group compared with the physician-only group. Financial modeling indicated that a dose-consolidation intervention could save \$0.03 to \$0.07 (in 2003 dollars) PMPM with full medication compliance, but only \$0.02 to \$0.03 PMPM when savings were calculated with realistic, partial-compliance rates. Findings indicated, therefore, that the letter-based dose-consolidation program did not decrease prescription-drug expenditures appreciably.

Cox ER, Henderson R, Motheral BR. Health plan member experience with point-of-service prescription step therapy. *Journal of Managed Care Pharmacy*. 2004;10(4):291-298.

The purpose of this study was to better understand the experience of members with point-of-service step-therapy edits and the outcomes associated with these edits in terms of the drug received. Self-administered surveys were mailed to members who experienced a step-therapy edit for proton pump inhibitors or non-steroidal anti-inflammatory drugs. Based on the results of the mailed survey, a telephone survey was conducted among a separate group who experienced a step-therapy edit and did not have a subsequent claim. Results of this study show that 59.4% of members received a medication covered by their health plan following a step-therapy edit. Among remaining members, 11.2% paid the total cost out of pocket, 11.2% did not fill the prescription at all and received no other similar medications, 8.1% received an over-the-counter medication, 3.6% obtained samples, and 6.6% didn't remember or filled their prescriptions another way. Results suggest that opportunities exist for better member and provider communications that help increase the use of first-line drugs and reduce the number of members who pay out of pocket or receive no medication.

Motheral BR, Henderson R, Cox ER. Plan-sponsor savings and member experience with point-of-service prescription step therapy. *American Journal of Managed Care*. 2004;10(7 Pt 1):457-464.

The study examined the effect of prescription step-therapy programs on plan-sponsor saving and member experience at the point of service. A quasi-experimental case-control study design was used to measure plan-sponsor savings. Member experience with step therapy was measured through a self-administered, mailed survey. Results of this study show a decrease of \$0.83 in net cost after implementing step therapy in the intervention group, while the comparison group had an increase of \$0.10 PMPM for these therapy classes. Members who did not receive a medication were less likely to be satisfied with their pharmacy benefit, compared with those who received first-line therapy or those who paid out of pocket for the brand medication. The study shows that step therapy can have significant drug savings; however, opportunities exist to further members' and providers' understanding of step-therapy programs.

Delate T, Henderson RR, Motheral BR. Financial impact of benefit design choice for non-sedating antihistamines. January 2004.

All forms and strengths of Claritin® — a prescription non-sedating antihistamine (NSA) — became available for sale over the counter (OTC) in December 2002. No generic for Claritin entered the market, and comparable drugs remained available by prescription only. As a result, health plans have a number of trend-management options for OTC Claritin and the prescription NSA products. This study presents an evaluation of the financial impact on health-plan decisions regarding NSA coverage.

This study is available at www.express-scripts.com.

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.

Clinical Therapeutics. 2003;25(12):3147-3161.

The purpose of this study was to examine the effect of a three-tier copayment system on utilization and cost of both prescription-drug and medical benefits. The study followed a group of commercially-insured, preferred-provider organization members for 30 months after the three-tier system was implemented. Results showed reduced growth in net cost and lower utilization of third-tier medications. The intervention and comparison groups did not differ significantly with respect to numbers of office visits, emergency department visits or inpatient hospitalizations.

Roe CM, Heinle SM, Cox ER. Design of a three-tier benefit and cost trend. *Drug Benefit Trends*. 2002;14(8):21-26.

This study explored how the design of a three-tier prescription benefit correlates to drug trend. Pre- to post-period change in payer cost was examined for 20 plans that switched from a two-tier to a three-tier copayment design. Pre- to post-period trends in PMPM net costs decreased when the aggressiveness of the three-tier structure and copayment per prescription increased. This study suggests that more aggressive three-tier structures are associated with lower net-cost trend.

COST-EFFECTIVENESS OF PHARMACEUTICALS

Cox ER, Motheral BR, Mager D. Verification of a decision analytic model assumption using real-world practice data: implications for the cost effectiveness of cyclo-oxygenase 2 inhibitors (COX-2s).

The American Journal of Managed Care. 2003;9(12):785-794.

This study evaluated the gastroprotective agent (GPA) rate assumption used to model cost-effectiveness for COX-2s and to re-estimate model outcomes using GPA rates from actual practice. This study found the rate of GPA use is positive and marginally higher among COX-2 users than among nonselective non-steroidal anti-inflammatory (NSAID) users. Findings suggest a re-evaluation of COX-2 cost-effectiveness models is warranted.

Cox ER, Motheral BR, Frisse M, Behm A, Mager D. Prescribing COX-2s for patients new to cyclo-oxygenase inhibition therapy.

The American Journal of Managed Care. 2003;9(11):735-742.

The purpose of this study was to profile the pattern of COX-2 use, including length of therapy, medical conditions treated and gastrointestinal (GI) risk. Medical- and prescription-claims data from a large, preferred-provider organization were used to evaluate diagnostic conditions and patterns of use among new COX-2 users. Approximately 19% of patients did not have a diagnosis associated with COX-2 therapy; 65% did not have an indication of being at risk for GI events; and 68% had no history of trying a lower-cost nonselective NSAID before beginning COX-2 therapy. Overall, 45% did not have a GI risk factor or prior use of nonselective NSAID therapy. Findings suggest that opportunities exist to encourage cost-effective prescribing of COX-2 therapy.

Fairman KA, Motheral BR. Do decision-analytic models identify cost-effective treatments? A retrospective look at *Helicobacter pylori* eradication. *Journal of Managed Care Pharmacy.* 2003;9(5):430-440.

This study was a retrospective examination of whether *H. pylori* pharmacoeconomic models lead to cost-effective therapeutic choices by decision-makers. When model assumptions were replaced with empirical data from a multi-payer claim database, model results were found to have overstated the cost-effectiveness of PPI-clarithromycin and understated the cost-effectiveness of bismuth-metronidazole-tetracycline (BMT).

POPULATION HEALTH AND PHARMACEUTICALS

Cox ER, Frisse M, Behm A, Fairman KA. Over-the-counter pain reliever and aspirin use within a sample of long-term cyclo-oxygenase 2 users. *Archives of Internal Medicine*. 2004;164(11):1243-1246.

The purpose of this study was to estimate the co-medication rates for aspirin, ibuprofen, acetaminophen and naproxen sodium among long-term COX-2 users. A telephone survey was used to measure co-medication use. The survey was conducted by nurses trained in survey administration. Members were asked about their use of COX-2s and OTC pain-relieving agents over the past 30 days. They were asked to report the number of days they took each medication, the dose or strength of the drugs and, for those taking aspirin, the reason for its use. Study results show a high rate of co-medication with aspirin for cardioprotection (99%) and a sizeable percentage of co-medication with OTC pain relievers (76%). These co-medication patterns, which have implications for patient gastrointestinal safety, may suggest the need for better pain management.

Motheral BR, Heinle SM. Predictors of satisfaction of health plan members with prescription drug benefits. *American Journal of Health-System Pharmacy*. 2004;61(10):1007-1014.

This study examined relationships between socio-demographic and health-plan characteristics, and member satisfaction with their prescription-drug benefits. Surveys were mailed to a stratified, random sample of members to assess knowledge of their prescription-drug benefits, as well as their experience and satisfaction with those benefits. Of the 14,141 surveys mailed, 3,819 were returned (27% response rate). Respondents were more likely to be home-delivery users and less likely to be enrolled in a plan with a closed formulary. Results indicated that the most important feature of the prescription-drug benefit is out-of-pocket cost. Lower satisfaction was associated with higher copayments, coinsurance, closed formularies, intensive managed care, large healthcare premiums, a recent increase in copayments and a recent denial of coverage. Greater satisfaction was associated with excellent health and home-delivery use.

Delate T, Simmons VA, Motheral BR. Patterns of use of sildenafil among commercially-insured adults in the United States: 1998-2002. *International Journal of Impotence Research*. 2004;16(4):313-318.

This study profiled the use of sildenafil (Viagra®) in the U.S. The percentage of Express Scripts members who used sildenafil increased substantially from 1998 to 2002. Males aged 18 years old to 45 years old — the current target of direct-to-consumer advertising — were the fastest-growing segment of sildenafil users. The proportion of users with an underlying medical reason declined in all age groups over the five years. The finding that a stable number of sildenafil tablets was dispensed per prescription over the study period suggests that plan-sponsor use of benefit strategies can help manage trend for this therapy class.

Delate T, Gelenberg AJ, Simmons VA, Motheral BR. Trends in the use of antidepressant medications in a nationwide sample of commercially insured pediatric patients, 1998-2002. *Psychiatric Services*. 2004;55(4):387-391.

The purpose of this study was to determine contemporary estimates for the prevalence of ambulatory antidepressant medication (ADM) use among commercially-insured children and adolescents. Results indicated that the growth in the prevalence of ADM use in these populations appears to be continuing at rates similar to those seen earlier for second-generation ADMs.

Cox ER, Motheral BR, Henderson RR, Mager D. Geographic variation in the prevalence of stimulant medication use among children 5 to 14 years old: Results from a commercially insured US sample. *Pediatrics*. 2003;111(2):237-243.

This study evaluated geographic variation in the use of stimulant medications in a sample of commercially-insured children aged 5 years old to 14 years old. The study also evaluated age, gender, income, urban or rural residence, and other factors thought to influence the use of stimulants in children. The study found significant variation in use of stimulants across geographic regions, with lower use in the West and higher use in the South and the Midwest.

Teitelbaum F, Parker AR, Frear RS, Vargas SL. The change in the use of hormone replacement therapies (HRT) combination products, estrogens and other agents used to treat osteoporosis since the release of HERS II and WHI findings. January 2003.

In July 2002, the *Journal of the American Medical Association* published two studies questioning the relative safety of combination estrogen/progestin hormone replacement therapy (HRT) products. To assess physician and member reaction to these studies, Express Scripts researchers analyzed the use of combination HRT products before and after the issuance of the HERS II and WHI information. More specifically, Express Scripts addressed the extent to which the use of estrogens, HRT combination products (Prempro® and Premphase®) and other agents (such as Evista®, Fosamax® and Actonel®) used to treat osteoporosis changed after these highly-publicized studies were released.

This study is available at www.express-scripts.com.

Cox ER, Henderson RR. Prescription use behavior among Medicare beneficiaries with capped prescription benefits. *Journal of Managed Care Pharmacy*. 2002;5(8):360-364.

The purpose of this study was to evaluate the strategies Medicare beneficiaries adopt to manage their out-of-pocket prescription-drug costs if their prescription-drug plan has a capped annual benefit of \$500 or \$1,000. A total of 786 surveys were mailed to Medicare+Choice members. Of the 28% response rate, 70% of respondents participated in at least one strategy — obtaining samples from their physicians, for instance — to manage prescription-drug costs. This strategy raises the question of whether prescription-drug samples may discourage the prescribing of lower-cost therapeutic alternatives.

Roe CM, McNamara AM, Motheral BR. Use of chronic medications among a large, commercially-insured U.S. population. *Pharmacoepidemiology and Drug Safety*. 2002;11(4):301-309.

This study examined how medications for chronic conditions are used in everyday life. Results showed that females were more likely than males to use medications for chronic conditions during the study year, and that medications commonly used to treat chronic conditions accounted for 53% of total drug costs for both sexes. Generally, the likelihood of using medications for chronic conditions increased with age for both sexes. Additionally, of those who took drugs to treat chronic conditions, 14% used combination therapy.

Roe CM, McNamara AM, Motheral BR. Gender- and age-related prescription-drug use patterns. *The Annals of Pharmacotherapy*. 2002;36(1):30-39.

The purpose of this study was to summarize gender- and age-related prescription-drug utilization patterns among a large, diverse, commercially-insured population within the U.S. Results indicated that most gender differences in medication use appear after or around the puberty years. Women were more likely to use several classes of medications, including antidepressants, anti-anxiety agents and pain medications.

Motheral BR, Cox ER, Mager DE, Henderson RR. 2000 *Prescription Drug Atlas*. January 2002.

This study was the first comprehensive state-by-state analysis of prescription-drug use. Age and gender have always been among the best indicators of prescription-drug use, but results from this study show that where one lives is also a good indicator of which and how many medications one uses. Prescription-drug use was tracked for a random sample of commercially-insured members who were continuously enrolled throughout 2000. Results showed that general prescription-drug use was lower in the Northeast and West, and higher in the South and Midwest. Even greater variation was found when the prevalence of prescription-drug use was evaluated for 23 of the most commonly-prescribed therapy categories. In observing prescription use for children, the study found that children exhibited greater overall variation than adults for most therapy classes.

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