

OVERALL TREND

Getting to Zero Waste

2008 DRUG TREND REPORT



EXPRESS SCRIPTS®

Overall Drug Trend

Continuing a pattern which began in 2003, per member per year (PMPY) pharmacy costs maintained their downward trend in 2008 to a rate of 3%, the lowest ever recorded by Express Scripts. All three components of overall trend — cost per prescription (cost/Rx), utilization and new drugs — were relatively flat at 2.3%, 0.4% and 0.2%, respectively. Utilization was moderated by multiple factors including movement of a popular brand, Zyrtec,[®] to over-the-counter (OTC) status, drug safety concerns and the economic downturn.

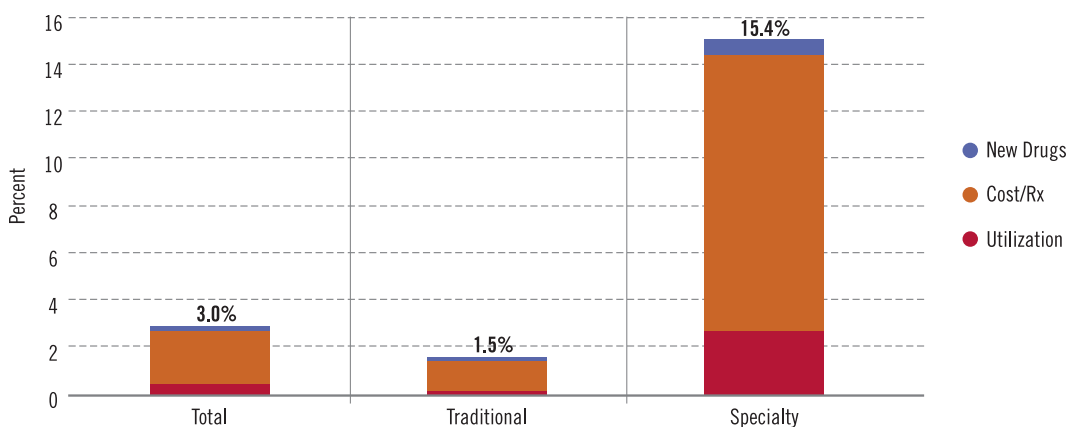
Trend for traditional (nonspecialty) drugs fell to a record low of 1.5%. Following a pattern similar to total trend, traditional trend components changed little — 1.3% for cost/Rx, 0.1% for utilization and 0.2% for new drugs.

However, spending for specialty drugs continued to grow at a double-digit rate. The specialty trend of 15.4% was driven by an 11.7% increase in cost/Rx, which was largely due to 9.4% price inflation. A modest 2.7% increase in utilization also contributed. Influencing the increase in specialty utilization were market-share shifts out of medical benefits into pharmacy spend and changes in prescribing practices away from traditional drugs as indications expand and newer specialty drugs enter the market. In 2008, new drugs added only 0.7% to specialty trend.

Beginning in 2008, the way we determine therapy categories has changed to mirror the classification system used in our plan-sponsor reporting. We moved to a proprietary system — most common indicators (MCIs). Developed by our clinical team, MCIs are named not for the type of drugs they contain (for example, anticonvulsants), but for the condition being treated (seizures). In addition, some nomenclature has changed for 2008. Classes previously named “nonspecialty” have been renamed “traditional.”

EXHIBIT 1

Components of Total, Traditional and Specialty Trend



TRADITIONAL TREND

Trend for traditional drugs fell to a record low of 1.5%. Although inflation had the greatest upward impact on trend at 2.9%, its influence was far below the 5.0% inflation rate reported in 2007. We calculated inflation as the change in ingredient cost net of rebate per prescription for common drugs, which are drugs that were available in both 2007 and 2008. Greater use of generic medications continued to drive trend lower in 2008 by 2.7%. Utilization, which had been growing at rates just over 2%, was flat in 2008 at 0.1%. Rounding out 2008 trend was the impact of new drugs at 0.2%. New drugs are branded drug products that were introduced to the market sometime in 2008.

To calculate cost/Rx, we used ingredient cost with the exclusion of plan sponsor rebates, which provides a more accurate representation of actual costs. The overall rate of price inflation was lower in 2008 driven primarily by a negative 9% inflation rate for generics compared to a 7.6% increase in inflation for brands — a rate identical to brand inflation in 2007. Lower generic inflation was driven by deeper discounts for plan sponsors, loss of generic exclusivity and price decreases by generic manufacturers.

EXHIBIT 2

Components of PMPY Traditional Cost Trend 2005 to 2008†

| | AWP Less Discount 2004 vs. 2005 | Ingredient Cost 2005 vs. 2006 | Ingredient Cost 2006 vs. 2007 | Ingredient Cost Net of Rebates 2007 vs. 2008 |
|--------------------------|------------------------------------|----------------------------------|----------------------------------|--|
| Price Inflation | 5.3% | 4.3% | 5.0% | 2.9% |
| X Units per Prescription | 0.1% | 0.4% | 0.5% | 0.3% |
| X Brand/Generic Mix | -2.7% | -2.9% | -4.4% | -2.7% |
| X Therapeutic Mix | 0.8% | 1.7% | 1.1% | 0.9% |
| = Cost/Rx | 3.3% | 3.5% | 2.0% | 1.3% |
| X Utilization | 4.0% | 2.2% | 2.5% | 0.1% |
| = Common Drugs | 7.5% | 5.8% | 4.6% | 1.3% |
| + New Drugs | 0.4% | 0.2% | 0.1% | 0.2% |
| = All Drugs | 7.9% | 5.9% | 4.7% | 1.5% |

* The percentage contribution of each factor does not total to the All Drugs percentage increase. The calculation takes the base cost for a given year and multiplies it by one plus the percentage contributed by the first factor (price inflation). The resulting total is then multiplied by the percentage contributed by the second factor (number of units dispensed), and so on for each Common Drugs factor. The percentage contribution of the New Drugs is then added to the total Common Drugs percentage, to yield an All Drugs percentage increase. Final results may differ due to rounding.

The current weak economy had various effects on traditional drug trend, including increased use of lower cost medications (measured by brand/generic mix) and utilization. Individuals have reduced spending across many sectors of the economy, including spending for healthcare. Utilization growth was more modest — particularly for traditional therapy classes that treat asymptomatic conditions, such as high blood pressure and high cholesterol. Fewer declines are being seen for classes that treat symptomatic conditions, such as ulcer disease, influenza and pain. Conversely, the weak economy is expected to increase utilization in other classes, such as drugs for the treatment of depression and insomnia. The impact on utilization by the economic downturn is expected to continue through 2009.

The fact that members were also looking for cost-savings opportunities is evidenced through greater use of lower cost generic medications. For traditional drugs, overall utilization of brands decreased by 10.9% while generic use increased by 7.5%. As a result, member cost share was lowered by 2.3% to \$12.70 per prescription for traditional drugs. In addition to the slowing economy, decreases in brand utilization were influenced by OTC strategies, drug safety concerns and patent expirations.

EXHIBIT 3

Traditional Drug Utilization by Generics and Brands

| | 2007 | 2008 | Trend |
|--------------|------------------|------------------|-------------|
| | PMPY Utilization | PMPY Utilization | |
| Generics | 8.64 | 9.28 | 7.5% |
| Brands | 5.65 | 5.04 | -10.9% |
| Total | 14.29 | 14.32 | 0.1% |

The top 20 traditional classes accounted for over 80% of traditional-drug spending. The top three — representing one quarter of traditional spend — all treat metabolic syndrome. A cluster of conditions, such as abdominal obesity and insulin resistance, metabolic syndrome increases the risk of heart disease, stroke and diabetes. Seven of the top 20 traditional classes had double-digit spending growth. Driven by increased utilization of drugs used to treat influenza, antiviral medications was the traditional drug class that had the highest rate of growth at 21%. Increased utilization of medications to treat viral infections likely was due to decreased vaccine effectiveness and the active 2007-2008 flu season which peaked in February of 2008.

Blood modifying agents (mainly drugs to prevent blood clots) and drugs used to treat mental and neurological disorders, such as Alzheimer's disease, psychoses and Parkinson's disease, both grew at rates of 17% due primarily to price inflation. The 32% negative trend for drugs used to treat allergies was due to Zyrtec® moving to OTC status early in 2008. An in-depth description of several therapy classes is provided in the Therapy Class Review Section of the *Drug Trend Report*.

EXHIBIT 4

**Components of Trend for the Top 20 Traditional Therapy Classes
Ranked by Percent of Total Traditional Spend**

| Therapy Class | % of Total Traditional Spend | PMPY Cost Trend | Components of Trend | | |
|-------------------------------------|------------------------------------|--------------------|---------------------|-------------|-------------|
| | | | Utilization | Cost/Rx | New Drugs |
| 1 High Blood Cholesterol | 9.1% | -8.0% | 2.5% | -10.2% | 0 |
| 2 High Blood Pressure/Heart Disease | 8.6% | -3.0% | 1.4% | -4.7% | 0.3% |
| 3 Diabetes | 8.0% | 9.7% | 1.6% | 7.9% | 0 |
| 4 Depression | 7.0% | -0.9% | 0.6% | -1.9% | 0.4% |
| 5 Ulcer Disease | 6.3% | -5.2% | 4.7% | -9.5% | 0 |
| 6 Asthma | 5.6% | 3.8% | -1.8% | 5.8% | 0 |
| 7 Seizures | 4.7% | 13.7% | 6.7% | 6.6% | 0 |
| 8 Infections | 4.4% | -0.8% | -0.5% | -0.3% | 0 |
| 9 Pain | 4.1% | 11.4% | 2.6% | 8.6% | 0 |
| 10 Mental/Neurological Disorders | 3.3% | 16.8% | 6.4% | 9.8% | 0 |
| 11 Viral Infections | 3.2% | 20.8% | 15.7% | 4.1% | 0.4% |
| 12 Attention Disorders | 2.8% | 13.7% | 5.6% | 7.6% | 0 |
| 13 Allergies | 2.3% | -32.2% | -22.6% | -12.8% | 0.3% |
| 14 Contraceptives | 2.3% | 8.0% | 2.2% | 5.7% | 0 |
| 15 Urinary Disorders | 1.9% | 9.9% | 2.7% | 6.9% | 0 |
| 16 Blood Modifying | 1.9% | 17.2% | 5.0% | 11.6% | 0 |
| 17 Skin Conditions | 1.8% | 9.9% | 0.3% | 9.6% | 0 |
| 18 Pain and Inflammation | 1.6% | -0.6% | -1.9% | -1.0% | 2.3% |
| 19 Migraine Headaches | 1.5% | 10.5% | -4.9% | 14.3% | 1.8% |
| 20 Hormonal Supplementation | 1.4% | 7.2% | -6.0% | 14.1% | 0 |
| Top 20 | 81.7% | 2.0% | 0.6% | 1.3% | 0.2% |
| All Other | 18.3% | -0.6% | -0.7% | 0 | 0.1% |
| Total | 100.0% | 1.5% | 0.1% | 1.3% | 0.2% |

SPECIALTY TREND

At 11.7%, increased cost/Rx was the main factor contributing to the 15.4% specialty-drug trend for 2008. The major driver was price inflation of 9.4%, a rate three times greater than for traditional medications. As was seen for traditional medications, though, the rate of utilization growth for specialty medications dropped by over 40% to 2.7%.

EXHIBIT 5

Components of PMPY Specialty Cost Trend 2006 to 2008†

| | Ingredient Cost | Ingredient Cost Net of Rebates |
|--------------------------|-----------------|--------------------------------|
| | 2006 vs. 2007 | 2007 vs. 2008 |
| Price Inflation | 7.3% | 9.4% |
| X Units per Prescription | -1.3% | -0.4% |
| X Brand/Generic Mix | 0 | 0 |
| X Therapeutic Mix | 2.2% | 2.6% |
| = Cost/Rx | 8.2% | 11.7% |
| X Utilization | 4.7% | 2.7% |
| = Common Drugs | 13.3% | 14.4% |
| + New Drugs | 0.7% | 0.7% |
| = All Drugs | 14.0% | 15.4% |

* The percentage contribution of each factor does not total to the All Drugs percentage increase. The calculation takes the base cost for a given year and multiplies it by one plus the percentage contributed by the first factor (price inflation). The resulting total is then multiplied by the percentage contributed by the second factor (number of units dispensed), and so on for each Common Drugs factor. The percentage contribution of the New Drugs is then added to the total Common Drugs percentage, to yield an All Drugs percentage increase. Final results may differ due to rounding.

In 2008, taken together as a separate class, specialty drugs lead all therapy classes in terms PMPY spending. At \$98.77, PMPY spend on specialty drugs outdistanced \$68.68 PMPY for the leading traditional class (drugs to treat high blood cholesterol). The top specialty class, inflammatory conditions, was in the top 10 of all therapy classes (traditional plus specialty) based on PMPY spend in 2008. The top three specialty classes accounted for well over 60% of total specialty spend, with seven of the top 10 specialty classes having total trends of over 10%. Blood cell deficiency was the only class that showed a negative trend. For some classes, utilization increases were the major factors in driving up trend; for others cost/Rx had bigger impact. In one class, pulmonary hypertension, both utilization and cost/Rx had large increases.

EXHIBIT 6

**Components of Trend for the Top 10 Specialty Therapy Classes
Ranked by Percent of Total Specialty Spend**

| Therapy Class | % of Total Specialty Spend | Total Trend | Components of Trend | | |
|---------------------------|----------------------------|--------------|---------------------|--------------|-------------|
| | | | Utilization | Cost/Rx | New Drugs |
| 1 Inflammatory Conditions | 27.5% | 17.0% | 10.5% | 5.7% | 0.2% |
| 2 Multiple Sclerosis | 20.2% | 18.3% | -2.9% | 21.9% | 0 |
| 3 Cancer | 16.0% | 18.6% | 2.0% | 15.7% | 0.7% |
| 4 Growth Deficiency | 5.2% | 20.3% | 12.9% | 6.5% | 0 |
| 5 Anticoagulant | 5.2% | 22.4% | 14.0% | 7.4% | 0 |
| 6 Blood Cell Deficiency | 4.3% | -11.4% | -17.3% | 7.1% | 0.1% |
| 7 Infertility | 3.6% | 14.4% | -2.4% | 17.2% | 0 |
| 8 Respiratory Conditions | 3.2% | -0.2% | -8.2% | 8.8% | 0 |
| 9 Hepatitis C | 2.9% | -7.3% | -11.4% | 4.6% | 0 |
| 10 Pulmonary Hypertension | 2.7% | 59.2% | 36.1% | 17.0% | 0 |
| Top 20 | 90.7% | 15.4% | 3.0% | 11.8% | 0.2% |
| All Other | 9.3% | 14.8% | 0.5% | 9.0% | 5.3% |
| Total | 100.0% | 15.4% | 2.7% | 11.7% | 0.7% |

MEMBER EXPERIENCE

Since first publishing the Drug Trend Report, Express Scripts has included member share in total cost calculations to capture total pharmaceutical spending. Examining trends in member copayments is critical to understanding utilization and cost trends because shifting costs to members, while decreasing plan-sponsor trend, may inappropriately decrease utilization and compliance with medication. Compliance is defined as taking medications as prescribed by the doctor.

For the second year, both total cost/Rx and member cost share dropped for traditional therapy classes. Overall, cost/Rx dropped by 2.2% to \$12.82. Members now pay 22.3% of total traditional-drug costs. The drop was influenced by increased utilization of lower cost generic medications and lower per-prescription copayments for generic medications. The average specialty copayment was higher at \$44 per prescription — primarily driven by plan sponsor copayment designs. However, due to the high per prescription specialty costs, members paid only 2.6% of total specialty costs, which remained the same in 2007 and 2008.

EXHIBIT 7

Member Copayment Trends

| | 2007 | | 2008 | | Trend |
|--------------|-------------------|--------------|-------------------|--------------|--------------|
| | Average Copayment | % Total Cost | Average Copayment | % Total Cost | |
| Traditional | \$13.00 | 23.3% | \$12.70 | 22.3% | -2.3% |
| Generics | \$7.45 | 29.6% | \$7.82 | 29.0% | -2.3% |
| Brands | \$21.48 | 20.9% | \$22.69 | 19.6% | 5.7% |
| Specialty | \$41.06 | 2.7% | \$44.04 | 2.6% | 7.3% |
| Total | \$13.11 | 21.3% | \$12.82 | 20.2% | -2.2% |

Trends in Compliance

Now estimated to affect over 130 million Americans, chronic diseases account for 70% of deaths and cost the U.S. \$1.3 trillion annually (\$1.1 trillion in lost productivity and another \$277 billion in direct treatment).¹

Prescription drugs are key elements in the appropriate treatment of many chronic diseases. However, not all patients use chronic prescriptions appropriately. According to a 2007 report from the National Council on Patient Information and Education, nonadherence with medications may result in unnecessary disease progression, disease complications, reduced functional abilities, a lower quality of life and even premature death.² Keeping patients adherent to prescription therapy is critical to improving health outcomes and controlling long-term healthcare costs. Recently, in light of the difficult economic environment, some consumers have begun taking less of their chronic medications or even foregoing care altogether.

To examine compliance patterns among Express Scripts membership, we evaluated compliance across three key chronic therapy classes: antidiabetics, antihypertensives and lipid-lowering agents for high cholesterol.

EXHIBIT 8

Unadjusted Medication Possession Ratios for Key Chronic Therapy Classes 2007 and 2008

| Therapy Class | Medication Possession Ratio | |
|-----------------------|-----------------------------|------|
| | 2007 | 2008 |
| Antidiabetic Agents | 77% | 77% |
| Antihypertensives | 83% | 83% |
| Lipid-lowering Agents | 84% | 83% |

Using a standard calculation of compliance called the Medication Possession Ratio (MPR), we evaluated the days supply of medication over a fixed period of time (measurement period) divided by the number of days in the measurement period. Our measurement period was one year beginning January 1 and ending December 31. For the calculation of MPR, we analyzed utilization for adult members who were continuously eligible in each year. All the members we studied were covered by plan sponsors in our commercial book of business. Compliance values represent only members with full employment (continuously eligible), not employees that lost employer-covered benefits in either year.

The numerator is the sum of the days' supply of all medications that fall within the measurement period, removing the day's supply that extends past the end of the measurement period and adding the days supply spilling into the current measurement period. The denominator is either 365 days for continuous users of medication or the difference in days between the initiation of therapy and the end of the measurement period for new users. To ensure at least 270 days of follow up, new users were included only if their initial claims were prior to March 31.

Our findings show no change in compliance for patients taking antidiabetic and antihypertensive medications among Express Scripts commercially insured members from 2007 to 2008. Compliance measures for patients taking medications to treat high blood cholesterol decreased by only 1%. In both years and for all three therapy classes, compliance rates were above or approaching 80%, a rate believed necessary for achieving optimal health outcomes.

Managing Trend

Even though Express Scripts pharmacy trend is the lowest in over a decade, significant spend still remains to be managed. Just because costs are not going up, does not mean that they cannot come down. Managing pharmaceutical spending involves not only weeding out waste or inappropriate use, but also advocating appropriate utilization to ensure that the right patient is taking the right drug in the right way at the right time.

MANAGING OUT WASTE IN PHARMACY BENEFITS

President Obama has made healthcare reform a key legislative initiative in his administration. While increasing access to care and reducing the number of uninsured are primary concerns, the administration also recognizes that the current inefficient system cannot support the number of individuals who need to be added. Healthcare spending, which made up 16.2% of GDP in 2007, is growing by about 6% yearly. If left unchecked, it is expected to account for 20% of GDP in 2018³, an unsustainable projection.

SO WHERE IS THE WASTE IN THE HEALTHCARE SYSTEM?

Waste is defined as spending more without improving health outcomes. Present at all levels of healthcare provision and utilization, waste takes many forms. On the provider side, current payment systems reward providers for the quantity of care, often leading to unnecessary diagnostic tests or marginally effective procedures. In prescription-drug spend, plan sponsors waste resources through ineffective plan designs that do not take advantage of programs designed to drive cost-effective utilization. Members waste benefits by using non-formulary drugs, by being nonadherent to treatment and by filling prescriptions through inefficient delivery channels.

For 2008, Express Scripts researchers estimated the waste within the commercially insured market from use of higher cost drugs instead of chemically or therapeutically equivalent lower cost generics. Estimated across 13 therapy classes and based upon clinically determined generic fill rate (GFR) potentials, potential savings of over \$18 billion were missed in the commercially insured market alone. Extrapolating to the U.S. population, including individuals covered by Medicare, Medicaid and other public insurance programs, Express Scripts estimated that missed saving opportunities amounted to over \$42 billion. Exhibit 9 summarizes our findings.

¹ The Partnership to Fight Chronic Disease. Almanac of Chronic Disease 2008. Available at: http://www.fightchronicdisease.org/pdfs/PFCD_FINAL_PRINT.pdf. Accessed March 17, 2009.

² National Council on Patient Information and Education. Enhancing prescription medication adherence: a national action plan. August 2007. Available at: http://www.talkaboutrx.org/documents/enhancing_prescription_medicine_adherence.pdf. Accessed March 17, 2009.

³ Sisko A, Truffer C, Smith S, et al. Health spending projections through 2018: recession effects add uncertainty to the outlook. *Health Aff (Millwood)*. 2009;28(2):w346-w357.

EXHIBIT 9

*Estimated Savings From Achieving Potential Generic Fill Rates**

| Therapy Class | Actual GFR | Potential GFR | Potential Savings (in \$ millions) |
|--|------------|---------------|---------------------------------------|
| Oral Contraceptives | 65.3% | 90% | \$454 |
| Antidiabetics | 55.3% | 60% | \$668 |
| Beta Blockers | 95.0% | 98% | \$167 |
| Antihypertensives | 64.5% | 83% | \$935 |
| Antihyperlipidemics | 43.9% | 80% | \$5,110 |
| Antihistamines | 79.2% | 100% | \$260 |
| Systemic and Topical Nasal Products | 49.4% | 90% | \$656 |
| Gastrointestinal Medications | 55.3% | 95% | \$4,508 |
| Antidepressants | 69.0% | 94% | \$2,559 |
| Antipsychotics | 32.5% | 45% | \$399 |
| Hypnotics | 69.4% | 95% | \$858 |
| Narcotic Analgesics | 93.8% | 95% | \$294 |
| Anticonvulsants | 57.7% | 75% | \$1,223 |
| Total (US Commercially Insured) | | | \$18,089 |
| Total (US population) | | | \$42,383 |

*Therapy class designation was based upon GPI codes

Specialty Drug Spending Patterns Between Pharmacy Benefits and Medical Benefits

Management of specialty-drug spending is another area where untapped savings exist. Because specialty medications can be reimbursed through both medical benefits and pharmacy benefits, the economic impact of specialty spending may be hidden within medical benefits, which often are not well-managed. Express Scripts conducted a study to identify how specialty-drug costs are distributed between medical and pharmacy benefits. We used an integrated medical and prescription claims database to evaluate specialty-spending distributions for 22 conditions from 2005 to 2007. Results from the top 10 specialty classes are presented in Exhibit 10.

EXHIBIT 10

Proportion of Pharmacy Cost as a Percentage of Total Specialty Spend 2005 to 2007 Ranked by 2007 Total PMPY Costs

| Rank | Disease State | 2005 | 2006 | 2007 |
|------|-------------------------|--------------|--------------|--------------|
| 1 | Cancer | 15.5% | 18.2% | 18.9% |
| 2 | Inflammatory Conditions | 65.8% | 66.1% | 65.3% |
| 3 | Blood Cell Deficiency | 32.5% | 17.4% | 15.3% |
| 4 | Multiple Sclerosis | 96.1% | 97.2% | 97.1% |
| 5 | Hemophilia | 38.0% | 33.9% | 30.4% |
| 6 | Growth Deficiency | 87.9% | 92.5% | 93.2% |
| 7 | Respiratory Conditions | 69.9% | 68.1% | 69.1% |
| 8 | Immune Deficiency | 60.6% | 23.1% | 20.4% |
| 9 | Anticoagulant | 93.9% | 94.5% | 94.4% |
| 10 | Hepatitis C | 98.0% | 98.6% | 98.3% |
| | Other | 52.8% | 52.6% | 52.0% |
| | Total | 48.9% | 45.2% | 44.9% |

Source: MarketScan® Commercial Claims and Encounters Database: 2005 to 2007

By viewing total medical and pharmacy costs together, a more complete picture of specialty spending is presented. When total medical and pharmacy spending is considered, specialty drugs used to treat cancer was the number one class. However, cancer was the number three therapy class in terms of total pharmacy specialty spend — representing only 16%.

Our results show that 55% of the costs for specialty medications in 2007 were billed through medical benefits — an increase from 51% in 2005. The transition of spending to the medical benefit likely is due to need for physician monitoring of some therapies, as well as to safety concerns for other treatments. Our findings show that conditions including immune deficiencies, blood cell deficiencies and hemophilia had significant movement of spending out of pharmacy benefits and into medical benefits. Administering specialty drugs is an important source of revenue for some physicians which may explain some of the transition. That said, however, many products can be managed appropriately and safely through specialty pharmacies that use drug-utilization monitoring specifically designed for hard-to-manage conditions. Given the significant savings under pharmacy benefits, plan sponsors should ensure that appropriate drugs are covered only under pharmacy benefits. They can also implement utilization-management programs under medical benefits for patients most appropriately managed by physicians.

The Solution

Clients have many tools available to capture the savings from increased generic usage depending on how actively they manage benefits. Taking an active stance, including tighter formulary management and adoption of clinical programs such as Step Therapy, has been shown to produce significant savings for plan sponsors and members. By the end of 2008, approximately 55% of Express Scripts' members were enrolled in plans that had implemented at least one Step Therapy program. Step Therapy, which encourages the use of lower-cost, equally effective, generic medications prior to stepping up to more costly branded therapies, produced average savings of \$5.11 per member per year (PMPM) for clients that adopted our standard package of modules.

Without active management, clients must rely on financial incentives through tiered copayment designs and copayment differentials to encourage cost-effective use of drugs and delivery channels. While optimal copayment design is necessary to establish the choice framework for members and their physicians to choose the appropriate drug therapy, relying solely on financial incentives leaves considerable savings on the table.

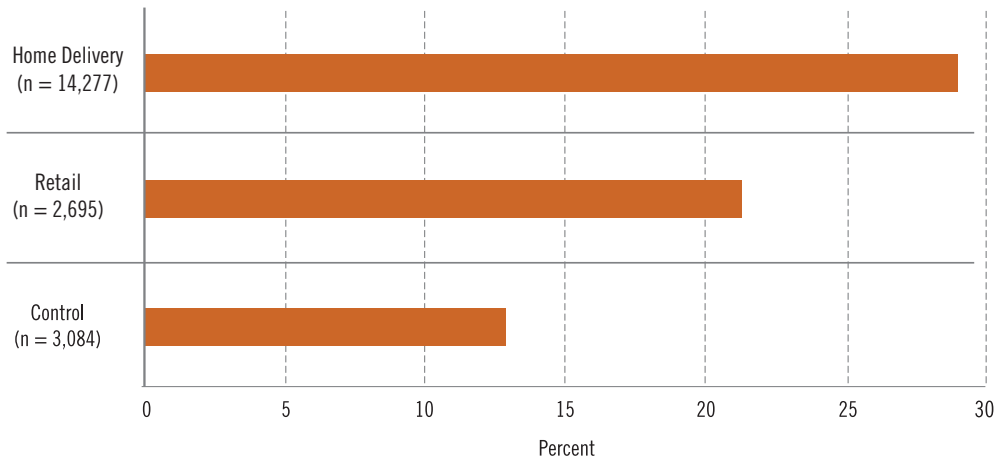
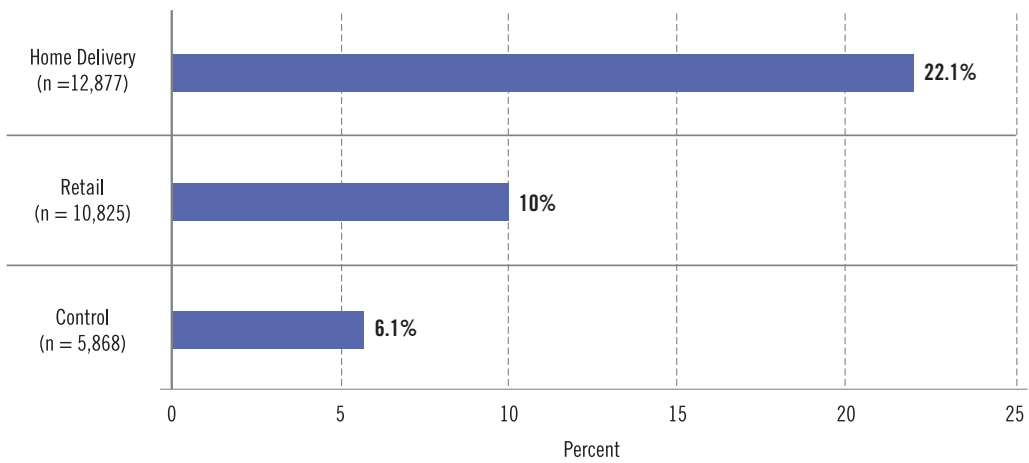
EDUCATION

Over the last five years, PBMs and plan sponsors have utilized member education with targeted and framed messaging to inform members of savings opportunities. Express Scripts has seen significant movement to lower cost options through the use of these educational initiatives.⁴ Two of our recent studies examined targeted and framed messaging about new therapeutic alternatives after the patent expirations of Ambien® (zolpidem) and Fosamax® (alendronate). These patent expirations provided the first therapeutically equivalent generic agents available in their respective therapy classes (hypnotics and bisphosphonates).

In both studies, movement to the generic alternative was more significant for members receiving targeted and framed messages than for members in control groups (who were given financial incentives alone). When categorized by delivery channel, members receiving medications through Home Delivery had a significantly greater rate of conversion than those receiving medication in retail pharmacies. The greater success in Home Delivery is consistent with other findings from letter campaigns encouraging use of lower cost alternatives. The implication is that once a relationship is established between Express Scripts and plan members through Home Delivery, members are more willing to receive, trust and act on suggestions about improving their health and capitalizing on the value of their prescription-drug benefits. Both studies are available on the Express Scripts.com website at: <http://www.express-scripts.com/industryresearch/outcomes/onlinepublications>.

⁴ Cox ER, Kulkarni A, Henderson R. The Impact of Patient and Plan Design Factors on Switching to Preferred Statin Therapy: The Case of Atorvastatin Formulary Status Change. *Annals of Pharmacotherapy*. 2007;41(12):1946-53.

EXHIBIT 11

*Adjusted Conversion Rates**Selected Brand Hypnotics to Zolpidem**A Brand Bisphosphonate to Alendronate*

AN ADVANCED UNDERSTANDING OF CONSUMER BEHAVIOR

Financial incentives and targeted patient education have been effective in motivating members to adopt preferred behaviors, but study results also suggest that standard approaches are not sufficient to wring out waste and improve health. In 2008, Express Scripts organized a distinguished team of behavior experts to start a new initiative aimed at enhancing consumer communications in healthcare. Our Center for Cost-Effective Consumerism studies human behavior specifically in relation to pharmacy benefits. We believe that an advanced understanding of human behavior, coupled with scientifically sound communications, will significantly improve pharmacy benefit management. We call this practice Consumerology. Through pilots and other testing methods, the Center has selected three behavioral economics principles to guide our research and development work:

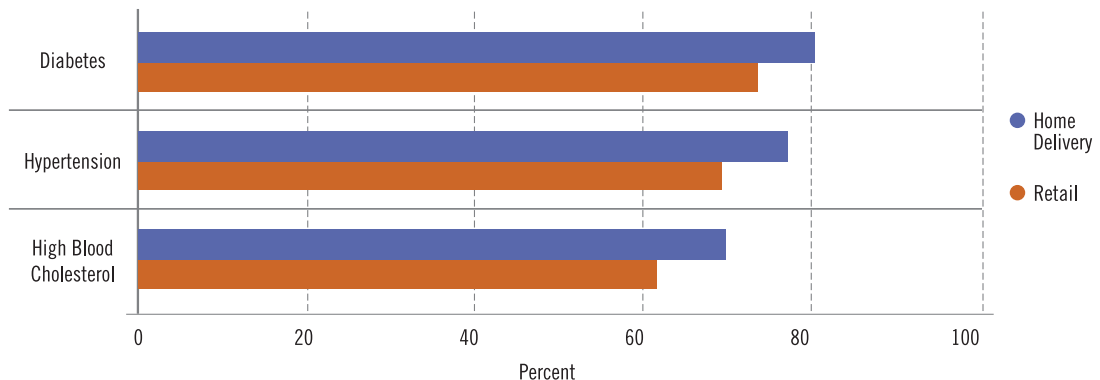
Social Comparison

Capturing the importance that people place on knowing how they are doing relative to others is known as social comparison. What other people think and how individuals fit in with the group influence behavior. We are investigating how to improve therapy adherence using this sensitivity. In one pilot, we are providing patients with information that compares their personal medication usage scores with average and minimally acceptable scores.

Hyperbolic Discounting

Hyperbolic discounting demonstrates that future events feel about half as important as events today. This psychological force, which causes current costs to loom surprisingly large relative to future benefits, often leads to procrastination. Hyperbolic discounting has important implications for almost every health-related behavior (such as exercising today to improve future health), as well as for Express Scripts products such as Home Delivery. Traditionally with Home Delivery, costs are incurred up front for a 90-day supply of medications. A better understanding of hyperbolic discounting has spurred us to conduct pilot studies aimed at greatly improving the use of Home Delivery. We think that, because members who fill maintenance medications through Home Delivery have two-thirds fewer opportunities to procrastinate, adherence to medications in Home Delivery is higher when compared with adherence rates to medications filled in retail pharmacies.

EXHIBIT 12

Adherence in Home Delivery Compared to Retail Across Three Chronic Therapy Classes

Source: Is compliance really better in home delivery? Evidence across three chronic therapy classes. September 2008.

Available at: <http://www.express-scripts.com/industryresearch/outcomes/onlinepublications/study/homeDeliveryCompliance.pdf>. Accessed April 2, 2009.

Loss Aversion

Loss aversion means that people work harder to avoid perceived losses than to obtain perceived gains. For example, people are more willing to undergo a surgical procedure characterized as having a 95% chance of success than one described as having a 5% chance of failure.

The loss-aversion principle has been tested in studies examining the impact of lowering copayments. One mechanism proposed to increase adherence is reducing barriers to care through reducing or eliminating copayments for high value medications. But do members react in the same way to lowering copayments as they do to increasing copayments? Studies have shown that copayment increases of 10% lead to declines in medication use between 2% and 6%.⁵

Does it follow, then, that lowering prescription-drug copayments improves medication adherence by the same proportions? In a study published in the December 2008 issue of the *American Journal of Managed Care*, Express Scripts researchers examined the relationships between lowered copayments and adherence.⁶ We based the study on lower copayments resulting from the patent expiration of the cholesterol-lowering drug Zocor® (simvastatin). We found only modest gains in overall adherence as copayments declined. Price elasticity of demand estimates from this study found that a 10% decrease in copayments led to utilization increases of only 0.2% — orders of magnitude smaller than the utilization decreases that result from increasing copayments.

So what does all of this mean for plan sponsors designing pharmacy benefits? It means that financial incentives are not the sole solution to influencing patient behavior. In addition to price, side effects, and drug effectiveness; important psychological principles, such as procrastination, expectations, social norms and framing, are also at play in shaping decisions about utilization of pharmaceutical products.

⁵ Goldman DP, Joyce GF, Zheng Y. Prescription drug cost sharing: associations with medication and medical utilization and spending and health. *JAMA*. 2007;298(1):61-69.

⁶ Sedjo RL, Cox ER. Lowering Copayments: Impact of Simvastatin Patent Expiration on Patient Adherence. *Am J Manag Care*. 2008;14(12):813-18.

Methods

In the 2008 *Drug Trend Report*, prescription-drug use was analyzed for two independent samples of approximately 3 million individual members each. The plan sponsors providing pharmacy benefits to the sampled members paid at least some portion of the cost for prescriptions dispensed to its members in both 2007 and 2008 and they had stable membership (50% or less of the membership changed in 2007 and 2008). Plan sponsors used Express Scripts for both retail and home-delivery pharmacy services. Prescription counts have been converted to equivalent quantities that would have been dispensed through retail pharmacies to allow for varying benefit structures and adjust for differential home-delivery usage rates.

Non-prescription medications (except for diabetic supplies, which were included for the first time) and prescriptions that were dispensed in hospitals, long-term care facilities and other institutional settings were not included in this analysis. Calculations also excluded claims for Medicaid recipients and Medicare beneficiaries receiving prescription-drug benefits through Medicare Part D plans or Managed Medicare Prescription Drug Plans (PDPs).

For the first time, plan sponsor rebates were included to provide a more accurate representation of actual costs.

Utilization was determined on a per member per year (PMPY) basis. It was calculated by dividing the total number of 30-day adjusted prescriptions by the total number of member-years for all members. A member-year is the total number of months of eligibility for all members in the sample divided by 12. Prevalence of use for each drug class was calculated as the number of members taking medications in the class divided by the total number of members (both utilizers and non-utilizers) in the sample. The average number of prescriptions per user per year (# Rx/User/Year) is the total number of 30-day adjusted prescriptions divided by the total number of user-years. A user-year is determined by adding the number of months of eligibility for all sample members who had at least one claim for a given drug class and then dividing the total by 12.