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Bright, bold colors splash across the panels of LeRoy Neiman’s energetic paintings—he is known for his semiabstract style that is instantly recognizable. He has been extremely successful, and his paintings of athletes, sporting events, and entertainers are world-renowned.

Neiman was born in 1921 in St. Paul, Minnesota. He believes that he is mostly of Turkish and Swedish descent. Neiman’s parents were Charles Runquist, an unskilled laborer, and Lydia (Serline) Runquist. His mother later remarried twice, and Neiman took his surname from one of his stepfathers. Raised in a blue-collar neighborhood in St. Paul, he described himself as a “street kid.” He attended a Roman Catholic primary school, where, as he told Max Millard for the New York City Westside TV Shopper (January 27-February 2, 1979), “he was always drawing pictures and getting special treatment . . . showing off, coping out of other things.” During recess periods he would inscribe pen-and-ink tattoos on his classmates’ arms.

A painting of a fish that he made in sixth grade won a prize in a national art competition. Starting in adolescence he earned money from local grocers by painting calcimine images of fruit, vegetables and meat as sale items, and portraits of the shopkeepers themselves on the windows of their stores. As a high school student, he created posters for school dances and athletic events.

The artist’s biography on his Web site (www.leroyneiman.com) says that, “In 1942, Neiman quit school and enlisted in the United States Army. While serving as a cook for four years, with two years of combat in Europe, he painted murals in military kitchens and dining halls that generated enthusiastic responses. He also painted stage sets for Red Cross shows under the auspices of the army’s Special Services division. ‘If nothing else, the army completely confirmed me as an artist,’ he wrote in his book LeRoy Neiman: Art and Life Style (1974). ‘During this period, I made my crucial discovery of the difference between the lifestyles of the officer and the PFC [Private First Class]. This was to be the basis of my later mission in art, to investigate life’s social strata from the workingman to the multimillionaire. I discovered that while the poor I knew so well are so often pitiable, the rich can be fools.’”

After getting out of the Army, Neiman used the G.I. Bill to pay for his art education at the School at the Art Institute of Chicago. He also taught there for 10 years. In addition, he studied art at the University of Chicago and the University of Illinois. Early in his career, Neiman worked as an illustrator for the Carson, Pirie, Scott department store.

Neiman said that he has painted just about every sport, but his favorite sport to watch and depict as art is boxing.

As a boy, he participated in boxing matches in the basement of his church, which started a lifelong interest in prize fighting. Neiman’s contributions to boxing-related art earned him induction into the International Boxing Hall of Fame in June 2007. Paintings of famous boxers such as Muhammad Ali, Joe Frazier, and George Foreman can be found on Neiman’s Web site in the boxing portion of the sports section. Other sports that are represented on the site include baseball, basketball, football, golf, hockey, sailing, skiing, tennis, and the Olympics. In 1972, ABC-TV broadcasts showed him creating plein air pictures at the Summer Olympic Games in Munich, Germany. For most of the Olympics sketches, Neiman used a combination of two or more mediums—watercolor, ink, gouache, felt-tip marker, chalk, colored pencil, graphite, and charcoal. He demonstrated his remarkable artistic skills for television audiences again at the Olympic Games in Montreal (1976), Lake Placid (1980), Sarajevo (1984), and Los Angeles (1984).

In American Artist magazine, Neiman said that the prime objective of his work is the “phenomenon of change.” He explained, “The spectator looking at a painting of mine must deal with this condition of change. Areas are broken up at close range and fit together only at a distance. As one advances on my painting, it becomes more abstract, more fluid, and as one moves away, it falls into focus and is realistic. . . .” This concept of flux is evident in End Around (Larry Brown). Brown was a running back for the Washington Redskins from 1969 to 1976 and winner of the Associated Press National Football League Most Valuable Player award in 1972. A running back needs to be fast, agile, and have good football instincts. Neiman captured these qualities in this painting with his positioning of the figure, as well as the use of contrasting colors that surround Brown.

Neiman is listed in Art Collector’s Almanac, Who’s Who in the East, Who’s Who in American Art, Who’s Who in America, and Who’s Who in the World. His paintings have been displayed in many museums and art galleries. Neiman’s works are distributed by Hammer Graphics (who has represented him for more than 35 years) and Knoedler Publishing Co. of New York.

Stan Isaacs of New York Newsday said of the artist, “Whether one approves of Neiman’s work or not, one must agree that he is a work of art himself.”

Sheila Macho
Cover Editor

COVER CREDIT

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http://www.leroyneiman.com
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Submit referenced tables and figures on separate pages with titles (and captions, as necessary) at the end of the manuscript; match symbols in tables and figures to explanatory notes, if included. May use 10-point font.

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REFERENCE

Health Care Costs of Adults Treated for Attention-Deficit/Hyperactivity Disorder Who Received Alternative Drug Therapies

Eric Q. Wu, PhD; Howard G. Birnbaum, PhD; Huabin F. Zhang, MD, MPH; Jasmina I. Ivanova, MA; Elaine Yang, PhD; and David Mallet, MBA

ABSTRACT

BACKGROUND: Many therapies exist for treating adult attention-deficit/hyperactivity disorder (ADHD), also referred to as attention-deficit disorder (ADD), but there is no research regarding cost differences associated with initiating alternative ADD/ADHD drug therapies in adults.

OBJECTIVE: To compare from the perspective of a large self-insured employer the risk-adjusted direct health care costs associated with 3 alternative drug therapies for ADHD in newly treated patients: extended-release methylphenidate (osmotic release oral system-MPH), mixed amphetamine salts extended release (MAS-XR), or atomoxetine.

METHODS: We analyzed data from a US claims database of 5 million beneficiaries from 31 large self-insured employers (1999-2004). Analysis was restricted to adults aged 18 to 64 years with at least 1 diagnosis of ADD/ADHD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 314.0x—attention deficit disorder; 314.00—attention-deficit disorder without hyperactivity; or 314.01—attention-deficit disorder with hyperactivity) and at least 1 pharmacy claim for OROS-MPH, MAS-XR, or atomoxetine identified using National Drug Codes. In preliminary analysis, we calculated the duration of index ADHD drug therapy as time from index therapy initiation to a minimum 60-day gap. Because the median duration of index ADHD drug therapy was found to be approximately 90 days, the primary measures were total direct medical plus drug costs and medical-only costs computed over 6 months following therapy initiation. Adults were required to have continuous eligibility 6 months before and 6 months after their latest drug therapy initiation and no ADHD therapy during the previous 6 months. Cost was measured as the payment amount made by the health plan to the provider rather than billed charges, and it excluded patient copayments and deductibles. Medical costs included costs incurred for all-cause inpatient provider rather than billed charges, and it excluded patient copayments and deductibles. Medical costs associated with initiating alternative ADHD treatments in adults with ADHD have not been evaluated. Studies in adults have focused on the economic burden of ADHD associated with an increase in comorbidity rates, risk of accidents, and health care costs but have not provided information about the health care costs associated with initiating alternative ADHD treatments in adults with ADHD.

RESULTS: Of the 4,569 patients who received 1 of these 3 drug therapies for ADHD, 31.8% received OROS-MPH for a median duration of 99 days of therapy, 34.0% received MAS-XR for a median 128 days, and 34.2% received atomoxetine for a median 86 days. In the 6-month follow-up period, the mean (standard deviation) total medical and drug costs were $2,008 ($3,231) for OROS-MPH, $2,169 ($4,828) for MAS-XR, and $2,540 ($4,269) for atomoxetine. 6 outlier patients were unrelated to ADHD. Approximately 30% of the cost difference compared with MAS-XR was attributable to 1 high-cost outlier with medical diagnoses for the highest-cost claims for these 2 outlier patients were unrelated to ADHD.

CONCLUSIONS: After adjusting for patient characteristics including substance abuse, depression, and the Charlson Comorbidity Index, adults treated with OROS-MPH had, on average, slightly lower medical and total medical and drug costs than those treated with MAS-XR or atomoxetine over the 6-month period after drug therapy initiation. Approximately 30% of the cost difference compared with MAS-XR was attributable to 1 high-cost outlier with medical diagnoses for the highest-cost claim that were unrelated to ADHD.

What is already known about this subject

• Previous studies have indicated that MPH is a cost-effective treatment for children with ADHD.

• Health care costs of alternative drug therapies in adults with ADHD have not been evaluated. Studies in adults have focused on the economic burden of ADHD associated with an increase in comorbidity rates, risk of accidents, and health care costs but have not provided information about the health care costs associated with initiating alternative ADHD treatments in adults with ADHD.

What this study adds

• Over the 6-month period after drug therapy initiation, adults with ADHD initiated on OROS-MPH had, on average, 8% lower risk-adjusted total medical and pharmaceutical costs than did those initiated on MAS-XR and 11% lower costs compared with atomoxetine. However, these differences were affected by 1 outlier case for each comparison with diagnoses, such as chronic kidney disease and acute myocardial infarction, that were unrelated to ADHD or to accidents.

Attention-deficit/hyperactivity disorder (ADHD) is estimated to affect 4.4% of the working adult population in the United States. Historically, ADHD has been consid-
ered a childhood condition; only recently has there been a heightened awareness among clinicians and researchers regarding ADHD in adulthood.\textsuperscript{2,3} Childhood ADHD persists into adulthood in up to 60\% of diagnosed cases.\textsuperscript{3,5}

The clinical features of ADHD-associated symptoms include poor concentration, general disorganization, tendency to leave projects incomplete, inattention, poor school/work performance, problems with time management, difficulty controlling temper, impulsivity, and being hyperfocused.\textsuperscript{4,7} ADHD patients also have an increased prevalence of comorbid conditions such as asthma, anxiety, bipolar disorder, depression, drug or alcohol abuse, antisocial disorder, or oppositional disorder.\textsuperscript{2,8,9}

The potential societal costs of adult ADHD are considerable. ADHD has been associated with an increased risk of accidents, which would have consequences regarding the use and cost of health care services.\textsuperscript{10} Productivity loss of adults with ADHD is estimated to be 35 days a year.\textsuperscript{1} The estimated burden of ADHD in the United States was $31.6 billion in 2000, and 45\% of that burden was attributable to excess health care costs of family members of patients with ADHD.\textsuperscript{11} Compared with a matched cohort, ADHD patients had almost 3 times greater annual health care costs, and family members had approximately 1.9 times higher annual health care expenditures compared with a matched cohort of family members of non-ADHD patients.\textsuperscript{12}

ADHD in adults is amenable to treatment and is best controlled by a combination of medications and psychosocial interventions.\textsuperscript{6,13,14} Common medications used for the treatment of ADHD in adults are stimulants (e.g., methylphenidate [MPH], mixed amphetamine salts [MAS], dextroamphetamine) or nonstimulants (e.g., atomoxetine).\textsuperscript{9,8,15,17} In the past, treatment options usually included either short- or intermediate-acting stimulants and antidepressants.\textsuperscript{18} Recently, stimulant products have entered the marketplace in extended-release formulations; the first methylphenidate product that lasts 12 hours with once-daily dosing is osmotic release oral system (OROS)-MPH, and the once-daily amphetamine preparation is MAS-XR. Atomoxetine hydrochloride is the first nonstimulant to receive an indication for ADHD in adults from the U.S. Food and Drug Administration.\textsuperscript{15} Both stimulant and nonstimulant treatments have been shown to be effective in improving ADHD symptoms.\textsuperscript{17,19} Stimulant therapy led to improvement in 65\% to 75\% versus 5\% to 30\% of patients randomized to placebo.\textsuperscript{18} Nonstimulant therapy has also been shown to improve symptoms assessed with the ADHD rating scales.\textsuperscript{17}

Quantifying costs related to ADHD and to alternative therapies is important in order to understand the economic impact of the condition and provide a basis for the development of programs and policies to assist patients suffering from this disability. The objective of this article is to compare risk-adjusted medical and total health care costs of adults diagnosed with ADHD initiated on extended-release methylphenidate (OROS-MPH, Concerta), mixed amphetamine salts extended release (MAS-XR, Adderall XR), or atomoxetine (Strattera) from the perspective of a large self-insured employer.

\section*{Methods}

\subsection*{Data}

Our study is based on data from a deidentified administrative claims database maintained by Ingenix, Inc. (Eden Prairie, MN) containing medical and demographic information on privately insured employees, retirees, and their spouses and dependents from 31 large self-insured companies in the United States. The claims cover services provided from January 1999 through December 2004. The 31 companies have national operations, span a broad array of industries and occupations, and cover approximately 5 million beneficiaries. On average, each employer has 2 to 3 health plans. The database includes medical and pharmacy claims for all employees plus their spouses and dependents. Data on the monthly eligibility of beneficiaries are available, as well as employee demographic information such as age, gender, geographic region of residence, and employee status of the primary beneficiary. The formulary status of ADHD drug therapies for these health plans is not known.

\subsection*{Sample Selection}

The study sample was drawn from all 31 companies and included adults between the ages of 18 and 64 years during the study period. Patients were included in the ADHD sample if they met the following criteria (outlined in the Figure):

- Adults aged 18 to 64 years with at least 1 ADHD diagnosis, defined as an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 314.0X (attention deficit disorder), 314.00 (attention deficit disorder without hyper-activity), or 314.01 (attention deficit disorder with hyper-activity) between January 1999 and December 2004.
- At least 1 pharmacy claim for OROS-MPH (National Drug Codes [NDC] 17314585002, 17314585102, 17314585202, 17314585302, 54868448900, 54868475900, 54868475901, 54868475902, 54868475903), MAS-XR (NDC codes 54092038101, 54092038301, 54092038501, 54092038701, 54092038901, 54092039101, 54868476001), or atomoxetine (NDC codes 00002322730, 00002322830, 00002322930, 000023232830, 00002323830, 00002323830).
- Continuous enrollment in a health care plan during the 6 months prior to and 6 months following the therapy index date. Therapy index date was the date of the most recent prescription fill date during the 5-year period from 1999 through 2004 for OROS-MPH, MAS-XR, or atomoxetine, with continuous eligibility 6 months prior to and after the claim date and no ADHD diagnosis or therapy during the previous 6 months (washout period). In addition to
Medical costs were calculated based on reimbursements from the employer to health care providers for inpatient care, hospital outpatient care (e.g., outpatient surgery), physician services, and emergency room visits, as well as other ancillary services (e.g., physical therapy, laboratory services). Costs were categorized in 2 mutually exclusive categories, inpatient services and outpatient/other services, based on the place of service code associated with each claim. We relied on place of service categories because revenue codes were not available in the data. Costs of inpatient services were defined using claims with a place of service specified as hospital inpatient, rehabilitation center, residential treatment center, or psychiatric facility. All other medical costs were grouped into an “outpatient and other costs” category that also included services with place of service specified as emergency treatment centers or hospital emergency rooms. Number of outpatient/other visits was defined as the summed number of unique days with a claim with place of service other than hospital inpatient, rehabilitation center, residential treatment center, or psychiatric facility. Total health care costs were defined as medical (inpatient and outpatient) plus prescription drug costs.

Costs attributable to psychotherapy, a subset of medical costs, were also reported. Psychotherapy encounters could have occurred in either an inpatient or outpatient setting, and we did not attempt to divide them into inpatient and outpatient subcategories. Psychotherapy costs were estimated using medical claims with Current Procedural Terminology (CPT) codes for psychotherapy (CPT codes 90804-90857, 96150-96155). Psychotherapy visits were defined as the summed number of unique days with at least 1 psychotherapy claim.

For each claim with an inpatient place of service, we identified the reason for the hospital use based on up to 2 primary or secondary diagnosis codes. The most frequently recorded diagnoses were designated as the reason for hospital services, irrespective of whether they appeared as primary or secondary on the claim.

About 0.1% of the medical claims had a missing amount paid. A procedure described as stratified hot-deck imputations, outlined by Little and Rubin, was applied to impute the missing paid amounts from randomly selected claims with complete paid amounts that contained the same procedure code, place of service, and type of service.

Analyses
All analyses were performed on an intent-to-treat basis (i.e., adults were grouped by their index therapy). Statistical significance was evaluated at the 0.05 significance level. The proportions of patients with at least 1 inpatient place of service claim, emergency room claim (defined as a claim with a place of service in an emergency treatment center or hospital emergency room), and outpatient or other claim over the 6-month follow-up period were compared between OROS-MPH and MAS-XR and between

ADHD = attention-deficit/hyperactivity disorder; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; MAS-XR = mixed amphetamine salts extended release; OROS-MPH = osmotic release oral system extended-release methylphenidate.
OROS-MPH and atomoxetine using chi-square tests.

Six-month medical (inpatient and outpatient) and drug costs were calculated for adults treated with OROS-MPH, MAS-XR, or atomoxetine. T tests were used for a descriptive comparison of observed costs among the treatment groups. Multivariate regression models were used to compare medical and direct health care costs between OROS-MPH and each of the other 2 therapies while adjusting for baseline patient characteristics.

A generalized linear model (GLM) specification with a log link function and gamma distribution for the error term was used to resolve the issue of a skewed cost distribution common in claims data analysis. In contrast with the traditional log-ordinary least squares regression, GLM provides more robust coefficient estimates. Also, the log link function of the mean response enables coefficients to be directly back-transformed into the original dollar scale and avoids the issue of potentially biased estimates that may result from using the Duan smearing estimation method.

Patient characteristics included age, gender, region, selected comorbidities (substance abuse and depression/anxiety), and the Charlson Comorbidity Index. Primary and secondary diagnoses during the 6 months prior to initiation of index therapy were used to identify the selected comorbidities and construct the Charlson Comorbidity Index. Substance abuse was defined as a diagnosis with 1 of the following ICD-9-CM codes: V65.42, 305.xx, 304.xx, 292.xx, 303.xx, 305.0x, or 291.xx. Depression/anxiety was defined as a diagnosis with ICD-9-CM codes 296.xx, V79.0x, 311.xx, or 300.0x. We chose to adjust for depression/anxiety and substance abuse based on prior studies reporting that patients diagnosed with ADHD were more likely to have anxiety, bipolar disorder, depression, drug or alcohol abuse, or conduct disorders compared with matched controls. Depression was found to be the most common comorbid condition among patients with ADHD. Another study reported that patients were more likely to receive atomoxetine compared with stimulants if they had a prior history of bipolar disorder, anxiety, substance abuse, or antidepressant use.

The Charlson Comorbidity Index is a weighted sum of 17 comorbidities in which comorbidity weights are based on adjusted risk of 1-year mortality; the higher the Charlson Comorbidity Index, the higher the illness burden. ICD-9-CM diagnosis codes defined by Romano et al. were used to identify the included comorbidities: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, moderate to severe liver disease, mild to moderate diabetes, diabetes with complications, hemiplegia or paraplegia, renal disease, any malignancy including lymphoma or leukemia, metastatic solid tumor, and AIDS. All analyses were performed using SAS Version 9.1 (SAS Institute, Cary, NC).

Results

Demographics: 6-Month Preperiod

Adults with a diagnosis of attention-deficit disorder (ADD)/ADHD receiving OROS-MPH, MAS-XR, or atomoxetine were, on average, 32 years old. Approximately 43% of the adults in the study sample were female, 3% had a diagnosis related to substance abuse in the previous 6 months, and 26% had a depression/anxiety-related diagnosis in the previous 6 months (Table 1).

A descriptive comparison of demographic characteristics indicated that patients initiated with MAS-XR were the youngest and atomoxetine users were the oldest. OROS-MPH patients had a lower rate of substance abuse (2.0%, P = 0.018) than

---

**TABLE 1** Baseline Characteristics of Adults Diagnosed With ADHD Receiving Different Drug Therapies

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>OROS-MPH (N = 1,452)</th>
<th>MAS-XR (N = 1,554)</th>
<th>Atomoxetine (N = 1,563)</th>
<th>P Value</th>
<th>P Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean [SD]</td>
<td>31.7 [13.2]</td>
<td>30.5 [12.5]</td>
<td>34.9 [13.1]</td>
<td>0.009</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>582 (40.1%)</td>
<td>704 (45.3%)</td>
<td>664 (42.5%)</td>
<td>0.004</td>
<td>0.181</td>
<td>0.113</td>
</tr>
<tr>
<td>Substance abuse, n (%)</td>
<td>29 (2.0%)</td>
<td>53 (3.4%)</td>
<td>51 (3.3%)</td>
<td>0.018</td>
<td>0.031</td>
<td>0.819</td>
</tr>
<tr>
<td>Depression/anxiety, n (%)</td>
<td>357 (24.6%)</td>
<td>423 (27.2%)</td>
<td>416 (26.6%)</td>
<td>0.100</td>
<td>0.202</td>
<td>0.704</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, mean [SD]</td>
<td>0.14 [0.52]</td>
<td>0.09 [0.44]</td>
<td>0.14 [0.55]</td>
<td>0.014</td>
<td>0.745</td>
<td>0.005</td>
</tr>
<tr>
<td>Patients with a hospitalization, n (%)</td>
<td>67 (4.6%)</td>
<td>63 (4.1%)</td>
<td>83 (5.3%)</td>
<td>0.451</td>
<td>0.380</td>
<td>0.097</td>
</tr>
</tbody>
</table>

* T tests were used to test for equality of means, and chi-squared tests were used to test for equality of proportions.

ADHD = attention-deficit/hyperactivity disorder; MAS-XR = mixed amphetamine salts extended release; OROS-MPH = extended-release methylphenidate.
Health Care Costs of Adults Treated for
Attention-Deficit/Hyperactivity Disorder Who Received Alternative Drug Therapies

### TABLE 2 6-month Utilization and Costs for Adults Diagnosed With ADHD Receiving Different Therapies

<table>
<thead>
<tr>
<th>Mean [SD]</th>
<th>OROS-MPH (N = 1,452)</th>
<th>MAS-XR (N = 1,554)</th>
<th>Atomoxetine (N = 1,563)</th>
<th>P Value*</th>
<th>P Value*</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of index ADHD therapy (in days)†</td>
<td>107 [66]</td>
<td>115 [65]</td>
<td>96 [65]</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. patients (%) on index ADHD drug therapy at 180 days</td>
<td>546 (37.6%)</td>
<td>655 (42.2%)</td>
<td>443 (28.3%)</td>
<td>0.011</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum/maximum duration of ADHD index therapy</td>
<td>3/180</td>
<td>7/180</td>
<td>4/180</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD drug cost</td>
<td>$282 [$215]</td>
<td>$322 [$250]</td>
<td>$392 [$298]</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total drug cost</td>
<td>$757 [$1,058]</td>
<td>$748 [$1,163]</td>
<td>$959 [$1,481]</td>
<td>0.812</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inpatient services‡, n (%)</td>
<td>50 (3.4%)</td>
<td>75 (4.8%)</td>
<td>80 (5.1%)</td>
<td>0.058</td>
<td>0.024</td>
<td>0.708</td>
</tr>
<tr>
<td>Hospital inpatient cost§</td>
<td>$139 [$1,336]</td>
<td>$261 [$2,060]</td>
<td>$334 [$2,480]</td>
<td>0.053</td>
<td>0.007</td>
<td>0.372</td>
</tr>
<tr>
<td>Medical outpatient visits</td>
<td>6.9 [7.2]</td>
<td>7.2 [7.2]</td>
<td>7.4 [8.2]</td>
<td>0.283</td>
<td>0.047</td>
<td>0.317</td>
</tr>
<tr>
<td>Medical outpatient cost‖</td>
<td>$1,112 [$2,183]</td>
<td>$1,161 [$3,956]</td>
<td>$1,247 [$2,424]</td>
<td>0.673</td>
<td>0.108</td>
<td>0.465</td>
</tr>
<tr>
<td>Psychotherapy visits</td>
<td>2.1 (4.8)</td>
<td>1.9 (4.3)</td>
<td>2.0 (4.6)</td>
<td>0.281</td>
<td>0.531</td>
<td>0.650</td>
</tr>
<tr>
<td>Psychotherapy cost</td>
<td>$132 ($342)</td>
<td>$122 ($320)</td>
<td>$106 ($702)</td>
<td>0.422</td>
<td>0.185</td>
<td>0.393</td>
</tr>
<tr>
<td>Total medical cost¶</td>
<td>$1,251 [$2,705]</td>
<td>$1,422 [$4,567]</td>
<td>$1,581 [$3,769]</td>
<td>0.209</td>
<td>0.006</td>
<td>0.290</td>
</tr>
<tr>
<td>Total medical and drug cost</td>
<td>$2,008 [$3,231]</td>
<td>$2,169 [$4,828]</td>
<td>$2,540 [$4,269]</td>
<td>0.280</td>
<td>&lt;0.001</td>
<td>0.023</td>
</tr>
</tbody>
</table>

* Tests were used to test for equality of means, and chi-squared tests were used to test for equality of proportions.
† Duration of index ADHD drug therapy was defined as time on index therapy until a minimum 60-day gap in the index therapy supply. We report the duration of therapy truncated at 180 days. The overall median duration of approximately 90 days guided our decision to compare 6-month costs.
‡ The 3 most common primary or secondary reasons for inpatient services were major depressive disorder (ICD-9-CM codes 296.2x and 296.3x), ADHD (ICD-9-CM code 314.0x), and depressive disorder (ICD-9-CM code 311.xx).
§ The minimum and maximum values for inpatient services costs for OROS-MPH were $0 to $32,930, $0 to $41,804 for MAS-XR, and $0 to $54,549 for atomoxetine.
‖ The minimum and maximum values for medical outpatient/other cost were $0 to $31,756 for OROS-MPH, $0 to $134,712 for MAS-XR, and $0 to $36,075 for atomoxetine.
¶ The minimum and maximum values for medical cost (inpatient and outpatient/other) were $0 to $35,597 for OROS-MPH, $0 to $134,712 for MAS-XR, and $0 to $55,950 for atomoxetine. By the criterion of medical cost in excess of $50,000, 2 patients were medical cost outliers. The diagnosis codes associated with the highest cost claim for the MAS-XR outlier were chronic kidney disease (ICD-9-CM code 585.xx) and iron deficiency anemia (ICD-9-CM code 280.9). The diagnosis codes associated with the highest cost claim for the atomoxetine outlier were acute myocardial infarction (ICD-9-CM code 410.21) and paroxysmal ventricular tachycardia (ICD-9-CM code 427.1).
ADHD = attention-deficit/hyperactivity disorder; ICD-9 = International Classification of Diseases, Ninth Revision, Clinical Modification; MAS-XR = mixed amphetamine salts extended release; OROS-MPH = extended-release methylphenidate.

Patients treated with MAS-XR (3.4%) and atomoxetine (3.3%, P = 0.031). Atomoxetine- and OROS-MPH-treated patients had higher Charlson Comorbidity Indexes than MAS-XR patients (P = 0.005 for comparison between atomoxetine and MAS-XR, P = 0.014 for comparison between OROS-MPH and MAS-XR). No significant differences were apparent across the 3 groups in the rate of depression or rate of hospital inpatient use in the 6-months before therapy initiation (Table 1).
Resource Use: 6-Month Postperiod

The mean (SD) duration of index ADHD drug therapy within 180 days was lower for atomoxetine (96 days [65]) compared with OROS-MPH (107 [66], P<0.001) or MAS-XR (115 [65], P<0.001) (Table 2). Median duration of therapy was 99 days for OROS-MPH, 128 days for MAS-XR, and 86 days for atomoxetine. Over the 6-month follow-up period, the proportion of patients with at least 1 inpatient place of service claim was not significantly lower in patients treated with OROS-MPH (3.4%) compared with MAS-XR (4.8%, P=0.058), but was lower than the 5.1% rate for atomoxetine-treated patients (P=0.024 for comparison with OROS-MPH). The proportions of patients having an outpatient claim or claim with an emergency room place of service were not significantly different between OROS-MPH-treated adults and those treated with MAS-XR or atomoxetine (data not shown).

Descriptive Cost Analysis

Six-month mean (SD, median) total health care (medical and drug) costs were $2,008 ($3,231, $1,062) for OROS-MPH, $2,169 ($4,828, $1,080) for MAS-XR, and $2,540 ($4,269, $1,271) for atomoxetine-treated adults (Table 2). Total health care costs were significantly higher for atomoxetine-treated adults compared with those treated with OROS-MPH (P<0.001) and MAS-XR (P=0.023).

The largest component of 6-month total health care costs was attributable to outpatient costs (52%). No significant differences were observed in outpatient costs or the subset of medical costs attributable to psychotherapy. Drug costs accounted for approximately 38% of total unadjusted costs for OROS-MPH and atomoxetine versus 34% for MAS-XR. Mean (SD, median) ADHD drug costs were higher with atomoxetine at $392 ($298, $325) compared with MAS-XR at $322 ($250, $275) and OROS-MPH at $282 ($215, $246) (P<0.001 for both comparisons).

Inpatient hospital cost accounted for 7% of total direct medical cost for OROS-MPH, 12% for MAS-XR, and 13% for atomoxetine. Mean (SD) inpatient service costs were not significantly lower for OROS-MPH patients at $139 ($1,336) compared with MAS-XR patients at $261 ($2,060, P=0.053), but were lower compared with atomoxetine patients at $334 ($2,480, P=0.007). The 3 most common reasons for inpatient service use were major depressive disorder (MDD; ICD-9-CM code 296.3x), ADHD (ICD-9-CM code 314.0x), and depressive disorder (ICD-9-CM code 311.xx).

By using the criteria of medical cost in excess of $50,000 or approximately the 99.96th percentile, 2 patients were medical cost outliers. One patient treated with MAS-XR had total medical and pharmacy costs of $136,300, of which $134,712 were medical costs; the highest cost claim for this patient was associated with diagnosis codes for chronic kidney disease (ICD-9-CM code 583.xx) and iron deficiency anemia (ICD-9-CM code 280.9x). One patient who received atomoxetine had total medical and pharmacy costs of $58,554, of which $55,950 were medical costs; the highest cost claim was associated with diagnosis codes for acute myocardial infarction (ICD-9-CM code 410.21) and paroxysmal ventricular tachycardia (ICD-9-CM code 427.1).

Multivariate Regression

The GLM comparison of health care costs in the 6 months after therapy initiation (adjusting for potential confounders, Table 3) found that risk-adjusted direct health care costs of OROS-MPH-treated adults were on average $156 (8.0%) lower than those of MAS-XR-treated adults (P=0.017) and $226 (11.3%) less than those of atomoxetine-treated adults (P=0.001). The health care cost difference was primarily due to differences in medical costs; average medical costs for OROS-MPH-treated adults were $142 (10.4%) less than those of MAS-XR-treated adults (P=0.022) and $132 (9.8%) less than those of atomoxetine-treated adults (P=0.033).

Discussion

Our analysis of a privately insured claims database indicates that over the 6-month period following therapy initiation, adults treated with OROS-MPH had, on average, lower all-cause medical and total health care costs than those treated with MAS-XR or atomoxetine after adjusting for patient characteristics. To our knowledge, this is the first study comparing all-cause health care costs of adults diagnosed with ADHD and receiving alternative ADHD drug therapies.28 Previous studies have indicated that MPH is a cost-effective treatment for children with ADHD.29–31 A study by Marchetti et al. developed a decision–analytic model to estimate the total expected costs for the treatment and management of school-age children with ADHD using 6 commonly prescribed pharmacotherapies: methylphenidate immediate release/extended release (MPH-IR/ER), methylphenidate immediate release (MPH-IR), branded MPH-IR/ER (Metadate CD), OROS-MPH (Concerta), branded MPH-IR (Ritalin), and a combination of dextroamphetamine and amphetamine salts (Adderal).32 This study found that dextroamphetamine and amphetamine salts had the highest total expected costs among the ADHD pharmacotherapies evaluated: the average total annual expected cost in 2001 U.S. dollars per treated patient was $1,710 for Metadate CD, $1,876 for Concerta, $2,061 for MPH-IR/ER, $2,122 for MPH-IR, $2,392 for Ritalin, and $2,567 for Adderal.

Other published studies have focused on the direct health care costs of adults with ADHD but did not provide cost comparisons of adults with ADHD on different drug therapies.8–11 Those studies compared the costs of care for adults with ADHD with the costs in matched controls and concluded that ADHD is associated with significant economic burden. Compared with the control group, adults diagnosed with ADHD were signifi-
Health Care Costs of Adults Treated for Attention-Deficit/Hyperactivity Disorder Who Received Alternative Drug Therapies

Significantly more likely to have a comorbid diagnosis of asthma, anxiety, bipolar disorder, depression, drug or alcohol abuse, antisocial disorder, or oppositional disorder (e.g., 4.7% vs. 2.9% for asthma and 4.5% vs. 0.58% for bipolar disorder). Adjusting for patient characteristics, adults with ADHD had an excess medical cost of $2,880 ($P < 0.001). Costs associated with accident claims are more than 3 times higher in adults with ADHD than in controls. The total excess cost of ADHD in the United States in 2000 was $31.6 billion, including the higher costs associated with family members of persons with ADHD. A recently published paper also reported national estimates and characteristics of ambulatory visits by adults with ADHD in the United States but did not compare the cost of alternative ADHD drug treatments. Our study assessed the real-world drug and total medical costs associated with initiation of 3 alternative drug therapies for adult patients with a diagnosis of ADHD.

Limitations

Foremost among the limitations of our study was its short duration. The overall median length of index ADHD drug therapy was approximately 90 days, ranging from a median of 86 days for atomoxetine to 99 days for OROS-MPH to 128 days for MAS-XR. We anticipated this relatively short therapy period based on a previous study by Perwien et al., which concluded that even though ADHD patients continued their ADHD medication for several months, they did not consistently take medication for more than 2 months.

Second, our study did not directly assess the clinical severity of ADHD. Like all administrative claims databases, ADHD severity could not be determined from the data that we accessed. To assess and control for subjects’ physical conditions, we used a common proxy of comorbidity risk measurement, the Charlson Comorbidity Index, and selected comorbidities. However, other risk-adjustment alternatives to the Charlson Comorbidity Index also exist. Studies have found similar mortality predictive accuracy with the Romano–Charlson Comorbidity Index (used in our analysis) and the Elixhauser comorbidities.

Third, we did not restrict ICD-9-CM codes specifically to ADHD. We included ICD-9-CM codes 314.00 (attention-deficit disorder without hyperactivity, also known as ADD of predominantly the inattentive type) and 314.0 (nonspecific attention-deficit disorder) as well as 314.01, which is specific to attention-deficit disorder with hyperactivity (ADHD). While other researchers have used ICD-9-CM codes 314.0x to describe ADHD, the correct definition of code 314.0x is ADD because ICD-9-CM code 314.00 is intended to describe ADHD.

Fourth, we did not require health care or hospital costs to be related to ADD/ADHD; hence, we report all-cause health care and hospital costs. While ADD/ADHD (ICD-9-CM code 314.0x) was 1 of the 3 most common primary or secondary reasons for hospital inpatient service use, we did not exclude any hospital service use during the follow-up period. The other 2 most common principal reasons for inpatient service use were MDD (ICD-9-CM codes 296.2x and 296.3x) and depres-

### TABLE 3

<table>
<thead>
<tr>
<th>Medical Costs†</th>
<th>Risk-Adjusted Cost Estimate ($)*</th>
<th>95% Confidence Limits ($)</th>
<th>P Value for Comparison With OROS-MPH</th>
<th>P Value for Comparison With MAS-XR</th>
</tr>
</thead>
<tbody>
<tr>
<td>OROS-MPH</td>
<td>1,220</td>
<td>1,141</td>
<td>1,305</td>
<td>0.022</td>
</tr>
<tr>
<td>MAS-XR</td>
<td>1,362</td>
<td>1,276</td>
<td>1,453</td>
<td>0.033</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>1,352</td>
<td>1,267</td>
<td>1,443</td>
<td>0.880</td>
</tr>
</tbody>
</table>

| Medical + Drug Costs‡ | | |
|----------------------| | |
| OROS-MPH             | 1,782 | 1,696 | 1,872 |
| MAS-XR               | 1,938 | 1,848 | 2,033 |
| Atomoxetine          | 2,008 | 1,915 | 2,106 |

* The risk-adjusted costs were estimated by a GLM with a log link and gamma distribution adjusting for patient demographic characteristics (i.e., age, gender, region) and comorbidities (substance abuse, depression, and Charlson Comorbidity Index).
† Medical costs include inpatient, outpatient and other costs.
‡ Total direct costs include medical costs and drug costs.
§ A sensitivity analysis excluding the 2 patients with medical costs in excess of $50,000 suggested that of the $156 6-month cost difference between OROS-MPH and MAS-XR and the $226 6-month cost difference between OROS-MPH and atomoxetine, $47 (30%) and $11 (5%), respectively, were attributable to high-cost outliers.
ADHD = attention-deficit/hyperactivity disorder; GLM = generalized linear model; MAS-XR = mixed amphetamine salts extended release; OROS-MPH = extended-release methylphenidate.
Health Care Costs of Adults Treated for Attention-Deficit/Hyperactivity Disorder Who Received Alternative Drug Therapies

Over the 6-month period following drug therapy initiation, adults with a diagnosis of ADHD initiated on OROS-MPH had, on average, 8% lower total all-cause drug and medical costs compared with MAS-XR or 11% lower total costs compared with atomoxetine. Further research is needed to evaluate clinical and economic outcomes in adults diagnosed with ADHD who are receiving alternative therapies.

Conclusions

Disclosures

Funding for this research was provided by McNeil Pediatrics Division of McNeil-PPC, Inc. to Analysis Group, Inc. Huabin Zhang is a former employee of McNeil-PPC. Authors Wu, Birnbaum, Ivanova, and Yang are employees of Analysis Group, Inc.

Author Eric Wu served as principal author of the study. Study concept and design were contributed primarily by Wu and authors Howard Birnbaum,
Huanbin Zhang, and David Mallet. Data collection and analysis was the work of authors Elaine Yang, Jasmina Ivanova, and Mallet; data interpretation was primarily the work of Wu, with input from Birnbaum, and Ivanova. Writing of the manuscript and its revision was primarily the work of Ivanova, with input from Wu, Birnbaum, Zhang, and Yang.

REFERENCES


Continuity in Methylphenidate Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

Mark Olson, MD, MPH; Steven C. Marcus, PhD; Huabin F. Zhang, MD, MPH; and George J. Wan, PhD, MPH

ABSTRACT

BACKGROUND: Although stimulant therapy is commonly discontinued early in adults with attention-deficit/hyperactivity disorder (ADHD), the factors that contribute to continuity of stimulant therapy remain largely unknown.

OBJECTIVE: To (1) compare the continuity of methylphenidate (MPH) therapy among adults who use immediate-release methylphenidate (IR-MPH) for ADHD with adults who use extended-release methylphenidate (ER-MPH) formulations, and (2) examine some of the methodological issues involved in research with administrative claims for ADHD.

METHODS: An analysis of pharmacy and medical claims for 75 US managed care plans representing approximately 55 million beneficiaries for dates of service from January 1, 2000 through December 31, 2004. Patients had to be adults (aged 18 to 64 years) who had 1 or more outpatient medical claims for ADHD (International Classification of Diseases, Ninth Revision, Clinical Modification code 314.xx) during the study period and who had initiated ER-MPH or IR-MPH treatment for ADHD. The study cohorts did not have a pharmacy claim for MPHs, amphetamines, pemoline, or atomoxetine for 6 months preceding the first (index) MPH pharmacy claim. Stimulant treatment episodes were defined to start on the index date and terminate on the last date supplied of the index medication. Episodes of treatment were also defined as terminated if there was a gap of ≥ 30 days between the end of the days supplied on the pharmacy claim and the date of the next pharmacy claim for the index medication.

RESULTS: Less than one third (30.0%) of the adult patients who were prescribed MPH had 1 or more medical claims with a diagnosis code for ADHD. For the adult MPH patients with at least 1 medical claim with a diagnosis code for ADHD, the patients who initiated therapy with ER-MPH (N = 2,833) were significantly younger, were more likely to be male, and were less likely to be treated by a psychiatrist than were the patients who initiated therapy with IR-MPH (N = 2,289). Only 50.5% (n = 1,156) of IR-MPH patients and 61.4% (n = 1,739) of ER-MPH patients had more than 1 pharmacy claim for the index MPH medication. Adults treated with ER-MPH also had a significantly longer median duration of treatment with the index medication (ER-MPH: 68 days, 95% confidence interval [CI], 65-71 days vs. IR-MPH 39 days, 95% CI, 33-52 days). Controlling for group differences in age, gender, treatment by a psychiatrist, recently prescribed psychotropic medications, treated mental disorders, emergency mental health treatment, and inpatient mental health care, ER-MPH initiation was associated with an average 27% longer duration of treatment than with IR-MPH (survival time ratio: 1.27, 95% CI, 1.20-1.35).

CONCLUSION: In management of adult ADHD, use of ER-MPH formulations was associated with a longer median duration of the initially prescribed medication than was use of IR-MPH. It is unknown whether the observed absolute unadjusted difference of 29 days in median length of therapy is clinically important.

KEYWORDS: Attention-deficit/hyperactivity disorder, Methylphenidate, Treatment continuity

What is already known about this subject

- Previous research indicates that episodes of treatment with stimulants such as methylphenidate (MPH) tend to be relatively brief in the community treatment of adult ADHD, with a mean of 50 days of therapy.

What this study adds

- Only 30% of adult patients who received either immediate-release MPH (IR-MPH) or extended-release MPH (ER-MPH) had a medical or facility claim with a diagnosis code for ADHD.
- For patients who received MPH and had at least 1 medical or facility claim with a diagnosis code for a diagnosis code for ADHD, ER-MPH had a longer median duration of therapy than did IR-MPH (68 days versus 39 days, respectively).
- The diagnosis codes for patients who received ER-MPH were distributed nearly equally between ADHD with hyperactivity (code 314.01, 46%) and ADHD without hyperactivity (code 314.00, 48%) compared with IR-MPH patients who had code 314.01 (ADHD with hyperactivity, 39%) and code 314.00 (ADHD without hyperactivity, 53%). The remainder, 5.5% for ER-MPH and 8.1% for IR-MPH, were ADHD other (code 314).

In the general adult population, the prevalence of attention-deficit/hyperactivity disorder (ADHD) is approximately 2% to 4%.1-4 Methylphenidate (MPH) effectively ameliorates many symptoms of adult ADHD.5-9 In 1 large 6-week randomized controlled trial of adults with ADHD,7 immediate-release methylphenidate (IR-MPH) was associated with a 76% response rate, compared with a 19% response rate for placebo. In a 6-week trial with the same response criteria, 66% of subjects treated with osmotic release oral system methylphenidate (OROS-MPH) responded, compared with 39% who received placebo.9 In both studies, response was defined as a 30% symptom reduction and, at least, much overall improvement.

Early discontinuation of treatment is common in the community care of patients initiating stimulant therapy.10-13 In 1 study,
adults initiating pharmacological treatment for ADHD continued their medications for an average of only 50 days. Although early discontinuation of treatment commonly occurs in the care of adult ADHD, the factors that promote continuity of stimulant treatment remain largely unknown.

Among youth with ADHD, extended-release methylphenidate (ER-MPH) formulations are associated with significantly greater treatment continuity than immediate-release formulations. This higher rate of treatment continuity with ER-MPH may be related to the simpler dosing regimen in which a single dose provides clinical effects for about 8 hours compared with IR-MPH, which requires several daily doses to provide coverage throughout the day.15

In the present study, we evaluated whether ER-MPH formulations are associated with greater treatment continuity than are IR-MPH formulations in the community management of adults with ADHD under managed care. We compare the duration of MPH treatment episodes of adults from various US managed care health plans, following initiation with either ER-MPH or IR-MPH formulations.

### Methods

#### Source of Data

Analyses of medical service and pharmacy claims from the PharMetrics (2000-2004) database are presented. This database contains standardized prescription, claims, and enrollment information from 75 managed care organizations that collectively cover more than 55 million lives,16 similar to the distribution of the US population by age and gender. Enrollment data include information on patient demographics and periods of eligibility for services. Claims data include diagnostic and provider information for all inpatient and outpatient services. Prescription claims include the name of the medication filled, the quantity of units dispensed, the days of supply, and the National Drug Code.

All study procedures were approved by the Institutional Review Board of the University of Pennsylvania.

#### Selection of Study Cohorts

Selected patients were between 18 and 64 years on the date of the first or index pharmacy claim for ER-MPH or IR-MPH. To assess patient characteristics before the index prescription and continuity of MPH after this prescription, the sample was limited to patients who were continuously enrolled in the health plan for 6 months before and 12 months after the index MPH prescription. Because we were interested in new stimulant treatment episodes, patients who received any stimulant prescription during the 6 months before the index MPH prescription were excluded from the analysis. The initial MPH claim was limited to a maximum of 90 days. To focus the analysis on patients receiving treatment for ADHD, we restricted the sample to adults who received 1 or more outpatient treatment claims for ADHD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 314.xx) during the study period. Patients were excluded if they were prescribed pemoline or atomoxetine during the study period (Figure 1).

For the primary analyses, we partitioned the selected sample into 2 study cohorts: patients who received an index MPH prescription of an ER-MPH (N=2,833) or IR-MPH
Continuity in Methylphenidate Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

(N = 2,289) formulation. The ER-MPH group included patients whose index prescription was OROS-MPH (Concerta; n = 2,067), MPH-LA (Ritalin-LA, n = 84), MPH-CD (Metadate-CD, n = 109), a residual group of other long-acting MPH preparations (MPH-ER, MPH-SR, MPH-CR, MPH-SA, Metadate-ER, and Methylin-ER, n = 505). The group also included patients treated with more than 1 ER-MPH (n = 68). In some analyses, the 4 ER-MPH formulations were compared. All other selected patients were assigned to the IR-MPH group.

Duration of MPH Treatment Episodes
Stimulant treatment episodes were defined to start on the index date and terminate on the last date supplied of the index medication. Episodes of treatment were also defined as terminated if there was a gap of ≥ 30 days between the end of the days supplied on the pharmacy claim and the date of the next pharmacy claim for the index medication. Each patient contributed only 1 stimulant treatment episode to the analysis. Once-per-day dosing was assumed to occur when the number of units in the pharmacy claim matched the number of days in the days supply field.

Background Characteristics
Study patients were first characterized with respect to patient age, gender, specialty of the prescribing physician (psychiatrist or other medical specialist treatment during the study period), and ADHD subtype. Three subtypes of ADHD were defined on the basis of the largest number of relevant claims for each patient during the study period: (1) ADHD without hyperactivity (ICD-9-CM code 314.00), (2) ADHD with hyperactivity (code 314.01), and (3) other ADHD subtypes (other code: 314). Mental health claims during the 6 months preceding the index MPH pharmacy claim were used to classify patients as having received treatment for mood disorders (codes 296, 300.4, 311), substance use disorders (codes 291, 292, 303-305), anxiety disorders (codes 300.0, 300.2, 300.3, 308.3, 309.81), and a residual diverse group of all other mental disorders, except mental retardation (codes 290-316, except above).

Analytic Strategy
Patients treated with ER-MPH or IR-MPH were first compared with respect to demographic and clinical background characteristics. Group comparisons are presented with 95% confidence intervals (CIs).

The mean and median duration of MPH treatment were calculated for both study groups with surrounding 95% CIs. Cox accelerated failure time regressions based on the Weibull distribution were performed, controlling for patient age, gender, treating specialist, other treated mental disorders, claims for other prescribed psychotropic medications, and claims for emergency and inpatient services in which the first listed diagnosis was a mental disorder (ICD-9-CM codes 290-316).

Emergency department and inpatient service use were identified using PharMetrics specified categories for place of service, procedure codes (Current Procedural Terminology [CPT-4], Healthcare Common Procedure Coding System [HCPCS], and revenue codes. In these analyses, the dependent variable was time to discontinuation of the index MPH medication. When the resulting parameter estimate for drug group was exponentiated, the regression provided a ratio of time to discontinuation between groups or the survival time ratio (STR). The time to discontinuation of the index MPH medication was also examined with a Kaplan-Meier survival curve, and the Wilcoxon test of equality over strata was used to compare the curves.

We also compared the mean and median duration of MPH treatment episodes among 4 subgroups of adult patients prescribed ER-MPH; those treated with OROS-MPH, MPH-LA, MPH-CD, or other extended-release MPH preparations. Separate

---

### TABLE 1

<table>
<thead>
<tr>
<th>Background Characteristics of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Age in years</strong></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td><strong>Prescription by psychiatrist</strong></td>
</tr>
<tr>
<td>ADHD subtype*</td>
</tr>
<tr>
<td>Hyperactive</td>
</tr>
<tr>
<td>Nonhyperactive</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

PharMetrics database for claims from January 1, 2002, to December 31, 2004. * ICD-9-CM code 314 is described as “hyperkinetic syndrome of childhood”, and 314.0 is described as “attention deficit disorder”. Modifiers to 314 include 314.00 for ADHD without mention of hyperactivity and 314.01 for ADHD with hyperactivity.

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Kaplan-Meier survival curves were also calculated. All statistical analyses were conducted using SAS software version 9.1.3.17

Results

Background and Clinical Characteristics

In the selection of study patients, 30.0% (5,122 of 17,093) of those prescribed MPH had 1 or more medical claims for the treatment of ADHD during the study period (Figure 1). Among selected study patients, roughly one half (55.3%) were initially prescribed an ER-MPH. Compared with patients started on IR-MPH, patients started on ER-MPH were primarily young adults (aged 18-35 years), male, treated by a doctor who was not a psychiatrist, and treated for the hyperactive subtype of ADHD (see Table 1). A significantly larger percentage of the IR-MPH patients received treatment with anxiolytic and antidepressant medications during the 6 months preceding the index MPH prescription (see Table 2). The two MPH groups did not differ significantly with respect to the proportion who received treatment for mood, anxiety, or substance use disorders or the proportion who received inpatient or emergency mental health treatment during the 6 months before the index prescription (Table 2). While 62% of ER-MPH patients had pharmacy claims with days supply that matched the units dispensed (i.e., once-daily use), only 8% of IR-MPH patients appeared to use only 1 unit per day (Table 2). Among the ER-MPH patients, those initiating OROS-MPH (68.1%) or MPH-LA (63.9%) were more likely than were those initiating MPH-CD (36.1%) or other ER-MPH preparations (45.8%) to start once-daily dosing regimens.

\[ \text{TABLE 2} \]

Characteristics of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ER Methylphenidate (n=2,833)</th>
<th>IR Methylphenidate (n=2,289)</th>
<th>Statistics</th>
<th>( \chi^2 )</th>
<th>df</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated comorbid disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance use</td>
<td>5.0</td>
<td>5.4</td>
<td>0.42</td>
<td>1</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>Mood disorders</td>
<td>28.2</td>
<td>27.6</td>
<td>0.20</td>
<td>1</td>
<td>0.66</td>
<td></td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>11.9</td>
<td>12.0</td>
<td>0.03</td>
<td>1</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>MH treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency</td>
<td>1.9</td>
<td>1.9</td>
<td>0</td>
<td>1</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Inpatient</td>
<td>1.8</td>
<td>1.9</td>
<td>0.04</td>
<td>1</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>34.8</td>
<td>37.3</td>
<td>3.33</td>
<td>1</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>1.7</td>
<td>2.1</td>
<td>0.73</td>
<td>1</td>
<td>0.40</td>
<td></td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>4.7</td>
<td>4.4</td>
<td>0.18</td>
<td>1</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>12.6</td>
<td>14.6</td>
<td>4.30</td>
<td>1</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Initial stimulant dosing</td>
<td></td>
<td></td>
<td>1,574.12</td>
<td>2</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>1 per day</td>
<td>62.3</td>
<td>7.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 per day</td>
<td>24.2</td>
<td>32.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 or more per day</td>
<td>13.5</td>
<td>60.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of patients with initial claim</td>
<td>11.42</td>
<td>2</td>
<td>0.003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤30 days</td>
<td>77.7</td>
<td>81.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31-60 days</td>
<td>13.5</td>
<td>11.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61-90 days</td>
<td>8.8</td>
<td>7.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PharMetrics database for claims from January 1, 2000, to December 31, 2004. ADHD = attention-deficit/hyperactivity disorder; MH = mental health.

\[ \text{TABLE 3} \]

Median Duration of Treatment Episodes for Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Methylphenidate for ADHD*

<table>
<thead>
<tr>
<th>Stimulant Group</th>
<th>Overall Median in Days (95% CI)</th>
<th>Number (%) With 2 or More Stimulant Pharmacy Claims</th>
<th>Median in Days for Those With 2 or More Stimulant Pharmacy Claims (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR methylphenidate (n=2,289)</td>
<td>39.0 (33.0-52.0)</td>
<td>1156 (50.5)†</td>
<td>121.0 (113.0-130.0)</td>
</tr>
<tr>
<td>ER methylphenidate (n=2,833)</td>
<td>68.0 (65.0-71.0)</td>
<td>1739 (61.4)†</td>
<td>138.0 (130.0-149.0)</td>
</tr>
<tr>
<td>- Osmotic release oral system (OROS) methylphenidate (n=2,067)</td>
<td>73.5 (76.0-79.0)</td>
<td>1322 (64.0)‡</td>
<td>145.5 (132.0-156.0)</td>
</tr>
<tr>
<td>- Metadate CD (n=109)</td>
<td>58.0 (30.0-80.0)</td>
<td>65 (59.0)‡</td>
<td>98.0 (86.0-142.0)</td>
</tr>
<tr>
<td>- Ritalin LA (n=84)</td>
<td>57.5 (30.0-64.0)</td>
<td>46 (54.8)‡</td>
<td>92.5 (71.0-175.0)</td>
</tr>
<tr>
<td>- Other ER methylphenidate (n=505)</td>
<td>34.0 (30.0-58.0)</td>
<td>238 (47.1)‡</td>
<td>121.0 (102.0-139.0)</td>
</tr>
</tbody>
</table>

* The number of patients in the extended-release methylphenidate group (n=2,833) exceeds the sum of the OROS-MPH (n=2,067), MPH-CD (n=109), MPH-LA (n=84), and Other ER methylphenidate (n=505) groups because 68 patients who were treated with more than 1 ER-MPH formulation do not appear in the individual medication subanalysis.
† Significantly different values, chi square = 61.0, P<0.001.
‡ Significantly different values, chi square = 49.3 (df=3) P<0.001.
CI = confidence interval; ADHD = attention-deficit/hyperactivity disorder; LA = long acting.
Continuity of MPH Treatment
The overall median continuity of MPH treatment was significantly longer for patients treated with ER-MPH than with IR-MPH (Table 3). Only 50.5% (n = 1,156) of IR-MPH patients and 61.4% (n = 1,739) of ER-MPH patients had more than 1 pharmacy claim for the index MPH. Adults treated with ER-MPH also had a significantly longer median duration of stimulant treatment (ER-MPH: 68 days, 95% CI, 65-71 days vs. IR-MPH: 39 days, 95% CI, 33-52 days). A Kaplan-Meier curve revealed significantly greater time to index MPH discontinuation for patients treated with ER-MPH rather than IR-MPH (Wilcoxon \( T = 77.7, df = 1, P < 0.001 \); see Figure 2). In a multivariate analysis, which controlled for background demographic and clinical characteristics, ER-MPH patients had an estimated 27% (STR = 1.27) longer duration of index MPH treatment than did IR-MPH patients (Table 4). In this multivariate analysis, the duration of MPH treatment was also significantly related to treatment by a psychiatrist and treatment with an antidepressant medication or mood stabilizer prior to the index MPH prescription (Table 4). Mental health treatment in an emergency department during the 6 months before initiation of MPH therapy and younger age (18-35 years) were each significantly and independently related to a shorter duration of index MPH treatment (Table 4). The generalized \( R^2 \) for this model was 0.061.

Among patients treated with ER-MPH preparations, those treated with OROS-MPH had the longest median duration of index stimulant treatment, followed by MPH-CD, MPH-LA, and the other ER-MPH group. The times to index MPH discontinuation of the 4 extended-release groups are displayed in Figure 3. The survival times of the curves significantly differ from each other (Wilcoxon \( T = 49.1, df = 3, P < 0.001 \)). Controlling for group differences in age, gender, treatment by a psychiatrist, recently prescribed psychotropic medications, treated mental disorders, emergency mental health treatment, and inpatient mental health care, OROS-MPH initiation was associated with an average 46% longer duration of treatment than was the other ER-MPH group.

Continuity in Methylphenidate Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

FIGURE 2 Survival Distribution in Days of Methylphenidate Treatment for Adults With Attention-Deficit/Hyperactivity Disorder

![Figure 2](image_url)

TABLE 4 Survival Time Ratios From an Accelerated Failure Time Model of Adults Treated With Extended-Release (ER) and Immediate-Release (IR) Stimulants for ADHD

<table>
<thead>
<tr>
<th>Characteristic (Versus Reference Category)</th>
<th>Survival Time Ratio</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER-methylphenidate (IR-MPH)</td>
<td>1.27</td>
<td>1.20-1.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient age, years (51-64)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>0.62</td>
<td>0.55-0.69</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>36-50</td>
<td>0.90</td>
<td>0.80-1.02</td>
<td>0.09</td>
</tr>
<tr>
<td>Patient gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (male)</td>
<td>1.01</td>
<td>0.95-1.08</td>
<td>0.72</td>
</tr>
<tr>
<td>ADHD subtype (other)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With hyperactivity</td>
<td>0.99</td>
<td>0.87-1.13</td>
<td>0.90</td>
</tr>
<tr>
<td>Without hyperactivity</td>
<td>1.00</td>
<td>0.88-1.14</td>
<td>0.95</td>
</tr>
<tr>
<td>Treatment by psychiatrist (none)</td>
<td>1.38</td>
<td>1.10-1.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Comorbidities*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance use (none)</td>
<td>0.92</td>
<td>0.79-1.07</td>
<td>0.27</td>
</tr>
<tr>
<td>Mood disorders (none)</td>
<td>0.98</td>
<td>0.90-1.07</td>
<td>0.63</td>
</tr>
<tr>
<td>Anxiety disorders (none)</td>
<td>1.01</td>
<td>0.91-1.12</td>
<td>0.85</td>
</tr>
<tr>
<td>MH treatment*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency (none)</td>
<td>0.76</td>
<td>0.59-0.98</td>
<td>0.03</td>
</tr>
<tr>
<td>Inpatient (none)</td>
<td>0.90</td>
<td>0.69-1.19</td>
<td>0.46</td>
</tr>
<tr>
<td>Medications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants (none)</td>
<td>1.19</td>
<td>1.10-1.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antipsychotics (none)</td>
<td>0.84</td>
<td>0.66-1.06</td>
<td>0.14</td>
</tr>
<tr>
<td>Mood stabilizers (none)</td>
<td>1.15</td>
<td>0.98-1.35</td>
<td>0.08</td>
</tr>
<tr>
<td>Anxiolytics (none)</td>
<td>0.97</td>
<td>0.87-1.07</td>
<td>0.51</td>
</tr>
</tbody>
</table>

*Based on claims during the 6 months before the index MPH pharmacy claim. ADHD = attention-deficit/hyperactivity disorder; LA = long acting; MH = mental health.
Continuity in Methylphenidate Treatment of Adults With Attention-Deficit/Hyperactivity Disorder

In this managed care population, adults starting ER-MPH formulations for the treatment of ADHD had greater continuity of treatment with the initially prescribed medication than adults starting IR-MPH formulations had. After controlling for several basic demographic, clinical, and treatment characteristics, ER-MPH was associated with a 27% longer duration of treatment than IR-MPH was, but the absolute difference was fewer than 30 days.

The reasons for the difference in treatment continuity are not known. It is possible that greater ease of administration associated with once-a-day dosing may help to account for the longer observed stimulant therapy episodes of patients treated with ER-MPH rather than with IR-MPH. Compared with once-a-day dosing, multiple daily doses may make patients more prone to missed doses and consequent decline in treatment response. In the management of several medical conditions, more complex dosing regimens have been related to problems with treatment continuity and poorer clinical outcome. At the same time, some patients and physicians may prefer IR-MPH because it allows for greater ease in dose titration and permits more flexible dosing schedules that may minimize side effects.

Of the ER-MPH products, OROS-MPH had the longest treatment continuity. This finding extends similar results concerning the continuity of MPH treatment for children and adolescents. Detailed clinical assessments, not available in administrative data, might help to reveal reasons for the differences in treatment duration among the ER-MPH formulations. It is possible that the greater treatment continuity of OROS-MPH compared with the other ER-MPH formulations is related to its longer half-life. Administration of OROS-MPH results in an immediate release of MPH, followed by a slower release of MPH over approximately 12 hours.

MPH-LA, MPH-CD, and the other extended-release preparations have somewhat faster release. MPH-LA, MPH is released over an 8-hour period. MPH-CD typically results in a peak MPH plasma concentration approximately 1.5 hours after dosing, followed by a second peak approximately 4.5 hours after dosing. It is also possible that the differences in the continuity of the ER-MPH formulations are explained by differences in unmeasured patient or physician characteristics that have confounded associations between MPH formulation and treatment continuity. Although the model controlled for several covariates, the generalized $R^2$ of 6.1% indicates that 94% of the variance in treatment continuation is attributed to unmeasured confounding factors.

The observed differences in stimulant continuity among MPH preparations occurred against a background of widespread early discontinuation of treatment. For both groups, the median duration of MPH treatment episodes was less than 70 days. An important priority remains the identification of patient, treatment, and contextual factors that contribute to pervasive early MPH discontinuation. An understanding of the most common reasons for early discontinuation may provide a framework for developing effective interventions to reduce premature discontinuation of MPH treatment in adults with ADHD. It may be especially important to determine the extent to which early MPH treatment discontinuation reflects problems with medication tolerability or side effects, including sleep difficulties, reduced appetite, stomach ache, exacerbation of tic disorders, or cardiovascular concerns.

Limitations

First and foremost among the study limitations is the fact that the clinical significance of MPH discontinuation cannot be determined from the current analysis. More specifically, it is not possible to distinguish clinically appropriate treatment discontinuation from premature treatment termination for cause, such as perceived lack of efficacy or adverse effects. Second,
patients initially prescribed IR-MPH may differ from those initially prescribed ER-MPH in important unmeasured clinical or treatment characteristics that may place the IR-MPH group at increased risk of early MPH discontinuation. In a variety of contexts, patient education, increased number of hours when the clinic is open, and improved communication between physicians and patients have been demonstrated to improve adherence to medication regimens.\(^5\)

Third, the present analysis was limited to patients treated with MPH rather than with mixed amphetamines, atomoxetine, or other medications commonly used to treat adult ADHD. Fourth, although pharmacy claims databases tend to be reliable and valid,\(^2,6,27\) a pharmacy claim does not guarantee actual medication consumption. In addition, some patients may take medications without generating a claim (e.g., out-of-pocket purchases), while other patients may take less than the amount prescribed. Fifth, because the study involved participants in private managed care plans, the results may not be generalizable to other patient populations, such as those insured by Medicaid or the Veterans Administration.

### Conclusions

In this observational study of adults treated for ADHD, ER-MPH was associated with significantly longer treatment episodes than was IR-MPH. In 1 study of pediatric ADHD, patients who were adherent with stimulants exhibited significantly greater symptom improvement at long-term follow-up than did patients who were nonadherent with stimulants.\(^24\) An important challenge for future research involves determining the effects of extending stimulant therapy continuity on key clinical and functional outcomes in the community treatment of adult ADHD.

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### DISCLOSURES

This research was supported by Ortho-McNeil Janssen Scientific Affairs, LLC. Author Steven C. Marcus received the grant from Ortho-McNeil Janssen Scientific Affairs, LLC and author Mark Olson worked as a consultant on the grant that supported this research. Both of these authors report receiving grant support from and consultative work for several companies with products in the subject area of this research, including Eli Lilly & Company, Janssen Pharmaceuticals, Bristol-Myers Squibb, McNeil Pediatrics, and Pfizer. Authors Huabin F. Zhang and George J. Wan are employees of Johnson & Johnson. Author Olsson served as principal author of the study Study concept and design were contributed primarily by Olsson with input from authors Marcus, Zhang, and Wan. Data interpretation was primarily the work of Marcus, with input from Olsson, Wan, and Zhang. Writing of the manuscript and its revision was the work of all authors.

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Evaluation of the Relationship Between a Chronic Disease Care Management Program and California Pay-for-Performance Diabetes Care Cholesterol Measures in One Medical Group

Timothy W. Cutler, PharmD; James Palmieri, PharmD; Maninder Khalsa, MD, MBA; and Marilyn Stebbins, PharmD

ABSTRACT

BACKGROUND: Pay for performance (P4P) is a business model in which health plans pay provider organizations (medical groups) financial incentives based on attainment of clinical quality, patient experience, and use of information technology. The California P4P program is the largest P4P program in the United States and represents a potential revenue source for all participating medical groups. The clinical specifications for the California P4P program are based on the National Committee for Quality Assurance (NCQA), Health Plan Employer Data, and Information Set (HEDIS), and each clinical measure has its own benchmark. In 2005, participating medical groups were paid on the basis of 9 clinical measures that were evaluated in the 2004 measurement year. The cholesterol testing measure represented 4.4%–7.14% of the total P4P dollars available to participating medical groups from the health plans.

OBJECTIVES: To (1) compare the percentage of medical group members aged 18 to 75 years with diabetes (type 1 or type 2) who received a low-density lipoprotein cholesterol (LDL-C) test and attained LDL-C control (<130 mg per dl) after enrolling in a chronic disease care management (CDCM) program with similar members managed by routine care, and to (2) assess the potential effect of CDCM on the quality performance ranking and financial reimbursement of a medical group reporting these measures in the 2004 California P4P measurement year.

METHODS: This is a retrospective database review of electronic laboratory (lab) values, medical and hospital claims, and encounter data collected between January 1, 2003 and December 31, 2004 at 1 California medical group comprising 160 multispecialty providers. Requirements were continuous patient enrollment in 1 of the 7 health plans participating in P4P during the measurement year (2004) with no more than 1 gap in enrollment of up to 45 days. Patients aged 18 to 75 years were included in the diabetes cholesterol measure (denominator) if they had at least 2 outpatient encounters coded for a primary, secondary, or tertiary diagnosis of diabetes (International Classification of Diseases, Ninth Revision, Clinical Modification code 250.xx, 357.2, 362.0, 366.41, 648.0) or 1 acute inpatient (Diagnosis Related Group code 294 or 295) or emergency room visit for diabetes. Lab values were obtained from multiple sources, including archived lab databases during the same measurement period (numerator). The CDCM program provided education and recommendations for diet, lifestyle, and medication modification delivered by a multidisciplinary team of nurses, pharmacists, and dieticians, and this intervention was compared with routine care for patients not enrolled in the CDCM program.

RESULTS: Of the 54,000 health plan members enrolled in this medical group under capitated reimbursement, 1,859 patients (3.4%) met the California P4P specifications for eligibility for the diabetes cholesterol measures and were evaluated. Of these, 8.9% (165/1,859) were followed by the CDCM program and 91.1% (1,694/1,859) by routine care. The LDL-C lab testing rate for patients in the CDCM program was 91.5% (151/165), and the LDL-C goal attainment rate was 78.2% (129/165) compared with 67.8% (1,148/1,694) and 55.7%, respectively, for routine care ($p < 0.001 for both comparisons). If the LDL-C lab testing and goal attainment rates for the CDCM group were compared with rates for peer medical groups, this medical group would have scored in the 75th and 90th percentiles, respectively, corresponding to an annual revenue potential of $28,512 for this medical group if the total incentive payment from the health plan was $1 per member per month (PMPM), or $57,024 if the total incentive P4P payment was $2 PMPM.

CONCLUSIONS: Preliminary data from 165 patients with diabetes managed in a CDCM program in a medical group operating under a small P4P financial incentive showed higher rates of LDL-C lab testing and goal attainment than from patients managed by routine care. Had these rates of LDL-C testing and goal attainment achieved in the CDCM program been extended to the entire P4P population with diabetes, this medical group would have generated incentive payments under the P4P program and ranked higher in publicly available quality scores.

KEYWORDS: Pay for Performance, Lipid management, Diabetes, Chronic Disease Care Management

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What is already known about this subject

- Pay for Performance (P4P) programs alone have not been shown to improve quality of care.
- Chronic disease care management (CDCM) programs have reportedly attained high rates of low-density lipoprotein cholesterol (LDL-C) testing (96.7%–97.3%) and goal LDL-C <100 mg per dl. (36.5%–83%) for patients with diabetes, but the study methods have lacked patient randomization.

What this study adds

- This is the first study to show the potential impact that CDCM may have on the P4P rankings and financial payouts for a medical group.

Pay for performance (P4P) is a business model by which health plans pay provider organizations (medical groups) for consistently demonstrating high levels of quality performance based on established criteria. The results of the P4P clinical measures are publicly available and are often discussed during contract negotiations between medical groups and health plans. California has the largest and most comprehensive P4P program; however, P4P programs exist nationwide. In fact, a recent survey demonstrated that most health plans that offer commercial health maintenance organization (HMO) products
in metropolitan areas use P4P in their medical group contracts.\(^5\)

The Integrated Healthcare Association (IHA) is the statewide leadership group that developed and coordinates the California P4P process. According to IHA, the purpose of the California P4P initiative is to create a business model that financially rewards quality performance through a standardized measurement set.\(^6\)

Clinical measures, patient satisfaction, and the ability of the medical group to integrate information technology into patient care are the criteria for payment in the California P4P model.\(^7\) Currently, Aetna, Blue Cross of California, Blue Shield of California, CIGNA, Health Net, PacifiCare, and Western Health Advantage participate in the California P4P initiative.\(^1,4,7\)

In 2004, the California P4P program payments were weighted 40\% for up to 9 clinical measures; 40\% for patient satisfaction, as determined by the consumer assessment survey comprising 16 primary questions; and 20\% for information technology, assessed by the ability of each medical group to integrate electronic clinical datasets for both population management and clinical decision making at the point of care.\(^8,7\)

The health plan provides payment on the basis of a dollar amount per member per month (PMPM) that is calculated in addition to the contracted PMPM amount for the delivery of care to members in the medical group.\(^7\) The medical group may receive incentive incremental P4P financial payment for scoring in any of the 3 category measures (clinical, patient experience, or information technology) and any number of the individual measures (i.e., as few as 1 of the possible clinical measures) as long as the medical group scores in the appropriate percentile ranking as determined by the health plan.\(^7\)

The data for the 2004 measurement year were not reported until May 27 of the 2005 reporting year.\(^4\) IHA then compiled the 2004 report data and submitted final information to the health plans by July 2005. Health plans had until the end of 2005 to pay the participating medical groups on the basis of their performance in 2004. This timeline contributed to significant delays in the availability of final P4P reporting numbers and final payment to the medical group.

The amount paid to the medical group varies by each health plan that participates in the California P4P program. The payment amount is determined from the medical group’s score in the 20th to 50th percentile (depending on the health plan) or higher when compared with a statewide benchmark of California medical groups.\(^8\) In the first 5 years of the P4P program, more than $145 million in incentive payments was distributed to 210 medical groups, representing 35,000 providers and more than 7 million commercial HMO members in California, or an amount that averaged less than $1 PMPM.\(^1,6,8\)

Few published studies have evaluated the effect of P4P incentive payments on improvements in clinical quality.\(^9,10\) Medical groups participating in the California P4P initiative may increase revenue if consistent quality performance can be demonstrated for any of the 9 clinical measures and/or the nonclinical measures. The clinical specifications for the California P4P program are based on the National Committee for Quality Assurance (NCQA) Health Plan Employer Data and Information Set (HEDIS), and each clinical measure has its own benchmark (see Table 1).\(^1,4\)

Of the 11 possible clinical measures in the 2004 California P4P initiative, 4 were based on comprehensive diabetes care, making diabetes care the most heavily weighted of the clinical measures.\(^4\) Although 11 clinical measures are listed in IHA specifications for the 2004 measurement year, the cholesterol measures for cardiovascular disease and for diabetes low-density lipoprotein cholesterol (LDL-C) measures are combined for reporting and payment purposes (see Table 1; measures 1 and 3 are combined for payment purposes).\(^4\)

The reason for the combined reporting of the diabetes cholesterol measure with the cardiovascular cholesterol measure is the extremely low reported numbers for the cardiovascular cholesterol clinical specifications.\(^4\)

All 11 clinical measures are included in the reporting of clinical quality to IHA, but plans may pay the medical group on only some or none of the clinical measures. For example, Health Net paid participating medical groups on 9 of the 11 possible clinical measures, while the remaining 6 health plans that participate in the California P4P initiative provided payment to medical groups on 7 of the 11 possible clinical measures.\(^7\)

The diabetes care measures not only evaluate the medical group’s ability to obtain laboratory values for glycosylated hemoglobin (A1C) and LDL-C for target patients, but also the medical group’s ability to attain goal A1C and LDL-C levels for its health plan members, as established by the California P4P initiative and HEDIS criteria.\(^4\) Under the comprehensive diabetes care clinical measures for the 2004 measurement year, goal levels for A1C were defined as <9\% and for LDL-C as <130 mg per dL.\(^4\) Current practice guidelines from the American Diabetes Association and the National Cholesterol Education Program Adult Treatment Panel III (NCEPATPI II) established goal A1C levels of <7\% and LDL-C levels of <100 mg per dL for the treatment of diabetes and dyslipidemia, respectively.\(^11,12\)

All 7 health plans provided payout to medical groups for the diabetes testing measures in 2005 (2004 measurement year).

Mercy Medical Group (MMG) is a 160-provider, multispecialty medical group with clinics throughout the greater Sacramento area. MMG is affiliated with Catholic Healthcare West (CHW) Medical Foundation and the CHW Mercy Hospitals in the Sacramento region. The 7 HMOs that contract with MMG on the basis of capitation reimbursement represent approximately 54,000 of the total (52\%) of about 104,000 health plan members; the remaining 50,000 health plan members (48\%) receive care under fee-for-service contracts. All 7 HMOs that contract with MMG participate in the California P4P initiative. MMG has participated in the California P4P initiative since 2003 and began self-reporting P4P clinical measures in the 2004 measurement year (2005 reporting year).\(^4\)

MMG has been using the Mercy Heart Institute’s chronic disease
## Evaluation of the Relationship Between a Chronic Disease Care Management Program and California Pay-for-Performance Diabetes Care Cholesterol Measures in One Medical Group

<table>
<thead>
<tr>
<th>Clinical Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Diabetes care LDL-C measurement and goal attainment‡</td>
<td></td>
</tr>
<tr>
<td>(counts as 2 independent measures)</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of enrolled members aged 18-75 years with diabetes (type 1 and type 2) who had:</td>
</tr>
<tr>
<td>• LDL-C testing during the measurement year or the year prior to the measurement year.</td>
<td></td>
</tr>
<tr>
<td>• LDL-C control &lt;130 mg per dL during the measurement year or the year prior to the measurement year.</td>
<td></td>
</tr>
<tr>
<td>2. Diabetes care A1C measurement and poor control</td>
<td></td>
</tr>
<tr>
<td>(counts as 2 independent measures)</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of members aged 18-75 years with diabetes (type 1 and type 2) who had:</td>
</tr>
<tr>
<td>• 1 or more hemoglobin A1C tests conducted during the measurement year.</td>
<td></td>
</tr>
<tr>
<td>• hemoglobin A1C poor control &gt;9%.</td>
<td></td>
</tr>
<tr>
<td>3. Cholesterol management LDL-C testing and goal attainment‡</td>
<td></td>
</tr>
<tr>
<td>(counts as 2 independent measures)</td>
<td></td>
</tr>
<tr>
<td>[0%]</td>
<td>The percentage of members aged 18-75 years as of December 31 of the measurement year who were discharged alive in the year prior to the measurement year for acute myocardial infarction, coronary artery bypass graft, or percutaneous transluminal coronary angioplasty and who had each of the following between 60 and 365 days after discharge:</td>
</tr>
<tr>
<td>• LDL-C test</td>
<td></td>
</tr>
<tr>
<td>• LDL-C &lt;130 mg per dL</td>
<td></td>
</tr>
<tr>
<td>4. Childhood immunization status</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14% for MMR and VZV rates only]</td>
<td>The percentage of enrolled children who turned 2 years old during the measurement year who were identified as having completed 1 or more of the following antigen series by the time period specified and by their second birthday:</td>
</tr>
<tr>
<td>• 4 DTaP/DT</td>
<td></td>
</tr>
<tr>
<td>• 3 IPV/OPV</td>
<td></td>
</tr>
<tr>
<td>• 1 MMR</td>
<td></td>
</tr>
<tr>
<td>• 3 H influenza type B</td>
<td></td>
</tr>
<tr>
<td>• 3 hepatitis B</td>
<td></td>
</tr>
<tr>
<td>• 1 chicken pox vaccine</td>
<td></td>
</tr>
<tr>
<td>Each antigen or antigen series is calculated and reported separately.</td>
<td></td>
</tr>
<tr>
<td>5. Breast cancer testing</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of women aged 50-69 years who had a mammogram during the measurement year or year prior to the measurement year.</td>
</tr>
<tr>
<td>6. Cervical cancer testing</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of women aged 18-64 years who received one or more Pap tests during the measurement year or the 2 years prior to the measurement year.</td>
</tr>
<tr>
<td>7. Chlamydia testing for women</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of women aged 16-25 years who were identified as sexually active and who had at least 1 test for chlamydia during the measurement year.</td>
</tr>
<tr>
<td>8. Use of appropriate medication for people with asthma</td>
<td></td>
</tr>
<tr>
<td>[4.44%-7.14%]</td>
<td>The percentage of enrolled members aged 5-56 years during the measurement year who were identified as having persistent asthma during the year prior to the measurement year and who were appropriately prescribed medication during the measurement year.</td>
</tr>
</tbody>
</table>

Adapted from the Integrated Health Care Association P4P 2004 Measurement Year/2005 Reporting and Payment Year Clinical Specifications.57

* All of the descriptions and data presented here are labeled 2005 clinical measure specifications that pertain to the 2004 measurement year from January 1, 2004, through December 31, 2004. These clinical measures account for 40% of total incentive payments to medical groups for health plans.

† The range of payment varies by health plan. The majority of plans paid 5.71% x 7 clinical measures (40%). The minimum payment of 4.44% x 9 clinical measures (40%) is based on 1 health plan, and the maximum of 7.14% x 7 clinical measures (50%) is also based on only 1 health plan.

‡ Cholesterol management refers specifically to CHD (secondary risk) patients. Although all 11 clinical measures are reported to IHA, P4P payouts are calculated on 9 clinical measures; the cholesterol and diabetes LDL-C testing and goal (<130 mg per dL) rates are combined, yielding up to 9 performance measures for P4P payment purposes.

§ Only the most recent lab test may be used, whether it is obtained in the measurement year (2004) or in the year prior to the measurement year (2003).

4 Hyperlipidemia risk-reduction program designed to educate and treat patients who are diagnosed with or who are at risk for developing cardiovascular disease. This program was developed collaboratively with MMG. The
first patients were enrolled in 1999, and approximately 1,000 patients are currently enrolled in the program. Physicians from the medical group make up the largest source of patient referrals and enrollment for the CDCM program. Initially, patients referred to the program are offered a 1-time patient education class, during which they receive information on cardiovascular disease, such as pathophysiology, risk factors, and ways to minimize risk, including dietary modifications and exercise recommendations. Follow-up includes ordering laboratory visits and prescribing lipid-lowering therapy as dictated by CDCM treatment protocol approved jointly by the medical group and the health plan.

The treatment protocol has 3 treatment tracks to which the patients are assigned. Approximately 35% of the patients are identified as cases for primary prevention (i.e., no history of coronary artery disease [CAD] or diabetes or stroke), 25% as cases for secondary prevention (i.e., history of CAD, myocardial infarction, stroke, etc.), and 40% as diabetes risk-equivalent prevention. This treatment protocol was developed using the NCEP ATP III as its framework. A multidisciplinary approach was chosen to ensure the best possible care for the patient. Physicians, dietitians, nurses, pharmacists, exercise physiologists, and social workers were all involved in the development of the treatment protocol. The protocol methodology was reviewed and approved by various hospital and physician committees. Additionally, the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) reviewed the program and as of the fall of 2005, the program has been recognized by JCAHO as a hyperlipidemia-certified program.

The treatment protocol includes both pharmacologic (medication algorithm) and nonpharmacologic (therapeutic lifestyle management education) methods for reducing risk. Nurse and pharmacist care managers are used to care for patients using the protocol and are allowed, under the physician’s signed order, to prescribe medications and order laboratory assessments as described in the protocol. Quality assessment takes place at regular intervals to assure the success of the program in achieving LDL-C targets while avoiding medication misadventure.

Enrollment and participation in the CDCM program in this medical group is voluntary. However, the referring physician in the medical group must provide a signed order that allows the CDCM program to care for the patient under the standardized treatment protocol. A diagnosis of dyslipidemia and a physician referral are the only criteria for enrollment in the CDCM lipid management program. There is no patient recruitment or other selection criteria. Once enrolled, patients are assessed, and an individualized care plan is established.

The purpose of this study was to (1) compare the percentage of medical group members aged 18 to 75 years with diabetes (type 1 or type 2) who received an LDL-C test and attained LDL-C control (<130 mg per dL) after enrolling in the CDCM program with similar members managed by routine care, and (2) assess the potential effect of CDCM on the quality performance ranking and financial reimbursement of a medical group reporting the diabetes cholesterol management measure of the 2004 California P4P initiative.

### Methods

This study was approved by the Committee on Human Research at the University of California, San Francisco, and the Institutional Review Board at Catholic Healthcare West. MMG is a 160-physician, multispecialty medical group in the greater Sacramento area that participates in the California P4P program. MMG uses a team-based CDCM program to help manage cholesterol for patients in the medical group.

A medical group can use 2 methods to report P4P clinical data—passive and active reporting. Passive reporting involves using the claims and encounter data already submitted to the health plan to calculate and report the clinical measures. With this health plan reporting method, the medical group is completely reliant on the plan to report data to IHA on the medical group’s behalf. In active reporting, the medical group uses internal records, including its claims, encounter, and electronic laboratory and pharmacy claims data to self-report the clinical measures to IHA.

MMG uses active (self-) reporting of P4P clinical measures. In order for a medical group to self-report clinical measures for the California P4P program, the medical group must undergo a rigorous audit process. An outside auditor approved by NCQA and IHA validates the self-reporting process used by the medical group. This audit process verifies that the medical group is accurately capturing data for the purposes of reporting P4P clinical measures by evaluating membership data, claims processing systems, data analysis, decision support processes, and the data linkage between electronic databases. This audit is performed every year.

Data collection and compilation for the California P4P clinical measures at this medical group are all electronic, using a combination of claims, encounter, and actual laboratory data. In 2004, MMG medical records were stored in paper charts, but encounter forms, claims, and some laboratory values were processed and stored electronically. The medical group used these electronic systems for P4P self-reporting. MMG started using an electronic medical record in 2006, but the P4P self-reporting process has not changed as a result. Laboratory data for LDL-C and A1C are stored electronically on a laboratory server and sent to the medical group on a monthly basis from the lab database vendor. Laboratory values may be obtained by the provider for individual patients in real time, but the group is dependent on the monthly laboratory reports for the purpose of P4P data aggregation.

New P4P measures for 2005 prompted targeted educational interventions and financial incentives by MMG to improve the medical group’s performance for these measures.1 Because of the substantive changes in physician education and medical
group interventions that took place in 2005 and 2006, it was determined that 2004 data were associated with fewer confounding variables and were perhaps the most valid for evaluating the efficacy of the CDCM program in achieving P4P target goals compared with usual care provided during in-office physician visits.

**Pay for Performance Clinical Measure: Diabetes Care—LDL-C Testing and Control**

The purpose of the diabetes care clinical (2-part) measure is to determine the percentage of medical group members aged 18 to 75 years with diabetes (type 1 or 2) who received an LDL-C test and had an LDL-C <130 mg per dL.

**Inclusion Criteria**

Patients included in this measure were commercial HMO members continuously enrolled in MMG and a P4P participating health plan during the measurement year (2004), with no more than 1 gap in enrollment of up to 45 days during that time. Patients with diabetes who were aged 18 to 75 years as of December 31, 2004 were included in the study. The eligible population for the diabetes care clinical measure was identified using pharmacy data and/or hospital/medical claims and encounter data. Complete pharmacy data were not available for MMG during the 2004 measurement year, and thus only the claims/encounter method was used to identify the eligible diabetes population. On the basis of the claims/encounter data, patients were identified as having diabetes if they had 2 face-to-face outpatient encounters for diabetes with different dates of service in an ambulatory setting or 1 face-to-face acute (inpatient or emergency department) visit for diabetes during 2003 or 2004. International Classification of Diseases, Ninth Revision, Clinical Modification codes, Diagnosis Related Group codes, and Current Procedural Terminology codes were used to identify diabetes as the primary, secondary, or tertiary reason for the visit and are listed in Table 2. These criteria determined the denominator for this measure. See Figure for a flow diagram describing patient selection.

The serum LDL-C value for the most recent cholesterol test and the number of patients with a LDL-C laboratory value in 2003 or 2004 were used for the numerator for this clinical measure. The medical group could use claims/encounter data to determine if the LDL-C was performed, or electronic laboratory data if at least the date and result of the LDL-C were included in the electronic information. Because the actual laboratory value is required to report “good” control, this medical group used the electronic laboratory data to determine the LDL-C level for patients in the eligible population. According to the 2005 Clinical Measure Specifications in the P4P program, patients who had no LDL-C performed in 2003 or 2004 were assumed to be in poor control. A triglyceride level >400 mg per dL would lead to inaccurate LDL-C calculations and, therefore, patients with a triglyceride level >400 mg per dL were considered to be in poor control but would meet the criteria for inclusion in the numerator for the proportion of patients who received LDL-C testing.

**Exclusion Criteria**

Medicare Advantage members were not included in any of the clinical measures for the 2004 measurement year and were not included in the P4P population for the diabetes care measures. Patients not assigned to a primary care physician, and patients enrolled in a health plan that did not participate in P4P, were also excluded from the study population.

The same denominator value was used for the LDL-C testing and control measures (the eligible population of patients with diabetes), but the numerator was reported separately for each measure. A patient may appear in the numerator for both LDL-C testing and LDL-C good control.

Health plans that participate in the California P4P program make incentive payment to the participating medical group based on that medical group’s quality performance measures compared with peer medical groups within the state. Each clinical measure

**TABLE 2** ICD-9-CM and DRG Codes to Identify Patients With Diabetes Using Claims/Encounter Data

<table>
<thead>
<tr>
<th>Description</th>
<th>ICD-9-CM Codes</th>
<th>DRGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes diagnosis</td>
<td>250, 357.2, 362.0, 366.41, 649.0</td>
<td>294, 295</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Description</th>
<th>CPT Codes</th>
<th>UB-92 Revenue Codes</th>
</tr>
</thead>
</table>

Used with permission from IHA: www.iha.org/p4pyr2/cspecy2.pdf.

receives a percentile ranking. The LDL-C testing and control measures for cardiovascular care and diabetes are evaluated separately by IHA. Because of the potentially small number of patients in the cardiovascular group, the cardiovascular and diabetes numbers are added together for the cholesterol measures for the purposes of payment to the medical group. The cardiovascular cholesterol numbers for this medical group were a small fraction (<2%) of total patients in the LDL-C P4P measure, and they were excluded from the final P4P numbers for the purposes of this paper. The total reported rates (%) for LDL-C testing and control did not change as a result of excluding the cardiovascular patients from the LDL-C P4P measure (Table 3).

### Diabetes Care—LDL-C Testing and Control 2005 Incentive Payment Amounts

Payment is generally based on the medical group’s ability to score in the 50th percentile or higher when compared with other (peer) medical groups. Generally, if the medical group scores between the 50th and 74th percentile, it is paid one half of the total possible incentive payment, and groups in the 75th to 99th percentile receive the full incentive payment amount. As previously mentioned, each of the 7 health plans determines the percentile ranking for incentive payment. No health plan provides payment for percentile rankings below the 20th percentile. Payment is commonly provided on a PMPM basis and is determined by each health plan.
Health plan payout for the testing and goal attainment for the LDL-C measures varied for the 2005 report year (2004 measurement year). All participating plans paid medical groups for LDL-C laboratory testing (from a low of 4.4% to a high of 7.14% of total available P4P dollars), but only 1 plan paid medical groups for the proportion of patients with LDL-C <130 mg per dL. Both LDL-C testing and goal attainment rates were reported to IHA in 2005. On the basis of the 2005 payment amounts, all potential P4P payouts for the LDL-C testing measure in the data analysis were based on the lowest plan payout of 4.44% of the total available P4P dollars. This method reduced the potential for overestimation of missed revenue opportunity for calculations involving the LDL-C testing measure. Because only 1 health plan out of 7 paid on the LDL-C goal rate <130 mg per dL, this measure was assumed to have insignificant reimbursement to the medical group and therefore was not considered in the potential payment calculations.

Data Analysis
Data were collected retrospectively from claims and encounter forms to determine the eligible population, as defined by the diabetes care cholesterol measures.*+ Laboratory data were obtained from the Mercy Laboratories electronic database. The entire eligible population (denominator) was identified, and then patients followed by the CDCM program were extracted from the whole P4P denominator and evaluated separately, using the available laboratory data. It was assumed that if a patient was not enrolled in the CDCM program, the patient received routine care. Patients enrolled in the CDCM program received care from their primary care providers as well as from CDCM team members. Queries using the Microsoft Access database were used to identify patients who had an LDL-C test performed and to determine the LDL-C value. This process was verified for accuracy by the NCQA- and IHA-approved P4P self-report auditor.

Statistical analysis was performed with Minitab release 14 statistical software. A chi-squared statistical test was used for all discrete data and 2-sample t test was used for continuous data to determine statistical differences between the CDCM program and the routine care group (P value was set to be <0.05 for statistical significance).

Results
Demographics
A total of 1,859 patients were evaluated in this study. The CDCM program enrolled 165 patients (8.9%), of whom 59.4% (98/165) were female. The average age for these patients was 57.8 years (Table 4). Of the total population for this measure, 91.1% (1,694/1,859) of the patients were managed by routine care, 49.5% of which (839/1,694) were female. The average age for the routine care group was 55.6 years (see Table 4).

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Patient Characteristics and Outcome Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>Total N= (1,859)</td>
</tr>
<tr>
<td>Female gender (n)</td>
<td>50.4% (937)</td>
</tr>
<tr>
<td>Average age [SD]</td>
<td>55.8 [10.54]</td>
</tr>
<tr>
<td>Patients with LDL-C value (n)</td>
<td>69.9% (1,299)</td>
</tr>
<tr>
<td>Patients at goal (&lt;130 mg per dL) LDL-C (n)</td>
<td>57.7% (1,072)</td>
</tr>
<tr>
<td>Patients with LDL-C &lt;100 mg per dL† (n)</td>
<td>36.3% (674)</td>
</tr>
</tbody>
</table>

* P values derived from chi-square test. † P value derived from 2-sample t test. ‡ LDL-C <100 mg per dL was not a clinical measure in this P4P program and is presented here for comparison with national guidelines. CDHM=chronic disease care management; LDL-C=low-density lipoprotein cholesterol; P4P=pay for performance; PCP=primary care physician.

LDL-C Testing Rates
The LDL-C testing rate for all P4P eligible patients (both CDCM program and routine care) in this medical group in 2004 was 69.9%. The LDL-C testing rate for patients in the CDCM program was 91.5% versus 67.8% for the routine care group (P <0.001, Table 4). When compared with peer groups, the patients in this medical group overall scored less than the 20th percentile for the lab testing rate (70% raw score), representing no revenue for this portion of the LDL-C testing measure. However, if the CDCM program patients’ LDL-C testing rate (92%) had been compared with peer groups, MMG would have scored higher than the 75th percentile. This score would have resulted in full payment from the health plans for this measure (see Table 5).

LDL-C Goal Attainment Rates
The LDL-C goal attainment rate (LDL-C <130 mg per dL) for all medical group patients (both CDCM and routine care patients) in 2004 was 57.7% (1,072/1,859). The LDL-C goal attainment rate for the CDCM program was 78.2%, significantly higher than the 55.7% rate for the routine care group (P <0.001; see Table 4). When compared with peer medical groups, MMG scored in the 75th percentile for the goal attainment rate, representing full revenue for this portion of the diabetes care LDL-C clinical measure from the 1 health plan that provided payout for the LDL-C goal attainment rate. However, if the CDCM goal...


<table>
<thead>
<tr>
<th>Performance Measure</th>
<th>Routine Care</th>
<th>CDCM</th>
<th>Medical Group Overall</th>
<th>Threshold for Maximum Payout</th>
<th>Payout Opportunity†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of LDL-C testing</td>
<td>&lt;20th</td>
<td>&gt;75th</td>
<td>&lt;20th</td>
<td>75th</td>
<td>$28,512-$56,024</td>
</tr>
<tr>
<td>Goal attainment at LDL-C &lt;130 mg per dL</td>
<td>75th</td>
<td>&gt;90th</td>
<td>75th</td>
<td>75th</td>
<td>–</td>
</tr>
</tbody>
</table>

* Percentile rankings are provided to the medical group as a range, not as discrete values on a continuous scale. Generally, if the medical group scores less than the 50th percentile, then it is not eligible for P4P incentive payment; the 50th-74th percentile range pays half of the P4P financial incentive, and medical groups that score higher than the 75th percentile are eligible for the full P4P incentive.
† Payment amount is based on 4.44% of total clinical dollars ($0.044 for $1 PMPM or $0.088 for $2 PMPM) X 54,000 members x 12 months = $28,512 for $1 PMPM to $56,024 for $2 PMPM. All 7 health plans provided incentive payments for the LDL-C testing rate, and only 1 health plan provided payment incentive for the LDL-C goal attainment <130 mg per dL; therefore, the LDL-C goal payment was considered negligible for the 2005 report year and was not included in this financial analysis.
CDCM = chronic disease care management; LDL-C = low-density lipoprotein cholesterol; P4P = pay for performance; PMPM = per member per month.

attainment rate had been compared with peer groups, MMG would have scored in the 90th percentile, which would have improved publicly reported scores for the medical group but would not have resulted in higher revenue for the medical group (see Table 5).

Although no financial award or public reporting exists in the P4P measures for medical groups that have LDL-C goal attainment at the higher standard of <100 mg per dL for patients with cardiovascular disease or cardiovascular disease risk-equivalent (diabetes), this rate was evaluated in the present analysis, since 100 mg per dL is the standard described in national guidelines. The medical groups’ overall rate for LDL-C <100 mg per dL was 36.3%. The CDCM program had an LDL-C <100 mg per dL rate of 46.7%, which was a statistically significant higher achievement than 35.2% in the routine care group (P = 0.004, Table 4).

**Potential Financial Payouts**

Because of confidentiality issues, the actual payment amount to the medical group cannot be disclosed. The contracted rates for P4P payment from each health plan are negotiated directly between the medical group and health plan and vary among the health plans. As previously discussed, all health plans pay the medical group a dollar amount PMPM based on their percentile rankings for each measure, with 100% payment for placement in the 75th percentile or higher among all medical groups, 50% payment for placement between the 50th and 74th percentiles, and minimal or no payment if lower than the 50th percentile (only Blue Cross of California provided payments on a sliding scale to medical groups that scored between the 20th and 49th percentiles).

All health plans made incentive payment to medical groups for LDL-C lab testing for the 2005 P4P reporting year, with a minimum of 4.44% of the total available PMPM dollar amount. Therefore, if $1 PMPM were provided to the medical group for all clinical measures, the payment amount for a medical group scoring in the 75th percentile or higher for the LDL-C testing rate would be $0.044 PMPM. However, if the medical group scored between the 50th and 74th percentiles for the LDL-C testing rate, the total payment would only be 2.22%, or $0.022 PMPM. If the medical group scored lower than the 20th percentile, then it would receive no payment for that clinical measure. If the contracted rate were $2 PMPM, then the diabetes LDL-C testing measure would represent a maximum payment of $0.088 PMPM.

The PMPM payout to the medical group is based on the number of commercial members that are enrolled in P4P participating health plans. This medical group had approximately 54,000 commercial members in 2004 that were members of P4P participating health plans, and therefore the payout for this LDL-C testing measure would be $0.044 PMPM x 54,000 members x 12 months, or $28,512 for a $1 PMPM payment incentive, and $0.088 PMPM x 54,000 members x 12 months, or $57,024 for a $2 PMPM payment incentive.

This medical group scored lower than the 20th percentile for the LDL-C testing rate in 2005 for the 2004 measurement period, and, therefore, no P4P revenue was earned for this part of the measure. If all 1,859 patients with diabetes in this medical group had been enrolled in the CDCM program in 2004, the LDL-C testing rate for this medical group could have scored in the 75th percentile. This rate represents a difference of 4.44% of the total contracted rate, or $28,512 for a $1 PMPM payment incentive or $57,024 for a $2 PMPM payment incentive (see Table 5).

**Discussion**

In this medical group, patients with diabetes who were followed by the CDCM program had significantly higher rates for both LDL-C testing and goal attainment than did those in routine care. Results of other studies on the effectiveness of team-based lipid management have also shown high LDL-C lab testing rates (96.7%-97.3%) and LDL-C <100 mg per dL goal attainment (56.5%-83.3%) in lipid management. Limitations of those studies include no patient randomization, no comparator-control group, and no evaluation of end point outcomes such as morbidity or mortality. This is the first study to pair the clinical results of team-based CDCM with emerging P4P initiatives showing both improved quality reporting and potential increased revenue.

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* Table 5: 2005 P4P Performance Measures, Percentile Rankings,* and Payout Opportunities
for the medical group.

Financially, had this medical group scored in the 75th percentile for both the LDL-C lab testing and goal attainment portions of the diabetes LDL-C measure, revenue would have increased from $0 payout to a hypothetical $28,512 for a $1 PMPM payment incentive. The results of the present study suggest that referring more patients to the CDCM program may be a viable way to improve the overall performance scores for the medical group.

Revenue sharing is one way to provide a financial incentive to increase medical group intervention in targeted DM programs. Currently, this hospital-based CDCM program does not generate revenue for the services it provides, but instead this not-for-profit hospital declares the expenses as a community benefit and part of its charity care obligation. This schema is consistent with the organization’s mission to provide direct services to the poor and to partner with others in the community to improve the quality of life in the community it serves.

Because the CDCM program receives referrals from outside MMG, a shared revenue model is not viable at this time since the program would then need to bill all referring providers in order to be compliant with the Omnibus Reconciliation Act of 1993. This law precludes preferential pricing for services to certain groups of physicians to avoid the potential for garnering referrals. As contracts with other medical groups are reviewed (or renegotiated) by the CDCM program, it might be worthwhile to develop a return-on-investment model to explore whether P4P revenue sharing would be beneficial to the program. Likewise, other medical groups wishing to contract for DM services may explore shared revenue as an incentive in contracting with a program that is structured to bill for services.

In 2006, all but 1 health plan provided payment for both LDL-C testing and LDL-C goal attainment <130 mg per dL for the 2005 measure year, making it even more important for medical groups to improve this clinical measure.16 Therefore, programs like the CDCM program that increase LDL-C testing and goal attainment <130 mg per dL are important from both a quality and financial perspective to P4P participating medical groups.

As previously described, a long time separates the reporting of the data to the health plans and the date that the payouts are received by the medical groups.4 Medical groups do not know their percentile rankings and actual payment amount from the health plan for up to 12 months after the close of the measurement year. This makes financial projections for the P4P initiative difficult to predict. However, medical groups who self-report do know the patients who are eligible for P4P reporting throughout the measurement year, allowing the groups to target the noncompliant patients in time to make a positive difference in the reported rate (e.g., referring noncompliant diabetes patients who miss an LDL-C lab test or are not at LDL-C goal to a CDCM program).

Reporting P4P clinical measures is a complicated and time-consuming process. A team of experts comprising physicians, data analysts, pharmacists, and other key organizational personnel is critical to successful self-reporting. Although self-reporting for MMG made the reporting process much more labor intensive, self-reporting was associated with improved MMG clinical measures compared with the passive report method that was used in the prior year for 2003. The self-report process also allows regular audits of the data so discrepancies can be clarified and gaps in care can be targeted at the organizational level.

The CDCM program described herein was an existing program and therefore did not incur any up-front costs to the medical group. Other medical groups would need to allocate funds to initiate targeted patient care (DM) programs. Since this P4P program does not pay for improvement but only for percentile ranking, poor-performing groups cannot earn P4P revenue to fund quality-improvement activities. This results in a potential situation in which the good get better and the poor do not improve enough to earn revenue. This situation has been previously described in the literature by Rosenthal et al. for the cervical cancer, breast cancer, and diabetes A1C clinical measures.9

The P4P process is dynamic. In the 2005 and 2006 measurement years, MMG targeted multiple clinical measures for improvement, including breast cancer testing, cervical cancer testing, childhood immunizations, LDL-C testing rate and LDL-C goal attainment, A1C measurement, and A1C goal attainment. In targeting these measures, new strategies were employed to improve disease prevention and quality of care, including physician detailing (modeled after the CDCM program), patient letter campaigns (modeled after the CDCM program), use of patient advocates, increase in the number of patients enrolled in the CDCM program, and other chronic DM programs, such as the Diabetes Care program. Furthermore, physicians at MMG were given financial incentives for their ability to meet certain quality measurement markers, including LDL-C testing and goal attainment rates for the diabetes care measure. This targeted approach was associated with significant improvement for this medical group, which was recognized as a top 20% performing medical group in the subsequent (2005 measurement) year. We chose the 2004 measurement year for the present study in an effort to reduce the confounding effects of these other medical group interventions that did not exist in 2004.

P4P programs have gained international attention, and there is great interest in whether P4P measures improve the quality of health care provided to patients at the medical group level.2,5,10 Until further studies are published evaluating the effect of P4P, medical groups must develop creative ways to improve their quality measures in order to keep pace with peer organizations. Team-based CDCM programs may become sources of revenue as well as a means to avoid costs associated with lower-quality care.
Our results suggest but do not prove that a focused CDCM intervention is effective in generating incentive revenue in a P4P program. A large opportunity also remains to show that a focused CDCM intervention could generate sufficient incentive payment to cover its costs. The literature is speckled with mostly anecdotes of success, including the results of a P4P program established to improve diabetes care that reportedly had a return on investment of 1.6 to 1 in the first year and 2.5 to 1 in the second year of the sponsoring health plan. This descriptive report without a control group was conducted in the Rochester area of upstate New York during 2003 to 2004.

LDL-C <100 mg per dL for patients with diabetes was not a clinical measure in this P4P program in 2004 but is the widely accepted LDL-C goal rate, according to NCEP ATP III. The CDCM program showed a significantly higher rate of attainment of the LDL-C <100 mg per dL goal than did routine care. The Mercy Heart Institute’s CDCM program described in this paper was previously shown to improve LDL-C goal attainment for diabetes patients from 23.2% before the intervention to 36% after only 6 months in the program. This 56% rate of LDL-C goal attainment compares with 47% in the present study.

Limitations
First and foremost among the study limitations is the small sample size, with only 165 patients in the CDCM program. Second, an opportunity for selection bias exists since this was not a prospective study with random assignment. We also did not control for confounding factors such as comorbid conditions, type of lipid-lowering agents, patient financial status, motivation, or intervention from other specialists (e.g., endocrinologist or cardiologist). The intervention and comparison groups in the present study were statistically different for age and gender. However, while the CDCM group might be different from the comparison, the practical significance of any differences would pertain to the goal attainment rate and not the testing rate because the patients in both groups needed lipid testing.

Third, we did not measure the amount of time and resources required to operate the CDCM program and therefore could not perform a calculation of return on investment. We are therefore unable to determine if the estimated payout opportunity for this medical group under the P4P program could have covered the cost of the CDCM program. While the CDCM program described in this paper does not represent a cost to the medical group, there are real costs that include salary and benefits. Because the CDCM program is based in a not-for-profit hospital, however, the program has been justified, in part, by the community benefit required by California State Senate Bill 697 for it to maintain not-for-profit tax-exempt status. Fourth, the CDCM program is not a mandatory program in this medical group, and there may be patients who choose not to participate, which would thereby reduce the opportunity for the CDCM program to elevate the entire medical group into the rankings that would generate P4P incentive payments. Fifth, since not all medical groups have access to team-based CDCM, these CDCM program results may not be generalizable to other medical groups.

Conclusions
This CDCM intervention in a medical group participating in P4P had a higher rate of LDL-C testing (92%) compared with routine care (68%) and a higher proportion of patients who attained LDL-C goal (<130 mg per dL) than did those treated in routine care (78% versus 56%, respectively). If all patients with diabetes who were measured by this P4P program had been enrolled in the CDCM intervention, this medical group would have attained the highest payout amount for the LDL-C testing measure and would have improved scores in public reporting of both P4P measures for LDL-C testing and LDL-C goal attainment.

References
Evaluation of the Relationship Between a Chronic Disease Care Management Program and California Pay-for-Performance Diabetes Care Cholesterol Measures in One Medical Group


Perceptions of Saskatchewan Community Pharmacists Regarding a Prior-Authorization Program

Jason Perpelkin, MSc, and Roy Thomas Dobson, PhD

ABSTRACT

BACKGROUND: In 1999, Saskatchewan Health authorized pharmacists to initiate exception drug status (EDS) requests, also known as prior authorization (PA). Before 1999, only those licensed to prescribe medications were authorized to initiate EDS requests. A pharmacist who submits an EDS request must obtain a patient diagnosis from the physician or agent of the physician; a diagnosis presented by the patient is insufficient.

OBJECTIVE: To obtain pharmacists’ opinions about the benefits of the PA program of the Saskatchewan Drug Plan and to identify factors associated with pharmacist-initiated EDS requests.

METHODS: A census survey of community pharmacy managers was conducted via a self-administered postal questionnaire in the province of Saskatchewan, Canada, in the fall of 2004. The survey questionnaire was addressed to pharmacy managers, some of whom may have delegated the response to a staff pharmacist. Pharmacy managers or their delegates were asked to respond on behalf of all pharmacists in their pharmacies.

RESULTS: A response rate of 82.6% was achieved (275/333). A majority of respondents agreed that the province’s PA program (EDS) benefited patients (87.3%) and the Saskatchewan Drug Plan (82.5%), whereas only 33.4% of respondents agreed that the EDS program benefited pharmacists. Pharmacists’ ability to obtain the requisite information (87.6%) and to contact the prescribing physician (87.3%), as well as patient-centered concerns such as the patient’s ability to pay for the prescription (85.1%), were the most important factors. The time required by the pharmacist to initiate the request was not important relative to other factors. Community pharmacies reported receipt of an average of 36.4 prescriptions for restricted and nonformulary drugs per week, of which 22 were submitted for PA coverage, 17 by the pharmacy and 5 by the pharmacy at the request of the physician.

CONCLUSIONS: The results of this study indicate that community pharmacists in Saskatchewan acknowledge that the EDS process is beneficial for their patients. However, pharmacists are burdened by an administrative process in which necessary information, particularly the patient diagnosis, is not readily available.

KEYWORDS: Pharmacist, Policy, Prior authorization, Step therapy, Drug plan

What is already known about this subject

- Prior-approval or prior-authorization (PA) programs reduce direct drug cost by imposing criteria for coverage such as prior use of first-line therapy (i.e., step therapy) or a patient diagnosis with a higher probability of a favorable response to the drug.
- As prescription drug use increases, drug and managed care plan administrators are developing and implementing cost-containment mechanisms to encourage the use of lower-cost drugs while promoting cost-effective use of more expensive and generally newer drug therapies.

What this study adds

- This is the first study of the opinions of pharmacists with regard to the administrative procedures involved in a PA program.
- Pharmacy managers and pharmacists are not opposed to PA programs but are dissatisfied with the administrative burden of the requirement to obtain the patient diagnosis from the physician.

Medicare in Canada is a federal program that has evolved over nearly 40 years to provide Canadians access to medically necessary physician and hospital services, including drugs administered in hospitals. However, each provincial and territorial government independently developed and continues to develop programs to provide drug coverage for some or all of its residents in the community or in nonhospital facilities. The federal government has also developed and continues to develop drug programs for select groups, including veterans and First Nations and Inuit peoples. However, more than half of all prescriptions are paid through private insurance or directly by individuals or patients.1,2 In 2005, Canada had 7,778 community pharmacies comprising chain and banner pharmacies (58.6%), independent pharmacies (21.4%), and pharmacies in food and mass merchandisers (20.0%).3 In 2005 in Saskatchewan, public funds paid for 48% of the $554 per capita spent on prescription drugs, whereas Canada as a whole spent $640 per capita on prescription drugs, with 46% of the expenditure paid for with public funds.4 The average retail price for a prescription in 2005 was $45.66, which included dispensing and professional fees.5 As in other countries, the final cost to the patient varied considerably depending on the markup and dispensing fee charged.
Over the years, increasing reliance on drug therapy and a tendency to abandon older drug therapies for newer, more expensive agents have caused drug utilization rates and expenditures for prescription drugs to grow substantially. Drug plans have attempted to control these rising costs in a variety of ways, including limiting coverage to certain cohorts of the population (i.e., low-income families), increasing copayments, or introducing deductibles. The result has been an ongoing shifting of costs to patients and private insurers.

In 1973, the Saskatchewan provincial government implemented a comprehensive drug plan via Saskatchewan Health’s Drug Plan and Extended Benefits (Drug Plan) Branch. All costs, with the exception of a small copayment, were publicly funded. Today, Saskatchewan residents are still covered by the provincial drug plan, but most beneficiaries must meet an annual, income-based deductible (3.4% of household income) before receiving any financial support from the government. Since July 2007, seniors (all Saskatchewan residents aged 65 years and older) pay no more than Can $15 per prescription (1-month supply) for drugs listed on the province’s formulary.

Utilization trends in Saskatchewan provide an interesting picture of drug expenditures in the province. In 1995-1996, 633,333 active beneficiaries in Saskatchewan received 5,798,090 prescriptions for a total prescription cost of Can $1,571,194,207 (Can $248 per beneficiary), and the Drug Plan paid Can $594,923,033 (37.8%) of the total cost. Ten years later, in 2005-2006, the number of active beneficiaries had increased by only 0.8% to 638,637, while the number of prescriptions increased 62% to 9,364,871 and total prescription costs increased by 239% to Can $375,304,926 (Can $588 per beneficiary); the Saskatchewan Drug Plan paid Can $181,288,493 (48.3%) of the total prescription cost, an increase of 305%.

Therefore, while the number of active beneficiaries remained virtually unchanged, the number of prescriptions per active beneficiary, average cost per prescription, and per prescription proportion paid by the Saskatchewan Drug Plan increased dramatically. Managed care interventions that have been implemented, such as prior authorization (PA) in the late 1970s and therapeutic maximum allowable cost, which began with proton pump inhibitors in July 2004, are attempts by the Saskatchewan Drug Plan to control escalating costs and thereby ensure its long-term viability.

Even with restrictive policies and cost shifting, drug utilization rates continue to rise and, with them, the cost of providing drug coverage. Both public and private drug plans have expanded various management strategies such as PA in an attempt to stem rising drug expenditures while maintaining access to effective drug therapies. PA limits the use of selected drugs by requiring advance approval for reimbursement of certain drugs when less costly alternatives are available. However, some aspects of these strategies can become sources of contention between payers, patients, and health care providers because they may be perceived as limiting access to needed drugs by requiring administrative approval for coverage. Additional administrative tasks are associated with these programs that health care professionals are expected to assume.

In Saskatchewan, PA is known as the Exception Drug Status (EDS) program. For the patient to receive provincial government coverage for restricted formulary drugs, EDS approval must first be obtained—a process that must be initiated by an authorized health care professional (physician, dentist, optometrist, nurse practitioner, or pharmacist). Some private drug plans have the same or similar requirements for drugs in the Saskatchewan EDS program. A few examples of EDS program drugs and coverage criteria include azithromycin permitted for patients intolerant to erythromycin and/or other antibiotics, insulin lispro permitted for treatment of patients using insulin pumps or difficult-to-control diabetes, and pioglitazone hydrochloride (HCl) or rosiglitazone maleate permitted for treatment of patients who previously received prescriptions for metformin or sulfonylureas and are not adequately controlled on or are intolerant to metformin or sulfonylureas.

When submitting an EDS request, the authorized health care professional can phone, mail, or fax the request to Saskatchewan Health; however, only the patient and prescribing physician receive confirmation letters. The pharmacist is notified when he or she access the patient profile via the Drug Plan’s database. Information required to submit an EDS request includes the (1) patient name, (2) patient health services number, (3) diagnosis relevant to use of drug, and (4) prescriber name and phone number. The information required to submit an EDS request for a nonapproved drug includes (1) the disease or problem treated, (2) the list of previous therapies and responses, (3) other non-EDS therapies tried and why they are not appropriate for the patient, (4) clinical evidence to support the therapy being requested, and (5) outcomes to assess effectiveness of the requested therapy. (Figure for EDS request form)

In July 2006, the Drug Plan implemented online adjudication for 2 drugs (pioglitazone HCl and rosiglitazone maleate) through an electronic step-therapy program. EDS claims for these 2 drugs can be submitted and adjudicated directly through the online claims transaction system. For these 2 drugs, the online transaction processing system checks the patient’s drug profile and if the first-line drugs (metformin or sulfonylureas) appear in the system, the coverage and approval letter is automatically generated for the patient.

Health care professionals as a whole are not compensated by the Saskatchewan Drug Plan for EDS requests. However, the Medical Services Branch (not the Saskatchewan Drug Plan and Extended Benefits Branch that administers the EDS program), compensates physicians Can $4 for information requests from health care professionals, including pharmacists, for a diagnosis from the physician to submit an EDS request. (written communication, G. Bradley, January 2005). Therefore, if the physician writes on the prescription “apply for EDS” but does not provide the required diagnosis on the written prescription, when the pharmacist contacts the physician to obtain the patient’s diagnosis, the physician may claim a Can $4 fee for that information request.
Perceptions of Saskatchewan Community Pharmacists Regarding a Prior-Authorization Program

**FIGURE** Saskatchewan Health Exception Drug Status Request Form

<table>
<thead>
<tr>
<th>Saskatchewan Health</th>
<th>Drug Plan &amp; Extended Benefits Branch</th>
</tr>
</thead>
<tbody>
<tr>
<td>3475 Albert Street</td>
<td>Regina SK SAS 6X6</td>
</tr>
<tr>
<td>306-787-3420 Phone</td>
<td>306-798-1089 Fax</td>
</tr>
</tbody>
</table>

**EXCEPTION DRUG STATUS REQUEST FORM**

**DATE:** ________/_______/_______

**DAY/MONTH/YEAR**

**PATIENT IDENTIFICATION**

Name: ________________________________________

Address: ________________________________________

__________________________________________________________________________

__________________________________________________________________________

Health Services Number: _____________________________

Date of Birth: ________/_______/_______

DAY/MONTH/YEAR

Sex: [ ] Male [ ] Female

**DRUG INFORMATION**

(See Appendix A for specific criteria)

Drug(s) Requested: ____________________________________________________________

Diagnosis (be specific): __________________________|

(include name, dosage form, and strength)

Alternative agents tried (be specific): __________________________________________

Drug allergies (be specific): _________________________________________________

Drug intolerances (be specific): ______________________________________________

Other information relevant to this request: ______________________________________

**For Pharmacy Use Only**

Pharmacist Name: ________________________________

Pharmacy Name: _________________________________

Pharmacy Phone Number: __________________________

Pharmacy Fax Number: _____________________________

Prescribing Physician: ____________________________

Physician M.S.P. Number: _________________________

Locum for Dr. (if applicable): _______________________

**For Physician Use Only**

Physician Name: _________________________________

Physician M.S.P. Number: _________________________

Locum for Dr. (if applicable): _______________________

Address: _______________________________________

**DRUG PLAN USE ONLY**

Fax Back Information: 

[ ] 30 [ ] P1 [ ] PC [ ] P2 [ ] SB [ ] P3

**HIRF INFO:**

**Drug Profile:**

Fax Request to Drug Plan (306) 798-1089

15/01/2003
Before 1999, only those practitioners licensed to prescribe in the province were able to initiate EDS requests. In 1999, Saskatchewan Health expanded the program to allow licensed pharmacists to apply for EDS on behalf of their patients. Allowing pharmacists to initiate these requests was seen as a way to improve access to prescription medication and assist patients in securing all available sources of funding for their prescription medications. However, the EDS program requires the pharmacist to obtain the patient’s diagnosis from the physician or physician’s agent in order to submit an EDS request.

Since 1999, when licensed pharmacists in Saskatchewan were allowed to initiate EDS requests, research has not been conducted on how the policy affects community pharmacy practice. As noted in previous studies on PA or step-therapy programs, often the drug costs and savings are evaluated while the perspective of the providers (e.g., pharmacists) are not addressed. This paper reports on the experiences and opinions of community pharmacy managers, or their delegates, and their pharmacies with regard to Saskatchewan Health’s EDS program and its effect on community pharmacy. Ethics approval was applied for and received from the University of Saskatchewan’s Behavioural Research Ethics Board before this survey was conducted.

Methods

Study Sample and Design

A census survey of community pharmacy managers in Saskatchewan was conducted in the fall of 2004. Pharmacy managers were chosen over individual pharmacists to reduce the potential of having 2 or more pharmacists’ perspectives represented from the same pharmacy. In September 2004, we received an up-to-date list of all 346 community pharmacies in the province from the Saskatchewan College of Pharmacists, the regulatory body for pharmacists in Saskatchewan. In identifying distinct community practices, we reduced the number to 333 as a result of pharmacy closure (1) and of pharmacies operating as satellites in remote communities that did not have a pharmacy manager and/or pharmacist specifically for the satellite location (12).

Following the Tailored Design Method for the conduct of surveys, we sent a prior notice letter in October 2004 to community pharmacy managers who were licensed pharmacists. In the letter, prospective survey respondents were asked to complete the questionnaire when it arrived or to designate a member of their staff whom they thought was most qualified to answer. This presurvey letter was followed 1 week later by the questionnaire, which included a cover letter and prestamped return envelope. A reminder postcard to nonresponders was sent 2 weeks later. A final mailing was sent 2 weeks after the reminder postcard to nonrespondents and included another copy of the questionnaire, a cover letter, and a prestamped return envelope. The study collection period closed 4 weeks after the final mailing.

Once the study period concluded, we performed a nonrespondent survey. A one-time questionnaire and cover letter, along with a prestamped return envelope, were sent to nonrespondents in an attempt to estimate potential biases in the sample.

Survey Instrument

Drawing on a review of the relevant literature, we constructed the questionnaire to address a series of topics relating to PA and the EDS program in Saskatchewan. These topic areas included potential stakeholder benefits from a PA program, the volume of EDS requests received by the pharmacy, factors influencing the decision to initiate a request, and the appropriateness of procedures used to submit a request. Information was also gathered with regard to the area, location, and type of pharmacy; the number of pharmacists and pharmacy technicians in the respondent’s pharmacy; the proximity of the prescribing physician; prescription volume; and hours the dispensary was open. Demographics were also collected on respondents’ gender, age, position, and years in their current position.

After the questionnaire was developed, content and format were evaluated using a pretest involving 5 community pharmacy managers. In the pretest, managers were asked to provide feedback on the design of the questionnaire, its relevance, and the flow of individual questions and between sections. Comments were also obtained from Saskatchewan Drug Plan representatives and an expert in questionnaire design from the Department of Management and Marketing, College of Commerce, University of Saskatchewan.

The final instrument contained 5 pages of questions with an average of 8 questions on each page (a copy of the instrument is available from the corresponding author). Items were measured primarily with 5-point and 7-point Likert-type scales. Respondents were also asked to complete a demographics page, and space was provided for additional comments, which are reported elsewhere.

Data Analysis

Descriptive statistics were calculated for all items. Comparative analysis was carried out using the Mann-Whitney U test and Kruskal-Wallis One-Way Analysis of Variance. Nonparametric tests were selected over parametric tests because of the primarily ordinal nature of the data. For post hoc analysis, the Bonferroni test was used to identify statistically significant differences between respondents when factors were compared. All statistical analyses were conducted using SPSS 13.0 for Windows (Chicago, IL).

Results

Study Population

A total of 279 questionnaires were returned. After data collection concluded, 4 additional questionnaires were received but were not included in the analysis. Of the eligible questionnaires received, 275 were properly completed, for a final response rate of 82.6% (275/333). Of the 50 nonrespondent questionnaires that were mailed after the study period, 15 were returned.
Pharmacy Characteristics and Exception Drug Status (EDS) Volumes

TABLE 1

<table>
<thead>
<tr>
<th>Pharmacy Characteristics – Saskatchewan (n = 275*)</th>
<th>Mean [SD]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pharmacists</td>
<td>2.8 [1.6]</td>
</tr>
<tr>
<td>Full-time equivalents</td>
<td>2.4 [1.4]</td>
</tr>
<tr>
<td>Number of pharmacy technicians</td>
<td>1.4 [1.7]</td>
</tr>
<tr>
<td>Full-time equivalents</td>
<td>1.0 [1.3]</td>
</tr>
<tr>
<td>Prescriptions per week</td>
<td>745 [504]</td>
</tr>
<tr>
<td>Pharmacy hours per week</td>
<td>62.0 [22.6]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exception Drug Status Volume Per Week</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of restricted/non-formulary prescriptions received – mean [SD]</td>
<td>36.4 [48.4]</td>
</tr>
<tr>
<td>Number (%) submitted for coverage†</td>
<td>22 (59.1%)</td>
</tr>
<tr>
<td>Number (%) initiated by the pharmacy</td>
<td>17 (78.8%)</td>
</tr>
<tr>
<td>Number (%) initiated by pharmacist’s request</td>
<td>5 (29.4%)</td>
</tr>
</tbody>
</table>

*48 (17.5%) of these 275 pharmacies were located in the same building with prescribers of EDS drugs.
† Circumstances such as the patient not meeting the EDS exception criteria (e.g., not having tried previous drug therapies required for approval or not having the tests done [such as culture and sensitivity for some antibiotics]) makes submission of some requests unnecessary.

(30%). There were no statistically significant differences between respondents of the original survey and respondents of the non-respondent survey on any common measures, including gender, respondents’ position, proximity to prescriber, community size, average number of prescriptions filled per week, and hours the pharmacy was open (data not presented).

Of the 273 respondents reporting their gender, nearly two thirds were male (64.2%). Almost half (49.1%) identified themselves as the manager, and more than one third of respondents identified themselves as the owner (36.4%). The reported average prescription volume per week (745, Table 1) is lower than the national average of 833. The average number of pharmacists (2.8) and pharmacy technicians (2.4) per location were also below the national average of 3.5 and 4.3, respectively.

An average of 36 restricted/nonformulary prescriptions were received per week which represented 5% of the reported prescription volume (Table 1). Compared with 1999, when pharmacies did not submit any EDS requests, we found that respondents reported that their pharmacies submitted 79% of all requests, with 29% of these EDS requests submitted by the pharmacy at the request of the prescribing physician. Therefore, community pharmacies submit an average of about 17 EDS requests per week out of the 59% of 22 of the restricted and nonformulary prescriptions received by the pharmacy and submitted by either the pharmacy or physician. Circumstances such as the patient not meeting the EDS exception criteria (e.g., not having tried previous drug therapies required for approval or not having the tests done [such as culture and sensitivity for some antibiotics]) makes submission of some requests unnecessary.

Stakeholders and the EDS Program

A majority of respondents (63%) agreed or strongly agreed that the EDS program benefited patients by expanding the number of prescription medications covered by the provincial drug plan (Table 2). A majority (64%) also agreed or strongly agreed that the provincial drug plan benefited from the EDS program by allowing costly medications to be available in a more controlled manner.

Fewer respondents agreed or strongly agreed that the EDS program benefited the health care system (39%) by promoting more appropriate utilization of drugs, while 37% of community pharmacy managers agreed or strongly agreed that the EDS program benefited physicians by providing them with more drug therapy choices for their patients. Only 15% of respondents agreed or strongly agreed that the EDS program benefited pharmacists by providing them with an opportunity to be more actively involved in securing the most appropriate drug therapy for their patients.

Factors Associated With a Pharmacist-Initiated EDS Request

In assessing the importance of factors that might influence whether a pharmacist initiated an EDS request on behalf of the patient, 74% of respondents indicated the ability of the patient to pay for the prescription was an important or very important factor (Table 3). Other factors seen as important or very important in initiating an EDS request included the ability to obtain all the information needed to make the request (77%) and the pharmacist’s ability to contact the prescribing physician (70%). Respondents who were in the same location (co-located in the same building) as the prescribing physician were less likely to consider proximity as a factor compared with those who were removed geographically (χ² = 18.41; P < 0.01, data not shown in tables). The time required to submit an EDS request was seen as the least important factor, with only 39% indicating this factor as important or very important.

Experience With EDS Requests

Seventy-nine percent of respondents agreed or strongly agreed that pharmacists in their pharmacy believe that initiating an EDS request is an important service for their patients, and 75% agreed or strongly agreed that they had adequate information on the administrative nature of the EDS program (Table 4).

With regard to the 1999 policy change allowing pharmacists to initiate EDS requests, 71% agreed or strongly agreed that the change in policy had been beneficial to patient care. However, most (96%) agreed that the change had significantly increased...
the administrative workload of pharmacists, but pharmacies that filled 0 to 250 prescriptions per week (15.9%) were less likely to agree with this statement than were those filling more than 500 (58.0%) prescriptions per week ($\chi^2 = 12.87; P < 0.01$, data not shown in tables).

Despite the administrative workload of pharmacists, there are less costly alternatives available. The principal stakeholders in PA programs are patients, pharmacists, physicians, drug plans, and administrators. Traditionally, physicians have been the health care professionals that apply for PA coverage for a patient, but some drug plans such as the Saskatchewan Drug Plan have authorized pharmacists to also initiate PA requests.

Other researchers have established the financial benefits of PA or step-therapy programs by identifying a reduction in direct drug costs. Through the examination of one aspect of the humanistic-service outcomes, the present study expands our understanding of PA programs. Specifically, we examined some of the factors associated with the uptake of a policy designed to allow pharmacists to apply for PA on behalf of their patients and the perceptions of community pharmacists associated with this policy.

While we did not measure the proportion of pharmacy staff time required for EDS submissions, the administrative burden is not small since preparing and submitting EDS requests requires more time than simply filling the prescription. Furthermore, pharmacists are not compensated financially for the service. It is not surprising that most respondents indicated that the current EDS policy was beneficial to patients and prescribers but viewed the policy as an additional burden for pharmacists.

Given the additional workload demands that the EDS program places on pharmacists, it was not unexpected that the respondents believed that pharmacists benefited the least from the EDS program. However, it was somewhat surprising that pharmacists reported that the time required to provide the service was the least important factor when deciding to initiate an EDS request. Factors such as the ability to obtain the required information and the ability to contact the prescriber were of greater concern. This suggests a need to improve communication and the role definition for both the pharmacist and the physician. Effective communication and collaboration between physicians and pharmacists will likely improve humanistic-service outcomes for patients, including reduction in the time delays in obtaining medications.

Respondents in the same location as prescribing physicians were less likely to be concerned with their ability to contact the physician. Co-locations and greater opportunity for face-to-face interaction allows the pharmacist(s) to establish good working relationships with prescribers. Good working relationships, in turn, would be expected to support greater accessibility when initiating an EDS request.

The ability of the patient to pay was also a key factor in pharmacist decisions to submit requests for EDS coverage. If a patient is unable to pay the cost share for the medication, even if approved via EDS, it is not productive for the pharmacist to apply for EDS coverage.

### Table 2

<table>
<thead>
<tr>
<th>The EDS program benefits . . .</th>
<th>Agree or Strongly Agree</th>
<th>Somewhat Agree</th>
<th>Neutral</th>
<th>Somewhat Disagree</th>
<th>Disagree or Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>patients by making their prescription drug more affordable</td>
<td>132 (48.1)</td>
<td>87 (31.8)</td>
<td>12 (4.4)</td>
<td>19 (6.9)</td>
<td>24 (8.8)</td>
</tr>
<tr>
<td>patients by expanding the number of drugs covered</td>
<td>173 (63.2)</td>
<td>67 (24.5)</td>
<td>8 (2.9)</td>
<td>11 (4.0)</td>
<td>15 (5.5)</td>
</tr>
<tr>
<td>physicians by providing more drug therapy choices for their patients</td>
<td>101 (37.0)</td>
<td>80 (29.1)</td>
<td>22 (8.1)</td>
<td>30 (10.9)</td>
<td>40 (14.3)</td>
</tr>
<tr>
<td>pharmacists by being more actively involved in securing the most appropriate drug therapy</td>
<td>41 (15.0)</td>
<td>51 (18.5)</td>
<td>36 (13.1)</td>
<td>46 (16.8)</td>
<td>100 (36.5)</td>
</tr>
<tr>
<td>drug plan by allowing costly drug therapies to be available in a more controlled fashion</td>
<td>176 (64.2)</td>
<td>51 (18.5)</td>
<td>19 (6.9)</td>
<td>12 (4.4)</td>
<td>16 (5.8)</td>
</tr>
<tr>
<td>health care system by promoting appropriate drug use</td>
<td>106 (38.7)</td>
<td>84 (30.7)</td>
<td>19 (6.9)</td>
<td>34 (12.4)</td>
<td>31 (11.3)</td>
</tr>
</tbody>
</table>

EDS = exception drug status.
Although it appears that respondents do not necessarily mind the time required to submit an EDS request, they are concerned about their ability to obtain the information necessary for initiating an EDS request. The fact that pharmacists are not likely to have the information required for an EDS request is troubling. The idea behind authorizing pharmacists to apply for EDS on behalf of patients was to increase timely access to prescription drugs for patients. However, when the pharmacist does not have the necessary information to make that request in a timely manner, the process may actually be lengthened.

An evolving partial solution may be found in the Saskatchewan Pharmaceutical Information Program (PIP). PIP is designed to link community physicians, pharmacies, and hospitals, providing confidential shared access to patient medication histories. However, while PIP may help alleviate some of the current barriers to pharmacist review of the complete medication history for a patient, it does not provide the pharmacist with access to other medical information.

### TABLE 3 Factors Associated With the Pharmacy Initiating an EDS

<table>
<thead>
<tr>
<th>Factors Determining Whether the Pharmacy Will Initiate an EDS Request</th>
<th>Very Important/Important n (%)</th>
<th>Somewhat Important n (%)</th>
<th>Neutral n (%)</th>
<th>Somewhat Unimportant n (%)</th>
<th>Very Unimportant/Unimportant n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Processing</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ability to obtain all the necessary information</td>
<td>211 (76.7)</td>
<td>30 (10.9)</td>
<td>10 (3.6)</td>
<td>6 (2.2)</td>
<td>18 (6.5)</td>
</tr>
<tr>
<td>Ability to track the status of the EDS request</td>
<td>141 (51.3)</td>
<td>54 (19.6)</td>
<td>38 (13.8)</td>
<td>6 (2.2)</td>
<td>36 (13.1)</td>
</tr>
<tr>
<td>Ability to contact the prescribing physician</td>
<td>193 (70.2)</td>
<td>47 (17.1)</td>
<td>14 (5.1)</td>
<td>2 (0.7)</td>
<td>19 (6.9)</td>
</tr>
<tr>
<td>Time needed to submit an EDS request</td>
<td>107 (38.9)</td>
<td>43 (15.6)</td>
<td>25 (9.1)</td>
<td>21 (7.6)</td>
<td>79 (28.7)</td>
</tr>
<tr>
<td>Familiarity with the EDS administrative processes</td>
<td>123 (44.7)</td>
<td>37 (13.5)</td>
<td>54 (19.7)</td>
<td>10 (3.6)</td>
<td>50 (18.2)</td>
</tr>
<tr>
<td><strong>Patient Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient will eventually exceed the deductible</td>
<td>163 (59.3)</td>
<td>60 (21.8)</td>
<td>21 (7.6)</td>
<td>12 (4.4)</td>
<td>19 (6.9)</td>
</tr>
<tr>
<td>Patient has exceeded the drug plan deductible</td>
<td>181 (65.8)</td>
<td>49 (17.8)</td>
<td>17 (6.2)</td>
<td>9 (3.3)</td>
<td>19 (6.9)</td>
</tr>
<tr>
<td>Ability of the patient to pay for the prescription</td>
<td>202 (73.5)</td>
<td>32 (11.6)</td>
<td>11 (4.0)</td>
<td>12 (4.4)</td>
<td>18 (6.5)</td>
</tr>
</tbody>
</table>

**EDS = exception drug status**

### TABLE 4 Pharmacist Opinions Regarding EDS Requests

<table>
<thead>
<tr>
<th>Pharmacist Opinions Regarding EDS Requests</th>
<th>Strongly Agree/Agree n (%)</th>
<th>Somewhat Agree n (%)</th>
<th>Neutral n (%)</th>
<th>Somewhat Disagree n (%)</th>
<th>Strongly Disagree/Disagree n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists have adequate information about program</td>
<td>207 (75.3)</td>
<td>44 (16.1)</td>
<td>13 (4.7)</td>
<td>7 (2.5)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Initiating EDS is an important service to patients</td>
<td>218 (79.3)</td>
<td>35 (12.7)</td>
<td>12 (4.4)</td>
<td>4 (1.5)</td>
<td>6 (2.2)</td>
</tr>
<tr>
<td>Policy change is beneficial to patient health care</td>
<td>195 (70.9)</td>
<td>43 (15.6)</td>
<td>19 (6.9)</td>
<td>6 (2.2)</td>
<td>12 (4.4)</td>
</tr>
<tr>
<td>Program contributes significantly to workload</td>
<td>238 (86.5)</td>
<td>25 (9.1)</td>
<td>7 (2.5)</td>
<td>2 (0.7)</td>
<td>3 (1.1)</td>
</tr>
</tbody>
</table>

**EDS = exception drug status.**
In July 2006, the Saskatchewan Drug Plan implemented 2 changes to help streamline the EDS application process. First, indefinite approval was permitted for 116 drugs or 442 EDS drug information numbers (DINs), analogous to National Drug Code (NDC) numbers in the United States. Second, online adjudication was implemented for 2 drugs, pioglitazone HCl and rosiglitazone maleate. EDS claims for these agents can be submitted and adjudicated directly through the online claims transactional processing system, which employs a “smart edit” to search for evidence of prior use of first-line therapy or prior use of the target drug that would have been associated with an EDS approval. While this is a positive step in addressing some of the issues around the administrative workload inherent in PA programs, the online adjudication system currently only includes 2 drugs.

Funding is clearly needed to institute measures that expedite and streamline the manner in which pharmacists apply for EDS, such as the move to online adjudication (smart edit). In addition, consideration must be given to paying pharmacists an appropriate fee for the service they provide. Financial compensation is important because it gives tangible recognition of the pharmacist’s professional role in delivering appropriate drug therapy while also providing an incentive for pharmacists and pharmacies to provide a service that clearly benefits patients in improved access to care and physicians in reduced administrative workload.

**Limitations**

First, this is a preliminary study of pharmacist perceptions that did not involve collecting information that might be used to improve processes such as the average time required of pharmacy staff per EDS submission and the proportion of total pharmacy time and payroll consumed by the EDS process. Second, the results obtained from the survey pertain only to the province of Saskatchewan, Canada, and may not be applicable to other jurisdictions. Third, since this survey was addressed to community pharmacy managers, the respondents tended to be older and were often the owners of the pharmacies. Therefore, the opinions recorded in this survey may not represent practicing pharmacists in general.

**Conclusions**

Pharmacists responding to the survey viewed the EDS program as being beneficial to patients but were concerned with the administrative burden. Concerns with the EDS program focus on the administrative nature of the program, including the inefficient manner in which pharmacists are required to apply for EDS due to lack of access to required patient information, including diagnosis and complete prescription drug history. To maintain pharmacists’ support for this managed care intervention, it will be necessary to reduce the administrative workload by providing access to required information and implementing smart edits that scan pharmacy claims history for evidence of prior use of first-line drug therapy. Further research is needed to capture the perceptions and experiences of all stakeholders of the EDS program, including pharmacists, physicians, patients, and drug plan personnel, to help assess humanistic-service outcomes of this managed care intervention.

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**ACKNOWLEDGMENT**

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**DISCLOSURES**

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Perceptions of Saskatchewan Community Pharmacists Regarding a Prior-Authorization Program

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Assessment of Eptifibatide Dosing in Renal Impairment Before and After In-Service Education Provided by Pharmacists

Jennifer L. Donovan, PharmD; Walter S. Schroeder, PharmD; Maichi T. Tran, PharmD; Keith Foster, PharmD; Alan Forrest, PharmD; Tamara B. Lee, PharmD; and Pritesh J. Gandhi, PharmD

BACKGROUND: Anticoagulant and antithrombotic agents are frequently cited as sources of medication errors. Several factors increase the risk of receiving excess dosing of glycoprotein IIb/IIIa inhibitors in the management of acute coronary syndrome (ACS), including older age, female gender, elevated serum creatinine, a history of diabetes mellitus, and a history of heart failure. In June 2003, the manufacturer of eptifibatide released a recommendation adjusting infusion rate downward to 1 mcg per kg per minute for eptifibatide in patients with renal impairment, defined as an estimated creatinine clearance (CrCl) < 50 ml per minute. Eptifibatide is known to accumulate in patients with renal impairment, thereby increasing hemorrhagic risk.

OBJECTIVE: To assess the impact of education on physician adherence to the renal dosing recommendation for eptifibatide at 2 academic medical centers. The primary outcome measure was the proportion of patients with renal impairment dosed appropriately with eptifibatide before and after in-service education provided by a clinical pharmacist. Secondary outcome measures included the difference in the improvement in dosing adherence between the 2 sites and the influence of patient variables on the incidence of bleeding events.

METHODS: This prospective study was conducted in patients with renal impairment who received eptifibatide for the management of unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI) or for the interventional management of chronic stable angina, UA, NSTEMI, or ST-elevation myocardial infarction (STEMI, not a Food and Drug Administration-approved use). Patient data were assessed at 2 tertiary care teaching institutions between June 2003 and December 2005. The preeducation phase for the sites ran from June 2003 through April 2005 for Site A and from June 2003 through May 2005 for Site B. The posteducation phase ran from May 2005 through December 2005 for Site A and from June 2005 through December 2005 for Site B.

At site A, a 1-hour educational seminar on ACS management strategies was employed, in which 5 minutes focused on adherence of prescribers to the guideline for renal dosing recommendations for eptifibatide. This tutorial was accomplished through (1) an in-service provided by 1 clinical pharmacist to the cardiology department, and (2) handouts containing the renal dosing recommendations for eptifibatide along with dosing for other medications used to manage ACS.

The intervention at Site B involved an eptifibatide-focused seminar presented to cardiologists by a clinical pharmacist, 10 minutes of which was devoted to renal dosing recommendations that included (1) a summary of literature supporting the infusion rate reduction in patients with renal impairment and (2) the specific updated dosing recommendation for eptifibatide. The data collected in retrospective chart review included patient demographics, baseline laboratory values, and risk factors for bleeding. An appropriate eptifibatide dose was defined as a physician order for a continuous infusion of 1 mcg per kg per minute in patients with an estimated CrCl < 50 ml per minute.

RESULTS: A total of 148 patients with renal impairment who received eptifibatide were evaluated (106 in the preeducation phase and 42 in the posteducation phase). A significant increase in the adherence rate for eptifibatide dosing in patients with renal impairment was observed from 36.8% in the preeducation phase to 69.0% in the posteducation phase (P < 0.001) for the 2 sites combined. The incidence of major and minor bleeding was 16.7% in the preeducation phase and 14.1% in the posteducation phase (P = 0.742). When bleeding incidence was stratified by the appropriateness of infusion, the incidence of major and minor bleeding was also similar for appropriate dosing (1 mcg per kg per minute, 16.4%) versus inappropriate dosing (2 mcg per kg per minute, 15.7%; P = 0.916).

CONCLUSION: This educational intervention provided by a clinical pharmacist was associated with improved prescriber adherence to dosing recommendations for eptifibatide in patients with renal impairment. Improved adherence to the dosing guideline and administration of an appropriate infusion rate were not associated with reduction in either minor or major bleeding events.

KEYWORDS: Eptifibatide, Dosing guideline, Renal impairment, Educational intervention, Clinical pharmacist

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What is already known about this subject

- Use of platelet glycoprotein IIb/IIIa inhibitors in patients with non–ST-segment-elevation ACS reduces ischemic complications before and after percutaneous coronary intervention but is associated with an increased risk of bleeding, and even greater hemorrhagic risk has been reported in patients with renal impairment.
- The acute nature in which eptifibatide is prepared and administered in the cardiac catheterization laboratory or emergency department does not permit pharmacist evaluation or the use of a computerized dosing system.
- There are 2 common types of interventions intended to improve adherence to medication dosing guidelines: education programs and computerized dosing aids.

What this study adds

- This intervention involving pharmacist-directed education of prescribers to reduce the dose of eptifibatide to 1 mcg per kg per minute for patients with renal impairment was associated with improved adherence to the dosing recommendation (the intermediate, process outcome) but no change in the proportion of patients who experienced major or minor bleeding episodes (end point, clinical outcome). These results cannot be attributed to the intervention, since this study lacked a control group.
Medication errors constitute a major problem in hospitalized patients and are associated with increased morbidity and mortality.1,2 The Institute of Medicine reported in 1999 that more than 98,000 people die each year as a result of medication errors.3 Furthermore, preventable adverse drug events (ADEs) are associated with a 4.6-day increase in a hospital stay with an estimated annual cost of $2.8 million for a 700-bed institution.4,5

Anticoagulant and antithrombotic agents are cited as frequent sources of these medication errors.1,3 The Institute of Safe Medication Practices has classified antithrombotic agents as high-alert medications because of their potential to cause significant patient harm.6 In a study by Fanikos and colleagues, anticoagulant drugs represented 7.2% of all medication errors; anticoagulants accounted for 1.72% of a total of 24 medication errors per 10,000 patient-days.5 Similarly, in a retrospective study, Saxer and colleagues compared actual doses of lepirudin with guideline-recommended doses in patients with heparin-induced thrombocytopenia and renal insufficiency.7 The authors found that 67% of patients who experienced a major bleeding event during therapy received a greater than recommended initial infusion rate.

More recently, CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the American College of Cardiology/American Heart Association Guidelines) investigators studied excess dosing of unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), and the glycoprotein IIb/IIIa inhibitors (eptifibatide [Integrilin] and tirofiban [Aggrastat]) in non–ST-elevation acute coronary syndrome (ACS).8 Excess dosing was found in 32.8% of UFH patients (n = 2,934), 13.8% of LMWH patients (n = 1,378), and 26.8% of glycoprotein IIb/IIIa inhibitor patients (n = 2,784). The CRUSADE investigators identified several patient characteristics that were associated with excess dosing of the glycoprotein IIb/IIIa inhibitors: age ≥ 75 years (odds ratio [OR] = 14.39, 95% confidence interval [CI], 12.24-16.90); female gender (OR = 3.74, 95% CI, 3.29-4.25); serum creatinine > 2 mg per dL (OR = 4.12, 95% CI, 2.95-5.75); a history of diabetes mellitus (OR = 1.35, 95% CI, 1.20-1.51); and a history of heart failure (OR = 1.49, 95% CI, 1.23-1.81).

Major bleeding occurred in 17.5% of patients (n = 374) with excess glycoprotein IIb/IIIa inhibitor dosing. Mortality was correlated with the degree of renal impairment in patients who received excess dosing of glycoprotein IIb/IIIa inhibitors. For eptifibatide, excess dosing was defined as full dose and creatinine clearance (CrCl) < 50 mL per minute, and for tirofiban, excess dosing was defined as full dose and CrCl < 30 mL per minute. Mortality was 1.2% (n = 73) for patients who received recommended doses of glycoprotein IIb/IIIa inhibitors compared with 4.3% (n = 83) for mild excess dosing (serum creatinine ≤ 2 mg per dL) and 12.4% (n = 22) for major excess dosing (serum creatinine > 2 mg per dL, P < 0.001). Higher mortality persisted after adjustment (adjusted OR = 1.50; 95% CI, 1.03-2.17).

In addition to the findings of the CRUSADE investigators, several articles described the incidence and cost implications of ADEs. Dosing errors were frequently identified as a major preventable ADE. Although the classes of medications varied widely, anticoagulants were frequently cited as the culprit of preventable ADE.4,9,10 Despite articles describing the frequency and preventability of ADE associated with anticoagulant and antiplatelet agents, no literature describes the impact of pharmacy-driven education to improve dosing adherence by physicians for these agents in the management of ACS. Because of this lack of data, we developed formal education programs for our health care professionals on appropriate dosing of eptifibatide, a glycoprotein IIb/IIIa inhibitor, in patients with renal insufficiency.

The purpose of this study was to compare the dosing appropriateness of eptifibatide in patients with renal impairment before and after education programs at 2 academic medical centers. This study was approved by the institutional review boards at both institutions.

Methods

Patients

We proposed that pharmacy-driven education at 2 academic medical centers would improve adherence to renal dosing recommendations for eptifibatide. On the basis of the eptifibatide package insert, patients with an estimated CrCl < 50 mL per minute require a 50% reduction in the continuous infusion rate, from 2 mcg per kg per minute to 1 mcg per kg per minute with no changes to the bolus dose (180 mcg per kg).5 Eptifibatide remains contraindicated in patients on hemodialysis. These recommendations provided the basis for our inclusion and exclusion criteria.

Patients were eligible for inclusion if they received eptifibatide for the medical management of unstable angina (UA) or non–ST-elevation myocardial infarction (NSTEMI), or as adjunct therapy in percutaneous coronary intervention for chronic stable angina (CSA), UA, NSTEMI, or ST-elevation myocardial infarction (STEMI). Eptifibatide is approved by the US Food and Drug Administration (FDA) for the medical management of UA and NSTEMI, as well as the interventional management of CSA, UA, and NSTEMI. Administration of eptifibatide in STEMI is not an FDA-approved indication and therefore represents off-label use. However, eptifibatide use as an adjunct to the interventional management of STEMI is given a Grade IIb recommendation where “treatment may be considered” by the 2005 American Heart Association (AHA)/American College of Cardiology (ACC)/
Assessment of Eptifibatide Dosing in Renal Impairment Before and After In-Service Education Provided by Pharmacists

Society for Cardiovascular Angiography and Interventions guideline update for percutaneous coronary intervention and the 2004 AHA/ACC guideline update for the management of STEMI. Additional inclusion criteria were age \( \geq 18 \) years and an estimated CrCl \(< 50\) ml per minute, as calculated by the Cockcroft and Gault equation. Actual body weight was used in the calculation of CrCl, according to the recommendation from Millennium Pharmaceuticals. CrCl was calculated from values closest to, but not following, eptifibatide initiation. We excluded patients if fibrinolytic therapy was administered within 48 hours preceding eptifibatide administration. All patients receiving eptifibatide during the pre- and posteducation phases were assessed for inclusion, using the inclusion/exclusion criteria described above.

**Study Design**

The study was divided into 2 phases: the preeducation phase and the posteducation phase. In the preeducation phase, we performed a retrospective eptifibatide utilization evaluation to identify eligible patients from June 2003 through April 2005 for Site A and from June 2003 through May 2005 for Site B. June 2003 was selected as the starting date because it correlated with the release of the renal dosing recommendations. We reviewed medical records to abstract patients’ age, gender, comorbidities, concomitant antiplatelet/anticogulant medications, renal function before administration of eptifibatide, hematologic status, blood product transfusions, and eptifibatide dose administered. These data are summarized in Table 1. The actual eptifibatide dose was compared with the recommended renal dosing guideline for appropriateness, defined as a physician order for a continuous infusion of 1 mcg per kg per minute in patients with an estimated CrCl \(< 50\) ml per minute. The preeducation and posteducation phases used the same inclusion criteria, exclusion criteria, and methods of patient identification and data abstraction. The eptifibatide utilization evaluation in the posteducation phase was conducted from May through December 2005 for Site A and from June through December 2005 for Site B.

**Education Programs**

The 2 sites used slightly different educational interventions for eptifibatide dosing. Site A incorporated the updated dosing recommendations as part of a larger seminar on ACS, whereas Site B provided an eptifibatide-focused seminar. Both sites developed an ACS treatment pathway that included all appropriate therapeutic options and incorporated dosing and monitoring recommendations. The education regarding the reduced dose for eptifibatide in patients with renal impairment took place at Site A in April 2005 and at Site B in May 2005.

The educational intervention at Site A included a 1-hour seminar on ACS management strategies. The in-service presentation by 1 clinical pharmacist focused on the recommendations from the CRUSADE trial, which recommends aggressive and early antiplatelet and anticoagulant therapy for patients presenting with ACS.

Review of the renal dosing of eptifibatide occurred over 5 minutes during the presentation and covered the infusion rate adjustment and the use of CrCl in identifying an appropriate infusion rate. A pocket reference card that included renal dosing recommendations for eptifibatide was distributed. The in-service presentation at Site A was attended by approximately 80% of the cardiology department and included cardiologists, nurses, and house officers.

The intervention at Site B employed a 10-minute eptifibatide-focused educational program. One lecture was provided to the interventional and clinical cardiologists by 1 clinical pharmacist who described eptifibatide renal dosing recommendations in the medical management of UA and NSTEMI and the interventional management of CSA, UA, NSTEMI, and STEMI. This seminar detailed the results from the ESPRIT (Enhanced Suppression of the Platelet IIb/IIIa Receptor With Integrilin Therapy) trial and Gretler and colleagues’ pharmacokinetic assessment of eptifibatide in patients with renal impairment. These studies provided the data to update the renal dosing recommendation for eptifibatide. The seminar concluded with a review of the Cockcroft-Gault equation to calculate an estimated CrCl. Physicians were given a handout of the information covered along with phone numbers to contact the central pharmacy to assist them with calculating an estimated CrCl. Approximately 67% of the cardiologists attended this in-service presentation at Site B.

**Outcomes**

The primary outcome measure was the overall adherence rate to eptifibatide renal dosing recommendations pre- and posteducation. Adherence to the dosing recommendation was defined as a physician order for a continuous infusion of 1 mcg per kg per minute in patients with an estimated CrCl \(< 50\) ml per minute. Our secondary outcome measure was the difference in adherence rates between Site A and Site B to identify differences in the effectiveness of the educational programs. The safety outcome measure was the number of hemorrhagic events observed pre- and posteducation and as a function of infusion appropriateness.

Independent, patient-specific variables were also assessed for their association with bleeding events. The incidence of hemorrhage was defined and stratified based on the criteria defined by the Thrombolysis In Myocardial Infarction (TIMI) study group. Minor bleeding was defined as overt bleeding associated with a decrease in hemoglobin between 3 g and 5 g per dL or a 9%-15% decrease in hematocrit. Major bleeding was defined as an intracranial hemorrhage or overt bleeding associated with a decrease in hemoglobin >5 g per dL or >15% decrease in hematocrit. Any bleeding was defined as the composite of minor and major bleeding.

To account for transfusions of packed red blood cells, the absolute number of units transfused was added to the difference between the baseline hemoglobin and the posttransfusion hemoglobin to obtain a true reflection of blood loss to be strati-
fied by the criteria above. Bleeding assessments were performed by reviewing laboratory data and chart review for annotations of overt or intracranial bleeding.

**Statistical Analysis**

Summary statistics, including 1-way and 2-way contingency tables, were computed for initial exploratory analyses. In the 2-group analysis, continuous variables were assessed via the Wilcoxon rank sum test. Dichotomous comparisons, including eptifibatide dosing adherence rates in the pre- and posteducation phases and bleeding incidence as a function of education and infusion appropriateness, were assessed by either the Fisher exact test or the Pearson chi-square test, depending on the expected value in each of the 4 cells.

### TABLE 1 Characteristics of Patients Who Received Eptifibatide (N=148)

<table>
<thead>
<tr>
<th></th>
<th>Preeducation n = 106</th>
<th>Posteducation N = 42</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of patients at Site A</td>
<td>77 (72.6)</td>
<td>29 (69.0)</td>
<td>–</td>
</tr>
<tr>
<td>Number (%) of patients at Site B</td>
<td>29 (27.4)</td>
<td>13 (31.0)</td>
<td>–</td>
</tr>
<tr>
<td>Age (years) – mean [SD]</td>
<td>75.6 [9.6]</td>
<td>77.8 [9.1]</td>
<td>0.159</td>
</tr>
<tr>
<td>Number of females (%)</td>
<td>49 (46.2)</td>
<td>19 (45.2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Actual weight (kg) – median [SD]</td>
<td>74 [15.4]</td>
<td>70 [13.7]</td>
<td>0.074</td>
</tr>
<tr>
<td>Length of stay (days) – mean [SD]</td>
<td>7.8 [8.0]</td>
<td>6.4 [6.2]</td>
<td>0.329</td>
</tr>
</tbody>
</table>

**Indication for eptifibatide – n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Preeducation</th>
<th>Posteducation</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic stable angina</td>
<td>10 (9.4)</td>
<td>8 (19.0)</td>
<td>0.177</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>31 (29.2)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>46 (43.3)</td>
<td>20 (47.6)</td>
<td>0.714</td>
</tr>
<tr>
<td>STEMI</td>
<td>19 (17.9)</td>
<td>14 (33.3)</td>
<td>0.050</td>
</tr>
</tbody>
</table>

**Past medical history – n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Preeducation</th>
<th>Posteducation</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>82 (77.3)</td>
<td>27 (64.2)</td>
<td>0.146</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>46 (43.3)</td>
<td>18 (42.8)</td>
<td>1.000</td>
</tr>
<tr>
<td>Heart failure</td>
<td>31 (29.2)</td>
<td>13 (31.0)</td>
<td>0.692</td>
</tr>
<tr>
<td>Cerebral vascular disease</td>
<td>8 (7.5)</td>
<td>2 (4.7)</td>
<td>0.725</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>19 (17.9)</td>
<td>5 (11.9)</td>
<td>0.463</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>50 (47.1)</td>
<td>23 (54.7)</td>
<td>0.467</td>
</tr>
<tr>
<td>Average comorbidities per patient [SD]</td>
<td>2.3 [1.2]</td>
<td>2.1 [1.2]</td>
<td>0.517</td>
</tr>
</tbody>
</table>

**Concurrent medications – n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Preeducation</th>
<th>Posteducation</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>98 (92.4)</td>
<td>41 (97.6)</td>
<td>0.446</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>87 (82.0)</td>
<td>38 (90.4)</td>
<td>0.313</td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>106 (100)</td>
<td>41 (97.6)</td>
<td>0.284</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>6 (5.6)</td>
<td>2 (4.7)</td>
<td>1.000</td>
</tr>
<tr>
<td>Warfarin</td>
<td>2 (1.8)</td>
<td>3 (7.1)</td>
<td>0.138</td>
</tr>
<tr>
<td>Nonsteroidal inflammatory agent</td>
<td>4 (3.7)</td>
<td>1 (2.4)</td>
<td>1.000</td>
</tr>
<tr>
<td>Average no. medications per patient [SD]</td>
<td>2.9 [0.64]</td>
<td>3.0 [0.54]</td>
<td>0.819</td>
</tr>
</tbody>
</table>

**Laboratory data**

<table>
<thead>
<tr>
<th></th>
<th>Preeducation</th>
<th>Posteducation</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline serum creatinine (mg per dL) [SD]</td>
<td>2.1 [1.11]</td>
<td>2.2 [1.67]</td>
<td>0.635</td>
</tr>
<tr>
<td>Baseline CrCl (ml per minute) [SD]</td>
<td>33.8 [9.45]</td>
<td>30.2 [9.6]</td>
<td>0.039</td>
</tr>
<tr>
<td>Baseline hemoglobin (g per dL) [SD]</td>
<td>11.8 [1.86]</td>
<td>11.6 [1.55]</td>
<td>0.504</td>
</tr>
</tbody>
</table>

* Continuous variables were assessed via the Wilcoxon rank sum test. Comparisons of dichotomous variables were assessed by either the Fisher exact test or Pearson chi-square test depending on the expected value in each of the 4 cells.

CrCl = creatinine clearance; NSTEMI = non–ST-elevation myocardial infarction; STEMI = ST-segment-elevation myocardial infarction.
Two logistic regression analyses were conducted. In the first analysis, the adherence rate (dependent variable) was assessed as a function of the study site and educational phase (independent variables) using multivariate, multinomial logistic regression with backwards stepping. Study site and educational phase were selected as independent variables to determine if the educational interventions conducted at the study sites were associated with a difference in dosing adherence. We did not include patient characteristics as covariates in this equation because our focus was to determine the impact of the educational program as opposed to factors contributing to excess dosing.

In the second logistic regression analysis, the bleeding rate (dependent variable) was assessed as a function of infusion appropriateness by the independent variables; percentage above ideal body weight; hours of eptifibatide infused; age > 80 years; weight < 65 kg; CrCl ≤ 30 ml per minute; female gender; use of aspirin, clopidogrel, UFH, enoxaparin, warfarin, or nonsteroidal anti-inflammatory drugs; or a history of coronary artery disease, chronic renal failure, cerebrovascular disease, peripheral vascular disease, abdominal aortic aneurysm, heart failure, or diabetes, using multivariable, multinomial logistic regression with backwards stepping. The independent variables were selected for logistic regression analysis for bleeding to determine if established risk factors associated with increasing bleeding risk as well as other cardiovascular comorbidities were associated with an increased likelihood of a hemorrhagic event. Continuous independent variables, including percentage above ideal body weight, hours of eptifibatide infusion, age, actual body weight, and CrCl were divided into ranges and were treated as categorical variables.

Goodness of fit for logistic regression analysis was assessed using the McFadden’s rho-squared statistic, analogous to an $R^2$. Analyses were performed using Systat version 11, Systat Software Inc., Richmond, California.

Patients undergoing coronary artery bypass grafting (CABG) were excluded from the bleeding analysis since intraoperative blood product use would skew the incidence of hemorrhage. Patients with incomplete data sets were excluded from logistic regression analysis, as calculations could not be performed without all tested variables.

## Results

A total of 106 patients in the preeducation phase and 42 patients in the posteducation phase were included in this analysis. No differences between phases were identified with respect to age, gender, or length of hospitalization (Table 1). In addition, both groups had a similar average number of comorbidities ($P = 0.517$). However, in the preeducation phase, significantly more patients presented with UA ($P < 0.001$). Furthermore, although statistical differences were found between groups with respect to baseline CrCl (preeducation phase 33.8 ml per minute vs. posteducation phase 30.2 ml per minute [$P = 0.039$]); these were not clinically significant.

### Impact of Education on Adherence

A significantly larger percentage of patients received an appropriate infusion of eptifibatide in the posteducation phase (69.0%) than in the preeducation phase (36.8%; $P < 0.001$, Table 2).

### Impact of Educational Program Type on Adherence

Site A included 77 and 29 patients in the preeducation phase and the posteducation phase, respectively. Site B enrolled 29 patients in the preeducation phase and 13 in the posteducation phase. Both sites experienced a statistically significant absolute improvement in dosing adherence for eptifibatide (Site A: 31.3%, $P = 0.005$, Site B: 34.7%, $P = 0.049$, Table 2). Logistic regression of eptifibatide infusion appropriateness was assessed as a function of study phase and site. A total of 148 patients were included in this analysis. This analysis did not identify any significant relationship between study site (OR = 0.98, $P = 0.986$) or the interaction between site and phase (OR = 1.162, $P = 0.860$). The McFadden’s rho-squared statistic for this analysis was 0.063. The lack of a difference observed between the 2 sites in comparison of the preeducation and posteducation phases suggests that the 2 intervention methods had similar effects in improving the adherence to renal dosing of eptifibatide. However, the small and unequal sample sizes reduced the power to detect a difference in the educational interventions.

### Bleeding

After removing data for patients who went on to CABG, we included 131 patients in the initial bleeding analysis. Data for patients who received CABG were removed in accordance with the TIMI bleeding criteria, as the transfusion requirements for this population skew bleeding results. A total of 11 minor and 10 major bleeding events occurred.

Table 3 describes bleeding incidence as a function of study phase. Minor bleeding occurred in 8 patients (8.3%) in the preeducation phase and in 3 patients (8.6%) in the posteducation phase ($P = 0.965$). Major bleeding in the pre- and posteducation phases occurred in 8 patients (8.3%) and 2 patients (5.7%), respectively ($P = 0.617$). When these patients were stratified by eptifibatide infusion appropriateness, minor bleeding occurred in 5 patients (8.2%) who received an appropriate infusion and in 6 patients (8.6%) who received an inappropriate infusion ($P = 0.939$). Major bleeding occurred in 5 patients (8.2%) who received an appropriate infusion and in 5 patients (7.1%) who received an inappropriate infusion ($P = 0.821$). Table 4 summarizes the bleeding incidence as a function of infusion appropriateness.

After the initial bleeding analysis, we performed logistic regression to identify other potential risk factors for bleeding. Data summarizing the bleeding responses and patient charac-
teristics are summarized in Table 5. Because of the large number and distribution of variables assessed and the uneven distribution of minor and major bleeding, patients were stratified as having any bleeding (minor or major) or no bleeding. As with the initial bleeding analysis, patients who received CABG were excluded from analysis. Patients who did not have complete data sets were also excluded, as logistic regression could not be performed on incomplete data sets. Most commonly, these patients did not have a height annotated for us to calculate an ideal body weight.

After these patients were removed, 119 were left for analysis. A total of 17 (8 minor, 9 major) bleeding events were identified, using the bleeding criteria established by the TIMI study group. Of the established and hypothesized risk factors for bleeding (female gender, age > 80 years; infusion appropriateness; CrCl < 30 ml per minute; a history of chronic renal failure, heart failure, or diabetes), only age > 80 years was associated with significantly increased odds of bleeding (OR = 4.74, 95% CI, 1.45-15.38, P = 0.010). The McFadden’s rho-squared statistic for this analysis was 0.101.

### Discussion

Our challenge was to develop an educational program to educate physicians not only on the updated dosing of eptifibatide, but also on the assessment of renal function in patients to determine the optimal dose. A wealth of literature exists on educational programs to increase physician awareness and recognition of disease states as well as strategies to improve prescribing of medications. However, no reports detail educational strategies to optimize the dose of medications to manage disease. Despite this limitation, we developed and applied educational strategies similar to those found in the literature to increase disease state awareness and adherence to disease state management guidelines.18,20

Schunemann and colleagues conducted an assessment of physician opinion regarding educational strategies to improve guideline adherence as part of the Seventh American College of Chest Physicians Conference on Antithrombotic and Thrombolytic Therapy.18 Their results identified dissemination of printed information and educational seminars as preferred methods that physicians believed would result in increased adherence. They also acknowledged active strategies, such as computerized reminders and patient-focused interventions, as established methods by which adherence may be improved.

These findings were echoed by Tooher and colleagues in their review of strategies to improve venous thromboembolism (VTE) prophylaxis.20 Their review assessed the effectiveness of educational strategies to improve prescribing of agents for VTE prophylaxis. The authors identified continuing education, audit and feedback, computerized decision aids, documentation aids, and quality assurance strategies as among the best ways to improve prescribing of VTE prophylaxis. They further went on to suggest that multiple educational strategies involving active programs like computerized reminders may be more effective than a single strategy.

The incidence of minor and major bleeding events did not significantly change between the preeducation (16.7%) and posteducation phases (14.3%). The overall bleeding rates appeared to be elevated in comparison with rates reported by large, prospective trials evaluating the safety and efficacy of eptifibatide in patients irrespective of renal function. In the IntegriLin to Minimise Platelet Aggregation and Coronary Thrombosis-II (IMPACT-II) trial, 2,682 patients were ran-

### Table 2

<table>
<thead>
<tr>
<th></th>
<th>Preeducation Phase</th>
<th>Posteducation Phase</th>
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<tbody>
<tr>
<td></td>
<td>Site A: June 2003–</td>
<td>Site B: June 2003–</td>
</tr>
<tr>
<td></td>
<td>April 2005</td>
<td>May 2005</td>
</tr>
<tr>
<td></td>
<td>Site A: May 2005–</td>
<td>Site B: June 2005–</td>
</tr>
<tr>
<td></td>
<td>December 2005</td>
<td>December 2005</td>
</tr>
<tr>
<td></td>
<td>n=106 (%)</td>
<td>n=42 (%)</td>
</tr>
<tr>
<td>Site A</td>
<td>29 (37.7)</td>
<td>20 (69.0)</td>
</tr>
<tr>
<td>Site B</td>
<td>10 (34.5)</td>
<td>9 (69.2)</td>
</tr>
<tr>
<td>Combined</td>
<td>39 (36.8)</td>
<td>29 (69.0)</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th></th>
<th>Preeducation Phase</th>
<th>Posteducation Phase</th>
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<tbody>
<tr>
<td></td>
<td>Site A: June 2003–</td>
<td>Site B: June 2003–</td>
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<tr>
<td></td>
<td>April 2005</td>
<td>May 2005</td>
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<tr>
<td></td>
<td>Site A: May 2005–</td>
<td>Site B: June 2005–</td>
</tr>
<tr>
<td></td>
<td>December 2005</td>
<td>December 2005</td>
</tr>
<tr>
<td></td>
<td>n=96 (%)</td>
<td>n=35 (%)</td>
</tr>
<tr>
<td>Minor†</td>
<td>8 (8.3)</td>
<td>3 (8.0)</td>
</tr>
<tr>
<td>Major‡</td>
<td>8 (8.3)</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Combined</td>
<td>16 (16.7)</td>
<td>5 (14.3)</td>
</tr>
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</table>

* Infusion appropriateness is defined as a physician order for a continuous infusion of 1 mg per kg per minute in patients with an estimated CrCl < 50 ml per minute.
† For each of the 2 sites, the Pearson chi-square test was used to assess the differences in adherence rates between the preeducation and posteducation phases. CrCl= creatinine clearance.
‡ Minor bleeding is defined as overt bleeding with a decrease in hemoglobin from 3 g to 5 g per dl or a 9-15% decrease in hematocrit.
§ Major bleeding is defined as overt bleeding with a decrease in hemoglobin > 5 g per dl or > 15% decrease in hematocrit.
$ The Fisher exact test was used to assess the difference in bleeding incidences between the educational phases.
domed to receive a 135 mcg per kg bolus of eptifibatide followed by continuous infusion of 0.5 mcg or 0.75 mcg per kg per minute. The incidence of major bleeding was 5.1% and 5.2% in each group, respectively. The rate of major and minor bleeding in 4,679 patients who received eptifibatide as a 1.80 mcg per kg per minute bolus followed by either a 1.3 mcg or 2 mcg per kg per minute infusion in the Platelet Glycoprotein Ib/IIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT) clinical trial was 14.0% for the subset of patients who did not undergo CABG. In the 1,040 patients randomized to receive two 180 mcg per kg boluses of eptifibatide followed by continuous infusion of 2 mcg per kg per minute in the ESPRIT trial, 4.8% of patients experienced a mild, moderate, or severe bleeding event.

In all 3 studies, the authors encouraged the use of aspirin and heparin therapy as part of standard ACS care. In the PURSUIT study, 93% of patients were administered aspirin and 89.8% of patients received heparin. These values are similar to aspirin and heparin use researchers found in our study (see Table 1). Data on the use of aspirin and heparin for the IMPACT-II and ESPRIT trials were not reported. The most notable variable that may explain the difference in bleeding rates between our results and these trials is the presence of renal impairment. We specifically enrolled patients with a CrCl < 50 ml per minute, whereas the IMPACT-II, PURSUIT, and ESPRIT trials enrolled patients irrespective of renal function. Furthermore, our patient population appeared to have an older mean age (75.6 years in the preeducation phase and 77.8 years in the posteducation phase) compared with the population in the IMPACT-II (62 years in the group receiving 0.5 mcg per kg per minute and 60 in the group receiving 0.75 mcg per kg per minute), PURSUIT (64 years), and ESPRIT (62 years) trials. Also, our study appeared to have more female patients (46.2% in the preeducation phase and 45.2% in the posteducation phase) compared with the IMPACT-II (23.6%), PURSUIT (34.9%), and ESPRIT (27%)
Assessment of Eptifibatide Dosing in Renal Impairment Before and After In-Service Education Provided by Pharmacists

Conclusions

Last, the median weight of our patient population (74 kg in the preeducation phase and 70 kg in the posteducation phase) appeared to be lower than that in the IMPACT-II (83 kg in patients who received 0.5 mcg per kg per minute and 84 kg in patients who received 0.75 mcg per kg per minute), PURSUIT (78 kg), and ESPRIT trials (84 kg). While the significance of the differences in these variables between our data and those of other researchers is unknown, our population appears to be at higher risk for receiving greater than recommended doses of eptifibatide and increased risk of bleeding associated with older patient age, a larger percentage of female patients, and lower actual body weight.

Limitations

First and foremost among the limitations of this study was the absence of a control group. Therefore, we cannot be certain that our educational intervention was the reason for the improved adherence to the dosing guideline in patients with renal impairment. Second, we chose to define the primary outcome measure as an intermediate measure (infusion appropriateness) and the proportion of patients who experienced either a major or minor bleeding episode as the secondary outcome. Our assumption was that adherence to renal dosing recommendations would result in a decrease in hemorrhagic complications.

Third, the small and unequal sample sizes in the preeducation and posteducation phases contributed to the absence of a significant difference in the incidence of minor and major hemorrhagic events in this analysis. Logistic regression demonstrated an increased likelihood of bleeding in patients > 80 years. We anticipated an increased risk of bleeding in patients in whom eptifibatide serum concentration should be elevated (history of chronic renal failure, CrCl < 30 ml per minute, inappropriate infusion rate, prolonged infusion). However, none of these factors was associated with increasing patients’ bleeding risk, most likely due to the small sample size in our study.

The pharmacokinetic study reported by Gretler and colleagues demonstrated a 2-fold increase in serum steady-state concentrations of eptifibatide and a 50% decrease in total clearance of eptifibatide in patients with a CrCl < 50 ml per minute. These pharmacokinetic data served as the foundation for the renal dosing recommendations for eptifibatide as opposed to actual observed bleeding rates between the cohorts of patients with renal impairment. While our study results are only descriptive, the 16% average rate of minor and major bleeding combined for both appropriate infusion (1 mcg per kg per minute) and inappropriate infusion (2 mcg per kg per minute) suggests that further research is warranted in eptifibatide use in patients with renal impairment.

Conclusion

To our knowledge, this is the first study in which researchers investigated the impact of pharmacist-driven education to improve dosing of an antiplatelet agent in the management of ACS. The education programs were associated with improvement in the dosing of eptifibatide in patients with renal impairment to the recommended dose of 1 mcg per kg per minute in 69.0% of patients compared with 36.8% before the intervention. The proportion of patients who experienced either major or minor bleeding was similar in the 2 periods, 16.7% (16 patients) in the preeducation period and 14.3% (5 patients) in the posteducation period, and there was no difference in the incidence of major or minor bleeding (approximately 16% for both infusion rates of 1 mcg or 2 mcg per kg per minute).

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Challenges and Opportunities in Pharmacogenomics and Therapeutics

The use of a patient's genetic data to inform decisions related to diagnostic and prognostic health care represents the ultimate achievement of 50 years of genomic research. The technology to realize this vision has emerged and continues to evolve. An emerging vision of the future involves deriving patient-specific genomic data before birth, which includes an exhaustive sampling of genomic information. In this envisioned future, genetic data will be periodically updated throughout a patient's lifetime on a tissue-specific basis to screen for genetic changes associated with age-related diseases. A patient's genotypic data will be further integrated with dedicated databases/warehouses harboring genetically linked health and adverse drug response risk information that will be utilized at the point of care for patient-specific therapeutic interventions.

Current and near-term uses of genomic information provide a glimpse of its future potential. For example, drugs are metabolized endogenously by a series of enzymes collectively referred to as the cytochrome P450 system. These enzymes are further characterized into subgroups, such as CYP1A1 and CYP2D6. It has been demonstrated that the metabolic activity and oral clearance of the immunosuppressant, sirolimus, is significantly decreased in patients with CYP3A5*3 single-nucleotide polymorphism (SNP).1 Furthermore, it is suggested that dose adjustments should be made in patients that harbor this SNP to reduce the risk of drug toxicity.1 In this context, an SNP refers to a single-nucleotide base change within the gene sequence of a P450 enzyme in the patient's genome, which decreases the enzyme's expression level and/or activity level.

This is distinct from a nucleotide base change commonly referred to as a "mutation" in which a change in the genome results in a disease state; this SNP predisposes the patient to an adverse drug response. Thus, patients who harbor this allele are at risk of drug toxicity associated with higher drug plasma levels if the "standard" dose is prescribed. Pharmacogenomic data could be used to suggest a more effective dose (in this case, a reduced dose) by predicting the metabolic capability of the patient.

Numerous current and near-term potential methods for DNA analysis support both SNP discovery and detection. The term SNP discovery refers to the utilization of biotechnology methods to uncover new SNPs in a subset of the population, which becomes more difficult (costly) if a specific SNP is rare in humans and inherently dependent upon DNA sequencing in human samples. SNP detection involves the use of laboratory testing to determine the allelic profile of a patient's sample within known polymorphic locations in their genome. Many known SNPs have been discovered within phase-1 metabolic enzymes, and some of these have been genetically linked to altered drug clearance and drug safety. These "drug safety" SNPs are best positioned to benefit the health care community in the near term because they are not inherently biomarkers of genetic illness in humans and may serve to reduce the incidence of adverse drug effects in the clinic.

The use of SNP information to identify drug safety issues could potentially produce a cultural shift in pharmaceutical drug development whereby new drug product development would require genomic screening to ensure safety and efficacy. Ultimately, clinical drug development (Phases I-IV) could be limited to patients with specific SNP genotypes to increase the overall safety and efficacy of new drug entities. This might benefit pharmaceutical firms by providing increased clarity in the creation of patient inclusion criteria for clinical dosing studies, thus reducing the variability in response that would occur without pharmacogenomic information. As a result, it might be anticipated that fewer promising drug entities will be abandoned due to erratic pharmacokinetics as well as safety and efficacy issues.

Future potential, however, does not equate to current reality. In a previous issue of JMCP, Morrow presented a thorough review of the literature focused on the clinical utility of pharmacogenomics in asthma.2 In addition, he considered the economic implications of pharmacogenomics, highlighting issues of importance to managed care pharmacy as the technology develops. We agree with Morrow that the developing field of pharmacogenomics represents an area of great opportunity for pharmacy in general and for managed care pharmacists in particular. Yet, Morrow reports that in regard to clinical utility, pharmacogenomic evaluation is not sufficiently developed to implement individualized asthma therapy on a population-wide basis. We concur with Morrow's assessment based on several points.

We suggest that the path to an optimal future in genomics-based health care is obscured by several independent factors that must be recognized and overcome to fully exploit genomic content in human health care. Ultimately, a functioning system for clinical genotyping requires (1) an information management system and data standards, (2) a secure interface between DNA analysis biotechnology and the clinical genotyping information system, (3) management of costs and opportunities to ensure that the clinical genotyping system provides value to health care, and (4) the education of pharmacy students and other health care professionals in the biological interplay between genomics and disease pathology.

At the heart of a large-scale clinical genomics implementation would be an information management system that can accommodate many different analysis methods (including new biotechnologies of the future) through the development of a group of scalable standards for genomic information. Given the very recent advances in human genomic knowledge and biotechnology methods, it is not feasible to assume that physicians, pharmacists, nurses, and other professionals within the health care industry have sufficient knowledge to translate raw genomic data into information relevant to health outcomes. Therefore, essentially all genomic data will be "automatically" filtered into categorical definitions by the data management system, and the
known (or potential) impact of a given SNP will then be presented to the health care professional. For example, if a patient is prescribed a drug in which an adverse response has been associated with 1 or more specific genotypes, then the patient’s electronic health record will indicate that the patient is “at risk for an adverse response due to genomic information” and make a recommendation to choose an alternate drug (including a specific drug recommendation if one is available) and/or reduce the dose of the drug.

Given patient privacy concerns, data standards for sharing genomic data must precede the practical use of genotyping in the medical clinic. Thus, with respect to system-wide adoption of a clinical genotyping system, it will be advantageous to categorically separate SNP data relevant to drug safety from SNP data relevant to general health outcomes. In other words, the utilization of pharmacogenomics will be more easily facilitated if the system is limited initially to the prediction of adverse drug reactions. This approach is not hindered by the limited knowledge of genomics in the health care community and overcomes patient privacy concerns as a fundamental adoption barrier. By categorically separating SNPs relevant to drug safety from SNPs linked to other health outcomes as well as SNPs with no known linkages (it is recognized that some small overlap in this distinction exists), consumers can (1) understand how their own genomic data are being used and gain trust in these systems, (2) indicate how their own genomic data are managed and who can gain access to these categorical data sets, and (3) provide a rationale for data security that is dependent on the category of the data. For example, data from an individual whose specific genomic profile is clearly associated with severe drug safety issues may be more easily accessed by worldwide health care institutions and pharmacies because these data would be needed in an emergency for an injured traveler. In contrast, other SNP categories associated with the propensity to develop chronic disease may not be shared across institutions. This concept assumes that (1) consumers will be able to control access to their genotypic information and (2) SNPs inherent to drug safety are far less likely to serve (or be abused) as indicators of general health for an individual.

This approach to facilitating the early adoption of pharmacogenomics in the medical clinic is consistent with the perceived value and use of pharmacogenomic data from the health care professional perspective. The integration of SNPs would be linked to drug safety outcomes within an information-based guidance system for ensuring drug safety (i.e., decision support for both the physician and pharmacist) for patients harboring potentially harmful SNPs. Early utilization of this genomic information will likely involve screening for drug safety at the pharmacy because a prescription/dispensing system exists that is already linked to an information system capable of providing guidance for patients and pharmacists. This type of system has the potential to impact nearly all health care consumers because it is not limited to a particular disease domain. Ultimately, the linkage of SNPs to the prediction of drug response within specific disease domains will be implemented on the heels of a pharmacogenomic drug safety system as the entire health care community becomes accustomed to working with information in the human genome.

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Opinions Regarding the Value and Use of the AMCP Format Still Unknown

Prior research has demonstrated the importance of pharmacoeconomics in drug research and formulary decisions.1,2,3 A recent JMCP letter to the editor from Lyles and Watkins encouraged increased assessments on the use of the AMCP Format for Formulary Submissions that produce clear inferences concerning the relationship between the dossier and subsequent formulary decisions.4 However, surprising little evidence of the impact of the AMCP Format and dossiers on drug formulary decisions is evident given that only one recent account by Spooner et al. exists detailing the real-world use of the AMCP Format.5

In a previous issue of JMCP, Nichol et al. surveyed representatives from managed care organizations (MCOs) and pharmaceutical manufacturers regarding their opinions of the AMCP Format.6 The results of this survey research are timely because they shed some light on the formerly unpublished perspectives of these representatives. Furthermore, because the survey was conducted from September 2004 to October 2005, these opinions coincide with the introduction of Version 2.1 of the AMCP Format for Formulary Submissions released in April 2005.7 It must be noted, however, that Version 2.1 had just been released and that the survey participants were likely responding based on their experience with the past version.

The Nichol et al. article is a “small survey” of MCOs and pharmaceutical manufacturers. The 20 MCO respondents surveyed came from a sample of both large and small companies from the National Directory of Managed Care Organizations database. The majority (70%) of the MCO respondents held the position of pharmacy director, responsible for evaluating dossiers and compiling/presenting the data to pharmacy and therapeutics committees. The 7 survey participants from pharmaceutical firms were all members of the Pharmaceutical Research and Manufacturers of America Foundations Health Outcomes Committee, which is composed of directors of health outcomes departments who have experience in developing dossiers in accordance with the AMCP dossier guidelines. Therefore, it cannot be assumed that they are representative of pharmaceutical manufacturers as a whole. There may be substantial differences in the opinions of employees of pharmaceutical manufacturers compared with this select group of directors.

It is surprising that only 40% of all drugs reviewed by MCOs included dossiers from the manufacturer. In their evaluation of pharmaceutical manufacturers’ responses to a request for a product dossier prepared using the AMCP Format, Spooner et al. noted that dossiers were received for only 58% of the products for which dossiers were requested.5 Nichol et al. did not report on the number and percentage of drugs for which dossiers had been developed and submitted to MCOs by the companies represented by respondents in their survey of manufacturer representatives.

Nichol et al. stated that 54% of the dossiers received by MCOs included budget impact models and 39% included other forms of economic analysis (cost-effectiveness or cost-benefit analyses). Nearly half of these models appeared to be cost-effectiveness evaluations, and a small number were reported to be tailored to the MCOs’ population. Spooner et al. claimed that 68% of the dossiers received by one MCO included a pharmacoeconomic or disease management impact model.6 Approximately half of the dossiers in the Nichols et al. study contained economic models that were regarded as being adequate by MCOs. In the Spooner et al. study, 20% of the models were unlocked, interactive budget impact models, whereas the other 48% essentially contained only reports on the analysis performed instead of actual models.7 Better communication between pharmaceutical manufacturers and MCOs appears to be the solution for the production of models that offer more value to MCOs to facilitate their decision to include/exclude drugs on their formularies.

Dossier confidentiality is clearly an area of concern for pharmaceutical manufacturers due to the lack of assurances by MCOs regarding this confidentiality. Given the business relationship between pharmaceutical manufacturers and MCOs, it seems unlikely that a manufacturer would attempt to benefit by pursuing legal action against an MCO concerning a breach of confidentiality related to a dossier.

Information presented in the Nichol et al. article contributes to the conclusion that the overall perceived value of the AMCP dossier format appears to be divided: certain MCOs seem to feel that dossiers should be used in their decision-making process, whereas others fail to see the value they provide. Pharmaceutical manufacturers viewed dossiers as a vehicle in which to convey the value of their products.

Going forward, it is interesting to note the divided (50/50) opinion of pharmaceutical manufacturers as to whether the new AMCP guidelines will improve the submission process as well as the transmission of data and information from pharmaceutical manufacturer to MCO. Pharmaceutical manufacturers expected that other groups besides MCOs, such as pharmacy benefit managers and Centers for Medicare and Medicaid Services, would use either a framework similar to the AMCP Format or the existing AMCP Format.

Besides inferring that the opinions of manufacturer representatives in the survey by Nichol et al. are most likely not representative of the opinions of employees of manufacturers in general, the question of the usefulness of the AMCP Format has not been answered by this research. Further research is war-
ranted, including additional case reports such as that described by Spooner et al., in the quest to maximize the usefulness and utilization of the AMCP Format.

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**REFERENCES**


Providing medical care for the uninsured population is a growing concern. Approximately 45 million people in this country have no health insurance and the percentage of uninsured continues to grow. Nearly 18% (8 million) of the uninsured are children while 1 in 5 are adults aged 25 to 64 years. In the face of this important social problem, the uninsured may forego health care services due to access issues, and in the end, utilize more costly medical services due to untreated diseases. It has been estimated that every year, as many as 18,000 unnecessary deaths were caused by lack of health insurance. In addition to the effect on quality of life, this issue has a major financial impact on the public health system. The Institute of Medicine estimated that the annual lost economic value of being uninsured in the United States is between $65 billion to $130 billion.

Escalating drug expenditures and reduced insurance coverage in the United States compounds the problem with access to prescription drugs. Pharmaceutical manufacturers offer prescription assistance programs (PAPs) to make certain brand-name prescription drugs available to low-income patients who are not eligible for public assistance programs and are without private insurance. It was hoped that PAPs would have a favorable effect on health outcomes such as hospitalization rates and emergency department visits through improved medication access and adherence. PAPs have evolved to become a safety net for millions of needy Americans who are not eligible for comprehensive assistance programs and unable to afford their medications. Much evidence justifies the benefits of establishing a PAP to assist indigent patients in obtaining their needed medications.

Since 2006, a majority of manufacturers have streamlined their PAPs to require 1 application per year with the exception of Novo Nordisk, Forest, Sanofi-aventis, Sankyo, and Biowaiv. The development of a ‘universal’ application process would greatly benefit patients and health care providers by reducing personnel time required to complete individual applications tailored to specific manufacturers. Even if the PAP form is simplified in a more universal format, our experience suggests that most patients will encounter difficulties completing the application on their own since the application requires an accurate interpretation of prescriptions to transcribe specific information such as drug name, strength, direction, quantity, duration, and number of authorized refills. Drug manufacturers frequently change their eligibility criteria and the list of drugs available in PAPs, making it difficult for indigent patients to stay abreast of the program changes. Additionally, many underserved patients may be challenged with limited health literacy, and some suffer from deteriorating health or cognitive status that prevents them from completing the application without assistance. Therefore, it is critical for health care providers to help these patients through the enrollment process to ensure that they have access to their required prescription drugs.

The increased need for PAPs makes the question of their operational cost important for administrators of medical clinics considering implementing such a program. In their time and motion study reported in a recent issue of JMCP, Clay et al. attempted to capture the overall cost of a PAP incurred by a free health clinic in Kansas City. The results showed the estimated annual cost of providing PAP service at the clinic was $81,835 at an average expense per patient ranging from $10.42 for a medication with 1 annual application up to $46.30 for manufacturers requiring 4 applications per year. The PAP enrollment process is time- and labor-intensive; therefore, personnel costs accounted for the highest component of the annual PAP expenditure. Clay et al. used the wage of a medical assistant with an hourly rate of $12.21 plus benefits ($4.23) as the basis of the personnel cost. This study establishes a benchmark for administrators who are considering the establishment of an onsite PAP at a medical facility similar in size and nature of the population served at the Kansas City Free Health Clinic. Additionally, this information is valuable for budget development while seeking funding or donations to establish or maintain a PAP.

A comparison with a PAP in another medical clinic provides insight into the considerations made by Clay et al. As the only Federally Qualified Health Center located in the Greater Lafayette, Indiana area, Tippecanoe Community Health Clinic (TCHC) provides coordinated primary health care to more than 9,000 uninsured county residents annually who have limited access to health care due to lack of financial resources or health care expense reimbursement. More than half of the clinic’s patients receive Medicaid assistance, and 40% are uninsured. Furthermore, approximately 67% of a patient’s income falls below the 100% federal poverty level. As the pharmacotherapist at TCHC, one of the authors provides comprehensive clinical pharmacy services through consultations with providers, PAP clerks, patients, and other allied health care professionals.

The PAP at TCHC began in 1999 with 1 part-time nurse working 10 to 15 hours per week and has expanded to its current staffing level of 1.8 full-time clerks with support from doctor of pharmacy candidates. The medical director and nursing supervisor provide managerial oversight of the PAP, and pharmacy consultation is accessible onsite. In 2005, TCHC processed 5,671 PAP applications (2,652 new and 3,019 renewals) contributing more than $1.7 million in acquisition costs for the medications received. The PAP office resides within TCHC and offers both scheduled and walk-in services. Clinic patients are referred to PAP by their providers or other patient advocates (e.g., pharmacist, specialists, dietitian, and nurses). If an uninsured patient is unable to afford low-cost drug regimens (e.g., discounted generics through the 340B program or $4 local pharmacy generic drugs), individual prescriptions written per specific manufacturer guidelines are given to patients to bring to the PAP office to determine enrollment eligibility and process the application. Some differences exist between the PAPs at the
Kansas City Free Health Clinic and TCHC. Due to the high volume of patient enrollments at TCHC, RxAssist Plus Patient and Medication Tracking Software was installed to streamline the application process and reduce personnel time. To offset clinical expenses and encourage patient accountability, a $3 processing fee for each application is required. All patients are required to pay, with the exception of homeless patients, for whom the fee is waived. If patients cannot afford the processing fee, the application is placed on hold until they can afford it, or other sources are identified to assist with the fee.

Individual credit checks are not preformed at TCHC because manufacturers do not require this as part of the supporting documents. At TCHC, all new applications are submitted via either fax or mail, with the latter method producing slightly longer application times. At TCHC, all new applications are submitted via either fax or mail, with the latter method producing slightly longer application times. The original PAP applications are never destroyed, and only 1 copy of the application is kept on record. Although some manufacturers accept online orders, the majority of refill renewals are communicated through a toll-free telephone number. The personnel time required to renew an application is significantly less than the time needed to process a new application. However, Clay et al. did not address the costs of renewing applications.

The monetary imputation estimated by Clay et al. may not have adequately captured the entire cost necessary to operate a PAP. First, the authors only accounted for the direct costs (e.g., personnel, supplies, application submission fees), required to process an application and dispense medications. Indirect costs such as utilities, office space, furnishings and equipment, as well as storage were not included in their final calculation. The overhead expenses may also include salary costs of providers and other patient advocates since they, too, have an active role in ensuring proper functioning of the PAP. In addition, if clinics wish to utilize the computerized application method, the cost of necessary software and associated expenses should be considered in the budget calculation.

Second, the authors’ personnel cost estimate was based solely on the salary of medical assistants, who have relatively low payroll expenses, and excluded costs for any managerial oversight or pharmacy involvement. Providing PAP with the goal of improving patient outcomes requires a team effort from a variety of patient advocates. One also needs to be mindful that the tasks required for PAP submissions and delivery are typical of the functions of a pharmacist, particularly the ability to accurately interpret a prescription, dispense the medication, and deliver appropriate patient education. Without patient education, the full benefit of PAP may not be evident because a lack of patient education may contribute to medication errors and can negatively affect patients’ health outcomes. Inclusion of a clinical pharmacist to support PAP is vital to its effectiveness given the specialized training pharmacists receive. Roles of a clinical pharmacist supporting PAP administration by a medical group or clinic may include but are not limited to: (a) making accessible and effective recommendations for therapeutic interchange; (b) serving as a liaison between the patient, other health care professionals, and the program; (c) dispensing sample medications while patients await PAP coverage; (d) providing coordination of care; (e) providing patient counseling; (f) overseeing other support staff to verify prescriptions; and (g) maintaining an updated formulary.

If inclusion of a pharmacist is not a viable option for the medical clinic, the time and resources needed to educate non-pharmacy personnel on methods to ensure medication safety should be accounted for as well as the potential for staff turnover. Alternatively, pharmacy technicians, social workers, or other support staff working under the supervision of a pharmacist may be an effective and less costly choice to administer the program. Pharmacist-coordinated PAP programs in various settings have demonstrated net cost-savings to justify the higher pharmacy personnel costs.

Third, medication delivery may take 2 to 6 weeks, so other means to bridge with an accessible and affordable therapeutically equivalent alternative may be necessary while waiting. This is a potential area for medication errors since patients are at risk of duplicating drug therapies if they do not receive proper counseling to discontinue the bridge medication. Furthermore, if dose adjustment is needed during this period, a patient may incorrectly administer the medication ordered at the previous dose without appropriate education.

Fourth, Clay et al. apparently did not measure the time required for providers to review patient charts to ensure that appropriate medication doses are dispensed. Additionally, staff to provide coordination of care is needed to avoid potential missets and overlap that can affect the effectiveness of the PAP. For example, the drug manufacturer only allows one shipping address but medications in a PAP could be ordered independently by a specialist that does not practice in the same location as the primary care provider. If a patient has an established PAP through the primary care provider, all medications from that manufacturer will be delivered to the patient’s primary care clinic. Hence, coordination of care between specialists and the primary care provider becomes essential for proper patient monitoring which makes outsourcing PAP a less attractive option.

Calculating the true cost to deliver PAP services is important to the implementation, maintenance, and improvement of these programs. However, while financial considerations play a significant role, other factors such as patient needs and outcomes are essential for consideration. Despite the necessary expenses involved in administering PAP, the net financial and human benefit generated from PAP for patients and health care providers can be enormous. Examples of cost-savings from the establishment of PAPs have been demonstrated in a renal transplant clinic (a minimum of $4 was returned to the institution for $1 spent in the pharmacist’s time). Additionally, a PAP at a medical center clinic resulted in cost savings of $237,985 over 6 months.
yielding a benefit-to-cost ratio of 2.2:1.\textsuperscript{18} Nykamp and Ruggles reported that maintaining adherence to needed medications improves care for underserved patients and leads to decreased health care expenditures.\textsuperscript{13} This financial information can be useful to help obtain funding or calculate cost-sharing strategies necessary to offset the administrative expenses.

Without PAPs, it will be nearly impossible for a nonprofit clinic serving a large underserved population to financially afford the high cost of medications through the discounted 340B drug-pricing program. Nevertheless, underserved patients will not be able to afford the sliding scale fee associated with the brand medications, and the uncompensated cost from medication expenditures will eventually be absorbed by the clinic, resulting in further debt. The last option would be to deny patients the medications they need that will, in turn, increase the overall health care expenditure through hospitalizations and nursing home admissions, and emergency services.\textsuperscript{13} Numerous patients at TCHC have affirmed, “If it were not for PAP, I would not take my medications.” Therefore, medical facilities that serve a large indigent population will benefit from investing in the programs by safety net providers.


Judy T. Chen is a pharmacotherapist responsible for providing pharmacy consultation through referrals from PAP clerks, providers, and other allied-health professionals at the Tippecanoe Community Health Clinic. Kent H. Summers discloses no potential bias or conflict of interest relating to the subject of this article.

DISCLOSURES

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Affordability is an especially significant problem for those on specialty pharmaceuticals. These products are substantially more expensive than traditional, chemical-based products. The Express Scripts Drug Trend Report indicates that the average cost of a prescription for a specialty product in 2006 was $1,454. Patients typically filled between 4 and 10 prescriptions per year for each specialty product prescribed for them. The Wall Street Journal reported that the price for cancer treatment with specialty products can range from $36,000 to $56,000 per patient. Some insurers have created specialty copayment tiers in pharmacy benefits for these products that require patient coinsurance of 20% to 50%. Even though coinsurance payments in these programs are often limited by out-of-pocket payment limits of $100 to $250 per prescription fill, these coinsurance amounts may exceed the ability to pay for many health plan members. Further, the high cost of most specialty products, many for chronic conditions, contributes to total medical costs that can push patients over insurance policy life-time maximum amounts, leaving them without insurance coverage. A recent Wall Street Journal article noted that the cost of treatment with Myozyme, a specialty drug used to treat a rare enzyme disorder, may be as much as $300,000 per year.

Pharmaceutical company patient assistance programs (PAPs) offer one potential solution to the problem of affordability of prescription drugs. These programs provide pharmaceuticals to medically indigent patients for free or for substantially reduced prices. The Pharmaceutical Research and Manufacturers Association (PhRMA) indicates that these programs provided $5 billion worth of free drugs to needy consumers in 2005. A number of studies have documented the savings generated by these programs for consumers, health centers, and hospitals. For example, Sarrafizadeh et al. reported that a private ambulatory care clinic in upstate New York saved $48,143 by using patient assistance programs for 44 patients during a 1-year study period. Johnson indicated that the H. Lee Moffitt Cancer Center saved $1.5 million in 2006 as a result of using PAPs for indigent patients. Hotchkiss reported savings of $7,000 per month in a state psychiatric facility that served about 46 patients each month. Chisholm et al. indicated that use of PAPs resulted in cost avoidance of between $69,000 and $125,000 in a transplant clinic in a university teaching hospital for the 1998 calendar year. Coleman et al. reported net savings of $57,000 over 6 months for indigent inpatients in a Connecticut hospital.

As Clay et al. documented in an article in a previous issue of JMCP, PAPs are not without costs. While the drug product may be provided free of charge, the health care provider or organization realizes substantial costs in applying for and distributing the products. An application must be submitted for each product requested. Different manufacturers have different application processes, many of which are complicated and lengthy. Some applications require documentation of patient need or require that documentation includes the patient’s tax returns. While some manufacturers allow for refills, many require a new application for each refill. Application processes may change without notice at any time. Pharmacists, social workers, and/or trained clerical personnel are typically involved in completing application forms and applications always require some degree of physician involvement. In a national survey of safety net clinics, Duke et al. reported that the most common reason for not using PAPs was that they were “too time consuming and complex,” followed closely by “unrealistic income documentation requirements for indigent patients.”

Large providers, such as pharmacies in university teaching hospitals, may have fewer problems administering PAPs because their large scale may allow the use of bulk replacement programs. These allow pharmacies to dispense PAP products to indigent patients without completing the manufacturer application.
process. Most hospitals have financial counselors or financial assistance specialists who determine patients' insurance status and ability to pay their hospital charges. These same financial assistance specialists can be used to determine whether patients qualify for PAPs. Once individuals are deemed to be qualified by the financial counselor, the pharmacy dispenses their PAP medications and notes that the medications were dispensed for a PAP patient. At the end of each month (or quarter, depending on the manufacturer's policy), the pharmacy determines the quantity of each manufacturer's drugs dispensed to PAP patients and sends a report with this information to the manufacturer. The manufacturer then ships the pharmacy a sufficient quantity of each product to replace what was dispensed to PAP patients.

The costs that providers, institutions, and patients incur in using PAPs have not been well documented. Most of the available research has been limited to estimation of the short-term, direct costs of operating PAPs from the health care institution's perspective. Most researchers have focused on the costs of pharmacists, technicians, and other employees—such as social workers or patient registration technicians—employed to manage the process of applying for and dispensing PAP drugs. For the most part, these studies have not included the time, overhead costs to the institution, or patients' time. However, the magnitude of savings that have been attributed to PAPs suggest that they would be cost-effective even after consideration of these additional costs. In one of the most comprehensive cost studies, Richardson and Basskin surveyed a national sample of safety net clinics and hospitals in 2000. They calculated the net benefit of PAPs by subtracting the cost of providing the program from the total value of medications received through the programs; the 340B acquisition prices were used to value the medications. Costs included labor, equipment, and miscellaneous (i.e., postage and mailing). The median annual net benefit for their sample ranged from $48,000 for clinics with outpatient medication budgets under $500,000 to $877,000 for hospitals with outpatient medication budgets over $500,000.

PAPs may also be associated with costs that are longer-term and more difficult to quantify. PAPs operated by the research-intensive pharmaceutical companies, which operate the great majority of PAPs, are almost always restricted to expensive, patented, brand-name products. Consequently, physicians who treat medically indigent patients frequently face the choice of providing a “free” PAP drug or an equally effective generic alternative. While the PAP drug is cheaper in the short run, it may be more expensive to both the health care system and the patient in the long run. In the short run, the “free” drug solves the physician's problem of providing therapy to a patient unable to pay for needed prescriptions. In the long run, however, PAPs may increase costs.

First, the use of PAP drugs may disrupt the formulary process. Physicians may become accustomed to using expensive, non-formulary PAP products rather than the generally less expensive formulary products. To the extent that this practice spills over to prescribing for non-indigent patients, health system costs increase. If, or when, PAP coverage ends, the patient faces paying for a much more expensive product or being switched to another product. Switching products is also not without costs; patients may be required to make additional physician visits and undergo additional laboratory tests to be stabilized on the new drug. Similarly, if an uninsured patient gains insurance coverage, the insurance company must either pay for a more expensive product or pay to have the patient switched to a new product.

Second, PAPs may also deflect attention from finding a more comprehensive solution to the problem of affordable drugs. The existence of PAPs supports the illusion that affordability of prescription drugs is not a problem because there is a mechanism through which all patients, regardless of income, can get the drugs they need. In fact, there are large numbers of consumers who are unable to afford needed prescription drugs and who are ineligible for or unaware of PAPs. The Partnership for Prescription Assistance program, which includes but is not restricted to pharmaceutical company PAPs, provided prescription drugs for more than 3.6 million consumers in its first 2 years of existence, from April 2005 to April 2007. While this is a substantial number of consumers, it is a fraction of the 81.8 million without insurance at sometime during that period. Further, it is a smaller number than the 5.5 million working and privately insured consumers who did not get needed medicines due to cost concerns during 2003.

Finally, PAP drugs, like all products and services, cannot be provided free of cost. Their cost is ultimately borne by cash-paying consumers in the form of higher drug prices and by insured consumers in the form of higher insurance premiums, deductibles, and copayments. PAP drugs are best used as part of a comprehensive program of therapeutic selection in which PAPs are one component of a multifaceted strategy to improve access to medications, such as the pharmacist-directed intervention described previously in JMCP by Stebbins et al. for one large medical group California.

How one views PAPs depends on one's perspective. In the short run, they provide billions of dollars of prescription drugs to consumers who might otherwise be denied needed drug therapy. In the long run, PAPs may actually exacerbate the problem of access to prescription drugs by deflecting concern about the issue of affordability and by contributing to the use of higher-cost drugs. Despite their long-term costs, it seems likely that PAPs will continue to be necessary and heavily-used until a more comprehensive solution to the problem of prescription drug affordability is developed.

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 ADD or ADHD or What Exactly?—GIGO Part II and Other Lessons in Research with Administrative Claims

In this issue of *JMCP*, Wu et al. examined administrative claims data for a population of approximately 5 million beneficiaries to identify 4,569 adult patients who received at least 1 pharmacy claim for long-acting (osmotic release oral system [OROS])-methylphenidate (MPH), mixed amphetamine salts extended release (MAS-XR), or atomoxetine, and had at least 1 medical or facility claim with a diagnosis code for attention deficit disorder (ADD) or attention deficit/hyperactivity disorder (ADHD). In 6 months of follow-up, the median duration of therapy with OROS-MPH was 99 days versus 128 days for MAS-XR and 86 days for atomoxetine. The unadjusted median total all-cause medical cost ($1,062) for the cohort of OROS-MPH patients (n=1,452) was 1.7% less than the total all-cause medical cost ($1,080) for MAS-XR patients (n=1,554), and 16.4% less than $1,271 for atomoxetine (n=1,563). The median total all-cause medical cost for the MAS-XR cohort was also less than the cost for the atomoxetine cohort. Mean total medical cost for the atomoxetine-treated patients was higher than for either OROS-MPH or MAS-XR, but the mean costs for OROS-MPH and MAS-XR patients did not differ significantly.

Wu et al. clearly warn us that these are all-cause medical costs, not ADD/ADHD-related medical costs. In fact, these authors identify for us that the difference in total medical costs among the 3 cohorts is influenced by a few cost-outlier cases. The highest-cost case for OROS-MPH was $35,597 versus $134,712 for MAS-XR, and $55,950 for atomoxetine. The diagnosis codes associated with the highest cost claim for the MAS-XR outlier were chronic kidney disease (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 585.xx) and iron deficiency anemia (ICD-9-CM code 280.9). The diagnosis codes associated with the highest-cost claim for the atomoxetine outlier were acute myocardial infarction (ICD-9-CM code 410.21) and paroxysmal ventricular tachycardia (ICD-9-CM code 427.1). These cost-outlier cases have no apparent relationship to ADD/ADHD itself or to an increased rate of accidents among ADD/ADHD patients, a premise underlying the measurement of total medical costs rather than only the costs for services with an ADD/ADHD diagnosis.

Also in this issue of *JMCP*, Olfson et al. examine administrative claims data for 55 million beneficiaries to derive 2 cohorts of non-elderly adult (age 18-64) users of extended-release (ER)-MPH drugs (n=2,833) versus immediate-release (IR)-MPH (n=2,289) who had at least 1 outpatient medical claim with a diagnosis code for ADD/ADHD. This research informs us that less than one-third (30%) of adult patients who received MPH had a medical claim for ADD or ADHD. The authors’ focus in this study was continuity or length of MPH therapy in adult ADD/ADHD patients, and the median duration of treatment with the index MPH medication was 68 days (95% confidence interval [CI], 65-71 days for ER-MPH versus 39 days [95% CI, 33-52 days] for IR-MPH). Although this difference of 29 days is statistically significant, the clinical and practical significance are unknown and no doubt small. Olfson et al. also inform us that only 51% of the IR-MPH patients and 61% of the ER-MPH patients had more than 1 pharmacy claim for the index MPH medication. Notably, the proxy measure for once-daily dosing employed in this study, a days supply equal to the number of units dispensed, was met by only 62% of ER-MPH patients even though ER-MPH’s 8-hour duration of effect was a premise underlying the authors’ comparison of ER-MPH with IR-MPH.

On the one hand, administrative claims aggregated in relational data warehouses create wonderful opportunities for data mining to answer research hypotheses. On the other hand, data torture can result when the limitations of claims data are underestimated. Researchers using administrative claims data would do well to remember that the primary purpose of a claim is obtaining payment for services rendered, not supporting research activities. Previously, Barbuto warned about the danger of garbage in, garbage out (GIGO) arising from manipulation of diagnosis codes for purposes of insurance coverage for patients or for reimbursement purposes for providers. For example, tension headache was replaced by migraine diagnoses in medical claims for reasons that had nothing to do with clinical presentation or actual diagnosis and everything to do with category of insurance coverage.

Some of the shortcomings of administrative claims to describe clinical conditions are made evident by example. In literature in which authors assess utilization or costs associated with ADD or ADHD, various ICD-9-CM codes are used to identify the condition. In their examination of the total health care costs of children with “ADHD” compared with children without ADHD and children with asthma, Chan et al. identified the ADHD sample by ICD-9-CM code 314, hyperkinetic syndrome of childhood. Kemner and Lage used more stringent criteria in their study of the association between MPH formulation and health care utilization in patients age 6 and older. Like Wu et al., Kemner and Lage identified ADHD using codes 314.00, attention deficit disorder without mention of hyperactivity, and 314.01, attention deficit disorder with hyperactivity. Yet another set of criteria was used in a study of psychotherapeutic medication utilization by children (ages 5 to 14) with ADHD. In this analysis, Zito and colleagues attributed a physician office visit to ADHD if it was coded with a diagnosis of 314.0, attention deficit disorder; 314.01, attention deficit disorder with hyperactivity; or 314.9, unspecified hyperkinetic syndrome; or if “restlessness” was indicated “as the reason for the visit” on a data collection form completed by the physician or office staff.

This variability in the diagnostic criteria employed in research possibly reflects ambiguities inherent in the coding...
Attention deficit disorder is also known as attention deficit/hyperactivity disorder (AD/HD or simply ADHD). The Guiding Principles for the Diagnosis and Treatment of Attention Deficit/Hyperactivity Disorder provide a succinct overview of the opportunities for misdiagnosis and variable quality of care in the treatment of patients suspected of having ADD or ADHD.\(^9\) The medical coding of ADD or ADHD can be precise or imprecise. ADHD if coded according to the apparent plain meaning of the language used in the ICD-9-CM would be identified on the medical or facility claim as 314.01 (attention deficit disorder with hyperactivity) which includes in the 2007 code descriptions “combined type”, “overactivity NOS” (not otherwise specified), “predominantly hyperactive/impulsive type,” and “simple disturbance of attention with overactivity.”\(^4\) But what about patients with ADD without hyperactivity? ICD-9-CM code 314.00 is defined as “attention deficit disorder without mention of hyperactivity.” Thus, the taxonomy of this disorder seems to produce the oxymoronic situation that patients with ADD coded as 314.00 (no hyperactivity) are a subset of 314 (hyperkinetic syndrome) but are commonly referred to as patients with “ADHD.”

So, what difference does it make if one researcher uses the broad ICD-9-CM code 314 to describe “ADHD” research, encompassing ADD both with and without hyperactivity, whereas another limits the study population to the specific code 314.01 that explicitly includes hyperactivity? The answer is that we do not know. However, it seems quite likely that a narrow code such as 314.01, specific to ADHD, will identify fewer patients in an administrative claims database compared with a broad code such as 314. For those that like symmetry, at least we can say about patients with ADD without hyperactivity? ICD-9-CM code 314.00 is defined as “attention deficit disorder without mention of hyperactivity.” Thus, the taxonomy of this disorder seems to produce the oxymoronic situation that patients with ADD coded as 314.00 (no hyperactivity) are a subset of 314 (hyperkinetic syndrome) but are commonly referred to as patients with “ADHD.”

The 3-character ICD-9-CM codes with 2-character modifiers create a seductive illusion of granularity in medical claims coding. The reality is less seductive. Although it is true that the medical diagnosis of ADD or ADHD can be precise, it is not known how many physicians spend the time necessary to precisely diagnosis these conditions and tailor treatment, including behavioral therapy as well as drug therapy. What is likely is that busy primary care physicians in submitting bills to payers do not typically make the fine differentiation between ICD-9-CM codes 314.00 and 314.01 for ADD without or with mention of hyperactivity, or for that matter, 314.0 for ADD alone. In fact, the Superbill maintained by the American Academy of Family Practice of the codes most common in office-based, outpatient practice lists “314.00, attention deficit w/o hyper-activity” as the only code under 314.\(^10\) So, it is probably acceptable to use ICD-9-CM code 314 with most suffixes for the purpose of research on ADD/ADHD when analyzing administrative claims, but this does not mean that the patients with medical claims having this code share a common pathology or, accordingly, that they would necessarily be expected to respond to the same drug treatments in the same way.

Olfson et al. describe the distribution of patients by “ADHD” subtype in their study of adult patients with “ADHD,” and the group that had an index pharmacy claim for ER-MPH was different than the group that received IR-MPH (\(P < 0.001\)).\(^2\) Code 314.01 accounted for 46% of the patients that received ER-MPH and 39% that received IR-MPH. Code 314.00 (without mention of hyperactivity) accounted for 48% of the patients that received ER-MPH and 53% of the patients that received IR-MPH. Approximately 6% of the ER-MPH patients and 8% of the IR-MPH patients had a 314 code other than 314.01 or 314.00. The clinical or practical significance of these differences is unclear.

This possibility of heterogeneity in patient populations designated with there results broad ICD-9-CM code 314 leads to a challenge in interpreting the existing literature that describes research on the utilization and costs associated with ADHD. Variability of sampling methods, and possibly of billing practices in different health care systems, means that readers have no way of knowing whether a sample population is sufficiently homogenous and representative of ADHD for the results to be clinically meaningful. Moreover, researchers face a challenge in trying to replicate the methods used in the published research when they are uncertain or skeptical of the specific rationale underlying methodological decisions. For example, Chan et al. examined health care resource utilization in children with ADHD and concluded that a diagnosis of ADHD was similar to a diagnosis of asthma in the magnitude of consumption of health care resources.\(^5\) The authors reported use of ICD-9-CM code “314” to identify “eligible children” with ADHD and assuage the reader by also requiring the presence of at least 2 pharmacy claims for “psychostimulant medications” (e.g., MPH, MAS, or pemoline) stating, “these medications are rarely used for other conditions, except narcolepsy.”

In the larger context, we need to maintain a healthy respect for the shortcomings of administrative claims data and resist the seduction inherent in thousands of specific codes that may or may not be used precisely by coders in medical clinics where the primary purpose of these codes is reimbursement, not differential diagnosis. This area of research in ADD/ADHD, perhaps representative of much of the field of research with administrative claims, needs a lot more specificity and consistency in description of the rationale underlying methods, particularly in the selection of patients by diagnosis and procedure codes.
Garbage in predicts garbage out even with thoroughness in description of methods, but complete and transparent description of methods and results will better inform us about what is in the “garbage.”

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The Elephant in the Pharmacy: Patient Choice Is the Big Challenge That No One Talks About in Affordability of Prescription Drugs

In May 2004, 66-year-old retired electrician Raymond Lindell was arrested in Mexico a few minutes after filling a prescription for 270 tablets of Valium 10 mg at a pharmacy in Nogales, Sonora. Lindell, an Arizona resident, was charged with failing to obtain a duplicate prescription for the controlled substance from a Mexican physician as required by Mexican law. He was further charged with obtaining the medication for another person, his 73-year-old chronically ill wife, and with obtaining more than the legally permissible 30-day supply. Lindell was released after 8 weeks in a Mexican prison, but not before triggering a highly publicized political fracas that included a citizen’s petition drive on his behalf, a boycott of Mexican border town pharmacies by frightened senior citizens, a media campaign by Nogales business leaders to restore customer confidence, and high-level discussions among government officials from the states of Arizona and Sonora. When asked why he had chosen to travel to Nogales, a driving distance of nearly 4 hours, to purchase brand-name Valium rather than fill his wife’s prescription for a much less expensive generic medication in the United States, Lindell answered that their insurance company had stopped paying for brand-name Valium and his wife was dissatisfied with generic alternatives because they “didn’t seem to work.”1,2

When health care professionals speak of prescription drug affordability, they typically refer to several important factors: rising medication cost, escalating copayments, and increasing health insurance premiums, to cite a few. But the problem that we too often fail to acknowledge openly—perhaps because it is so much more difficult to address than the others—is the ubiquitous and sometimes counterproductive effects of the choices made by patients and family members.

Human beings do not always make wise decisions, and there is much about consumers’ health care decision making that we do not know. How many of the uninsured could afford health insurance premiums but are simply taking the gamble that they are young and healthy now and do not need coverage? Among non-elderly adults in the United States, the likelihood of being uninsured peaks in the 18- to 24-year-old age group at 50%, compared with 33% for those aged 25 to 44 years and 17%-20% for those aged 45 to 64 years.3 How many of those who report that they have foregone medical insurance coverage because of its cost choose to spend the money on leisure activities or consumer goods? Lower income is clearly associated with lack of medical coverage; of those with annual incomes below 200% of poverty level ($37,320 for a family of 4), 57% are uninsured.3 Yet of 81.8 million Americans under age 65 without health insurance in 2002-2003, 13.5 million, about 16%, had incomes exceeding 400% of poverty level ($74,040 annually for a family of 4), and 22.6 million, about 28%, had incomes exceeding 300% of poverty level ($55,980 annually for a family of 4).3

Medication choices are not always made wisely either, as the Lindell case illustrated with nearly tragic results. How often do patients seek an expensive brand drug out of ignorance of the benefits and therapeutic or chemical equivalence of generic medications, with the unfortunate consequence that they find full compliance too expensive and curb or even terminate their treatment? In a study of medication-taking behavior following the initiation of chronic therapy, patients initially treated with generic medication were less likely (13.6%) than those treated with preferred brands (19.9%) or nonpreferred brands (28.3%) to switch to a product in a different tier.4 The percentage of days covered (PDC) was 6.6 percentage points higher for generic users (58.8%) than for users of nonpreferred brands (52.2%), and the odds of adherence (defined as PDC > 80%) were 62% higher for generic users than for nonpreferred brand users.

National Medical Expenditure Panel Survey data suggest that only 61% of U.S. multisource drug sales from 1997 to 2000 were dispensed as generic; an estimated 11% savings would have resulted from generic conversions on the basis of chemical equivalence alone.5 An unpublished pharmacy benefits manager study estimated unrealized potential savings from combined therapeutic and chemically equivalent substitution in 6 therapy classes (antidepressants, antihyperlipidemics, antihypertensives, calcium channel blockers, gastrointestinal, and nonsteroidal anti-inflammatory drugs) at $21.7 billion for commercially insured members in 48 states during 2005.6

Yet, in surveys, about 20%-40% of health care consumers express the belief that generic medications are lower in quality or effectiveness than brand medications.7-10 Moreover, the perceived risk of using a generic instead of a brand medication varies with seriousness of illness, with the percentage increasing for the chronic illnesses most often targeted by generic substitution programs. In a willingness-to-pay survey assessing the likelihood of generic use by health condition, the percentage of consumers rating a generic drug as riskier than a brand drug to treat a heart condition (53.8%) was higher than comparable ratings for hypertension (44.0%), strep throat (22.0%), pain (18.9%), or cough (14.2%).8

In addressing the question of health care choices, including patients’ decisions about whether to comply with treatment, policy analysts too often limit their focus to out-of-pocket cost, sometimes ignoring human idiosyncrasy. The willingness-to-pay survey results suggest that a single-minded focus on out-of-pocket cost is likely to yield limited results; when rating how much of a generic versus brand cost differential would be necessary to encourage the acceptance of generic medication to treat a heart condition, 27.2% of respondents said that they would not use a generic at any cost saving.8 Given the reality that evidence does not always support the choices that human beings make, how can we do a better job of promoting good choices?

Put 20 health care economists in a room, and you might get 20 different opinions about the crucial question of aligning
consumer and provider behavior with desired outcomes. Critics of tiered copayment structures or other cost-sharing schemes point out that an insured worker's average out-of-pocket cost for a brand drug has increased considerably in recent years, by 84% for preferred brand medications (from $13 in 2000 to $24 in 2006) according to recent estimates, but rarely mention that the average out-of-pocket cost per prescription for a generic medication—$11—is much lower than the brand cost. Nor do these critics typically put the problem into context by pointing out that the share of total pharmaceutical spending paid by consumers has dramatically declined over time. In 1990, consumers paid 56% of prescription drug expenditures out of pocket. Just 10 years later, the consumer share of prescription drug cost declined to 28%. In 2005 it was 25%, and in 2006 it is projected to decline even further to 19% in large part because of the Medicare Part D program. \(^{11}\) Are further declines in the share paid by consumers the solution to the (as yet not completely understood) problem of prescription drug affordability? Would such declines be sustainable over the long term, or even the short term, in any third-party coverage system?

Some have argued that the solution to aligning consumer behavior with desired outcomes lies in value-based insurance design in which out-of-pocket cost would be highly targeted based on the presumed value of the medication in a patient's particular clinical situation. For example, a very low copayment would be charged for beta-blocker therapy in congestive heart failure patients. \(^{12}\) A similar proposal in England would require the National Health Service to pay for branded medication based on value, with higher payments for more effective drugs and lower payments for "me too" and less effective drugs. \(^{13}\) While the value-based approach is promising, it is also untested; the industry awaits comparative studies of its merit, much as it implemented 3-tier copayment designs some 15 years ago, before their outcomes had been assessed. And when long-held assumptions are tested using strong research designs, they are not always supported. For example, in the run-up to passage of Medicare Part D coverage, assertions that better access to prescription drugs would reduce medical expenses were common. Yet in a well-controlled study of the effect of providing prescription coverage to seniors, Briesacher and colleagues found that acquiring prescription drug coverage resulted in increased expense for prescription medications without any observable consistent effect on medical service costs. \(^{14}\)

While we await evidence, payers, providers, and patients seek solutions to the problem of prescription drug affordability as they understand it. This issue of JMCP has 2 commentaries regarding the value versus cost of prescription assistance or patient (medication) assistance programs (PAPs). In a previous article in JMCP, Clay et al. found that a medical clinic incurred administrative costs of $10.42 per patient for a brand drug that requires 1 application per year and up to $46.30 per patient for a drug in a PAP that requires 4 (re)applications per year. \(^{15}\) Chen and Summers assert in their follow-up commentary in this issue of JMCP that PAPs are an essential part of the frayed fabric that supports health care services for low-income persons who don't qualify for Medicaid or other public programs. \(^{16}\) Carroll, in a second follow-up commentary in this issue, presents an alternative view, that PAPs may incent providers to adopt a short-term solution—providing a "free" brand-name drug to a lower-income patient instead of a generic medication that might be less expensive and equally effective. \(^{17}\)

Examples of potentially perverse incentives associated with PAPs abound. Paroxetine (Paxil) CR costs approximately $107 per month of therapy in mid-2007 compared with generic paroxetine at $21 per month of therapy, both dosed once per day. Paxil CR has no generic equivalent but is the same molecule as generic paroxetine, with no evidence of therapeutic inequivalence to paroxetine, meaning that 5 patients can be treated with generic paroxetine for the same cost as 1 patient treated with brand paroxetine CR. \(^{18}\) Or consider the cost of generic simvastatin at $26 per month of therapy in mid-2007 versus $100 per month of therapy with therapeutically equivalent atorvastatin (Lipitor). All of this leaves us with another fundamental question: Is subsidizing poor decisions necessary or even prudent?

These are difficult questions, perhaps even offensive questions to some, but they are essential questions if we are to define accurately the problem of affordability of prescription medications and to face head on and realistically the challenge of healthcare reform. To find evidence-based solutions, we need more answers—specifically, more answers to questions about why some patients comply with treatment, including prescribed medication, and why some do not. We need better information about the degree to which out-of-pocket cost reductions and cost differentials influence patient behavior and how pharmacist-directed intervention such as that described previously by Stebbins et al. \(^{19}\) and suggested by Chen and Summers might affect the actual realized value of pharmacotherapy. Clay et al. helped define the administrative cost incurred by a medical clinic in assisting patients with PAPs but did not address pharmacist intervention or other systematic education of patients in how to use the drugs. \(^{15}\) However, Clay et al. opened the door a little wider for others to measure what patients do with these brand drugs obtained via PAPs and how these outcomes compare with a more comprehensive pharmacist-directed intervention in which PAPs are a relatively small part of attaining affordable drug therapy.

Finally, to base decision making on evidence instead of presupposition, we need rigorous studies to determine which interventions effectively influence patient choice and which do not. Much of the research in benefit design policy is plagued by weak cross-sectional and pre-post analyses, which are prone to confounding even after appropriate statistical controls are used. We call for studies employing stronger quasi-experimental
and experimental research designs to provide solid information about how to persuade the elephant in the pharmacy to move in the desired direction—at least occasionally.

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Join Us in Boston and Make History!

It’s fitting that AMCP will convene its 2007 Educational Conference in the city where American history began — and this fall, the “shot heard ‘round the world” will not be the advance of the redcoats, but advances in managed care pharmacy. As in 1776, the winds of change are blowing.

No pharmacist is unaware of the erupting opportunities now assailing our practice: and chief among them, Medication Therapy Management is about to change the world (and health care) as we know it. Those who are already involved in these efforts know this revolution will require seamless integration across all pharmacy practice settings — managed care, community, consultant and specialty pharmacy. It’s clear that we’ll all have to work together and leverage each other’s strengths to deliver the value-added, high-quality patient care and services we all espouse.

And as usual, AMCP will feature the newest quality improvement and formulary management data, the most sought-after faculty, the hottest topics and newest clinical studies, as well as popular stand-bys such as the Managed Care Industry Forum, roundtable discussions, poster displays and networking receptions.

It’s also fitting that October is American Pharmacists Month — a time when each of us celebrates our unique place in the provision of health care and brings our contributions to the attention of the public. We urge you to join us in Boston this fall, and make history.

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AMCP’s Managed Care Industry Forum
Friday, October 26 | 12:30 pm–2:45 pm

A highlight of AMCP’s Educational Conference is the Managed Care Industry Forum. This unique event provides a setting in which to network with pharmacy colleagues in a relaxed, non-commercial environment. Every attendee is invited to attend this long-standing favorite event, featuring many returning key players in pharmacy as well as new faces representing innovative ways in which the managed care industry is evolving. The Forum serves as a separate but complementary event to AMCP’s Annual Showcase (our commercial exhibit show in the spring) by allowing both participants and exhibitors to network equally through the exchange of educational information only. Take advantage of this opportunity to discuss the latest issues and trends with other managed care pharmacy professionals. If your company would like to participate in the Forum, please call AMCP at 800-827-2627 or click on “MCIF Prospectus” under the Meetings/2007 Educational Conference section on our website to download the Prospectus.

Please see page 12 for a list of participants as of August 10, 2007.

Managed Care Pharmacy Residency Showcase
Friday, October 26 | 2:45 pm–6:00 pm

AMCP’s 10th Annual Managed Care Residency Showcase features a focused and intimate forum for pharmacy students to meet one-on-one with representatives from managed care pharmacy residency and fellowship programs across the country in preparation for post-graduate activities. This event provides students with the opportunity to determine firsthand if a particular residency program meets their needs and expectations, while networking with fellow students and sharing ideas on their future career plans. The Residency Showcase is also an opportunity for promotion of programs to potential candidates as well as to foster new relationships and exchange valuable information. As in the past, AMCP will hold its Student and New Member Reception in conjunction with the Residency Showcase to enhance attendance! If you are interested in showcasing your program, please call AMCP at 800-827-2627 or visit www.amcp.org to download the Prospectus.

Please note that there will be a Residency Preceptors Meeting on Friday, October 26. For more information, please contact Mark Brueckl at 800-827-2627 or via email at mbrueckl@amcp.org. Details will be posted on AMCP’s website as they become available.

Opening Night Reception
Wednesday, October 24 | 5:30 pm–7:00 pm

The Academy of Managed Care Pharmacy will welcome you to Boston and the 2007 Educational Conference at the Opening Night Reception. Join your colleagues for a relaxed evening of catching up and making plans for the days ahead. It’s a wonderful way to begin the 2007 Educational Conference.

Reception for Students and New Members
Friday, October 26 | 5:00 pm–6:00 pm

Don’t miss this special reception where you’ll have an opportunity to mingle with AMCP’s Board of Directors, AMCP Leadership, students from various schools of pharmacy, and new AMCP members in a relaxed, social environment. This reception will be held during the last hour of the Managed Care Pharmacy Residency Showcase. Please also make sure to stay for the student and new member drawing for complimentary registration to the 20th Annual Meeting & Showcase in San Francisco!
Thursday General Session — Christopher Gardner

Surmounting acute obstacles on his road to success, the amazing story of Gardner’s life was published as an autobiography, *The Pursuit of Happyness*, and inspired the Columbia Pictures’ movie of the same title, starring Will Smith.

Always hard-working and tenacious, a series of circumstances in the early 1980s left Gardner homeless in San Francisco and the sole guardian of his toddler son. Unwilling to give up Chris Jr. or his dream of financial independence, Gardner started at the bottom. Without connections or a college degree, he earned a spot in the Dean Witter Reynolds training program.

Often spending his nights in a church shelter or the bathroom of a Bay Area Rapid Transit station in Oakland, Gardner was the sole trainee offered a job at Dean Witter Reynolds in 1981. He spent 1983–1987 at Bear Stearns & Co., where he became a top earner, and then in 1987, he founded the brokerage firm Gardner Rich & Co. in Chicago.

Friday General Session — Regina Herzlinger, PhD

One of the most significant voices in health care reform today, Regina Herzlinger is known as the “Godmother” of consumer-driven health care — a term she coined and a movement she helped create.

An important researcher and analyst, she was an early predictor of the unraveling of managed care. Her solutions for structuring, financing and delivering health care are innovative, yet commonsensical.

Herzlinger has written three books on health care reform, including most recently, *Who Killed Health Care? America’s $2 Trillion Medical Problem — and the Consumer-Driven Cure*. This book is more than just an assault on the forces that are driving health care costs, driving down the number of people who are covered, and degrading patient care. It is also a manifesto, a powerful argument for consumer-driven reforms that already are transforming the system.

She is the first woman to be tenured and chaired at Harvard Business School, the first woman to teach in the school’s executive programs and the first to serve on a number of corporate boards.

Don’t Miss This Workshop!

Boston is fabulous in the fall! Stick around for a Saturday hands-on experience on building and interpreting pharmacoeconomic models with Dan Malone, PhD, and Ed Armstrong, PharmD, professors at the University of Arizona College of Pharmacy.

**Advanced Issues in Pharmacoeconomic Modeling: Evaluating Uncertainty and Interpreting Cost-Effectiveness Data**

Saturday, October 27
8:30 am–10:30 am

Keep checking back on the AMCP website for updates, schedules and final programming — we’re putting together a compelling roster of speakers, programs and events designed to keep you at the forefront of your profession!
You won’t want to miss the Academy of Managed Care Pharmacy’s (AMCP’s) 2007 Educational Conference — the largest assembly of pharmacy and health care professionals dedicated solely to the issues of managed care pharmacy. This conference will highlight a myriad of activities, initiatives, breakthroughs and partnerships that are shaping the future of managed care pharmacy.

Join your colleagues in Boston for this premier educational and networking event!

Featured Speakers cont’d

Friday Afternoon Session — Mark McClellan, MPA, MD, PhD

The Feature Presenter on Friday afternoon will be Dr. Mark McClellan, former Administrator for the Centers of Medicare & Medicaid Services.

Mark McClellan has had a highly distinguished tenure of public service. In the George W. Bush administration, he served as a member of the President’s Council of Economic Advisers and senior director for Health Care Policy at the White House (2001–2002), FDA commissioner (2002–2004), and CMS administrator from March 2004 until October, 2006.

Upon his retirement from government service, he joined the AEI-Brookings Joint Center for Regulatory Studies as a visiting senior fellow to work on developing and implementing ideas to drive improvements in high-quality, innovative, affordable health care. He is also an associate professor of Economics and associate professor of Medicine at Stanford University.

During the Clinton administration, Dr. McClellan was deputy assistant secretary of the Treasury for Economic Policy from 1998–1999, supervising economic analysis and policy development on a range of domestic policy issues. He subsequently directed Stanford’s Program on Health Outcomes Research and was a research associate of the National Bureau of Economic Research and a visiting scholar at the American Enterprise Institute.

Additionally, he was associate editor of the Journal of Health Economics and co-principal investigator of the Health and Retirement Study (HRS), a longitudinal study of the health and economic well-being of older Americans.

www.amcp.org
Tuesday, October 23
8:00 am – 5:30 pm
FMCP Program: Learning Institute for Management of Chronic Kidney Disease
(invitation only – please visit www.fmcpnet.org)

Wednesday, October 24
8:00 am – 2:30 pm
FMCP Program continued from Tuesday: Learning Institute for Management of Chronic Kidney Disease
8:00 am – 5:30 pm
AMCP Committee Meetings
12:00 noon – 7:00 pm
Registration
1:00 pm – 5:00 pm
Pre-Conference Symposia
5:30 pm – 7:00 pm
Opening Night Reception

Thursday, October 25
6:00 am – 8:00 am
Breakfast Symposia
7:00 am – 5:30 pm
Registration
continued below ...
7:00 am – 5:00 pm
AMCP Committee Meetings
8:15 am – 9:15 am
Educational Sessions
8:30 am – 12:00 noon
Managed Care Essentials
9:00 am – 1:00 pm
Lunch Symposia
9:30 am – 11:00 am
Workshop
11:30 am – 1:00 pm
Leadership Luncheon (invitation only)
Student Session I: Meeting Orientation/Luncheon
1:30 pm – 2:30 pm
Opening General Session
2:45 pm – 5:30 pm
Educational Sessions

Friday, October 26
6:00 am – 8:00 am
Breakfast Symposia
7:00 am – 5:00 pm
Registration
8:30 am – 9:30 am
Educational Sessions
9:00 am – 11:00 am
Round Table Discussions
9:45 am – 10:45 am
Educational Sessions
11:00 am – 12:30 pm
General Session
12:30 pm – 2:45 pm
Managed Care Industry Forum
Poster Presentations
Lunch in Hall
2:45 pm – 6:00 pm
Managed Care Pharmacy Residency Showcase
2:45 pm – 3:45 pm
Educational Sessions
4:00 pm – 5:00 pm
Educational Sessions
5:00 pm – 6:00 pm
Student and New Member Reception

Saturday, October 27
8:00 am – 10:30 am
Registration
8:30 am – 10:30 am
Workshop
10:30 am
Adjourn
SS1  Optimizing Antidementia Therapy to Provide Cost-Effective Quality Care for Patients with Alzheimer’s Disease: A Primer for Managed Care Pharmacists
Wednesday, October 24 | 1:00 pm–5:00 pm
Program Manager: Jacqueline Harracksingh | QED Communications/SCEPTER | Tel 914-829-4153
jacqueline.harracksingh@quintiles.com
This Satellite Symposium was made possible through an educational grant provided by Forest Laboratories.

SS2  The Unhidden Cost of Non-Compliance
Wednesday, October 24 | 1:00 pm–5:00 pm
Program Manager: Lauren Cole | Impact Education, LLC | Tel 704-548-5137 | lauren.cole@impactedu.net
This Satellite Symposium was made possible through an educational grant provided by MERCK/Schering-Plough Pharmaceuticals.

SS3  Blurring Lines of Medical and Pharmacy Management: The New Role of Specialty Pharmaceuticals
Wednesday, October 24 | 1:00 pm–5:00 pm
Program Manager: Lauren Cole | Impact Education, LLC | Tel 704-548-5137 | lauren.cole@impactedu.net
This Satellite Symposium was made possible through an educational grant provided by Merck & Co, Inc.

SS4  Specialty Pharmacy and Treatment Optimization: Applications for the Multiple Sclerosis Population
Thursday, October 25 | 6:00 am–8:00 am
Program Manager: Mara Simpson | Consensus Medical Education | Tel 303-662-1144
msimpson@consensusmedical.com
This Satellite Symposium was made possible through an educational grant provided by Teva Neuroscience.

SS5  Pharmacy Benefit Design: The Impact on Clinical and Economic Outcomes
Thursday, October 25 | 6:00 am–8:00 am
Program Manager: Chris Smelser | ProCE, Inc. | Tel 319-626-7680 | csmelser@proce.com
This Satellite Symposium was made possible through an educational grant provided by Takeda Pharmaceuticals North America.

SS6  The Benefits and Impact of Proper COPD Management
Thursday, October 25 | 9:00 am–1:00 pm
Program Manager: Nelson Rosado | CME Fission | Tel 646-742-3654 | nelson.rosado@fissioncommunications.com
This Satellite Symposium was made possible through an educational grant provided by Dey, L.P.

SS7  Optimal Formulary Design for Chronic Disease States: Balancing Outcomes and Costs
Thursday, October 25 | 9:00 am–1:00 pm
Program Manager: Nancy Fox | Health Insights | Tel 267-419-1710 | nfox@healthinsightsslc.com
This Satellite Symposium was made possible through an educational grant provided by P&G Pharmaceuticals, sanofi-aventis, and Bayer Healthcare Pharmaceuticals.

SS8  Optimizing Management of Schizophrenia and Bipolar Disorder Through Individualized Treatment Strategies
Friday, October 26 | 6:00 am–8:00 am
Program Manager: Chris Tebbin | CME Enterprise | Tel 317-208-3629 | christine.tebben@cmeenterprise.com
This Satellite Symposium was made possible through an educational grant provided by Solvay Pharmaceuticals, Inc. / Wyeth Pharmaceuticals.

SS9  A Case-Based Approach to Understanding the Expanding Challenge of Diabetes and Implications for Managed Care Organizations
Friday, October 26 | 6:00 am–8:00 am
Program Manager: Carla Brink | ASHP Advantage | Tel 218-728-1816 | cbrink@ashpadvantage.com
This Satellite Symposium was made possible through an educational grant provided by Novo Nordisk Inc.
Registration Policies

- **Government Rate**
  To receive the Government Rate, you must be a full-time employee of the federal government, a state government, or the U.S. Military.

- **Substitutions**
  Registrant substitutions will be accepted with written notification from the original registrant. An administrative fee of $30 (other fees may apply) will be assessed. Only one substitution per registrant is allowed. Registration cannot be transferred to other AMCP national meetings.

- **Cancellations/Refunds**
  Cancellation of participant registration must be requested in writing and must be received by Wednesday, September 26, 2007 in order to receive a partial refund. A $150 administrative fee will be assessed on all cancellations. No cancellation/refund requests will be granted after Wednesday, September 26, 2007.

- **No Shows**
  Registrants who do not cancel prior to AMCP’s 2007 Educational Conference and do not attend will be responsible for the full registration fee.

- **Suites and Meeting Rooms**
  Please visit AMCP’s website at www.amcp.org for information regarding suites and meeting rooms.

- **Grievance Policy**
  Should any registrant be dissatisfied with the quality of the continuing education programming during AMCP’s 2007 Educational Conference, a request in writing must be submitted to AMCP within five days of the conclusion of the program for consideration of a refund of registration fees.

- **Spouse Registration**
  Your spouse can register onsite to attend the receptions and the Managed Care Industry Forum. To register a spouse onsite, the meeting attendee must have a regular meeting registration. Identification is required for registration or pick-up of registration materials. Cost: $50.

- **Opening Night Reception Only Registration**
  Have friends and associates join you at this popular event. Cost: $95.

- **Just a reminder ...**
  All conference registrants must register either in advance or onsite at the conference. A valid photo ID must be presented at the registration desk when you check in to obtain your name badge and program materials.
Registration Form

AMCP’s 2007 Educational Conference • October 24–27, 2007 • Hynes Convention Center

Full registration fees must accompany this form for registration to be processed. Confirmations will be sent to all confirmed participants. If an email address is provided, confirmations will be sent via email. Questions? Call Experient at (847) 940-2107.

ATTENDEE INFORMATION [required]

First Name ___________________________ Last Name ___________________________

My AMCP Membership Number (if applicable) ___________________________ Title ___________________________

Company ___________________________ Address ___________________________

City ___________________________ State ___________________________ Zip Code ___________________________

Registrant’s Telephone ___________________________ Fax ___________________________

Registrant’s E-mail Address ___________________________

Administrative Assistant’s Email Address [optional] ___________________________

Emergency Contact and Telephone Number ___________________________

REGISTRATION FEES/CATEGORIES [please check the appropriate circle below]

Health Care Practitioner Member (physicians/nurses) $370 $190 $475 $295
Pharmacist Member (licensed pharmacists) $370 $190 $475 $295
Associate Member (non-pharmacists/physicians/nurses) $580 $295 $680 $390
Government Employee (AMCP member) $345 $195 $450 $300
Government Employee (non-member pharmacists/physicians/nurses)** $585 $345 $690 $450
Government Employee (non-member non-pharmacists/physicians/nurses)** $785 $635 $890 $540 Non-Member $795 $435 $895 $540
Student Member $40 N/A $40 N/A
Resident/Fellow/Graduate Member $80 N/A $80 N/A
Student Non-Member $60 N/A $60 N/A
Press N/A N/A N/A N/A

*If registering for one day, please indicate which day you will be attending: ☐ Wednesday ☐ Thursday ☐ Friday ☐ Saturday

**Registration provides a one-year AMCP membership (Government Employees only).

METHOD OF PAYMENT

☐ Check made payable to Experient/AMCP for $ __________ (in U.S. funds drawn on a U.S. bank)

☐ Charge $ __________ to my credit card (credit card will be charged immediately)

Visa ☐ MasterCard ☐ American Express ☐ Discover

CARD NUMBER ___________________________ EXPIRATION DATE (MONTH/YEAR) ___________________________

CARDHOLDER PRINTED NAME (as it appears on your card) ___________________________

CARDHOLDER SIGNATURE ___________________________

Ways to Register

• Online: www.amcp.org    • By fax: 800 521-6077

Mail: Experient/AMCP 108 Wilmot Road, Suite 400 Deerfield, IL 60015-5124

III. Which of the following best describes your job function(s)? (check one)

1. Pharmacists
2. Sales/Marketing
3. Administrative
4. Health Care/Pharma
5. Medical
6. Financial
7. Information Management
8. Health Plan/Managed Care
9. Other (specify)

IV. Are you a pharmacist?

☑ Yes ☐ No

V. Your reason for attending AMCP’s national meetings? (please choose all that apply)

1. Obtain Continuing Education Credits
2. Enhance Knowledge and Skills
3. Opportunity for Networking
4. Develop Personal and Leadership Skills

VI. Is this your first AMCP meeting? ☐ Yes ☑ No

Cancellation of participant registration must be requested in writing and must be received by Wednesday, September 26, 2007. A $150 administrative fee will be assessed on all cancellations. No cancellation/refund requests will be granted after Wednesday, September 26, 2007. Registrant substitutions will be accepted with written notification from the original registrant. An administrative fee of $30 (other fees may apply) will be assessed. Only one substitution per registrant is allowed. No registration transfers to other AMCP national meetings. Note: A valid photo ID must be presented during registration check-in to obtain your badge and meeting materials.
**Audience**

Health care professionals interested in, or who practice in, managed care, those who want to increase their knowledge of managing and coordinating pharmaceutical care programs, and those responsible for optimizing patient care and satisfaction with managed care.

**Learning Objectives**

By attending continuing education programming at AMCP’s 2007 Educational Conference, you will be able to:

- Discuss emerging issues and trends in health care and managed care pharmacy
- Describe successful collaborative practice models and their role in improving medication compliance, patient care, and outcomes
- Employ new professional development tools in your career in managed care pharmacy
- Cite new programs for formulary design, pharmacotherapies and disease management tools that will affect patient quality of life
- Identify and analyze new drugs, new classes of drugs, drugs for new indications, and the impact of new generic drug approvals that are currently moving down the pipeline
- Examine and discuss legislative and regulatory action influencing managed care pharmacy
- Summarize the important aspects of FDA Reform
- Discuss current and future issues related to the Medicare Part D prescription drug benefit and its impact on managed care pharmacy
- Examine and discuss different aspects of biotechnology and specialty pharmacy and their impact on managed care

Contact hours include all Managed Care Essentials, Contemporary Issues, Pharmacy Partnership Briefings, Round Table Discussions, Workshops, Friday General Session and the Saturday Workshop. Posters are not eligible for CE or CME. Your actual contact hours may vary depending on the number of sessions you attend.

**Accreditation Statement**

The Academy of Managed Care Pharmacy is approved by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. Individuals may obtain up to 12.5 contact hours of credit (excluding satellite symposia) or 1.25 Continuing Education Units (CEUs) during AMCP’s 2007 Educational Conference.

This Activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through joint sponsorship of CME Consultants and the Academy of Managed Care Pharmacy. CME Consultants is accredited by the ACCME to provide continuing medical education for physicians.

CME Consultants designates this educational activity for a maximum of 12.5 AMA PRA category I credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Attendees will be able to submit for their CE and CME certificates online via AMCP’s website and download a certificate of proof of attendance after the meeting has concluded. A certificate cannot be printed onsite. All CE and CME accredited activities have been brought to you by AMCP and are free of any commercial product endorsement.

**Americans with Disabilities Act**

AMCP and CME Consultants fully intend to comply with the legal requirements of the American with Disabilities Act. If any participant of this conference is in need of accommodation, please do not hesitate to contact AMCP at 800-827-2627 or visit the AMCP registration desk onsite at the meeting.

**FDA Disclosure**

The contents of some CME activities may contain discussions of off-label uses of some of the agents mentioned. Please consult the prescribing information for full disclosure of approved uses. The faculty is also aware it is their responsibility to inform the audience if discussion of any non-FDA approved uses of pharmaceutical, medical equipment, prostheses, etc. will be included in their presentation.

**Disclosure Statement**

In accordance with Policy, presenters have indicated if they have a conflict of interest and if so, it has been resolved.
MEMBER INFORMATION

Mr. Ms. Mrs. Dr. 

FIRST NAME LAST NAME 

TITLE 

ORGANIZATION NAME 

ORGANIZATION ADDRESS 

CITY STATE ZIP CODE 

HOME ADDRESS 

CITY STATE ZIP CODE 

SEND ALL MAILINGS TO MY: Company Address Home Address 

WORK TELEPHONE FAX 

HOME TELEPHONE CELLULAR TELEPHONE 

EMAIL ADDRESS (PRIMARY) 

EMAIL ADDRESS (SECONDARY) 

ANNUAL MEMBERSHIP RATES INFORMATION 

Pharmacist Member $240 per year 

Health Care Practitioner (Non-Pharmacist) Member $240 per year 

Associate Member $440 per year 

Student Member $35 per year 

Resident/Fellow/Graduate Member $85 per year 

METHOD OF PAYMENT 

Check made payable to AMCP for $ (in US funds drawn on a US bank) 

Charge $ to my credit card: Visa MasterCard American Express 

CARD NUMBER EXPIRATION DATE 

DEMOGRAPHIC INFORMATION 

PLEASE TELL US: 

I. What degrees/designations do you hold? 

B.S. Pharmacy Pharm.D. 

M.P.A. M.P.H. 

Ph.D. J.D. 

M.B.A. R.Ph. 

M.D. N.D. 

Other (specify) 

II. Which of the following best describes your employer? (check one) 

Association Medical Education 

Claims Processor Med/Physician Group 

College/University Not Employed/Retired 

Community Service Provider PBM/PBM Mail Service 

Consulting Firm Pharm Management/PSAO 

Government/Military Pharmaceutical Manufacturer 

HMO/PPO/Health Plan/IHS Press 

Home Care Retail Pharmacy 

Hospital Spec Pharmacy 

Information Management Wholesale/Distribution/GPO 

Legal/Advertising/Professional Services 

Long-term Care 

Mail Service Only 

Other (specify) 

III. Which of the following best describes your job function(s)? (check one) 

Asst Pharm Director/Not Employed/Retired 

Senior Pharm Management Nurse 

Clinical Coord/Operations Outcomes Research/Clinical Science 

Contracting/Purchasing Consultant 

Consultant Pharm Director 

Customer Service Pharm Manager 

Distrib/Supply Chain Physician 

Editorial President/CEO 

Editorial Prof/Trade Relations 

Formulary Management School/College Faculty 

Financial Management Staff/Clinical 

Formulary Management Pharmacists 

Legal/Govt Affairs 

Medical Affairs 

Marketing/Sales 

Medical Affairs 

Medical Director/CMO 

Med-Pharm Information Management/Education 

Network Management 

Other (specify) 

IV. How many years have you been in your current role? 

year(s) 

To join, return this form to AMCP:

AMCP
Academy of Managed Care Pharmacy
100 North Pitt Street Suite 400
Alexandria, VA 22314
Tel: 703-683-8416 Toll-Free: 800-827-2627
Fax: 703-683-8417 http://www.amcp.org
Thank You to Our Premium Level Sponsors!

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  - GlaxoSmithKline
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- **Silver**
  - AstraZeneca
  - sanofi-aventis
  - Sepracor

- **Bronze**
  - Astellas Pharma US, Inc.
  - Solvay Pharmaceuticals, Inc./Wyeth Pharmaceuticals

*as of August 10, 2007*
Please print or type. Please return this form with your conference registration. If an email address is provided, confirmations will be sent via email. Note: To arrange hotel accommodations, you must be registered for the conference.

**ATTENDEE INFORMATION [required]**

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**HOTEL INFORMATION**

- **Marriott Copley Place**
  - Rates: $249 single occupancy / $257 double occupancy

- **Westin Copley Place**
  - Rates: $249 single/double occupancy

- **Hilton Back Bay**
  - Rates: $249 single/double occupancy

**Arrival Date:** October __________, 2007  
**Departure Date:** October __________, 2007  
**Occupancy of Room:** [please check one]  
  - Single  
  - Double  

**ADA Requests:** [please check all that apply]  
  - Mobile  
  - Audio  
  - Visual  

**Special Requests:** [Based on availability. Special requests will be made on your behalf, but cannot be guaranteed. Non-smoking room, double/double beds, cribs, etc.]

**METHOD OF PAYMENT [All reservations require a $249 room deposit plus registration fee]**

- Check deposit made payable to Experient/AMCP for $ __________ (in U.S. funds drawn on a U.S. bank)
- Charge my credit card —  
  - Visa  
  - MasterCard  
  - American Express  
  - Discover

**Ways to Make Hotel Accommodations**

- **Online:** [www.amcp.org](http://www.amcp.org)  
- **By fax:** 800 521 6017  
- **By mail:** Experient/AMCP  
  - 108 Wilmot Road, Suite 400  
  - Deerfield, IL 60015-5124

**IMPORTANT HOUSING NOTES**

- You must be a confirmed registrant to obtain housing under AMCP’s block.
- All reservations require a $249 room deposit. Please note that your credit card will be charged when this form is submitted to confirm your room reservation.
- In the event that you decide to depart earlier than confirmed at the time you check-in, you will be charged a $50 early departure fee by the hotel.
- All new reservations should be made directly with Experient by 5:00 pm CDT Monday, September 24, 2007. After September 24, you may continue to contact Experient for reservation changes, cancel requests or new reservations (based on availability) until 5:00 pm CDT Wednesday, October 3, 2007. You can begin contacting hotels directly for all reservation needs starting Friday, October 12, 2007. Room cancellations must occur 14 business days prior to your arrival. Failure to cancel within the appropriate time frame will result in forfeiture of your entire $249 room deposit.
- When cancelling a reservation by telephone with the hotel, record the date, cancellation number, and the name of the person accepting the cancellation.
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<td>Managed Care/Biotechnology Healthcare/P&amp;T Journals</td>
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<td>Managed Healthcare Executive/Formulary</td>
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<td>Medco Health Solutions, Inc.</td>
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<td>MediMedia USA, Inc.</td>
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<td>Organon USA Inc.</td>
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<td>P&amp;G Pharmaceuticals</td>
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- Indicates Corporate Members
Boston, the big city in the convenient small city size!

AMCP looks forward to welcoming you to Boston! The City of Boston hosts over 12 million annual visitors from across the country and around the globe. This vibrant, thriving city is renowned for its cultural facilities, world-class educational institutions, champion sports franchises, as well as its place at the very forefront of American history. Tourism is one of New England’s largest industries; as the region’s social and commercial “hub” Boston is willing to accommodate and entertain you as few other cities can.

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A range of presentation formats is sought for managed care pharmacists and health care professionals working in managed care pharmacy and interested in increasing their knowledge of the management and coordination of clinical, pharmacy benefit and pharmaceutical care programs. AMCP is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education [CE]. In addition to CE, AMCP will offer Continuing Medical Education [CME] through an Accreditation Council for Continuing Medical Education [ACCME] accredited provider for those sessions that meet ACCME criteria.

To submit a proposal, visit www.amcp.org for more information. Sample proposal submissions are available in the online Call for Proposals pdf brochure.

DEADLINE FOR SUBMISSION: NOVEMBER 2, 2007
AMCP recognizes those who share our vision with peers as its AMCP Visionaries.

- **AMCP Visionary**
  Those recruiting one to three new members will be recognized each month in the AMCP News, posted on the AMCP website, and listed in the Year in Review.

- **Four to Seven Referrals: Sapphire Level**
  In addition to the above, Sapphire Visionaries will be recognized at AMCP conferences with a special ribbon to attach to their meeting badge.

- **Eight to Fourteen Referrals: Ruby Level**
  In addition to the above, Ruby Visionaries will receive a ruby lapel pin and a personal letter of thanks from the AMCP president.

- **Fifteen to Twenty-Four Referrals: Emerald Level**
  In addition to above, Emerald Visionaries will receive an emerald lapel pin and a certificate of appreciation presented at the AMCP Leadership Luncheon during the Annual Meeting.

- **More Than Twenty-Five Referrals: Diamond Level**
  In addition to the above, Diamond Visionaries will receive a diamond lapel pin and an invitation to attend the gala Awards Dinner held during the Annual Meeting each spring.

See the AMCP website for membership applications and additional information, www.amcp.org.