Evaluation of Product Switching After a State Medicaid Program Began Covering Loratadine OTC 1 Year After Market Availability

Utilization and Costs for Compliant Patients Initiating Therapy With Pioglitazone or Rosiglitazone Versus Insulin in a Medicaid Fee-for-Service Population

Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature

Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis

Suboptimal Pneumococcal Pneumonia Vaccination Rates Among Patients at Risk in a Managed Care Organization in Israel
CONTENTS

ORIGINAL RESEARCH

108 Evaluation of Product Switching After a State Medicaid Program Began Covering Loratadine OTC 1 Year After Market Availability
   Troy K. Trygstad, PharmD, MBA; Richard A. Hansen, PhD, RPh; and Steven E. Wegner, MD, JD

121 Utilization and Costs for Compliant Patients Initiating Therapy With Pioglitazone or Rosiglitazone Versus Insulin in a Medicaid Fee-for-Service Population
   Ittekhar Kalsekar, PhD; Shrividiya Iyer, PhD; Reema Modi, PhD, MBA; Rukmini Rajagopalan, DrPh, MBA, RN; and Jan Kavookjian, PhD, MBA

SUBJECT REVIEW

130 Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature
   Jennifer M. Stephens, PharmD, BCPS; Marc F. Botteman, MSc, MA; and Joel W. Hay, PhD

FORMULARY MANAGEMENT

143 Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis
   Parthiv Mahadevia, MD, MPh; Shallen Shah, MD; Sally Mannix, BA; Jessica Brewster-Jordan, BA; Leah Kleinman, DrPh; Christopher Leibman, PharmD, MS; and Liza O'Dowd, MD

CONTEMPORARY SUBJECT

152 Suboptimal Pneumococcal Pneumonia Vaccination Rates Among Patients at Risk in a Managed Care Organization in Israel
   Natan R. Kahan, RPh, MHA; Dan-Andrei Waitman, MD, MPH; Shimon Blackman, BScPharm; and David P. Chinitz, PhD

DEPARTMENTS

96  Cover Impressions
   Pike Place Market, Seattle (1999)
   Thomas Kinkade
   Sheila Macho
   Cover Editor

157 Commentary
   • The Estimated Impact of Drug Importation, Mandatory Mail Service, and Medicaid Fee Reduction on Community Pharmacies in Michigan
     Patrick L. McKercher, PhD
   • Mail-Service Pharmacy Savings: A Conclusion in Search of Evidence
     Norman V. Carroll, PhD, RPh

168  Editorial Subjects—In This Issue and in Previous Issues
   • Measuring Value in the Treatment of Symptoms of Allergic Rhinitis With Nasal Steroids
   • What Is the Future of Thiazolidinediones (TZDs) After Market Introduction of Inhaled Insulin?
     Frederic R. Curtiss, PhD, RPh, CEBS
     Editor-in-Chief

173 Abstracts From Professional Poster Presentations at AMCP’s 18th Annual Meeting & Showcase
Editorial Content and Peer Review

All articles, editorials, and commentary in JMCP undergo peer review; articles undergo blinded peer review. Letters may be peer reviewed to ensure accuracy. The fundamental departments for manuscript submission are:

- Original Research
- Subject Reviews
- Formulary Management
- Contemporary Subjects
- Editorials/Commentary
- Letters

For manuscript preparation requirements, see “JMCP Author Guidelines” in this Journal or at www.amcp.org.

Original Research

These are well-referenced articles based on original research that has not been published elsewhere and reflects use of the scientific method. The research is guided by explicit hypotheses that are stated clearly by the authors.

Subject Reviews

These are well-referenced, comprehensive reviews of subjects relevant to managed care pharmacy.

Formulary Management

These are well-referenced, comprehensive reviews of subjects relevant to formulary management methods or procedures in the conduct of pharmacy and therapeutics (P&T) committees and may include description and interpretation of clinical evidence.

Contemporary Subjects

These are well-referenced submissions that describe pilot projects or other subjects that are not intended to be comprehensive reviews of the subject.

Editorials/Commentary

These submissions should be relevant to managed care pharmacy and address a topic of contemporary interest.

Letters

If the letter addresses a previously published article, an author response may be appropriate. (See “Letter to the Editor” instructions at www.amcp.org.)

Advertising/Disclosure Policy

A copy of the full advertising policy for JMCP is available from AMCP headquarters and the Advertising Representative. All aspects of the advertising sales and solicitation process are completely independent of the editorial process. Advertising is positioned either at the front or back of the Journal; it is not accepted for placement opposite or near subject-related editorial copy.

Employees of advertisers may submit articles for publication in the editorial sections of JMCP, subject to the usual peer-review process. Financial disclosure, conflict-of-interest statements, and author attestations are required when manuscripts are submitted, and these disclosures generally accompany the article in abstracted form if the article is published.

See “Advertising Opportunities” at www.amcp.org. Contact the Advertising Representative to receive a Media Kit.

JMCP employs extensive bias-management procedures that include (a) full disclosure of all sources of potential bias and conflicts of interest, nonfinancial as well as financial; (b) full disclosure of potential conflicts of interest by reviewers as well as authors; and (c) accurate attribution of each author’s contribution to the article. Aggressive bias-management methods are necessary to ensure the integrity and reliability of published work.

Editorial content is determined by the Editor-in-Chief with suggestions from the Editorial Advisory Board. The views and opinions expressed in JMCP do not necessarily reflect or represent official policy of the Academy of Managed Care Pharmacy or the authors’ institutions unless specifically stated.

Editorial Office

Academy of Managed Care Pharmacy
100 North Pitt St., Suite 400
Alexandria, VA 22314
Tel: (703) 683-8416
Fax: (703) 683-8417
E-mail: jmcpreview@amcp.org
tfaggen@amcp.org

Advertising Sales Office

Professional Media Group, Inc.
40 N. Woodbury Rd.,
Pitman, NJ 08071
Tel: (800) 486-5454
or (856) 589-5454
Fax: (856) 582-7611
E-mail: peter@promedgroup.net
JMCP employs extensive bias-management procedures intended to ensure the integrity and reliability of published work.
Thomas Kinkade is known as the “Painter of Light.” Because of the tremendous popularity of his paintings depicting light, he has become America’s most-collected living artist. Whether it’s the amber glow from cottage windows, the reflection of street lamps upon wet pavement, or the smoldering hues of a sunset, viewers of his paintings are naturally drawn to the warmth and peacefulness evoked by the light. In an article written by Kinkade posted on California State University Fullerton Grand Central Art Center’s Web site, he stated, “For many millions, my art provides an escape from the pressures of contemporary life and a gentle affirmation of such foundational values as home, family, faith, and simpler ways of living. This same function has been served by populist iconography in every American generation: be it Currier & Ives prints, Frank Capra films, or Norman Rockwell [Saturday Evening] Post covers.”

Kinkade was born in 1958 in Sacramento, California, and shortly thereafter moved with his family to the nearby town of Placerville in the foothills of the Sierra Nevada Mountains (called the “Range of Light” by American naturalist John Muir). Kinkade showed an early interest in art and would often explore the outdoors, taking along his sketchpad to record the beautiful scenery around him. By the time he was 16, he had begun to paint in oil, becoming an apprentice to Glen Wessels, a prominent California artist. After his graduation from high school, Kinkade studied art at the University of California at Berkeley, where his roommate was James Gurney, the artist renowned for the Dinotopia books and television miniseries. Kinkade furthered his studies at the Art Center College of Design in Pasadena, California.

Following their student years, Kinkade and Gurney set out on a summer adventure across America. According to the Kinkade biography found on the Geocities Web site, “Together they traveled throughout the country by freight train accompanied [by] their painting gear . . . sketching in a fashion that was called plein air, [so named] by nineteenth-century Impressionists. Roughly translated, this referred to a studio in the open air, without surrounding walls. Working outdoors, Kinkade studied how the light brought forth brilliant colors that sparkled, and how the movement of clouds created shadows over the landscape . . . .

“Upon return[ing] from their trip, Kinkade and Gurney collaborated on a book titled The Artist’s Guide to Sketching. Based on the drawings they had done while on their cross-country trek, Kinkade and Gurney approached the method of plein air art. The book, published in 1982, quickly became a bestseller and has continued to be ranked as a classic for pupils.” The book’s success helped the two young artists land jobs in Hollywood’s film industry—specifically, Ralph Bakshi Studios, where they created more than 600 background paintings for the animated feature film Fire and Ice.

In the spring of 1982, Kinkade married his childhood sweetheart, Nanette. With his wife’s encouragement, he left his position at the movie studio the following year to pursue a solo career as an artist. For the next several years, Kinkade sold his paintings in galleries throughout California. By 1989, he had decided to publish prints of his paintings and launched Lightpost Publishing with Ken Raasch.

Kinkade is a deeply spiritual man, a devoted husband, and the father of four daughters. He spends most of his time at his home-based studio, “Ivy Gate,” located in California’s Santa Clara Valley.

The Thomas Kinkade Company Web site reveals that throughout his career, Kinkade “. . . has been recognized around the world for his many charitable efforts. He has received the World Children’s Center Humanitarian Award, has worked extensively with World Vision Charities, and has been the national spokesperson for the Make-A-Wish Foundation. His most recent humanitarian efforts include his appointment as the Ambassador of the Points of Light Foundation, founded by former President George Bush, an organization devoted to encouraging volunteerism and community service throughout the United States.”

Although not as well-known as his light-filled, romantic landscapes, Kinkade’s plein air paintings are equally impressive. Pike Place Market, Seattle is a splendid example of his plein air style. He paints quickly on a small canvas, utilizing a moderate number of brushstrokes to capture the essence of a particular scene. In his depiction of the famous Seattle landmark, Kinkade has masterfully woven the familiar elements of the market together, including the large neon “Public Market” sign, the crowded fish stalls, and the shoppers beneath their umbrellas. His trademark glow of warm light beaming from the stalls beckons the viewer into the picture, while the plume of smoke from the stovepipe on the roof conjures up the coolness of the air on this rainy day.

If you attend AMCP’s 18th Annual Meeting & Showcase held from April 5-8, in Seattle, don’t miss Pike Place Market, where vociferous fishmongers throw fish and have fun with visitors.

Sheila Macho
Cover Editor


**JMCP Author Guidelines**

The Journal of Managed Care Pharmacy is indexed by Index Medicus/MEDLINE and International Pharmaceutical Abstracts (IPA).

1. **Standard journal article**
   (List all authors when 6 or less; if more than 6, list only the first 3 and add et al.)

2. **No author given**

3. **Journal paginated by issue**

4. **Book or monograph by authors**

5. **Book or monograph with editor, compiler, or chairman as author**

6. **Chapter in a book**

7. **Government agency publication**

8. **Paper (or Poster) presented at a meeting**
   Reagan ME. Workers’ compensation, managed care, and reform. Paper (poster) presented at: 1995 AMCRA Midyear Managed Care Summit; March 13, 1995; San Diego, CA.

9. **Newspaper**

10. **Web site**

---

**Manuscript Submission**

A paper copy of the manuscript, including orignals of figures and tables and author attestation forms (see Submission Checklist), should be submitted to the JMCP Peer Review Administrator at the Academy of Managed Care Pharmacy, 100 North Pitt St., Suite 400, Alexandria, VA 22314; Tel: (800) 827-2627 or (703) 683-8416 or Fax: (703) 683-8417. The paper copy is necessary to ensure proper presentation and placement of text, figures, tables, and graphs. Please submit the manuscripts electronically at jmcp.msubmit.net. All text should be in a word processing program (preferably Microsoft Word). Tables should be prepared in a word processing program using the tab function to create columns, not using “tables” or “cells.” Figures should be saved in Photoshop or Illustrator and may be re-created by us. Figures may also be prepared in a word processing program (preferably Microsoft Word). We can accept PowerPoint graphics. Please identify the format (PC or MAC), all programs used, and all file names. P values should be expressed to no more than 3 decimal points in the format 0.xxx.

**Note:** Please do not include author identification in the electronic manuscript document.

---

**Submission Checklist**

Before submitting the paper copy of your manuscript to the Journal of Managed Care Pharmacy, please check to see that your package includes the following:

- **Cover letter**

- **Manuscript:** prepared in 12-point type, 1.5 line spacing, including

- **abstract:** no more than 500 words

- **keywords:** follows the abstract

- **references:** cited in numerical order as they appear in the text (use superscript numbers) and prepared following modified AMA style; do not include footnotes in the manuscript

- **tables and figures:** generally no more than a total of 6. 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.

- **Disclosures and conflict-of-interest forms:** completed and signed author attestation forms (available at www.amcp.org); clearly indicate source(s) of funding and financial support.

**Note:** Please do not include author identification in the electronic manuscript document.

For “Manuscript Submission Checklist” and “Peer Review Checklist,” see www.amcp.org.

---

**Reference Style**

References should be prepared following modified AMA style. All reference number in manuscript should be superscript (e.g., 1). See the following examples of common types of references:

Evaluation of Product Switching After a State Medicaid Program Began Covering Loratadine OTC 1 Year After Market Availability

TROY K. TRYGSTAD, PharmD, MBA; RICHARD A. HANSEN, PhD, RPh; and STEVEN E. WEGNER, MD, JD

ABSTRACT

OBJECTIVE: The conversion of loratadine from prescription (Rx)-only to over-the-counter (OTC) status on November 27, 2002, brought about the question of how OTC products may influence utilization of both OTC and Rx-only low-sedating antihistamines (LSAs) simultaneously. This study examined product switching following OTC conversion of loratadine but subsequently changed the policy 1 year after OTC conversion, on November 23, 2003. The objective of this study was to determine patterns of LSA utilization in relation to changes in OTC availability and Medicaid coverage policy and to assess the rate of product switching associated with these policies.

METHODS: Administrative pharmacy claims from the NC Medicaid population of approximately 1.1 million eligible recipients were used to study the 3 years of LSA use between July 1, 2001, and June 30, 2004. Two general methods were employed to evaluate the extent of product switching. First, monthly rates of incident use, new starts (i.e., no LSA use in the prior 12-month period) and product switching in time series were determined. These series were constructed to include a baseline period of no OTC availability, a period of OTC availability without coverage, and a period of OTC availability with coverage. Second, product switching was assessed through the use of rate-ratio calculations. Three equal 12-month periods were compared using rate ratios: (1) a baseline referent period (July 1, 2001, to June 30, 2002) during which loratadine OTC was not yet available, (2) a noncoverage period (July 1, 2002, to June 30, 2003) during which loratadine OTC was introduced to the market but not covered by NC Medicaid, and (3) a coverage period (July 1, 2003, to June 30, 2004). The primary comparison periods for the 3 years were the 5-month periods from February to June of each year.

RESULTS: The use of individual drugs within the LSA class responded to coverage changes as expected, with alternative LSAs replacing loratadine use in the loratadine noncoverage period. Switching behavior for individual drugs within the LSA class was strongly associated with coverage changes. Recipients using loratadine were 2.16 times more likely to switch to an alternative Rx-only antihistamine in the noncoverage period (95% confidence interval [CI], 2.10-2.22) as compared with the baseline period. Yet they were only 1.11 times as likely not to use an Rx LSA during the last 5 months of the noncoverage period (95% CI, 1.09-1.13), as compared with the baseline period, suggesting minimal OTC uptake. The largest 12-month percentage increase in market share was observed for cetirizine (13.4%), although desloratadine accounted for the largest switch rate from loratadine at 3.10 (95% CI, 2.91-3.30), as compared with the baseline period, with a total market share increase of 7.8%. This suggests that new users of LSAs were most likely to initiate therapy with cetirizine, while existing loratadine users were most likely to switch to desloratadine. Compared with baseline switch rates, LSA users were only 0.34 (95% CI, 0.32-0.37) times as likely to switch to loratadine OTC from another (Rx-only) LSA during the subsequent OTC coverage period. LSA expenditure per member per month (PMPM) was essentially constant over time, at $3.03 in the 5-month pre-OTC period, $2.96 in the 5-month loratadine noncoverage period, and $2.93 in the 5-month coverage period for loratadine OTC. Total LSA utilization increased slightly, from 1.37 days PMPM in the 5-month pre-OTC period to 1.41 in the 5-month loratadine noncoverage period and 1.45 in the 5-month coverage period for loratadine OTC. Loratadine OTC accounted for only 4.1% of the total LSA days of therapy and 4.2% of the LSA patients in the 5-month OTC coverage period from February to June 2004.

CONCLUSION: Medicaid recipients switched to another covered (Rx) LSA when loratadine became available as an OTC and was not covered. After the subsequent policy change 1 year later to cover loratadine OTC, there was little switching to loratadine OTC. Though the average cost per LSA claim dropped $4.15 (6.6%), from $62.79 in the baseline period to $58.64 in the OTC coverage period, time-series and rate-ratio results suggest that an additional $6.01 (10.2%) could have been saved per LSA claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Although coverage of loratadine OTC offers a substantial cost-savings opportunity for the Medicaid program compared with Rx-only LSAs, not covering the OTC product immediately at the time of OTC availability contributed to (a) increased switching to Rx-only LSA products and (b) little use of loratadine OTC in the subsequent OTC coverage period.

KEYWORDS: Loratadine, Medicaid, Over the counter, OTC, Low-sedating antihistamine, LSA, Drug utilization, Switching

J Manag Care Pharm. 2006;12(2):108-20

Since the introduction of loratadine (Claritin) in 1993, expenditures on low-sedating antihistamines (LSAs) have accounted for a significant portion of prescription (Rx) drug spending. Oral antihistamines accounted for more than $5.1 billion1 (approximately 4.0%) of total community pharmacy sales in the United States in 2001, ranking ninth among all drug classes.2 On November 27, 2002, the U.S. Food and Drug Administration (FDA) approved loratadine as the first-ever LSA for over-the-counter (OTC) sale.3 Loratadine was officially introduced to the OTC market in December 2002, first marketed as Claritin and Alavert (Wyeth Consumer Healthcare) and subsequently under several label names.

Following OTC approval, many private health plans responded by moving loratadine to the highest copayment tier or by removing loratadine from coverage in the pharmacy benefit.4 For state Medicaid programs, benefit design is largely determined at the state level, and there is wide variability in OTC coverage, types of drugs covered, and copayment amounts among the states.5 At the time of initial OTC marketing of loratadine in 2002, 31 states had partial coverage of OTC antihistamines, and 19 states had some form of prior authorization for Rx antihistamines.6 For those states not covering OTC products, loratadine OTC was removed from the pharmacy benefit altogether. Since copayments for Medicaid recipients are generally nominal, a covered Rx-only alternative almost always costs less out of pocket than a comparable OTC product at retail cost, creating an incentive for the Medicaid recipient to use a more expensive Rx-only product.

In the case of the OTC conversion of loratadine Rx, the Rx version of the drug was removed completely from the market.7 This is in contrast with other OTC conversions in which availability was tied to strength (as with histamine-2 blockers and...
nonsteroidal anti-inflammatory agents in which lower-strength products were OTC and higher-strength products continued to be available by Rx) or chemical moiety (as with omeprazole magnesium). Therefore, in the Rx-to-OTC conversion of loratadine, there was no dual OTC and Rx market existence. Thus, pharmacy benefit plans that did not cover OTC products were left with 2 options: (1) drop loratadine from the pharmacy benefit or (2) initiate coverage of OTC products in general or loratadine OTC as an exception.

Either of these options may result in drug cost savings relative to pre-OTC availability. One study using decision analysis to model the budgetary impact of Medicaid policies following the loratadine OTC conversion reported a $.02 per-member-per-month (PMPM) savings for coverage.7 A separate analysis from a societal perspective found that availability of LSAs over the counter would be associated with annual savings of $4 billion, or $100 dollars per allergic rhinitis sufferer per year, and 135,061 time-discounted quality-adjusted life-years.8

Another study modeled the impact of discontinuing OTC coverage in the Oregon Medicaid program. Using a time-series analysis to evaluate the 1993 policy change, the authors concluded that eliminating OTC coverage reduced program costs, with limited evidence of substitution to Rx-only products.7 Empirical evidence from a study considering a number of different managed care pharmacy benefit plans found that the Rx-to-OTC switch of loratadine resulted in a decrease in all allergic rhinitis-related utilization, suggesting that the decrease in LSA utilization was not associated with a commensurate increase in use of other allergic rhinitis drugs such as nasal steroids or montelukast.10 However, none of these studies reflects the specific effect within a Medicaid environment, and none directly assesses loratadine OTC coverage or its use. In fact, Sullivan et al. point to the inability to readily measure OTC use as a serious limitation that needs to be addressed in future papers.10

The study of concurrent OTC and Rx drug use will become increasingly important as more drugs become available over the counter. Nearly 4 out of every 5 Americans report using an OTC product in the previous 6 months,11 and nearly two thirds of all OTC purchases in 1996 were for products containing ingredients that were once Rx-only.12 Studying the transition and subsequent use of formerly Rx-only products is becoming essential to understanding overall drug use in member populations.

The opportunity costs associated with noncoverage of OTC products is of interest to all benefit managers, regardless of payer type. Despite the studies that have suggested reductions in payer cost associated with the marketing of OTC products, none have examined the opportunity costs associated with not covering OTC products. Benefit managers and health plan sponsors are interested in determining if and by how much plan benefit dollars can be saved by noncoverage of OTC drugs versus coverage of OTC drugs. This determination is becoming more important given the OTC conversions of costly drugs such as omeprazole OTC (Prilosec) and the recent consideration of OTC availability of select statins.13

The State Employee Health Plan of North Carolina (NC) likely considered this matter when redesigning the benefit structure for proton pump inhibitors (PPIs) for state employees. The customary $10 generic copayment was reduced to $5 for omeprazole OTC to create a financial incentive for its use.14 Evidence of the value of OTC coverage was produced by the study of the Arkansas State Employee Health Plan, which added coverage of omeprazole OTC at a reduced copayment. Coverage of omeprazole OTC resulted in 47% market share for the OTC drug in the first week of the policy change, with a consequent cost reduction to the state of approximately 50% for the entire PPI class of drugs.15

Historically, Medicaid coverage of OTC products was extended only to insulin in NC. Hence, when loratadine was approved for OTC sale, NC Medicaid recipients were no longer able to obtain it as a covered benefit except for existing pharmacy stock of loratadine Rx, which could be dispensed and reimbursed. When the pharmacy stock of loratadine Rx was depleted, NC Medicaid recipients taking loratadine had 3 options: (1) obtain an Rx for an alternative covered product such as cetirizine (Zyrtec), desloratadine (Clarinex), or fexofenadine (Allegra); (2) purchase the OTC product out of pocket; or (3) stop using an LSA. Given the higher cost of the OTC product ($8-$15) relative to the $3.00 copayment for the branded Rx LSA in the Medicaid pharmacy benefit at the time, it is likely that most NC Medicaid recipients switched to a covered Rx-only LSA. Approximately 1 year following OTC availability, NC Medicaid changed its OTC policy to cover select products, including loratadine OTC on November 23, 2003, citing both access and potential cost savings.16

The present study takes advantage of the natural timing of these 2 policy changes: the FDA approval of loratadine OTC in late November 2002 and the approval of coverage of loratadine OTC in the state Medicaid program the next year, in November 2003. In the private sector, the conversion of loratadine from an Rx-only to an OTC product greatly increased access to the drug for individuals who can afford the OTC price and also made a physician visit unnecessary to obtain the drug. For NC Medicaid recipients, however, this change caused an increase in out-of-pocket costs since OTC products were not included as a pharmacy benefit (loratadine Rx had a $3.00 copayment before OTC conversion). One year after OTC conversion, a change in NC Medicaid drug policy allowed OTC products to be covered for a copayment of $1.00 per claim.

Given the potential drug cost savings of loratadine OTC, the effect of NC Medicaid coverage policies on LSA utilization and product switching was evaluated. Despite coverage of loratadine 1 year after its OTC conversion, failing to cover the product at the time of conversion may have diminished those
savings through increased product switching. This hypothesized effect was evaluated by (1) determining the patterns of LSA utilization in relation to changes in OTC availability and coverage policy and (2) assessing the rate of LSA product switching as a function of OTC availability and coverage policy.

**Methods**

A retrospective analysis of pharmacy claims was undertaken for the NC Medicaid program for the 3-year period from July 1, 2001, through June 30, 2004. This period includes both the federal policy change (OTC conversion on November 27, 2002) and the state policy change (loratadine OTC coverage on November 23, 2003). Specifically, the following products were considered in the present analysis: loratadine Rx, loratadine OTC, cetirizine, desloratadine, and fexofenadine. During the period of this study, there was no mail-service pharmacy option available to NC Medicaid recipients, and there was a supply limit of 34 days per community pharmacy claim.

Two general methods were employed to evaluate the extent of product switching. First, we determined 3 types of monthly rates in time series: aggregate LSA use (the total number of respective LSA claims), incident LSA starts (the number of enrollees initiating an LSA following a year of nonuse), and incident product switching (the number of enrollees switching from loratadine Rx to another LSA following a year of exclusive loratadine Rx use). These monthly rates were used to construct time series that were inclusive of both federal and state (Medicaid) policy changes over the 3-year study period. This approach provided a qualitative illustration of the effect of these policy changes on utilization patterns and switching behavior but did not allow statistical testing due to limitations associated with the use of time-series analysis. To overcome this limitation, the second approach employed the construction of rate ratios to quantify product switching. Year-long rates of switching among 3 discrete periods were compared: (1) a baseline period of no policy changes, (2) an OTC noncoverage period, and (3) an OTC coverage period.

Each of the 3 time series provided a separate but necessary component of the overall analysis to determine the effect of policy changes. Monthly aggregate (all) LSA use was used to determine general trends in total LSA use that could be linked directly to each policy change. However, since this time-series method could not parse out the specific effect of policy changes between new users and product switchers, incident LSA starts (at least 1 year of prior nonuse) and incident product switching were determined to separate the effect of coverage changes for new LSA users from the effect of coverage changes on existing LSA users.

Monthly aggregate LSA use was calculated from the total number of paid LSA claims per 1,000 eligible recipients per month for the time period from July 1, 2001, to June 30, 2004. Over this 3-year period, the number of Medicaid recipients increased from 990,000 to 1.1 million. Thus, an analysis of 1,000 recipients was employed to normalize the growth in number of eligible recipients over time. Utilization was defined as paid pharmacy claims for any quantity, strength, or dosage of LSAs, regardless of Medicaid recipient eligibility.

To assess the frequency and product distribution of incident LSA starts over time, LSA starts per 1,000 nonusers (no LSA use) per month were calculated. Since LSAs are often used on an as-needed basis and seasonal utilization of LSAs is common, incident LSA starts were determined by 1 year of nonuse. Enrollees were considered nonusers if, prior to initiating LSA use, no LSA claim had been filed in the year prior to that LSA pharmacy claim. Continuous Medicaid eligibility was not required for these analyses since this requirement would have reduced the study population by almost half. Monthly LSA start rates are reported for the period from January 2002 through June 2004, and claim data spanning the 12-month period from January 2001 through December 2001 were used to determine nonuse for the monthly rates in January 2002, with subsequent 1-year run-in periods to determine nonuse for respective monthly rates.

To assess product switching, the number of enrollees switching from loratadine Rx to other LSAs per 1,000 loratadine Rx users per month was calculated over time. A loratadine Rx user was required to have a 1-year run-in period of exclusive loratadine Rx use. As was the case with the new-start classification, continuous eligibility was not required to be considered a loratadine Rx user due to the transient eligibility commonly found with Medicaid recipients. Rather, loratadine Rx users were defined as those recipients having any eligibility in the prior 12 months, with no LSA claim other than at least 1 claim for loratadine Rx. Subsequent 1-year run-in periods of exclusive loratadine Rx use were used to determine the denominator for each monthly rate, and the numerator was determined from the LSA product switches in the respective months.

While the time-series approach provides a good visual depiction of switching behavior over time, it does not show clearly the specific magnitude of the policy effect. Furthermore, traditional statistical modeling techniques typically employed with time-series analysis are limited in that they require significant longitudinal history and are often difficult for policy makers to interpret. Therefore, the rate-ratio method was employed as a second, adjunct approach to compare the rate of product switching between both exposure periods (noncoverage and coverage) and the baseline referent period. This approach also has been used to characterize the seasonality of emergency department visits for asthma in schoolchildren.

This rate-ratio method of quantification was also necessary for precision and for testing for statistical significance. More importantly, this approach also enabled use of LSA persistence as a proxy for OTC use in the absence of claims for OTC products during the noncoverage period. Specifically, this was achieved...
by determining the number of persons who did not persist in LSA use across each policy period. With a rate-ratio approach, rates of baseline discontinuation (persistence) are canceled out by the division of rates from both the referent-baseline and the policy periods. The definition of LSA discontinuation for the purposes of this analysis was the absence of a pharmacy claim for an LSA during the period of interest. Thus, an LSA persistence rate ratio of 1.0 indicates constant baseline LSA discontinuation over time, whereas a rate ratio greater than 1.0 indicates 1 of 2 possible scenarios: (1) increased discontinuation or (2) OTC uptake. The magnitude of change is multiplicative. Thus, a rate ratio of 2.0 results from a 2-fold increase in LSA discontinuation in the exposure period (OTC noncoverage) versus the baseline period (referent). The validity of this ratio with respect to policy attribution is dependant on the absence of confounding factors. While this assumption is an important limitation, it is common to all quasi-experimentation in policy analysis, especially time-series applications.

Using the rate-ratio approach, switching behavior was measured for 3 different 12-month time periods, using the natural timing of OTC conversion and changes in NC Medicaid OTC coverage. In each 12-month period, switch rates were calculated by comparing LSA users in the first 5 months of the year-long period with LSA users in the last 5 months of the year-long period. The first 5 months of each year-long period were used to identify LSA users and classify eligible users according to which LSA(s) they used. The last 5 months of each period were used to compare changes in LSA utilization with prepolicy use; an LSA switcher was defined as an LSA user with an LSA product change.

Exclusive use of a given product was required, meaning that a Medicaid recipient with a pharmacy claim for more than 1 type of LSA (e.g., cetirizine and fexofenadine) was excluded from the data when calculating the rate ratios. Requiring mutual exclusivity ensured that comparisons could be made across
drug products and that the number of switchers for each type of drug product added up to the sum total of LSA switchers.

In each exposure period, the 5-month intervals were centered over the spring and fall, the peak seasons of LSA use. The middle 2 months (December and January) were used as a washout interval when pharmacy claims were not evaluated. Both policy changes occurred at the end of the month of November, immediately before the beginning of the washout interval. The purpose of the washout interval was 2-fold: (1) to account for minimal differences in the timing of market and policy changes within the periods (loratadine was approved for OTC status on November 27, 2002, and Medicaid coverage of loratadine OTC began on November 23, 2003) and (2) to allow for policy uptake. In the case of OTC noncoverage, time was needed for patients to get an Rx to switch to alternative products. For the OTC coverage period, the washout interval provided a lag time to allow the OTC product to get to market in sufficient supply (e.g., the first 3 National Drug Code [NDC] numbers to become available for online adjudication occurred for loratadine 10 mg tablets on November 25, 2003, December 19, 2003, and January 8, 2004).19)

For the calculation of the rate ratios, the first 12-month period (July 1, 2001-June 30, 2002) was used as a reference (the referent, or baseline, period) (Figure 1). The second 12-month period (July 1, 2002-June 30, 2003) was the period of loratadine OTC availability without coverage by NC Medicaid (the OTC noncoverage period). The final 12 months (July 1, 2003-June 30, 2004) represented a period of loratadine OTC coverage by NC Medicaid (the OTC coverage period). Each period comprised the same calendar months (July-June) in an attempt to account for the seasonality of LSA claims.

The first rate-ratio calculation (Equation 1) compared the rate of switching in the OTC noncoverage period with the rate of switching in the referent period. Note that the numerators and denominators of this equation are seasonally equal, 5-month intervals with equal 2-month washout intervals to a total 1-year period for each policy. [July-November] + [December-January] + [February-June] = 12 months. Specifically, the comparison was the rate of switching from loratadine Rx to another LSA or stopping use of an LSA altogether (i.e., nonuse). As previously mentioned, the term nonuse describes the absence of an LSA claim in the period of interest. More specifically, the nonuse classification includes 2 types of Medicaid recipients: (1) true nonusers and (2) users who purchased loratadine OTC on their own. By constructing a rate ratio comparing nonuse in different policy periods, the baseline discontinuation that frequently occurs with as-needed products such as LSAs is cancelled out. Thus, if the rate of recipients discontinuing Rx-only LSA use is larger in the policy period than in the referent period, the increased discontinuation in pharmacy claims may be attributed to the policy change at hand. Subsequently, the rate ratio represents the multiplicative magnitude of combined (1) loratadine OTC uptake and (2) class-wide LSA discontinuation regardless of legend (Rx or OTC) status. This method alone does not allow parsing the dominant effect. This approach does, however, help overcome the confounding of OTC use not accounted for in pharmacy claims.
Under the null hypothesis, the rate ratio should be equal to 1.0 if no NC Medicaid recipients were purchasing an OTC product on their own following the availability of loratadine OTC. Rate ratios greater than 1.0 indicate increased switching to the nonuse category. More specifically, rate ratios greater than 1.0 indicate either greater discontinuation of LSA products after the policy change or initiation of self-purchased OTC use. Determining which of these scenarios dominates is beyond the capability of this method although one may refer to the analysis of aggregate LSA utilization in time series (as well as LSA starts) to confirm persistence and constancy of overall LSA use. If aggregate LSA use remained constant over time, one might infer that no OTC uptake occurred when the resultant discontinuation (persistence) rate ratio is 1.0.

The second set of rate ratios was designed to represent the degree to which recipients using an Rx-only LSA switched to loratadine OTC once OTC coverage was implemented. The numerator is the rate of persons switching from an Rx-only LSA to loratadine OTC after OTC coverage became effective (in November 2003). A rate for new LSA starts was also determined (nonuse to loratadine OTC use). To be consistent and to permit inclusion of more data, the “any eligibility” criterion used for the time-series approach was also used for these rate-ratio calculations. Thus, for any categorization in any period of interest, only if aggregate LSA use remained constant over time, one might infer that no OTC uptake occurred when the resultant discontinuation (persistence) rate ratio is 1.0.

As before, rate ratios greater than 1.0 represent more switching to loratadine OTC in a period of coverage versus switching to loratadine Rx in a referent period. Ratios less than 1.0 reflect less use of the OTC product as compared with baseline switching patterns with the Rx product. Ratios equal to 1.0 would imply no difference in loratadine OTC uptake versus loratadine Rx uptake.

Desloratadine was introduced to the market in January 2002 (FDA-approved on December 21, 2001) and was not available to the U.S. market during the referent-baseline period. Therefore, it was not possible to calculate rate ratios for switching from desloratadine to loratadine OTC.

Chi-square tests and corresponding 95% confidence intervals (CIs) were calculated to compare the rate of switching for each drug. All data management and statistical testing was performed using Statistical Analysis Software, SAS version 9, Cary, NC.

### Results

Over the 3-year study period, NC Medicaid accumulated 1.7 million pharmacy claims for LSAs, totaling $106 million for 377,722 recipients. The prevalence of LSA use was 4.7% of eligible Medicaid recipients in the 5-month pre-loratadine OTC period from February through June 2002 and 4.8% in each of the latter 2 periods, from February through June 2003 (the loratadine OTC noncoverage period) and February through June 2004 (the loratadine OTC coverage period) (Table 1). The mean age as of the first claim on file during the study period was 26 years, whereas the median age was 15 years. Nearly two thirds (63.3%) were female, and 94.1% were community-dwelling Medicaid recipients. The remaining 5.9% of eligible recipients were in institutional care, including domiciliary care and mental hospital care. The days supply limit (34) was the same for institutional care recipients as for community-dwelling recipients.

LSA use remained steady and seasonal, with remarkable predictability throughout the 3-year study period. The highest use was observed during the months of April and May, peaking

### TABLE 1 LSA Utilization and Cost for the 3 Measurement Periods

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>LSA Rxs</td>
<td>243,857</td>
<td>262,426</td>
<td>276,329</td>
</tr>
<tr>
<td>LSA days</td>
<td>6,906,738</td>
<td>7,498,730</td>
<td>7,991,652</td>
</tr>
<tr>
<td>LSA patients</td>
<td>47,088</td>
<td>50,529</td>
<td>53,281</td>
</tr>
<tr>
<td>LSA expenditures</td>
<td>$15,311,733</td>
<td>$15,698,614</td>
<td>$16,205,124</td>
</tr>
<tr>
<td>Loratadine Rxs</td>
<td>92,906</td>
<td>24,447</td>
<td>11,453</td>
</tr>
<tr>
<td>Loratadine days</td>
<td>2,657,009</td>
<td>706,199</td>
<td>330,122</td>
</tr>
<tr>
<td>Loratadine patients</td>
<td>18,107</td>
<td>4,798</td>
<td>2,233</td>
</tr>
<tr>
<td>Loratadine expenditures</td>
<td>$7,185,016</td>
<td>$2,172,901</td>
<td>$233,932</td>
</tr>
<tr>
<td>Eligible member-months</td>
<td>5,057,242</td>
<td>5,312,670</td>
<td>5,529,713</td>
</tr>
<tr>
<td>LSA days/Rx</td>
<td>28.3</td>
<td>28.6</td>
<td>28.9</td>
</tr>
<tr>
<td>Loratadine days/Rx</td>
<td>28.6</td>
<td>28.9</td>
<td>28.8</td>
</tr>
<tr>
<td>Loratadine Rx %</td>
<td>38.1%</td>
<td>9.3%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Loratadine days %</td>
<td>38.5%</td>
<td>9.4%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Loratadine patients %</td>
<td>38.5%</td>
<td>9.5%</td>
<td>4.2%</td>
</tr>
<tr>
<td>Loratadine dollar %</td>
<td>46.9%</td>
<td>13.8%</td>
<td>1.4%</td>
</tr>
<tr>
<td>Avg. LSA cost per day</td>
<td>$2.22</td>
<td>$2.09</td>
<td>$2.03</td>
</tr>
<tr>
<td>Avg. loratadine cost per day</td>
<td>$2.70</td>
<td>$3.08</td>
<td>$0.71</td>
</tr>
<tr>
<td>Avg. cost per LSA Rx</td>
<td>$62.79</td>
<td>$59.82</td>
<td>$58.64</td>
</tr>
<tr>
<td>Avg. cost per loratadine Rx</td>
<td>$77.34</td>
<td>$88.88</td>
<td>$20.43</td>
</tr>
<tr>
<td>Prevalence of LSA use</td>
<td>4.7%</td>
<td>4.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td>LSA days PMPM</td>
<td>1.37</td>
<td>1.41</td>
<td>1.45</td>
</tr>
<tr>
<td>LSA expenditures PMPM</td>
<td>$3.03</td>
<td>$2.96</td>
<td>$2.93</td>
</tr>
</tbody>
</table>

LSA = low-sedating antihistamine; OTC = over the counter; PMPM = per member per month; Rx = prescription.
at approximately 60 pharmacy claims per 1,000 eligible Medicaid enrollees every spring (Figure 2). A fall peak was found in the month of October, with approximately 50 pharmacy LSA claims per 1,000 eligible Medicaid enrollees. In general, LSA use varied between 40 and 60 pharmacy claims per 1,000 recipients, with no apparent upward trend. This occurred despite a dramatic shift in market share for cetirizine and the market introduction of desloratadine.

New LSA starts also were steady, with remarkable seasonal predictability. A surge in new starts in April of each policy period coincided with notable trends in 1-month prevalence results. Using our method of defining eligibility and nonuse, approximately one third of all LSA users (17-18 new starts per 1,000 recipients compared with 60 prevalent fills per 1,000 recipients) were new starters in the peak use month of April (Figure 3). During the month of July, an off-season in NC, only one sixth
of all LSA use was the result of new LSA starts (7 new starts per 1,000 recipients versus 41-43 fills per 1,000 recipients). The difference in ratios is seasonal and likely reflects the addition of seasonal LSA starters to a baseline rate of perennial starters.

In assessing the users who had switched from loratadine Rx to other products, we observed 3 distinct results in the 3 periods of interest (i.e., referent-baseline, OTC noncoverage, and OTC coverage). The baseline rate of switching from Rx loratadine to another LSA ranged from 10 per 1,000 recipients in the low-use months to a peak of 31 per 1,000 in the month of April (Figure 4). In contrast, during the OTC noncoverage period, switching from loratadine Rx ranged from 30 to 35 per 1,000 recipients in the low-use months to a peak of 63 per 1,000 in the month of April. For the months with comparable data (January-November), the difference in the area under the curve amounted to a difference of 237 switches per 1,000 recipients, or a 112% increase from a baseline of 212 to 449 switches per 1,000 recipients over that period. These time-series results in conjunction with rate-ratio results suggest that there was very little out-of-pocket loratadine OTC use (shown later) and that the 112% increase in switching, representing 8,380 switchers, was the result of noncoverage of loratadine OTC.

A small increase above seasonal trends in switching to loratadine OTC was found in May 2004 during the loratadine OTC coverage period. This spike coincides with the rollout of a pharmacist-based OTC initiative put forth by the NC Medicaid
Drug Utilization Review Board. Despite the resultant increase in switching to loratadine OTC, loratadine Rx users were much less prevalent in the month immediately preceding the initiation of OTC coverage (n = 734) versus the month immediately preceding initiation of OTC availability (n = 13,773), meaning that there were fewer existing loratadine Rx users to switch to the much cheaper OTC product when coverage was initiated (approximately 1 user during coverage for every 20 during noncoverage).

Recipients in the OTC noncoverage interval were 2.16 (95% CI, 2.10-2.22) times more likely to switch from loratadine Rx to a different Rx LSA than recipients in the referent-baseline period using the rate-ratio method (Table 2). Using the same ratio construction, recipients were only slightly more likely to discontinue use in the noncoverage period than in the coverage period (rate ratio, 1.11 [95% CI, 1.09-1.13]). This suggests that very few recipients either self-purchased loratadine OTC after it became available or discontinued LSA use as a result of the policy change. An examination of the other LSAs on the market showed that the largest gain in market share was observed for cetirizine (13.4%, Table 3) although desloratadine had the largest rate of switching from loratadine Rx (rate ratio, 3.1 [95% CI, 2.91-3.3]), with a market share increase of 7.8% (Table 3). This suggests that new LSA users were most likely to initiate therapy with cetirizine, while existing loratadine users were most likely to switch to desloratadine. The reverse outcome occurred in the OTC coverage interval during which switch rates to loratadine OTC were consistently lower. Recipients were only 0.34 (95% CI, 0.32-0.37) times as likely to switch to loratadine OTC from another Rx LSA during the OTC coverage period as they were to switch to loratadine Rx in the referent-baseline period (Table 4). Additionally, the rate of starting loratadine OTC was only 0.18 (95% CI, 0.17-0.18) times that of loratadine Rx in the referent period.

### Discussion

Medicaid OTC coverage continues to vary significantly by state. At least 1 OTC drug other than insulin was covered by all states with the exception of Louisiana in 2004.20 Most OTC drugs are covered in Delaware, Minnesota, Nevada, New Hampshire, New Mexico, Oregon, Texas, Virginia, and Wyoming.21 Many OTC drugs (e.g., histamine-2 antagonists, allergy drugs, analgesics) are covered in states like California, Indiana, Nebraska, South Carolina, and Vermont although restrictions and/or limitations were placed on certain drugs.22 Other states, including NC, cover only a few select OTC drugs (e.g., loratadine and omeprazole).23 Of relevance to this study, coverage decisions for OTC products are typically made coincident with OTC approvals from the FDA. A delay in extending coverage to the new OTC availability may lead to increased product switching to alternative covered products.

Following OTC conversion of loratadine, most NC Medicaid recipients seem to have switched from loratadine Rx to an alternative covered Rx (Medicaid-covered) product. Although all other LSAs accounted for some portion of loratadine Rx’s loss of market share, the largest rate of switching was
Evaluation of Product Switching After a State Medicaid Program Began Covering Loratadine OTC 1 Year After Market Availability

<table>
<thead>
<tr>
<th>Switch from</th>
<th>Switch to*</th>
<th>Rate/1,000†</th>
<th>Rate/1,000†</th>
<th>Rate Ratio</th>
<th>95% CI for Rate Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No LSA</td>
<td>Loratadine (Rx/OTC)</td>
<td>23</td>
<td>4</td>
<td>0.18†</td>
<td>0.17-0.18</td>
</tr>
<tr>
<td>Another LSA§</td>
<td>Loratadine (Rx/OTC)</td>
<td>44</td>
<td>15</td>
<td>0.34†</td>
<td>0.32-0.37</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Loratadine (Rx/OTC)</td>
<td>48</td>
<td>12</td>
<td>0.25†</td>
<td>0.23-0.28</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>Loratadine (Rx/OTC)</td>
<td>–</td>
<td></td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>Loratadine (Rx/OTC)</td>
<td>38</td>
<td>17</td>
<td>0.44†</td>
<td>0.39-0.49</td>
</tr>
</tbody>
</table>

* Switches to Rx or loratadine OTC are dependent on the period; in the referent period, the switch is to loratadine Rx while in the OTC coverage period, the switch is to loratadine OTC.
† Rate/1,000 is defined as the number of switchers per 1,000 eligible users. For this table, LSA users had to appear in both the 5-month preinterval of the referent period (Jul.-Nov. 2001) and the 5-month preinterval of the noncoverage period (Jul.-Nov. 2003). In the preinterval of the referent period, there were 1,020,856 nonusers of LSAs, 16,563 users of fexofenadine, and 28,317 users of cetirizine. In the preinterval of the OTC coverage period, there were 1,150,548 nonusers of LSAs, 30,570 users of fexofenadine, and 57,270 users of cetirizine.
‡ P < 0.001 for chi-square test of the null hypothesis that the rate of switching in the referent period was the same as the rate of switching in the OTC coverage period.
§ Another LSA refers to the combination of switches from the covered drugs: cetirizine, desloratadine, or fexofenadine.
|| Desloratadine was not available during the referent period; therefore it was not possible to calculate a rate ratio for this switch.
CI = confidence interval; LSA = low-sedating antihistamine; OTC = over the counter; Rx = prescription.

observed for desloratadine (loratadine Rx → desloratadine). The switch rate for desloratadine was more than 3 times greater following OTC conversion. This result is not surprising since desloratadine is the principal active entity of loratadine. Even so, the rate of switching from loratadine Rx to cetirizine and from loratadine Rx to fexofenadine was nearly twice as great after the OTC conversion of loratadine compared with the rates prior to OTC conversion. While this result seems inherently obvious given the noncoverage of loratadine OTC, it is the magnitude of switching and attribution of the policy effect above and beyond baseline switch rates that is germane to the analysis.

Unlike the effect observed in the noncoverage period, product switching following coverage of loratadine OTC a year later lagged behind that of the referent-baseline period. In comparison with baseline switch rates, our results indicate that there was relatively little switching to loratadine OTC from another (Rx) LSA product. This could indicate that once they have switched to an alternative product, physicians and patients were hesitant to switch back or initiate the use of an OTC product despite an economic incentive (i.e., $2 lower copay [$1 versus $3] per loratadine pharmacy claim). One explanation may be that the economic incentive was not large enough in the NC Medicaid population. In a privately insured population, a $10 differential in recipient out-of-pocket cost has been shown to influence utilization.22

Our data support the intuitive hypothesis that Medicaid programs will realize more use of the Rx-to-OTC conversion if OTC coverage is coincident with OTC availability rather than delayed. This conclusion is supported by the relative success in converting persons to loratadine OTC who previously used loratadine Rx as a result of the grace period associated with the legacy stock provision (Figure 4).

In fact, switches to loratadine OTC outpaced all other LSAs in May and June 2004 for existing users of loratadine Rx. In the month immediately preceding the federal policy change (Rx-to-OTC conversion of loratadine) in November 2002, there were 13,773 enrollees with loratadine claims. By the time the state policy change occurred (OTC coverage) in November 2003, there were only 743 enrollees with loratadine claims. While not all of the 13,773 prepolicy users would have remained on loratadine after the Rx-to-OTC conversion, our results suggest that most would have transitioned to the Medicaid-covered OTC product.

Various approaches have been employed by researchers to evaluate OTC switching behavior.7-10,15 However, we are unaware of previous literature that has been able to measure or approximate OTC use empirically using administrative claims data. In large part, this is because OTC use is difficult to track in the absence of administrative claims data. Using the trend and market-share analysis of pharmacy claims alone, researchers would tend to overestimate the relationship between policy changes and switching to alternative, covered products because of the loss of OTC claims in the denominator. In this study, we utilized an alternative method of quantifying switching behavior in the absence of administrative claims for loratadine OTC.

Discontinuation of paid claims (a proxy for combined
discontinuation and OTC use) remained steady over time, thus suggesting very minimal, if any, loratadine OTC use during the noncoverage period (rate ratio, 1.11). The additional 11% increase in discontinuation from the referent-baseline period to the noncoverage period may be the result of either (1) loratadine OTC use or (2) LSA discontinuation altogether. It is impossible to determine from pharmacy claims which of these outcomes was more common. The use of a patient survey would be necessary to determine out-of-pocket OTC use.

The minimal change in discontinuation rates over time in combination with time-series results suggests an additional 8,380 switchers above baseline rates and permits an estimate of lost cost savings. The policy effect can be translated into monetary terms by multiplying the cost difference between the average paid claim amounts for Rx-only LSAs in the coverage period ($58.64 in Table 1) and loratadine OTC claims ($20.43 in Table 1) by the number of switchers attributed to noncoverage (8,380). The resulting first-fill opportunity cost associated with noncoverage would be $320,200. Given a monthly average of 53,281 LSA users during the OTC coverage period (Table 1), this translates to an opportunity cost of $6.01 per LSA pharmacy claim that is directly attributable to not covering the OTC product at the time of conversion (federal policy change). Though the average cost per LSA pharmacy claim dropped $4.15 (-6.6%) from $62.79 in the baseline period to $58.64 in the OTC coverage period, the time-series and rate-ratio results above suggest that an additional $6.01 (10.2%) could have been saved per LSA claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Of course, this extrapolation is based on many assumptions, and this study was not designed as a cost study to account for nondrug costs such as physician office visits or other variables involved in calculating total health care and indirect costs. However, these nondrug factors are more likely to increase this opportunity cost (lost savings).

Cetirizine was the most common choice for new LSA starts (Figure 3), while desloratadine was the most common LSA switch as a result of the policy change (Table 2). Drawing conclusions from the time-series results alone, one may infer that cetirizine was the dominant choice for switchers. This conclusion would be erroneous, however, since baseline switching to cetirizine (66/1,000 loratadine Rx users [Table 2]) was already pronounced prior to OTC conversion of loratadine, while desloratadine lagged (30/1,000 loratadine Rx users [Table 2]). The rate-ratio approach accounted for baseline switching, thus accounting for prepolicy market conditions so that a direct attribution of effect could be given to the policy change in question.

**Limitations**

Foremost among the limitations of this study is the relatively large number of Medicaid recipients who continued to incur claims for loratadine Rx through the noncoverage period. This is the result of a Medicaid legacy stock (grace period) provision that is part of the federal Medicaid rebate program whereby pharmacies can continue to bill (and receive payment) for the Rx-only product until the stock is depleted. These claims are for NDC numbers representing previously Rx-only products whereas loratadine OTC claims were new NDC numbers for the newly marketed brand and generic OTC products. This is an important distinction, given the cost differential for reimbursement ($88.88 for the Rx NDC vs. $20.43 for the OTC NDC [Table 1]). The legacy stock provision may have reduced the immediate impact of the noncoverage effect in time series, though most pharmacies did not have legacy stock for more than a few months. This limitation may make the time-series results less generalizable to private-payment pharmacy benefit plans that may have NDC blocks for OTC-equivalent drugs. However, this limitation is reduced in importance because the majority of pharmacies did not have legacy stock remaining at 7 months post-OTC conversion (November 27, 2002-June 30, 2003); therefore, nearly all switching behavior was captured using the second quantifiable approach. In fact, another value of the rate-ratio method used in the present study was the ability to capture longitudinal switching behavior.

Second, factors uncommon to both policy and referent-baseline periods may have confounded the results. When constructing rate ratios, the researcher must ensure that participants differ only in exposure.25 Any factor, other than the policy itself that exists in the policy period and not in the referent period or vice versa may lead to spurious results. Certainly, the latter half of 2002 and all of 2003 and 2004 were marked by heavy promotion of both desloratadine Rx and loratadine OTC. It is not clear what role these or other factors played in the interpretation of the results found in the present study.

We also did not assess the use of therapeutic alternatives to LSAs in allergic rhinitis, including nasal steroids or montelukast (Singular), which was approved by the FDA for the additional indication of allergic rhinitis on December 31, 2002.24 Lakomski and Chitre estimated that as much as 25% of the use of montelukast was for allergic rhinitis in the 12-month period ended August 31, 2002, long before the FDA approval for this indication.

We were also not able to calculate a rate ratio for switching from desloratadine to loratadine OTC because of the timing of the FDA approval of desloratadine. The likely effect was to diminish the rate ratio for the sum total of switching from other LSAs to loratadine OTC. Visual inspection of the rates (not rate ratios) found in the OTC coverage period (switching from desloratadine to loratadine OTC was found to occur at a rate of 25 enrollees per 1,000 desloratadine users [Table 4], outpacing all other drug class members) suggests that the effect of this limitation may not be large. This result is consistent with the effect seen from the noncoverage period in which the most common switch was from loratadine to the nearly chemically identical desloratadine.
As an alternative to the rate-ratio method, we conducted a supplementary analysis of incident use in this Medicaid population over 3 years using an autoregressive integrated moving average (ARIMA) model. We used an ARIMA (0,0,1) model with adjustment for 12-month seasonality. This model was used to forecast LSA use under varying policy scenarios. However, 2 major limitations arose from the ARIMA analysis. Since loratadine OTC was not a covered product during the period from November 2002 to November 2003, we cannot accurately capture nor assume OTC use or nonuse from administrative claims data using time series alone. Furthermore, we had less than the preferred 20 months of data to identify (overlay) our model (after adjusting for seasonality). Thus, this approach was determined to be inadequate for our study and probably for other studies of Rx-to-OTC conversions.

In our analysis, we chose to use eligibility criteria that maximized the inclusion of LSA pharmacy claims. Using the “any eligibility” criterion for all analyses with run-in periods enabled us to capture 80% to 90% of all LSA use. Had we used continuous eligibility criteria, we would have captured only 50% to 60% of all LSA use. We conducted a separate supplementary analysis that required continuous eligibility, and only small differences in rates (less than 2%) were observed when compared with the “any eligibility” models; thus, we present here the more inclusive analysis using the “any eligibility” criterion.

We also required exclusive use of drug products for all of the analyses in prepolicy periods. Requiring 1 year of exclusive use for incident switching in time series and the prepolicy period, exclusive use for the rate-ratio calculations was necessary to elicit a more true policy effect. Inclusion of recipients making multiple switches during the prepolicy periods might have led to misclassification errors. An infinite number of user classifications exists for these multiple switchers. Requiring exclusive use of a given LSA for a predefined period ensures appropriate classification for true users of specific drugs. Using an alternative criterion such as “drug of last fill” simplifies classification but would appear to increase the likelihood of misclassification of drug switches attributable to the policy change. Since the focus of the present study was on switching rates and not aggregate switching or aggregate costs, we chose the more conservative approach. We acknowledge that rates of switching due to the policy changes may be slightly different for these “multiple” switchers but that these actual rates would be quite difficult to determine, and these types of switchers were substantially less common.

We believe that our multifaceted approach is necessary when evaluating product switching for LSAs in a Medicaid program, as well as other populations, especially when considering drugs that are used as needed. The rate-ratio approach should perform even more robustly with medications that are used for chronic conditions where continuous use affords more precise measures and reduces the likelihood of misclassification resulting from the exclusion of subjects with use of multiple products in a therapeutic class. We also believe that the rate-ratio approach described herein has useful application to analyses of multiple insurance plans over a single period, using one of these plans as a referent.

The policy change made in November 2003 to cover loratadine OTC was the first such OTC coverage for other than insulin products in the NC Medicaid program. The dissemination of OTC coverage information to prescribers and pharmacists as well as the learning curve associated with claims adjudication for nonlegend drugs likely contributed to the slow uptake of loratadine OTC. It is likely that there will be additional benefits from this policy change to cover loratadine OTC, both for additional loratadine OTC claims as well as future OTC products. The NC Medicaid program is now better positioned for future LSA conversions, as well as potential class conversions such as the possible introduction of OTC statin drugs.

### Conclusion

Medicaid recipients switched to another covered Rx-only LSA in the loratadine noncoverage period at a rate greater than twice that of the baseline period of coverage (2.16 [95% CI, 2.10-2.22]). After a subsequent policy change to extend coverage to loratadine OTC, there was minimal switching to loratadine OTC from another Rx LSA despite a copayment differential of $2 ($3 for an Rx LSA versus $1 for loratadine OTC). Though the average cost per LSA pharmacy claim dropped $4.15 (6.6%), from $62.79 in the baseline period to $58.64 in the OTC coverage period, time-series and rate-ratio results suggest that an additional $6.01 (10.2%) could have been saved per LSA pharmacy claim had OTC coverage been in effect at the time of the conversion of loratadine to OTC status. Though OTC conversion and subsequent OTC coverage both seem to have reduced overall LSA expenditures, failure to cover the OTC product at the time of OTC conversion resulted in substantial opportunity costs in lost savings. Medicaid programs, as well as perhaps private plans, may capture these savings and prevent accelerated switching at the time of OTC conversion by making coverage decisions before FDA approval of conversion of drugs from Rx to OTC status.

### ACKNOWLEDGMENTS

The authors would like to thank Emily Brouwer, MPH, PharmD candidate, University of North Carolina School of Pharmacy, Chapel Hill, and the JMCP peer reviewers and editor-in-chief for their constructive advice with this manuscript.

### DISCLOSURES

Funding for this research was provided by the Pharmacy Foundation of North Carolina, the University of North Carolina School of Pharmacy, and AccessCare of North Carolina (a nonprofit organization) and was obtained by authors Troy K. Trygstad, Richard A. Hansen, and Steven E. Wegner.
The authors disclose no potential bias or conflict of interest relating to this article. Trygstad served as principal author of the study. Study concept and design were contributed primarily by Trygstad and Hansen, with input from Wegner. Data collection was primarily the work of Trygstad, with input from Wegner. Data interpretation was the work of Trygstad and Hansen. Drafting of the manuscript was the work of all authors; its revision was the work of Trygstad.

REFERENCES

Diabetes is one of the leading causes of morbidity and mortality in the United States. An estimated 17 million Americans are affected by the disease, with nearly 1 million new cases of diabetes being diagnosed per year.\(^1\) Type 2 diabetes is more prevalent than type 1 diabetes and accounts for more than 90% of diabetes cases. The economic burden of diabetes cost the United States an estimated $132 billion in 2002 in medical expenditures and lost productivity.\(^2\)

Poor glycemic control is most often a cause of diabetic complications, which form an important component of the excess direct medical costs of treating patients with type 2 diabetes.\(^3\) Results from the United Kingdom Prospective Diabetes Study (UKPDS) have indicated that tight glycemic control is improved by use of pharmacotherapy involving oral hypoglycemic agents or insulin.\(^4\) Emerging therapies are designed to offer an alternative to standard therapies, which may improve glycemic control and help reduce incidence or the severity of complications and, hence, the cost of type 2 diabetes. Despite evidence that tight glycemic control reduces both short- and long-term costs in type 2 diabetes, most patients do not have good control.\(^5\) This may be due to the progressive nature of type 2 diabetes or the fact that type 2 diabetes is not managed adequately in clinical practice.

**CONCLUSION:** Medicaid fee-for-service patients initiated on either pioglitazone or rosiglitazone incurred higher diabetes-related pharmacy costs, which were offset by lower costs for ER visits and hospitalizations in this 12-month analysis.

**AUTHORS**

IFTEKHAR KALSEKAR, PhD, is an assistant professor, College of Pharmacy and Health Sciences, Butler University, Indianapolis, Indiana; SHRIVIDYA IYER, PhD, is a pharmacoeconomic scientist, outcomes research, medical and scientific affairs, Takeda Pharmaceuticals North America, Inc., Lincolnshire, Illinois; RUKMINI RAJAGOPALAN, DrPH, MBA, RN, is a strategic consultant, health economics and statistics, Vernon Hills, Illinois (she was an employee of Takeda Pharmaceuticals North America, Inc. at the time of this study); REEMA MODY, PhD, MBA, is a manager, health economics and outcomes research, TAP Pharmaceutical Products, Inc., Lake Forest, Illinois (she was a doctoral student, Department of Pharmaceutical Systems and Policy, West Virginia University, Morgantown, at the time of this study); JAN KAVOOGKIAN, PhD, MBA, is an assistant professor, Department of Pharmaceutical Systems and Policy, School of Pharmacy, West Virginia University, Morgantown.

**AUTHOR CORRESPONDENCE:** Iftekhar Kalsekar, PhD, Assistant Professor, College of Pharmacy and Health Sciences, Butler University, 4600 Sunset Ave., Indianapolis, IN 46208. Tel: (317) 940-9421; Fax: (317) 940-8520; E-mail: ilalsek@butler.edu

"Note: An editorial on the subject of this article appears on pages 160-72 of this issue."
practice. The difficulty and expense of achieving tight glycemic control, coupled with the high prevalence of the disease and possibilities of long-term complications, make it important to consider the best strategy of choosing a therapy directed at tight control while simultaneously controlling for resource utilization.

Failure to control glycemic levels by diet and exercise typically leads to prescribing one of the many classes of oral hypoglycemic agents available in the market. The most recent class of oral hypoglycemic agents is the thiazolidinediones (TZDs), which were introduced into the U.S. health care delivery system in the 1990s. TZDs have a unique mechanism of action in improving insulin sensitivity. They are used as monotherapy as well as combination therapy and have been associated with effective glycemic control and reductions in various macrovascular complications associated with type 2 diabetes. In addition to their ability to decrease insulin resistance and lower glucose concentrations, TZDs have been found to be associated with favorable effects on lipids, including an increase in high-density lipoprotein cholesterol (HDL-C) and reductions in triglyceride and free fatty acid levels.8

Insulin has been utilized for more than 80 years in the management of diabetes and continues to serve as the definitive treatment for type 1 diabetes.9 However, the pharmacoeconomics and medical indications for insulin are controversial in treatment of type 2 diabetes. It is not proven that use of insulin would produce benefits such as lower incidence of complications and better quality of life in patients with type 2 diabetes.10 Because of favorable results from clinical trials, it has been recommended that insulin be used more aggressively and much earlier in the treatment of patients with type 2 diabetes.11,12 However, the glycemic control demonstrated by insulin and TZDs in clinical trials might not be consistent with results in actual practice because of a lack of supervision and presumably decreased adherence to medication regimens.

In addition to the effect of choice of therapy on glycemic control, impact on economic outcomes must also be considered. Although the direct costs of hypoglycemic medications and supplies can be easily compared, data on how insulin therapy affects overall resource utilization in patients with type 2 diabetes are very limited, especially when compared with newer oral hypoglycemic agents such as TZDs. Experimental studies such as clinical trials typically do not include estimates of resource utilization, and this measure might not be valid because clinical trials require additional administrative costs in medical supervision and the resource use is mandated in large part by study protocols.13,16

Pharmacotherapy for patients with type 2 diabetes entails continuous use of medications. Insurance sources may restrict the use of more expensive medications through cost control mechanisms like drug formularies, thus limiting access to expensive therapies. As part of efforts to avoid a dramatic increase in health care costs for type 2 diabetes patients and also ensure widespread access to efficient treatments, it is critical to compare health care costs incurred with new therapies versus conventional therapies. Although cost-effectiveness of TZDs as compared with older oral hypoglycemic agents has been documented in some studies using simulation models,17,18 no study has reported cost-estimate comparisons between TZDs and insulin therapies in actual practice settings.

The objective of this study was to compare health care utilization and costs between type 2 diabetes patients initiating therapy with TZD or insulin in a Medicaid population.

**Methods**

**Data Source**

The study was conducted using medical and pharmacy claims data of a state Medicaid program (West Virginia [WV])
Medicaid). Insurance claims data are a valid source for identifying disease conditions and assessing utilization parameters and thus provide an opportunity to conduct inexpensive, nonintrusive research providing high statistical power in real-world settings. This study was approved by WV Medicaid and the Institutional Review Board at West Virginia University.

Patient Identification
We identified patients with at least 1 inpatient admission with principal diagnoses of type 2 diabetes (identified using International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 250.0x-250.9x, where x = 0 or 2) or at least 2 inpatient admissions/2 outpatient facility or physician office visit claims for which any diagnoses was recorded as type 2 diabetes.

Study Design
The study used a retrospective cohort design. The study compared a cohort of patients initiating TZDs (pioglitazone or rosiglitazone) with those initiating insulin in terms of their health care utilization and costs. The enrollment period extended from January 1, 1999, to December 31, 2001. The first pharmacy claim for a TZD (pioglitazone or rosiglitazone) or insulin was treated as the index pharmacy claim. A 12-month preperiod without a pharmacy claim for a TZD or insulin confirmed that the patient was new to the use of these medications. The analysis was restricted to patients with at least 6 pharmacy claims for the index drug in the 12-month follow-up period (Table 1).

Exclusion Criteria
• Troglitazone belongs to the thiazolidinedione class of OHAs and was removed from the U.S. market in March 2000 due to its hepatotoxicity. Hence, patients initiating therapy with troglitazone were not included in the TZD group, but troglitazone use was permitted in the preperiod (Table 1).
• Patients initiating polytherapy with a combination involving both insulin and TZDs were also excluded.
• The Medicaid fee-for-service medical and pharmacy claims in the administrative database did not include medical and pharmacy claims reimbursed through either Medicare or Medicaid managed care. Since Medicaid recipients aged 65 years and older are eligible for coverage under both Medicaid and Medicare, the subjects of this research were limited to all Medicaid recipients older than 18 years and younger than 65 years to avoid the issue of coverage under both Medicaid and Medicare. For similar reasons, Medicaid recipients who were part of managed care were not included in the study. Patients who were not continuously eligible in the follow-up periods were also excluded from the study. These exclusion criteria were used to ensure the availability of comprehensive health care utilization data for our study sample.

Study Outcomes
Health care utilization and costs were assessed over the period of 12 months postindex pharmacy claim.

Health Care Utilization
Physician office visits, emergency room (ER)/hospitalization episodes, and pharmacy claims were identified in the follow-up period. The number of physician office visits, ER/hospitalization episodes, and pharmacy claims were computed; ER visits that subsequently led to a hospitalization were not included, to avoid double counting. Overall health care utilization was computed irrespective of the diagnoses codes or National Drug Codes (NDCs). Type 2 diabetes-related utilization was computed by restricting the calculation of utilization variables to claims with a primary or secondary diagnosis of type 2 diabetes (ICD-9-CM codes: 250.0x-250.9x, where x=0 or 2) and NDCs for diabetes medications or insulin.

Health Care Costs
Payments made by the Medicaid program to hospitals, medical providers, and pharmacies were used to compute the costs. For hospital costs, WV Medicaid reimbursement rates on the basis of diagnosis-related group (DRG) codes in the year 2002 were used. For DRG codes that did not have a reimbursement value from WV Medicaid, the relative weight of the DRG was used to assign hospitalization costs. (Each DRG code is associated with a relative weight. WV Medicaid reimbursement values on the basis of DRG codes were used to obtain an average reimbursement rate for a unit relative weight. For DRG codes that did not have a reimbursement value from WV Medicaid, the relative weight of the DRG was used to assign hospitalization costs. (A DRG weight of 1 was equal to $ 4,632.66, based on reimbursements from WV Medicaid in the year 2002.) This value was used in the calculation of costs for hospitalizations based on the relative weight of the DRG.) Since the administrative claims for patients were selected over the period of a few years, the costs were inflation-adjusted to 2002 costs using the medical care and prescription drug price indexes.

Overall health care costs were computed irrespective of the diagnoses codes. The components of ER/hospitalization, outpatient, and pharmacy costs were computed separately. Type 2 diabetes-related costs were computed by summing paid amounts for claims with a primary or secondary diagnosis code for type 2 diabetes. Pharmacy claims for oral hypoglycemic agents and insulin were identified on the basis of NDCs. Pharmacy claims for diabetic supplies such as syringes, needles, and glucose testing equipment were also identified using NDCs. Type 2 diabetes-related costs were examined separately in terms of ER/hospitalization costs, outpatient costs, and pharmacy costs.

Statistical Analysis
Descriptive frequencies were used to describe the study popu-
Propensity Score Model to Predict the Initiation of Thiazolidinediones (Pioglitazone or Rosiglitazone) Therapy

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (in years)</td>
<td>0.03</td>
<td>0.01</td>
<td>0.00*</td>
<td>1.03 (1.01-1.04)</td>
</tr>
<tr>
<td>Males (reference: females)</td>
<td>-0.12</td>
<td>0.13</td>
<td>0.36</td>
<td>0.89 (0.68-1.15)</td>
</tr>
<tr>
<td>Whites (reference: nonwhites)</td>
<td>0.16</td>
<td>0.29</td>
<td>0.57</td>
<td>1.17 (0.67-2.05)</td>
</tr>
<tr>
<td>Urban (reference: rural)</td>
<td>0.08</td>
<td>0.22</td>
<td>0.73</td>
<td>1.08 (0.70-1.68)</td>
</tr>
<tr>
<td><strong>Year of index prescription (reference: 2001)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>-1.88</td>
<td>0.17</td>
<td>0.00*</td>
<td>0.15 (0.11-0.22)</td>
</tr>
<tr>
<td>2000</td>
<td>-0.09</td>
<td>0.17</td>
<td>0.60</td>
<td>0.92 (0.66-1.27)</td>
</tr>
<tr>
<td><strong>Presence of microvascular complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>0.74</td>
<td>0.18</td>
<td>0.69</td>
<td>1.08 (0.75-1.54)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>-0.36</td>
<td>0.22</td>
<td>0.09</td>
<td>0.70 (0.46-1.06)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>-0.25</td>
<td>0.32</td>
<td>0.44</td>
<td>0.79 (0.41-1.46)</td>
</tr>
<tr>
<td><strong>Presence of macrovascular complications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>-0.31</td>
<td>0.17</td>
<td>0.07</td>
<td>0.74 (0.53-1.02)</td>
</tr>
<tr>
<td>Peripheral vascular</td>
<td>0.06</td>
<td>0.19</td>
<td>0.74</td>
<td>1.06 (0.74-1.53)</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>-0.10</td>
<td>0.26</td>
<td>0.71</td>
<td>0.91 (0.55-1.50)</td>
</tr>
<tr>
<td><strong>Presence of comorbid conditions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.67</td>
<td>0.16</td>
<td>0.00*</td>
<td>1.95 (1.43-2.67)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>-0.31</td>
<td>0.13</td>
<td>0.02*</td>
<td>1.36 (1.05-1.77)</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.11</td>
<td>0.28</td>
<td>0.71</td>
<td>1.11 (0.64-1.94)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>-0.72</td>
<td>0.26</td>
<td>0.01*</td>
<td>0.49 (0.29-0.82)</td>
</tr>
<tr>
<td>Asthma</td>
<td>-0.19</td>
<td>0.16</td>
<td>0.23</td>
<td>0.83 (0.60-1.13)</td>
</tr>
<tr>
<td><strong>Diabetes-related utilization and costs in the preperiod</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>0.00</td>
<td>0.00</td>
<td>0.90</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>ER/hospital costs</td>
<td>0.00</td>
<td>0.00</td>
<td>0.48</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Pharmacy costs</td>
<td>0.00</td>
<td>0.00</td>
<td>0.45</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Total costs</td>
<td>0.00</td>
<td>0.00</td>
<td>0.23</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>No. of physician visits</td>
<td>0.01</td>
<td>0.02</td>
<td>0.55</td>
<td>1.01 (0.97-1.06)</td>
</tr>
<tr>
<td>No. of visits to an endocrinologist</td>
<td>0.09</td>
<td>1.00</td>
<td>0.35</td>
<td>1.09 (0.91-1.32)</td>
</tr>
<tr>
<td>No. of ER/hospital episodes</td>
<td>-0.17</td>
<td>0.07</td>
<td>0.02*</td>
<td>0.84 (0.73-0.97)</td>
</tr>
<tr>
<td><strong>Other medications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>-0.63</td>
<td>0.27</td>
<td>0.02*</td>
<td>0.53 (0.31-0.91)</td>
</tr>
<tr>
<td>Nitrates</td>
<td>0.18</td>
<td>0.19</td>
<td>0.34</td>
<td>1.20 (0.82-1.75)</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>2.00</td>
<td>1.15</td>
<td>0.09</td>
<td>7.27 (0.76-69.70)</td>
</tr>
<tr>
<td>Antithrombolytic agents</td>
<td>-0.01</td>
<td>0.31</td>
<td>0.99</td>
<td>0.99 (0.54-1.84)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>0.09</td>
<td>0.29</td>
<td>0.75</td>
<td>1.10 (0.62-1.94)</td>
</tr>
<tr>
<td>Other cardiovascular agents</td>
<td>0.32</td>
<td>0.42</td>
<td>0.45</td>
<td>1.37 (0.60-3.13)</td>
</tr>
<tr>
<td><strong>Total health care utilization and cost in the preperiod</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient costs ($)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.35</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>ER/hospital costs ($)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.03*</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Pharmacy costs ($)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.64</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Total costs ($)</td>
<td>0.00</td>
<td>0.00</td>
<td>0.32</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>No. of ER/hospital episodes</td>
<td>0.03</td>
<td>0.03</td>
<td>0.32</td>
<td>1.03 (0.98-1.08)</td>
</tr>
<tr>
<td><strong>Type of oral hypoglycemic therapy in the preperiod</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No therapy (incident case of type 2 diabetes)</td>
<td>-0.34</td>
<td>0.27</td>
<td>0.21</td>
<td>0.71 (0.42-1.21)</td>
</tr>
<tr>
<td>Alpha glucosidase inhibitors</td>
<td>-0.54</td>
<td>0.28</td>
<td>0.06</td>
<td>0.58 (0.33-1.01)</td>
</tr>
<tr>
<td>Biguanides</td>
<td>-0.11</td>
<td>0.15</td>
<td>0.48</td>
<td>1.11 (0.83-1.50)</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>-0.65</td>
<td>0.31</td>
<td>0.04*</td>
<td>0.52 (0.28-0.97)</td>
</tr>
<tr>
<td>Rezulin</td>
<td>0.81</td>
<td>0.25</td>
<td>0.00*</td>
<td>2.25 (1.37-3.69)</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>0.28</td>
<td>0.15</td>
<td>0.07</td>
<td>1.32 (0.97-1.78)</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>-0.01</td>
<td>0.38</td>
<td>0.97</td>
<td>0.99 (0.47-2.08)</td>
</tr>
</tbody>
</table>

MODEL FIT:
-2 log-likelihood = 1636.947; chi-square statistic = 392.914; P = 0.000.
Nagelkerke’s R² statistic = 0.28.

* Indicates significant difference at the 0.05 level (2-sided). CI = confidence interval; ER = emergency room.
ulation. Evaluation of the choice of diabetes therapy on type 2 diabetes economic outcomes may be subject to selection bias since it is likely that the patients receive specific diabetes therapy based on the severity of their conditions. It is possible that patients prescribed insulin had higher A1c (glycosylated hemoglobin) levels at baseline compared with those prescribedTZDs. Since normal regression techniques cannot adequately control this selection bias, propensity matching was used for analysis.22 This technique employed an initial logistic regression model to obtain estimated probabilities of receiving TZDs as compared with receiving insulin on the basis of demographics, year of index prescription, presence of microvascular/macrovascular complications, comorbidity, type 2 diabetes-related utilization and costs in the 12-month preperiod, overall health care utilization and costs in the preperiod, and type of oral hypoglycemic agent/other medications in the preperiod. Patients with similar probabilities (± 0.01) to receive TZDs were matched, and analysis was restricted to this matched sample.

This propensity matching technique helped in substantially reducing selection bias in estimating the impact of choice of diabetes therapy on subsequent health care utilization and costs. As the process of propensity matching leads to a comparable sample, further statistical control was not required. However, since utilization and cost data are not normally distributed, univariate tests such as t tests are inappropriate. Nonparametric tests such as the Mann-Whitney U test cannot be applied since they conduct significance testing on ranks as opposed to means. Hence, after propensity matching, nonparametric bootstrapping was used to evaluate utilization and cost differences between patients initiating therapy with TZDs or insulin.23,24 The bias-corrected and accelerated (BCa) method, which adjusts for skewness and nonconstant variance in the bootstrap sampling distribution was used. General guidelines recommend the use of 1,000 or more repetitions during bootstrapping.25 Hence, 2,500 repetitions were used for calculating the BCa confidence intervals in the study. The statistical analyses were conducted using Statistical Package for Social Sciences, version 13.0 (SPSS Inc., Chicago, IL) and Stata, version 9 (Stata Corporation, College Station, TX).

Results

A total of 32,183 patients, from a Medicaid population of approximately 230,000 recipients, were identified as having type 2 diabetes in the enrollment period (1999-2001). After accounting for the inclusion/exclusion criteria, the study sample consisted of 1,961 type 2 diabetes patients initiating therapy with TZDs or insulin in the 3-year enrollment period (TZDs = 1,523; insulin = 438) (See Table 1). A propensity matching technique was used to restrict the analysis to patients who had comparable baseline demographics, utilization, complications, and comorbidities. The propensity score model used to predict the receipt of TZDs was found to be significant with a Nagelkerke R² value of 28.4% (Table 2). Patients were then matched based on their predicted probability (± 0.01) to receive TZDs. Three hundred forty-five patients initiating insulin therapy were matched on a 1:1 basis to 345 patients initiating TZDs. Ninety-three patients initiating insulin could not be matched to a patient receiving TZD and represented a distinct group of insulin patients to whom the study results are not generalizable. These unmatched patients were probably more severe at baseline since they had higher utilization and expenditures in the 12-month preperiod compared with the insulin patients who could be matched to patients initiating therapy with TZDs (Number of diabetes-related ER/hospitalization episodes in the 12-month preperiod [mean ± SD]: Matched insulin patients = 0.9 ± 1.4, Unmatched insulin patients = 1.5 ± 2.5); Total diabetes-related costs in the 12-month preperiod [mean ± SD]: Matched insulin patients = $3,931.3 ± $5,745.0, Unmatched insulin patients = $6,415.3 ± $10,671.3).

Table 3 indicates clearly that the propensity-matched sample of TZD and insulin patients was more similar on baseline variables as compared with the sample before propensity matching. Chi-square tests were used to examine differences in categorical baseline characteristics. For continuous data, bootstrapping on independent sample t tests was used to conduct the significance testing. The propensity-matched sample did not demonstrate significant differences between patients initiating insulin or TZDs on any of the variables related to patient demographics, year of index prescription, presence of complications, comorbidity, overall and type 2 diabetes-related utilization and costs in the 12-month preperiod, and type of oral hypoglycemic agent/other medications in the preperiod. Since the propensity-matched sample of patients receiving TZDs and insulin had similar demographic and utilization characteristics, the utilization and cost outcomes were compared using appropriate univariate analysis.

Health Care Utilization in the 12-Month Follow-up Period (Table 4)

Overall Utilization

Nonparametric bootstrapping revealed that there was no significant difference in the number of ER/hospitalization episodes or the number of pharmacy claims between patients initiating therapy with TZDs or insulin. However, patients initiating TZDs had 11.4% fewer physician office visits as compared with patients initiating insulin therapy (P < 0.05).

Type 2 Diabetes-Related Utilization

A subsequent analysis, restricted to type 2 diabetes-related utilization, indicated that patients initiating therapy with TZDs had 18.2% fewer type 2 diabetes-related physician office visits in the 12-month follow-up period (P < 0.05). However, TZD patients filled 14.1% more diabetes prescriptions than patients initiating therapy with insulin (P < 0.01). There were no significant differences in the number of diabetes-related ER/hospitalization episodes.
### TABLE 3
Baseline Differences Between Patients Initiating Thiazolidinediones (Pioglitazone or Rosiglitazone) Therapy Versus Insulin, Before and After Propensity Matching

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Before Propensity Matching</th>
<th>After Propensity Matching</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TZDs (n = 1,523)</td>
<td>Insulin (n = 438)</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>51.0 ± 9.0*</td>
<td>48.1 ± 10.5*</td>
</tr>
<tr>
<td>Males</td>
<td>35.6%</td>
<td>38.5%</td>
</tr>
<tr>
<td>Whites</td>
<td>95.4%</td>
<td>94.0%</td>
</tr>
<tr>
<td>Urban</td>
<td>91.4%</td>
<td>91.1%</td>
</tr>
<tr>
<td>Year of index prescription</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>16.2%*</td>
<td>49.3%*</td>
</tr>
<tr>
<td>2000</td>
<td>50.4%*</td>
<td>28.1%*</td>
</tr>
<tr>
<td>Presence of microvascular complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>16.6%</td>
<td>15.3%</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>7.9%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>3.9%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Presence of macrovascular complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>31.9%*</td>
<td>38.8%*</td>
</tr>
<tr>
<td>Peripheral vascular</td>
<td>14.6%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>6.2%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Presence of comorbid conditions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>82.9%*</td>
<td>69.6%*</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>61.3%*</td>
<td>46.8%*</td>
</tr>
<tr>
<td>Cancer</td>
<td>5.6%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Liver disease</td>
<td>3.7%</td>
<td>8.7%</td>
</tr>
<tr>
<td>Asthma</td>
<td>18.3%*</td>
<td>24.2%*</td>
</tr>
<tr>
<td>Diabetes-related utilization and costs in the preperiod (mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient costs ($)</td>
<td>511 ± 1685</td>
<td>582 ± 1024</td>
</tr>
<tr>
<td>ER and hospital costs ($)</td>
<td>1,499 ± 4,619*</td>
<td>3,298 ± 6,655*</td>
</tr>
<tr>
<td>Pharmacy cost ($)</td>
<td>835 ± 803*</td>
<td>579 ± 733</td>
</tr>
<tr>
<td>Total costs ($)</td>
<td>2,845 ± 5,252*</td>
<td>4,490 ± 7,141*</td>
</tr>
<tr>
<td>No. of physician visits</td>
<td>2.6 ± 3.1</td>
<td>2.3 ± 3.3</td>
</tr>
<tr>
<td>No. of visits to an endocrinologist</td>
<td>0.1 ± 0.7</td>
<td>0.1 ± 0.7</td>
</tr>
<tr>
<td>No. of ER/hospital episodes</td>
<td>0.6 ± 1.3*</td>
<td>1.00 ± 1.7*</td>
</tr>
<tr>
<td>Other medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>5.4%*</td>
<td>8.4%*</td>
</tr>
<tr>
<td>Nitrates</td>
<td>18.2%</td>
<td>18.3%</td>
</tr>
<tr>
<td>Antiarrhythmics</td>
<td>1.4%*</td>
<td>0.2%*</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>3.8%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>4.9%</td>
<td>6.2%</td>
</tr>
<tr>
<td>Other cardiovascular agents</td>
<td>3.0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Overall health care utilization and cost in the preperiod (mean ± SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient costs ($)</td>
<td>3,004 ± 6,227*</td>
<td>4,733 ± 9,554*</td>
</tr>
<tr>
<td>ER and hospital costs ($)</td>
<td>2,368 ± 6,257</td>
<td>6,674 ± 17,156*</td>
</tr>
<tr>
<td>Pharmacy costs ($)</td>
<td>3,370 ± 2,455</td>
<td>3,284 ± 3,652</td>
</tr>
<tr>
<td>Total health care cost ($)</td>
<td>8,742 ± 10,851*</td>
<td>14,692 ± 23,578*</td>
</tr>
<tr>
<td>No. of ER/hospital episodes</td>
<td>1.5 ± 3.1*</td>
<td>2.6 ± 5.1*</td>
</tr>
<tr>
<td>Type of oral hypoglycemic therapy in the preperiod</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No therapy (incident case of type 2 diabetes)</td>
<td>4.4%*</td>
<td>8.0%*</td>
</tr>
<tr>
<td>Alpha glucosidase inhibitors</td>
<td>4.2%</td>
<td>6.2%</td>
</tr>
<tr>
<td>Biguanides</td>
<td>54.4%*</td>
<td>46.3%*</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>3.0%*</td>
<td>5.3%*</td>
</tr>
<tr>
<td>Troglitazone†</td>
<td>21.6%*</td>
<td>11.2%*</td>
</tr>
<tr>
<td>Sullfonylureas</td>
<td>70.6%*</td>
<td>57.8%*</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>4.7%*</td>
<td>2.3%*</td>
</tr>
</tbody>
</table>

* Indicates significant difference at the 0.05 level (2-sided).
† Patients initiating therapy with troglitazone were excluded from the analysis, but prior use of troglitazone was allowed. After propensity matching, the extent of troglitazone use in insulin versus TZD (pioglitazone or rosiglitazone) initiators was found to be similar, 13.0% and 12.8%, respectively.

ER = emergency room; TZD = thiazolidinedione.
Health Care Costs in the 12-Month Follow-up Period (Table 5)

Overall Costs
The type of diabetes therapy was found to have a significant impact on overall health care costs in the 12-month follow-up period, with TZD patients incurring 18.2% lower overall health care costs as compared with patients initiating therapy with insulin ($P < 0.05$). These differences in overall health care costs were primarily due to 35.7% higher ER/hospitalization costs in patients initiating therapy with insulin than initiating therapy with TZD ($P < 0.05$). No significant differences were observed in terms of outpatient and prescription costs between these groups.

Type 2 Diabetes-Related Costs
The choice of diabetes therapy was also found to have a significant impact on total type 2 diabetes-related health care costs, with patients initiating TZDs incurring 25.2% lower costs than patients initiating insulin therapy ($P < 0.05$). Although the diabetes-related prescription costs were 53.1% higher for patients initiating TZDs than patients initiating insulin ($P < 0.001$), they were offset by significantly lower type 2 diabetes-related ER/hospitalization costs for patients with TZDs (43.9%; $P = 0.003$). No significant differences were observed in terms of type 2 diabetes-related outpatient costs between these groups.

Discussion
The results of our study demonstrated that overall health care and type 2 diabetes-related costs for a 12-month follow-up period were significantly lower for patients initiating therapy with TZDs as compared with those initiating therapy with insulin. The high acquisition costs of TZDs contributed to higher pharmacy costs for patients initiating TZDs versus insulin. However, these higher pharmacy costs were offset by lower costs for ER/hospitalization for the TZD group as compared with the insulin group.

Though direct cost comparisons between TZDs and insulin have not been previously reported, other studies have reported resource utilization and cost comparisons between insulin and other oral therapies like metformin and sulfonylurea. Brown et al. reported that, in a retrospective chart review of type 2 diabetes patients who had failed prior sulfonylurea therapy, addition of metformin was more cost effective than was the addition of insulin. Overall treatment costs were higher for insulin-treated patients.

Hayward et al. reported an increase in outpatient visits, laboratory tests, and glucose monitoring devices for patients initiating insulin therapy as compared with those using sulfonylureas. These results were controlled for selection bias by adjusting for baseline severity of illness of the patients. This study also indicated that although insulin therapy was associated with lower A1c levels in all type 2 diabetes patients, it was only

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Comparison of Overall Type 2 Diabetes-Related Health Care Utilization in the 12-Month Follow-up Period Between Thiazolidinediones (TZDs, Pioglitazone or Rosiglitazone) Versus Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Total costs ($3,727 ± 9,962)</td>
</tr>
<tr>
<td>Thiazolidinediones (n = 345) (Mean ± SD) Insulin (n = 345) (Mean ± SD) (TZD-Insulin)</td>
<td></td>
</tr>
<tr>
<td>No. physician office visits</td>
<td>9.3 ± 8.9</td>
</tr>
<tr>
<td>No. ER visits or hospitalization</td>
<td>2.1 ± 4.9</td>
</tr>
<tr>
<td>No. pharmacy claims</td>
<td>88.1 ± 38.4</td>
</tr>
<tr>
<td>Type 2 diabetes-related utilization</td>
<td>3.6 ± 3.8</td>
</tr>
<tr>
<td>No. physician office visits</td>
<td>1.1 ± 2.5</td>
</tr>
<tr>
<td>No. pharmacy claims</td>
<td>21.9 ± 8.9</td>
</tr>
</tbody>
</table>

* Indicates significant difference at the 0.05 level (2-sided).
CI = confidence interval; ER = emergency room.

<table>
<thead>
<tr>
<th>TABLE 5</th>
<th>Comparison of Overall and Type 2 Diabetes-Related Health Care Costs in the 12-Month Follow-up Period Between Thiazolidinediones (TZDs, Pioglitazone or Rosiglitazone) Versus Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall health care costs ($)</td>
<td>3,727 ± 9,962</td>
</tr>
<tr>
<td>Thiazolidinediones (n = 345) (Mean ± SD) Insulin (n = 345) (Mean ± SD) (TZD-Insulin)</td>
<td></td>
</tr>
<tr>
<td>ER and hospital costs</td>
<td>3,895 ± 7,577</td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>12,377 ± 15,435</td>
</tr>
<tr>
<td>Pharmacy costs</td>
<td>5,116 ± 3,167</td>
</tr>
<tr>
<td>Total costs</td>
<td>2,179 ± 8.9</td>
</tr>
<tr>
<td>Type 2 diabetes-related costs ($)</td>
<td>2,855 ± 8.4</td>
</tr>
<tr>
<td>Thiazolidinediones (n = 345) (Mean ± SD) Insulin (n = 345) (Mean ± SD) (TZD-Insulin)</td>
<td></td>
</tr>
<tr>
<td>ER and hospital costs</td>
<td>893 ± 2.9</td>
</tr>
<tr>
<td>Outpatient costs</td>
<td>1,678 ± 7.0</td>
</tr>
<tr>
<td>Pharmacy costs</td>
<td>5,423 ± 9.2</td>
</tr>
</tbody>
</table>

* Indicates significant difference at the 0.05 level (2-sided).
ER = emergency room.
modestly effective when prescribed for those who initially had A1c levels lower than 10%. Aggressive insulin therapy in such patients was associated with increased health care utilization, with only marginal benefits in glycemic control. Similar results in the present study show that a group of type 2 diabetes patients initiated on TZDs incurred lower resource utilization and costs as compared with a matched sample of patients initiated on insulin.

The higher incidence of ER/hospitalization in the insulin group in our study could be attributed to the high rate of complications reported with insulin therapy. Insulin has been reported to be much less effective in routine clinical practice than in trials because patients may be less motivated and have fewer resources, such as regularly available expert advice for prompt dose adjustments. Hypoglycemia, a frequent complication of intensive diabetes therapy may be mild or severe and necessitate hospitalization. The incidence of hypoglycemia during insulin treatment is reported to be higher than during oral treatment. In a study using medical and pharmacy administrative data, Heaton et al. reported that, during the 6 years of follow-up, more than 16% of insulin-treated patients experienced hypoglycemia profound enough to warrant medical attention. The mean cost per episode was found to be $1,186 (range $181-$4,924) or $7.04 per patient per month. Although the financial burden is smaller than that of late complications of diabetes, hypoglycemia associated with insulin therapy may be associated with significant cost to the health care system.

With respect to insulin therapy, in addition to the costs associated with hypoglycemia, the costs of complications related to therapeutic hyperinsulinemia should be considered. Increased plasma insulin level is considered by some as an independent risk factor for the development of atherosclerosis. TZDs, on the other hand, have been reported to reduce blood pressure and appear to reduce atherosclerotic risk factors through several mechanisms. Results of a case control study by Koro et al. indicated that TZD use was associated with a 49% reduction in myocardial infarction compared with the use of insulin, potentially translating into economic benefits.

Hospitalizations have been reported to account for 40% to 80% of the direct costs of diabetes mellitus and include a high proportion of rehospitalizations, mainly conditioned by poor metabolic control and the presence of chronic complications. Interventions designed to decrease the need for hospitalizations or more efficiently use services during a hospitalization can help lower the total costs of care associated with diabetes.

Limitations

Foremost among the limitations of this study was the imperfect measure of disease severity. Resource utilization in patients with type 2 diabetes can be affected significantly by baseline disease severity. Our analysis controlled for severity of diabetes based on information available from administrative claims data. Lack of clinical values such as A1c and blood glucose levels can raise concerns regarding the comparability of patients initiating insulin or TZD therapy. Selection bias was controlled by restricting the analysis to a comparable group of insulin and TZD users obtained after propensity matching. However, use of propensity matching may have resulted in the exclusion of type 2 diabetes patients who had higher disease severity and were therefore prescribed insulin. This could have resulted in the inability of our technique to match such insulin users to any TZD users in our study population. No comparative information for this severe group can be derived from our results, thus restricting the generalizability of our study results to presumably type 2 diabetes patients without extreme glycemic levels.

Second, it is also possible that patients initiated on insulin may demonstrate higher initial treatment costs due to an increased frequency of physician office visits for dosing adjustments and instruction/education. These short-term start-up costs may not be an important factor over a longer follow-up period. Because of a short duration of follow-up in our study (1 year), treatment costs for insulin may appear artificially higher. However, our study showed that the increased costs for patients initiated on insulin were primarily a result of ER/hospitalization episodes not increased outpatient visits.

Third, the study results are limited to recipients younger than 65 years who were part of a state Medicaid fee-for-service program. Since the present study was conducted in WV Medicaid, it is not necessarily representative of other state Medicaid programs and may differ significantly from a managed Medicaid population.

Fourth, administrative claims data more recent than 2002 were not available, resulting in the use of claims data from 1999 through 2002. Troglitazone was the most frequently prescribed TZD in 1999 but was withdrawn from the U.S. market in March 2000. In this study period, we restricted our analyses to rosiglitazone and pioglitazone. Troglitazone was excluded from consideration as an index medication in 1999 through March 2000, when it was withdrawn from the market. It is not known how this factor might have confounded the study results, but some patients with an index pharmacy claim for troglitazone would have been excluded from the present study.

This study is also subject to several limitations that are inherent in investigations that rely on the use of administrative claims data. Since administrative claims data were used to determine cost estimates, errors due to billing and coding cannot be ruled out. Only those costs incurred by the WV Medicaid Program were examined. Expenses for health care services incurred by sources other than the WV Medicaid Program were not included in the analysis. For example, drug utilization information about over-the-counter drugs and prescription samples received in the physician’s office were not measurable. This may lead to potential misclassification and an underestimation of overall resource utilization.

Utilization and Costs for Compliant Patients Initiating Therapy With Pioglitazone or Rosiglitazone Versus Insulin in a Medicaid Fee-for-Service Population

March 2006    Vol. 12, No. 2 www.amcp.org
Conclusion

Clinicians treating patients with type 2 diabetes are faced with the task of selecting therapy that can maintain appropriate glycemic levels as well as control resource utilization and expenditures. The best therapeutic alternatives may differ based on the baseline glycemic levels and disease severity of the patients. Our study results indicate that, in a population of type 2 diabetes patients without significantly high utilization and costs at baseline, the initiation of TZDs was associated with lower health care resource utilization and costs compared with patients initiated on insulin therapy.

DISCLOSURES

This study was presented, in part, as a podium session at the annual meeting of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), Washington, D.C., May 18, 2005. It was supported by a grant from the Outcomes Research (Medical and Scientific Affairs) Department at Takeda Pharmaceuticals North America Inc., Lincolnshire, IL. Author Shrividya Iyer is an employee of Takeda Pharmaceuticals; Rukmini Rajagopalan was an employee of Takeda Pharmaceuticals at the time of this study. Funding was obtained by author Jan Kavookjian. The authors disclose no other potential bias or conflicts of interest related to this article.

Ifelkhar Kalsekar served as principal author of the study. Study concept and design were contributed by Kalsekar, Iyer, Rajagopalan, and Kavookjian. Data collection was primarily the work of Kalsekar, Iyer, and author Reema Mody, with input from Kavookjian and Rajagopalan; data interpretation was the work of Kalsekar, Mody, and Kavookjian, with input from Iyer and Rajagopalan. Drafting of the manuscript was primarily the work of Kalsekar and Iyer; its revision was the work of all authors.

REFERENCES

Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature

JENNIFER M. STEPHENS, PharmD, BCPS; MARC F. BOTTEMAN, MSc, MA; and JOEL W. HAY, PhD

ABSTRACT

OBJECTIVE: To review the recent literature (January 2000–November 2005) regarding the impact of antidiabetic medications and glycemic control on the overall costs of care for patients with diabetes in U.S. managed care organizations (MCOs).

SUMMARY: The pharmacy component accounts for typically 20% to 30% (full range, 10%-65%) of overall costs for MCO patients with diabetes. About 30% of pharmacy expenses are directly related to glycemic control, while the balance is spent on the management of macrovascular and microvascular complications related to diabetes and other common comorbidities such as hypertension and hyperlipidemia. Cost offsets and/or cost savings have been shown with the initiation of insulin therapy, including the use of newer short-acting insulins. Increasing medication possession ratios for antidiabetic medications (including insulins) are correlated with reduced overall health care costs, particularly reductions in hospitalization rates. Patients with diagnosed diabetes not receiving medications have significantly increased health care resource utilization. We identified 8 studies that indicated that improvements in glycemic control lower overall per-patient direct costs within MCOs.

CONCLUSIONS: The literature to date suggests that improving glycemic control and antidiabetic medication persistence reduce overall medical costs for patients with diabetes in managed care plans. Continued expansion of antidiabetic medication options will place increasing pressure on MCOs to assess the return on investment for newer pharmacotherapies. Routine measurement of economic and quality-of-life outcomes alongside clinical outcomes will become necessary for assessing the total value that new antidiabetic medications provide and whether cost offsets to managed care exist. Appropriate use of antidiabetic medications, including medication compliance, is an important component in a strategy to achieve glycemic control and may improve outcomes for patients with diabetes.

KEYWORDS: Managed care, Diabetes, Economics, Review, Burden, Resource utilization, Cost of treatment, Trends, Medications, Glycemic control

J Manag Care Pharm. 2006;12(2):130-42

Authors

JENNIFER M. STEPHENS, PharmD, BCPS, is clinical director, and MARC F BOTTEMAN, MSc, MA, is director, health economics, Pharmerit North America, LLC, Bethesda, Maryland; JOEL W. HAY, PhD, is an associate professor, Department of Pharmaceutical Economics and Policy, University of Southern California School of Pharmacy, Los Angeles.

AUTHOR CORRESPONDENCE: Jennifer M. Stephens, PharmD, BCPS, Clinical Director, Pharmerit North America, LLC, 7272 Wisconsin Ave., Suite 300, Bethesda, MD 20814. Tel: (301) 941-1942; Fax: (301) 656-0183; E-mail: jstephens@pharmerit.com

Copyright © 2006, Academy of Managed Care Pharmacy. All rights reserved.

Diabetes is a high-profile, costly disease to society and payers, including managed care organizations (MCOs). Most recent estimates put the overall annual economic burden of diabetes in the United States at more than $132 billion. Since more than 60% of the U.S. population is covered by some form of managed care, MCOs certainly bear a substantial portion of the diabetes burden in this country.

Depending on patient mix, anywhere from 3% to 10% of members of a typical MCO have diabetes, and these patients consume approximately 15% of health care budgets. At the individual patient level, managed care 3-year health care costs are a minimum of 2 times higher (with no complications) than age-matched controls without diabetes. Excess per-patient expenditures for diabetes averaged more than $3,400 annually in 1994, with most of these excess costs related to hospitalizations and treatment of complications. In fact, costs of diabetes have increased over time for MCOs because of increased utilization of appropriate laboratory testing, outpatient services, and medications to manage diabetes. The increasing expenditures, along with the broad penetration of managed care in the United States, make diabetes a key disease for management of financial risk within an MCO.

Over the past decade, national organizations such as the American Diabetes Association (ADA) have recommended specific target levels of glycemic control (hemoglobin A1c [A1c] <7%) for patients with diabetes to reduce microvascular and macrovascular complications related to hyperglycemia. These recommendations were based upon the landmark results of the 1993 Diabetes Control and Complications Trial in type 1 diabetes and the 1998 United Kingdom Prospective Diabetes Study in type 2 diabetes, which demonstrated that intensive blood glucose control significantly lowers diabetes-related complications. In addition, it is now well established that intensive glucose control is cost effective over the long term, even for newly diagnosed patients. During the last decade, several new classes of oral antidiabetic medications, as well as multiple agents within a class, have become available, opening a variety of new opportunities for achieving the recommendations for more aggressive glycemic control.

The National Committee on Quality Assurance (NCQA), the ADA, and other national diabetes organizations advocating for early diagnosis and optimized glycemic control have spurred MCO investment of significant resources in disease management and pharmacotherapy to improve the management of their diabetic populations. While MCOs have invested significantly in aggressive diabetes management, the overall public health
and economic impacts of these investments remain to be fully appreciated and investigated. Understanding the impact of the investment is important as the diabetes epidemic grows and as new medications become available.

The objective of this review was to synthesize the recent literature regarding the impact of antidiabetic medications and glycemic control on the overall costs of care for patients with diabetes in MCOs. Ultimately, our hope is that a better understanding and appreciation of the value associated with pharmacotherapy as a component of glycemic control will be useful as decision makers for diabetes management adapt their strategies, particularly as the diabetes pharmacologic armamentarium continues to expand.

## Methods

We conducted a systematic literature review focused on the recent economic and resource utilization burden of diabetes in U.S. MCOs, with specific emphasis on antidiabetic medications and glycemic control. Research topics for the review included general burden and cost of diabetes to MCOs, pharmacy utilization patterns for patients with diabetes, impact of diabetes medication on resource utilization (including oral agents, insulin, insulin-related hypoglycemia, and persistence with therapy), the link between glycemic control and costs, and whether investments in pharmacotherapy to achieve glycemic control provide cost offsets to managed care.

The primary electronic database search was conducted in MEDLINE and was limited to English-language articles published from January 2000 through November 2005. The review focused on the past 5 years in order to identify the most recent economic data and trends for the current standards of care. The core search terms were “diabetes and managed care” with the following terms added for specificity: “economics,” “costs,” “medications,” “cost drivers,” “financial trends,” and “complications.”

In addition to the basic MEDLINE search, attempts were made (using the same search terms) to ensure that all potentially relevant information was identified by (1) searching sources represented through MEDLINE’s “related articles/links” feature, (2) searching abstract archives from the ADA and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), (3) searching the Web sites of the NCQA and the Pharmaceutical Research and Manufacturers of America, and (4) using common Internet search engines (Google, Yahoo) to find abstracts, research reports, and information not otherwise identified. Finally, manual reviews of the subject index of the Journal of Managed Care Pharmacy and the bibliographies of relevant retrieved references were also conducted.

The combined MEDLINE and supplemental search strategies resulted in more than 500 abstracts, which were imported into a reference manager database and independently screened by 2 authors to assess relevance. An abstract was deemed relevant and the article retrieved in full text if it had information that addressed diabetes medication utilization within a managed care setting, including prescribing trends, relationship between cost and glycemic control, health care resource utilization patterns, cost information by various areas of care, or overall costs for various medication strategies. Abstracts were excluded if the primary topic of the paper was mental health comorbidities with diabetes, gestational diabetes, or impact of diabetes on employers.

After detailed abstract review, approximately 110 articles were selected and retrieved in full text. Because the focus of the search was on economic impact within MCOs, we selected 37 articles that specifically reported costs or resource utilization trends as key, relevant papers for inclusion in the Results section of this review. These key papers were specifically designed to answer issues related to the research questions and most commonly utilized longitudinal retrospective claims data analyses. Another 31 articles did not meet strict inclusion criteria but did contain information relevant to support background or discussion of the results; among these were studies reporting trends in medication use, studies related to glycemic control or disease management without specific cost data, and studies published prior to the year 2000 that were identified from manual review of bibliographies that reported economic or resource utilization data useful for comparisons with more recent data in this review.

We retrieved articles even if there appeared to be a small chance that they would address economic or resource utilization issues; thus 42 out of 110 retrieved articles were excluded. The most common types of papers excluded were those identified as potentially relevant from the abstract (e.g., the abstract had mentioned economics or resource utilization) but, as we determined by reviewing the full paper, focused only on clinical data. For example, most of the managed care literature on disease management programs (DMPs) focuses on reporting clinical outcomes and performance measures, without linking clinical end points to the economic or resource utilization data at the patient level for overall cost of care. Other common reasons for exclusion of papers were that the study population was not managed care (e.g., the paper made extrapolations to MCOs, but the retrospective data set or study population used was not managed care) or the article was a general review paper without reporting specific economic data.

Where possible, we identify the type of cost reported in the articles (charges, reimbursements, claims paid, total vs. diabetes-attributable). Cost information is reported as it appeared in the original articles to avoid an artificial presentation of results given changing patterns of care and the long time frames of data analysis (>10 years in some studies); however, as an aid for the reader, we used the medical component of the Consumer Price Index to inflate original costs to current 2005 values. The 2005 inflated values are reported in parentheses next to the original
Results

Annual Costs of Diabetes Within MCOs
[expressed in 2005 dollars]
The average per-member (patient) annual cost for a typical mix of patients with diabetes is between $3,715 [$4,614 in 2005 dollars] and $5,760 [$6,532] in closed-model health maintenance organizations (HMOs) or MCOs with some type of DMP, and may be as high as $7,000 [$9,046] without a DMP.\(^7,12-15\) When compared with other diseases, diabetes is neither the least nor most expensive disease to MCOs on a per-patient basis. The annual average cost of diabetes per patient ($4,878 [$6,058]) was higher than asthma ($3,707 [$4,604]) but was half that of the average annual cost for coronary artery disease (CAD, $9,512 [$11,814]) across old and new patients.\(^16\) This study, following patients the year before and after (1999-2000) implementation of a DMP, used predictive modeling from medical and pharmacy claims for total costs and was not limited to disease-specific costs. This study may have failed to exclude diabetes patients from the CAD analysis, thus inflating the burden of CAD as a single diagnosis. For comparison, Nichols and Brown (2002) reported the annual cost of cardiovascular disease (CVD) with no diabetes at $6,396 [$8,257] and CVD with diabetes at $10,172 [$13,132].\(^14\)

For newly diagnosed patients without complications, overall costs are more than 50% lower than for the average patient with diabetes.\(^14\) In a large Michigan HMO, the baseline annual cost for a patient with no complications and diet-controlled diabetes was ~$1,600 [$1,987] for male patients and ~$2,100 [$2,608] for female patients.\(^13\)

Breakdown of Expenditures
Within managed care, the top expenditure category for the broad diabetes population is typically inpatient care. For patients newly diagnosed with no complications, top expenditure categories are pharmacy and outpatient services. Breakdown of costs (as a percentage of total medical costs) within MCOs range as follows: inpatient, 12 to 58%; outpatient, 18 to 50%; and pharmacy, 10 to 65%. By comparison, on the national level across all payers (including Medicare), major expenditures by
category for patients with diabetes were inpatient care (44%), nursing home care (15%), outpatient care (20%), and medications/supplies (19%).

Table 1 shows the breakdown of recent MCO overall direct costs that have been reported in the literature for patients with diabetes.1,7,12,14,17-24

Pharmacy Utilization Patterns for Patients With Diabetes
Several studies have described the general medication and health care resource utilization patterns in patients with diabetes in MCOs. The pharmacy component ranges from 10% to 65% of overall costs for MCOs. Approximately 30% of prescription costs are directly related to glycemic control, while the rest are for management of the macrovascular and microvascular complications of diabetes and common comorbidities such as hypertension and hyperlipidemia.23 Diabetes patients in MCOs often receive many medications. At a closed-model HMO, patients with diabetes received an average of 20 to 24 prescription medications annually for any reason (diabetes and comorbidities).25 Though MCOs may restrict use of new medications, enrollees in MCOs are significantly more likely to be treated with antidiabetic medications in the first place and are also more likely to receive newer, more progressive antidiabetic medications (such as the insulin sensitizers and newer sulfonylureas) compared with patients covered by regular indemnity health plans.26 However, MCOs may also use member cost-sharing (copay) for medications, including oral diabetes medications, which may adversely affect persistence with oral antidiabetic medications.27

Glycemic control (achieving target A1c) is managed with a variety of agents, and the use of insulin is common. Across a variety of studies and types of MCOs, the proportion of diabetes patients receiving insulin typically ranges from 23% to 32%.24,31,32,38,39,40 This rate of insulin use has fallen from more than 40% in the mid-1990s with the entry of newer oral agents that improve insulin resistance and reduce insulin needs, as well as a surge in newly diagnosed patients that do not require insulin early in their disease.7 Similar trends were seen nationally across a variety of payers in the late 1990s, where insulin use decreased and the use of combination regimens of oral antidiabetic agents increased.31 Interestingly, glycemic control rates (A1c <7%) declined from 44.5% to 35.8% during this same time frame.31 Thus, despite a substantial growth in the number of therapeutic options available to treat diabetes in the last decade, a significant proportion of patients with diabetes were still not achieving glycemic goals.

A 5-year (data from 1997-2001) cross-sectional study reported a “snapshot” of drug use patterns each year at 2 HMOs and found that overall utilization of prescriptions for diabetes patients increased because of emphasis on achieving glycemic, blood pressure, and lipid goals.7 In this time frame, both overall drug and diabetes drug expenditures more than doubled in urban/suburban plans. Utilization of metformin, thiazolidinediones (otherwise referred to as glitazones), multiple-drug diabetes regimens, cholesterol-lowering agents, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers more than doubled, while the use of insulin, sulfonylureas, and alpha-glucosidase inhibitors declined or remained stable.7

Another study examined diabetes drug therapy trends using data from 1997 to 2000, of which more than 50% of the patients were covered by some type of managed care.32 During this period, treatment with any insulin therapy (monotherapy or in combination) fell from approximately 22% to 18% of patients, insulin monotherapy fell from 18% to 13%, and insulin therapy in combination with an oral antidiabetic agent essentially remained constant (5.8%-5.9%). For oral agents, the proportion of patients receiving monotherapy with sulfonylureas dropped from 35% to 26%, yet the proportion receiving monotherapy with either metformin or a glitazone doubled. Combination therapies (2 or more drugs) increased by >2 to 8 times over the 4-year period. Use of 3 oral agents in combination, albeit low, increased 6-fold (0.5%-3%).

Drug therapy prescribing patterns in 1,085 MCO enrollees were examined over 36 months (1997-2000).32 The study population was starting its initial drug therapy and had high proportions of elderly persons (67% aged >60 years) and those with complications (76%). Drug therapy patterns from initiation to 36 months found that 11% were receiving no drug therapy at the end of the study, 54% were receiving oral monotherapy (down from 82% at initiation), 27% were receiving combination therapy (up from 6%), and insulin monotherapy was down from 12% to 9%. Despite escalation to combination therapies over 36 months, more than 80% of the population did not reach recommended glycemic goals, and mean A1c was essentially unchanged from the baseline to the end of the study. Though glycemic goals are difficult to achieve, it is not for lack of trying. Once patients initiate oral therapy, there appears to be frequent adjustment of the regimen, with most patients requiring at least 2 modifications to their regimen in the first 12 months of pharmacologic treatment.33

Impact of Diabetes Medications on Resource Utilization and Costs
The proportion of total costs spent on the pharmacy category in patients with diabetes has increased in recent years, in part because of emphasis on achieving glycemic targets; the use of newer, more expensive medications; and a trend toward multidrug strategies. Several MCO studies examined the relationship between total health care costs and antidiabetic drug regimens. These studies are generally not comparable, as patient population characteristics, time frames, and drug therapy comparisons were different. Nevertheless, they do provide valuable insight on the impact of medication on total cost of care within a managed care setting.
Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature

### Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature

#### Study/Year Comparisons Data and Methods Key Findings*

**Rosennblum and Kane**

2003<br>Preinsulin vs. postinsulin initiation<br>1997-2000 MCO claims data (medical, facility, pharmacy) from 1,177 patients with T2D aged 18-65 years with continuous claims data 9 months before and after start of insulin; trend analysis on standardized costs (plan payments) at 60-day increments postinsulin<br>Totals costs increased 10% in the first 2 months following initiation of insulin, however, from month 2 through month 8 costs decreased 40%. Costs were significantly lower at each time point after the first 2 months, including pharmacy, medical, and facility costs (all P<0.001). Pharmacy costs did not return to preinsulin levels, however, medical (P<0.003), facility (P<0.013) and total costs (P<0.002) decreased below preinsulin levels by months 4-6.

**Thiebaud et al.**

2005 (abstract)<sup>15</sup> Insulin users vs. nonusers (oral antidiabetic meds)<br>2001-2004 medical and pharmacy claims data for 359 patients with T2D enrolled in a single Midwest HMO; propensity score weighted regression to assess insulin on costs<br>Patients aged >60 years using insulin experience a reduction of 42% in total costs and 32% in ambulatory costs relative to other patients receiving oral antidiabetic agents (both P<0.05). Insulin patients aged 30-40 years have a 33% reduction in total costs (NS), while those 40-60 years have 4%-17% increases in effect of total costs (NS).

**Chen et al.**

2005<sup>34</sup> Insulin lispro vs. regular human insulin<br>2000-2001 MCO claims data for 6,436 subjects on insulin (30.6% lispro, 69.4% regular); during a 12-month follow-up; propensity score model methods; charges for hospital and outpatient services; acquisition price for drugs<br>Pharmacy costs were higher for lispro users by $212 [$252] per year (P<0.001), but this was offset by reduced hospitalization for cost savings of $2,286 [$2,713] (P<0.011) in nondiabetes medical and total medical savings of $2,327 [$2,762] (P<0.072) annually for insulin lispro users compared with regular insulin. Patients less likely to receive lispro were older, on oral medications, and had more comorbidities.

**Hall et al.**

2003<sup>21</sup> Insulin lispro vs. regular insulin<br>1998-1999 medical and pharmacy claims data from 14 health plans with 11,443 patients on insulin (29.2% lispro, 70.8% regular); propensity score matched 1:1, resulting in >1,800 pairs that were then followed for 12 months<br>Insulin lispro users at baseline were younger, more likely to have T1D, a history of insulin use, and fewer comorbidities; more likely to visit endocrinologists, and had lower total costs. After matching 1:1, lispro users had more office visits (P=0.002) and more prescriptions filled (P=0.017) than regular insulin users but fewer inpatient admissions (P=0.003), lower hypoglycemia inpatient admissions (P=0.001), and lower total inpatient costs (P=0.023). Overall cost for lispro users was $216 [$268] less per year (NS).

**Stockel et al.**

2003<sup>18</sup> 4 oral agent regimens: • repaglinide monotherapy • metformin monotherapy • repaglinide+metformin • metformin + glyburide<br>1999-2001 medical and pharmacy claims data from large West Coast MCO with 44,367 subjects in 4 cohorts: metformin (n = 26,535), repaglinide (n = 500), metformin+glyburide (n = 17,160); follow-up period was 9 months<br>Repaglinide provided cost offsets only when used in combination with metformin. Mean total costs were: $8,924 [$10,593] for repaglinide + metformin, $9,448 [$11,214] for metformin, $9,576 [$11,367] for metformin + glyburide, and $11,910 [$13,594] for repaglinide. Differences were not significant due to sample size and variability in costs.

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Comparisons</th>
<th>Data and Methods</th>
<th>Key Findings*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosennblum and Kane 2003</td>
<td>Preinsulin vs. postinsulin initiation</td>
<td>1997-2000 MCO claims data (medical, facility, pharmacy) from 1,177 patients with T2D aged 18-65 years with continuous claims data 9 months before and after start of insulin; trend analysis on standardized costs (plan payments) at 60-day increments postinsulin</td>
<td>Totals costs increased 10% in the first 2 months following initiation of insulin, however, from month 2 through month 8 costs decreased 40%. Costs were significantly lower at each time point after the first 2 months, including pharmacy, medical, and facility costs (all P&lt;0.001). Pharmacy costs did not return to preinsulin levels, however, medical (P&lt;0.003), facility (P&lt;0.013) and total costs (P&lt;0.002) decreased below preinsulin levels by months 4-6.</td>
</tr>
<tr>
<td>Thiebaud et al. 2005 (abstract)</td>
<td>Insulin users vs. nonusers (oral antidiabetic meds)</td>
<td>2001-2004 medical and pharmacy claims data for 359 patients with T2D enrolled in a single Midwest HMO; propensity score weighted regression to assess insulin on costs</td>
<td>Patients aged &gt;60 years using insulin experience a reduction of 42% in total costs and 32% in ambulatory costs relative to other patients receiving oral antidiabetic agents (both P&lt;0.05). Insulin patients aged 30-40 years have a 33% reduction in total costs (NS), while those 40-60 years have 4%-17% increases in effect of total costs (NS).</td>
</tr>
<tr>
<td>Chen et al. 2005</td>
<td>Insulin lispro vs. regular human insulin</td>
<td>2000-2001 MCO claims data for 6,436 subjects on insulin (30.6% lispro, 69.4% regular); during a 12-month follow-up; propensity score model methods; charges for hospital and outpatient services; acquisition price for drugs</td>
<td>Pharmacy costs were higher for lispro users by $212 [$252] per year (P&lt;0.001), but this was offset by reduced hospitalization for cost savings of $2,286 [$2,713] (P&lt;0.011) in nondiabetes medical and total medical savings of $2,327 [$2,762] (P&lt;0.072) annually for insulin lispro users compared with regular insulin. Patients less likely to receive lispro were older, on oral medications, and had more comorbidities.</td>
</tr>
<tr>
<td>Hall et al. 2003</td>
<td>Insulin lispro vs. regular insulin</td>
<td>1998-1999 medical and pharmacy claims data from 14 health plans with 11,443 patients on insulin (29.2% lispro, 70.8% regular); propensity score matched 1:1, resulting in &gt;1,800 pairs that were then followed for 12 months</td>
<td>Insulin lispro users at baseline were younger, more likely to have T1D, a history of insulin use, and fewer comorbidities; more likely to visit endocrinologists, and had lower total costs. After matching 1:1, lispro users had more office visits (P=0.002) and more prescriptions filled (P=0.017) than regular insulin users but fewer inpatient admissions (P=0.003), lower hypoglycemia inpatient admissions (P=0.001), and lower total inpatient costs (P=0.023). Overall cost for lispro users was $216 [$268] less per year (NS).</td>
</tr>
<tr>
<td>Stockel et al. 2003</td>
<td>4 oral agent regimens: • repaglinide monotherapy • metformin monotherapy • repaglinide+metformin • metformin + glyburide</td>
<td>1999-2001 medical and pharmacy claims data from large West Coast MCO with 44,367 subjects in 4 cohorts: metformin (n = 26,535), repaglinide (n = 500), metformin+glyburide (n = 17,160); follow-up period was 9 months</td>
<td>Repaglinide provided cost offsets only when used in combination with metformin. Mean total costs were: $8,924 [$10,593] for repaglinide + metformin, $9,448 [$11,214] for metformin, $9,576 [$11,367] for metformin + glyburide, and $11,910 [$13,594] for repaglinide. Differences were not significant due to sample size and variability in costs.</td>
</tr>
</tbody>
</table>

* Costs updated to 2005 dollars in brackets [ ].

HMO=health maintenance organization; MCO=managed care organization; NS=nonsignificant; T1D=type 1 diabetes; T2D=type 2 diabetes.

### Intensity of Drug Therapy and Total Costs

Two studies researched the relationship between antidiabetic classes of medication and total medical care expenditures in MCOs. In the first study, a large Midwest MCO reviewed its 25,000 members with diabetes and examined annual diabetes treatment costs by drug therapy. Annual total treatment costs (inpatient, outpatient, emergency room [ER], and pharmacy, including supplies) for those diabetes patients with no complications in 1999 ranged from ~$600 [$775] for no drug treatment to ~$2,600 [$3,357] for those receiving 3 or more drugs in combination therapy. In newly diagnosed patients without complications, the pharmacy costs became a major component of their total expenditures (as much as 65% in triple therapy [3 agents used in combination]).

An older study using California HMO data from the mid-1990s also found that overall costs increased as antidiabetic therapies were escalated. Nevertheless, the total contribution of diabetes medications to the overall enrollee cost was relatively...
As summarized in Table 2, 5 studies using retrospective claims data addressed the impact of medication strategies on total diabetes treatment costs in managed care settings.18,21,34,35 Four studies were insulin-specific, evaluating the general cost impact of initiating insulin36,37 or the cost offsets associated with newer insulin formulations31,34; only 1 study examined specific oral medication strategies.15 As presented in more detail in Table 2, key findings from these studies were the following: (1) insulin initiation does not increase overall costs when considering a short-term perspective of 4 to 8 months but rather reduces costs by as much as 40% over the preinsulin period,10 (2) cost offsets with initiation of insulin may be specific to elderly populations,10 (3) increased pharmacy expenditures for new short-acting insulins are offset by medical cost savings and reductions in medical resource utilization,21,34 and (4) cost savings with oral medication strategies may be related to the specific combinations of medications used and not a single agent used alone.38

### Impact of Insulin-Induced Hypoglycemia

Reluctance to use insulin for intensification of glycemic control often includes a fear of adverse events, particularly hypoglycemia. The incidence and economic impact of insulin-induced hypoglycemia in MCOs has been reported in 2 studies.36,37 At a New England staff-model HMO, the incidence and resource utilization patterns of serious hypoglycemia (defined as a hypoglycemic episode requiring care in an ER or hospital) were evaluated retrospectively in 1,113 patients, aged 20 to 64 years, who used insulin monotherapy from 1993 to 1997.36 The overall incidence of serious hypoglycemia during the study period was ~5 episodes per 100 patient-years (95% confidence interval [CI], 4.14-6.00) and was higher (5.71-8.23 episodes per 100 patient-years) in younger female patients (aged 20-44 years). Ninety-four percent of cases were managed in the ER. Another study at a large Midwestern MCO followed 2,118 patients for 6 years (1992-1998) who were prescribed some type of insulin regimen.37 Hypoglycemia significant enough to warrant medical attention occurred in 16% of patients receiving insulin, with 7.1 episodes per 100 patient-years. Overall mean

---

**TABLE 3** Impact of Antidiabetic Medication Persistence on Managed Care Costs

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Data Details</th>
<th>Relationship of Persistence to Total Costs and Resource Utilization*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balkrishnan et al 200320</td>
<td>1996-2002 claims data, mid-Atlantic Medicare HMO, N = 775, aged 265 years, T2D, oral agents and/or insulin, 1-5 year follow-up (2,450 patient years)</td>
<td>Increased antidiabetic MPR was the strongest predictor of decreased total annual health care costs. A 10% relative increase in antidiabetic MPR was associated with an 8.6% relative decrease in total annual health care costs (P &lt; 0.001), with sensitivity analyses suggesting that cost savings may be as high as 28%, with a 10% relative increase in MPR. Reduced costs with increased MPR held true for all agents, including insulin.</td>
</tr>
<tr>
<td>PhRMA 200436</td>
<td>1999-2001 claims data, proprietary database of &gt;70 plans, N = 46,000, age not specified, T2D, new starts on oral agents, 1-year follow-up</td>
<td>The patients most persistent (top one third) with their antidiabetic medications had a 40% reduction in hospitalization rates (10% vs. 16%) compared with those with lowest persistence. Patients with highest persistence had annual pharmacy costs that were $300 [5356] higher per patient, but this was offset by a $600 [5712] per-patient savings on inpatient care.</td>
</tr>
<tr>
<td>Lau and Nau 200446</td>
<td>2000-2001 claims data; Midwestern MCO; N = 900, aged &gt;18 years; T2D, oral agents, excluded insulin, 1-year follow-up (2000 adherence relationship to 2001 hospitalization)</td>
<td>Nonadherence to oral antidiabetic medications increased total and diabetes-attributable costs for patients with the highest diabetes-attributable costs, worsening adherence increased the medical services portion of diabetes-attributable costs.</td>
</tr>
<tr>
<td>Curkendall et al. 2005 (abstract)10</td>
<td>2000-2001 claims data; large MCO; N = 54,505; aged &gt;18 years; overall (P &lt; 0.001); T2D; oral agents, insulin not excluded; 1-year follow-up, stratified by baseline resource intensity</td>
<td>When 2000 MPR dropped below 80%, risk of 2001 hospitalization (diabetes or CV causes) significantly increased (OR 2.53; 95% CI, 1.38-4.64) within a 1-year time frame. Rate of hospitalization increased from 5.2% to 10.3% when MPR was &lt;80% (P=0.01), with rate of hospitalization highest at 14.8% when MPR was &lt;40%.</td>
</tr>
</tbody>
</table>

* Costs updated to 2005 dollars in brackets [ ]

CV = cardiovascular; HMO = health maintenance organization; MCO = managed care organization; MPR = medication possession ratio; OR = odds ratio; PhRMA = Pharmaceutical Research and Manufacturers of America; T2D = type 2 diabetes.

---

small (5%-13%). Within the medication category, glycemic control medications for diabetes accounted for between 4% and 47% of the total pharmacy budget. Overall costs appeared higher for patients on insulin, but when their diabetes drugs were examined as a proportion of the overall cost and proportion of the pharmacy budget, drug costs were not the drivers (diabetes drugs were 6% of total costs and ~30% of the pharmacy budget); inpatient care drove the costs for patients on insulin, indicating that these patients were further along in their disease progression and had more complications.

### Impact of Medications: Comparative Studies

As summarized in Table 2, 5 studies using retrospective claims data addressed the impact of medication strategies on total diabetes treatment costs in managed care settings.18,19,21,34,35 Four studies were insulin-specific, evaluating the general cost impact of initiating insulin36,37 or the cost offsets associated with newer insulin formulations31,34; only 1 study examined specific oral medication strategies.15 As presented in more detail in Table 2, key findings from these studies were the following: (1) insulin initiation does not increase overall costs when considering a short-term perspective of 4 to 8 months but rather reduces costs by as much as 40% over the preinsulin period,10 (2) cost offsets with initiation of insulin may be specific to elderly populations,10 (3) increased pharmacy expenditures for new short-acting insulins are offset by medical cost savings and reductions in medical resource utilization,21,34 and (4) cost savings with oral medication strategies may be related to the specific combinations of medications used and not a single agent used alone.38
cost per episode was $1,186 [$1,583] (range $181-$4,924 [$242-$6,574]) or ~$7 per member per month (PMPM) (~$9 PMPM). Costs were driven by the hospitalizations occurring in 15% of episodes but representing more than 60% of the total costs to the MCO. Treatment facility frequency and associated mean cost per episode were as follows: hospital, 15% ($4,924 [$6,574]); ER, 30% ($812 [$1,084]); and physician office, 50% ($181 [$242]).

**Impact of Antidiabetic Medication Persistence**

Several important studies, summarized in Table 3, have linked increased persistence with/adherence to antidiabetic medications to reduced health care utilization/costs in MCO settings. These studies, all using managed care claims data, demonstrate that the increase in medication possession ratios for antidiabetic medications (including insulins) is correlated with reduced overall health care costs, particularly with reductions in hospitalization rates. In addition, patients with diagnosed diabetes not receiving medications have significantly increased health care resource utilization. And finally, in patients with high baseline diabetes-attributable costs, worsening adherence predicts an increase in diabetes-related medical costs.

**Link Between Glycemic Control and Costs**

The relationship between improved glycemic control and reduced costs in MCOs has been fairly well established in a variety of studies, including retrospective claims analyses, studies of antidiabetic medication persistence, and evaluations of the overall impact of DMPs. We identified 4 published articles and 1 study in abstract form that were specifically designed to address the relationship between glycemic control and total costs. Three supportive studies were also identified that reported relevant information.

In the first study, a claims data analysis from a New England HMO compared patients with good (A1c <8%), fair (A1c 8-10%), and poor glycermic control (A1c >10%). They found a statistically significant inverse relationship between the level of control and the likelihood of inpatient admissions on both an adjusted (for each patient’s follow-up time) and unadjusted basis (P <0.01 for both). Patients with poor control had the highest corresponding charges for inpatient admissions (over a 3-year timeframe) primarily related to short-term complications (e.g., hyperglycemia or hypoglycemia, infections, electrolyte disturbances). The study was designed to assess short-term impact; thus, it did not link long-term complications to glycemic control.

Another claims data analysis at a Pacific Northwest HMO compared patients with 1% absolute A1c reduction with unimproved patients and linked the glycemic control to cost savings from reduced complications over 4 years. In this study, cost savings were seen in all patients improved but occurred even for those already close to glycemic targets and for those with baseline complications or CVD (~$800 savings annually for those with complications or CVD vs. ~$400 annually for those with no baseline complications). During the study years of 1994 to 1997, the total per-patient costs were consistently lower in the improved group (by $685-$950 [$944-$1,309] per patient per year) and were significantly lower in years 1995 to 1997 (P <0.01).

Two recent additional studies provided data on the relationship between glycemic control and costs in managed care settings in both short-term and intermediate time frames. The first study examined the 1-year impact of glycemic control on direct medical costs in a large national health plan. Patient medical claims were analyzed using 2 groups for comparison: those at their target A1c level (≤7%) and those above the target. After controlling for confounding variables, the patients above target had 30% higher medical costs at 1 year (P <0.01). A second study also used managed care claims data from a Southeastern health plan of >10,000 patients with diabetes in a longitudinal analysis of up to 43 months. Patients were stratified into good (A1c ≤7%), fair (A1c >7%), and poor (A1c >9%) glycemic control. Patients with good glycemic control had total diabetes attributable costs that were 20% and 24% lower (P <0.05) than the fair and poor glycemic control groups, respectively.

Finally, Gilmer and colleagues (2005) updated their earlier landmark analysis of the relationship between incremental changes in baseline A1c level and subsequent 3-year total costs in a Minnesota health plan with more than 600,000 members. For this study, multivariate regression analysis was conducted on prospective patient survey, baseline laboratory, and 3-year retrospective claims data (1999-2002) from 1,694 patients with complete information. After controlling for age, sex, diabetes duration, education, and income, they found that A1c levels higher than 7.5% continued to be a significant independent predictor of total cost (P = 0.015) although stronger predictors of total costs were coronary heart disease, hypertension, and depression.

Another study demonstrated that higher total health care costs were significantly related to both higher A1c levels and higher disease severity index or a larger number of comorbidities. The cost difference was more than $600 [$775] for a change in HbA1c from 8.7 to 7.2% with 0 to 1 comorbidities but was more than $16,000 [$20,636] different with 4 comorbidities.

Finally, some evaluations of DMPs of various types show a reduction in health care resource utilization and costs with improved glycemic control. For example, a single health plan DMP produced an absolute decrease in A1c levels of 0.5% (8.2%->7.7%), a 22% decrease in hospital admissions, a 34% decrease in hospital length of stay, and a 12% decrease in PMPM costs only 9 months after program initiation. An academic health system similarly found that its DMP produced a more than 1% absolute reduction in A1c (8.51%->7.41%), which was associated with a $108 [$128] PMPM cost reduction, or an annual savings of $1,294 [$1,536] per member with diabetes. And finally, a Midwestern HMO found limited
short-term cost savings from its DMP but estimated that the improved A1c levels produced from the program had a value related to improved length and quality of life of $31,000 [$33,790] per patient achieving a 1% absolute reduction in A1c.12

Table 4 provides a summary of the reported annual per-patient economic value of glycemic control across the variety of studies discussed in this section.24-41-47

### Discussion
This review provides a unique assessment of published literature reporting economic or resource utilization outcomes for patients with diabetes enrolled in managed care. Our findings suggest that, despite concerns of rising drug costs, the pharmacy costs have not been the driver of overall diabetes costs to MCOs. In addition, the pharmacy component is dominated by
medications to treat CVD and other complications/comorbidities of diabetes, while only ~30% of medications are related to glycemic control. Furthermore, the recent published comparisons of insulin in MCO settings suggest that higher pharmacy costs associated with starting insulin or using newer insulin formulations may be offset by medical cost savings within 1 year or less.

Most importantly, the results of this review suggest that there are potential overall cost savings to managed care plans from improving glycemic control and antidiabetic medication persistence, regardless of the specific medications used. These cost savings occurred despite additional spending in areas such as pharmacy for patients who achieved goals. In most studies, the cost offsets occurred from reduced inpatient admissions. Cost savings occurred even for patients already close to their goals who were making small changes (e.g., those going from an A1c level of 8% to 7%).

Given these interesting findings between glycemic control and costs, it is worth discussing one older (pre-2000) study not included in the results. This landmark study in a Midwestern HMO found that charges for medical care from 1993 to 1995 were related to the level of glycemic control the year before (in 1992). Charges significantly increased for every absolute 1% increase above an A1c of 7%. Compared with a person with an A1c of 6% (normal level), every additional 1% increase in A1c above this level resulted in cumulative charge increases of approximately 4% for A1c = 7% (P = not significant), 10% increase for A1c = 8% (P <0.05), 20% increase for A1c = 9%, (P <0.01), and 30% higher charges for A1c = 10% (P <0.01). This study also found that the cost savings differential for even modest A1c reductions (8% to 7%) was ~3.5 times higher in patients with diabetes plus comorbidities (heart disease and hypertension) compared with those with diabetes only. The finding that higher cost savings with glycemic control are achieved in sicker patients may also be consistent with Goetzel's review, which reported that glycemic control measures in prediabetes (less sick) did not produce a positive return on investment. Studies presented in this review suggest annual cost savings from improved glycemic control were more than double from 2001 to 2002 found that ~50% of patients were at goal (HbA1c <7%) compared with ~36% of patients in the 1999 to 2000 NHANES data set. A California HMO recently reported that the proportion of its patients achieving recommended glycemic control had improved from 30% in 1999 to 2000 to more than 50% in 2004 because of more intensive drug regimens, including combination therapy. Though improvements have occurred over the last 4 years, nearly half of all patients with diabetes are still not at recommended glycemic goals.

Implications for Managed Care

The relationship between improved glycemic control and reduced cost is fairly well established; however, implementing the appropriate interventions to achieve glycemic control in patients with diabetes continues to be a challenge for managed care. The NCQA estimates that failing to deliver recommended care for diabetes in managed care results in the following annual costs: 13,600 avoidable deaths, $178 ($194) million in avoidable hospital costs because of heart attack and stroke in patients with uncontrolled diabetes, and 11.6 million avoidable sick days. Surprisingly, the proportions of patients who still have poor glycemic control (A1c >9.5%) were 25% in Medicare managed care, 34% in commercial MCOs, and as high as 48% in Medicaid managed care.

Emerging reports indicate some improvement in glycemic control in recent years. At the national level, the National Health and Nutrition Examination Survey (NHANES) analysis from 2001 to 2002 found that ~50% of patients were at goal (HbA1c <7%) compared with ~36% of patients in the 1999 to 2000 NHANES data set. A California HMO recently reported that the proportion of its patients achieving recommended glycemic control had improved from 30% in 1999 to 2000 to more than 50% in 2004 because of more intensive drug regimens, including combination therapy. Though improvements have occurred over the last 4 years, nearly half of all patients with diabetes are still not at recommended glycemic goals.

There are many likely reasons for the continued lack of glycemic control; clearly, diabetes is a complex and challenging disease with no silver bullet for achieving success. There are a number of issues that come into play with the general lack of glycemic control across managed care. MCOs have been at the forefront of proactively managing diabetes through a variety of “disease management” initiatives, including programs targeting clinicians and patients. Part of the incentive for this focus on diabetes has been the Health Plan Employer Data and Information Set (HEDIS) performance measures, which allow comparison of managed health plans.

The HEDIS performance measures focus on frequency of measuring clinical parameters (blood pressure, lipids, A1c) as a proxy for quality of care, but measurement does not necessarily result in improved A1c levels. For example, a review of Medicare managed care plans in Oregon showed that, while HEDIS performance rate for A1c testing was 87%, two thirds of the patients were not at recommended glycemic goals, with 24% in very poor control (>9.5%). Similarly, a large Southwestern HMO found that, while A1c testing rates were...
77%, only 29% of those receiving antidiabetic medications met their glycemic goal. Similar problems occur with not achieving blood pressure goals in diabetes.57

Not surprisingly, DMPs have limited success when the focus is on improving the numbers of tests performed.58 Programs associated with the greatest improvements in A1c levels include pharmacist evaluation and counseling, medication adjustment, and physician/patient interactions.59,60 Despite limitations with DMPs, a recent survey of programs in health plans covering more than 15 million members found that diabetes DMPs were the most frequently implemented (compared with other diseases) and that the average return on investment for MCOs was approximately 2 to 1.60

**Investment in Pharmacotherapy**

Another important issue related to the lack of glycemic control is a “silo” mentality on the pharmacy component of the costs of care for patients with diabetes (e.g., focus on drug budget impact without considering potential cost offsets in medical resource utilization). As our review indicates, only about 30% of the pharmacy costs for patients with diabetes are related to glycemic control, with the majority of costs related to managing comorbidities and complications. In addition, there is now substantial evidence that the investment in diabetes drug therapy provides cost offsets, particularly reductions in inpatient care. Yet, surprisingly, more patients than ever are not being treated with any drug therapy for their diabetes.32,38,45

From 1990 to 2001, there was a rapid shift toward oral medication combinations and a reduction in insulin use.7,38,61 One might ask whether the reduction in insulin use in the 1990s could have slowed progress in population glycemic control. However, patients most likely to achieve glycemic goals are using insulin in combination with other oral medications.54 Newer formulations of insulin are now emerging and will continue to emerge.62 Current trends in insulin use are difficult to ascertain using peer-reviewed literature because of lag times in publication of study results. However, market research information indicates that the pendulum is now swinging back toward insulin, with insulin analogs primarily driving the growth in the insulin market at more than 5% annually and oral agents showing declines.53,64 While recent insulin studies discussed in this review have shown positive clinical and economic results,19,21,34,35 additional studies will be continually needed as new insulin options increase in the next few years. These studies suggest that restrictions placed on newer insulin therapies based solely on drug acquisition price may not be defensible without assessment of the entire cost impact of a drug on other medical expenditures (inpatient and outpatient care). Outcomes studies will help determine if newer insulin formulations and delivery systems will improve glycemic control and economic outcomes for MCOs.

The current economic burden of diabetes to managed care is accelerating. Over the past decade, the number of adults in the United States diagnosed with diabetes has increased by more than 35%, and the age at diagnosis has decreased by an average of 6 years, from 52 to 46 years.65 The obesity epidemic and the continued aging of the U.S. population will also amplify the costs of diabetes to the health care system.66,67 Investments in pharmacotherapy and lifestyle interventions for patients with prediabetes have not produced a positive return on investment.68 However, for patients with diagnosed diabetes in managed care plans, there does appear to be a link between glycemic control and lower overall costs, demonstrated both in this review and other papers.69

Given the favorable economic impact of achieving glycemic control, MCOs will need to continue to evaluate the way that medications are managed. Managed care’s continued investment in drug therapies to achieve glycemic control may improve quality of care and possibly reduce overall costs in the future. The Veterans Affairs system found that as their national annual medication expenditures increased from 1994 to 2000 for patients with diabetes, so did glycemic control.68 New research must be conducted to better understand the most recent economic impact of medications over the last 2 to 3 years. Furthermore, the benefits of new products in terms of glycemic control must be weighed along with their safety profiles and potential for rare, severe adverse events (e.g., the glitazones, muraglitazar).

**Limitations**

Key limitations of this review include the lack of information on the economic impact of the newest medications marketed in the past several years because of the common lag times associated with conducting and publishing research. Thus, the impact of newer medications is underrepresented; however, we attempted to address this limitation through review of abstracts presented at key professional meetings, including those of the ADA and ISPOR. Likewise, given publication lag time, much of the literature published between 2000 and 2005 uses older claims data with dates of service often before 2001.

Since our search terms and focus were on economic and resource utilization issues, our study eliminated much of the disease management literature reporting primarily clinical outcomes, which could have potentially biased the results. In addition, many of the studies reviewed reported only descriptive point estimates of cost savings with improved glycemic control, and these estimates are subject to statistical uncertainty. The potential weaknesses of the study designs may also lead to a favorable bias toward the benefits of medication use and glycemic control. Nevertheless, the review represents the current state of managed care literature in this area. Newer studies should attempt to correct for some of the potential sample selection bias issues using appropriate econometric methods in future retrospective data analyses.31
Economic Impact of Antidiabetic Medications and Glycemic Control on Managed Care Organizations: A Review of the Literature

Conclusions

The recent managed care economic literature suggests that improving glycemic control and antidiabetic medication persistence results in lower overall medical costs for patients with diabetes in managed care plans. Continued expansion of antidiabetic medication options will place increasing pressure on MCOs to assess the return on investment for newer pharmacotherapies. Routine measurement of economic and quality-of-life outcomes alongside clinical outcomes will become necessary for assessing the total value that new antidiabetic medications provide and whether cost offsets to managed care exist. Novel insulin therapies will continue to be an area of increasing focus and research given the recent studies suggesting overall cost savings (even in the short term) for newer agents, with reduced adverse events and improved patient compliance.

Appropriate use of antidiabetic medications, including medication compliance, is an important component in the strategy to achieve glycemic control and may improve outcomes for patients with diabetes. Whether managed care's significant investments in pharmacotherapies over the past 5 years have produced broad cost offsets and/or cost savings remains unclear. This question will probably continue to be addressed on a case-by-case basis, using head-to-head comparisons to establish whether cost offsets occur for MCOs when newer medications and combination therapies are used to achieve glycemic control.

DISCLOSURES

Funding for this study was provided by Pfizer, Inc. and sanofi-aventis and was obtained by authors Jennifer M. Stephens, Marc F Botteman, and Joel W. Hay. The authors disclose no potential bias or conflict of interest relating to this article. Stephens served as principal author of the study. Study concept and design were contributed by all authors. Data collection was the work of Stephens, with input from Botteman; data interpretation was primarily the work of Stephens, with input from Botteman and Hay. Drafting and revision of the manuscript was primarily the work of Stephens, with input from Botteman and Hay.

REFERENCES


50. Parris ES, Lawrence DB, Mohn LA, Long LB. Sulfonlurea adherence is associated with A1c goal attainment in a managed care diabetes disease management program. Poster presented at: 64th Annual Scientific Sessions of the American Diabetes Association; June 4-8, 2004; Orlando, FL. Abstract 1187-P.


Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis

PARTHIV MAHADEVIA, MD, MPH; SHAILEN SHAH, MD; SALLY MANNIX, BA; JESSICA BREWSTER-JORDAN, BA; LEAH KLEINMAN, DrPH; CHRISTOPHER LEIBMAN, PharmD, MS; and LIZA O’DOWD, MD

ABSTRACT

OBJECTIVE: Sensory attributes of intranasal corticosteroids (INSs) differ by product based on chemical composition. We previously reported that patients are able to demonstrate preferences for certain INS sensory attributes, which may affect their willingness to adhere to therapy. As part of the same study, we also sought to determine if these same patients are willing to pay for products not containing certain sensory attributes.

METHODS: We conducted a 2-part cross-sectional study of 120 patients with allergic rhinitis at 4 allergy and immunology clinics in the United States in November and December 2003. In the first part of the study, the patients chose between pairs of hypothetical INS products that differed in the intensity of 6 sensory attributes (smell, taste, aftertaste, throat rundown, nose runout, and feel of spray in nose/throat; results were reported in the Annals of Allergy, Asthma & Immunology [2004;93:345-50]). In the second part of the study, reported here, discrete choice experiment methodology was used in which the patients chose among hypothetical INS products that differed in the intensity of the 6 sensory attributes and monthly copayments of $15, $30, and $50. Each sensory attribute was characterized by 3 intensity levels, e.g., no aftertaste (mild intensity), weak aftertaste (moderate intensity), or strong aftertaste (severe intensity). The strength of preferences, shown as marginal willingness to pay to avoid certain sensory attributes, was measured in U.S. dollars per month. We also evaluated the effect of annual household income on willingness to pay.

RESULTS: Demographic results indicated that 86.7% of participants had prior experience with at least 2 INS products. Seven patients (5.8%) were excluded from the willingness-to-pay analysis due to inconsistent responses to the logic checks used to confirm patient engagement in the study instrument. On average, the 113 remaining patients were willing to pay $11 (95% confidence interval [CI], $9-$13) per month in 2003 dollars to get an INS with no smell instead of strong smell, $12 (95% CI, $10-$14) for no taste instead of strong taste, $20 (95% CI, $18-$22) for no aftertaste instead of strong aftertaste, $10 (95% CI, $9-$12) for no throat rundown instead of a lot of throat rundown, $11 (95% CI, $9-$13) for no nose runout instead of a lot of nose runout, and $6 (95% CI, $4-$8) for a spray with a wet feel instead of a dry feel. Comparing moderate intensity levels of each sensory attribute with the mildest, only 3 attributes had statistically significant willingness to pay: aftertaste, throat rundown, and nose runout. Patients with a higher income were willing to pay more to avoid a lot of throat rundown and nose runout than those with a low income (P <0.01), but this relationship did not hold for the other sensory attributes.

CONCLUSION: Patients demonstrated significant willingness to pay to avoid certain sensory attributes of INSs. Sensory attributes of INS products appear to be potentially important considerations when evaluating alternative INS products for drug therapy selection or formulary placement.

KEYWORDS: Patient preferences, Allergic rhinitis, Intranasal corticosteroids, Willingness to pay

J Manag Care Pharm. 2006;12(2):143-51

Intranasal corticosteroids (INSs) are a mainstay in the clinical management of allergic rhinitis. Consensus guidelines and reviews agree that of the 6 INSs on the U.S. market, none has shown advantages in efficacy or differences in safety profile. However, INSs have unique formulations, chemical composition, and delivery devices that produce a variety of sensory perceptions. Some sensory perceptions, such as aftertaste, can be unpleasant, leading to decreased preference toward a product and reductions in willingness to adhere to treatment. Therefore, selection of an INS based on patient preferences of sensory attributes may increase satisfaction and treatment adherence.

INSs commonly used to treat allergic rhinitis include budesonide aqueous nasal spray (Rhinocort Aqua), flunisolide (generic and Nasarel), beclamethasone dipropionate (Beconase AQ), fluticasone propionate nasal spray (Flonase), mometasone furoate nasal spray (Nasonex), and triamcinolone acetone nasal spray (Nasacort AQ). Prior head-to-head studies of sensory attributes conducted with these INSs have shown that patients can discern sensory attribute differences among INSs and formulate clear preferences. An article by Shah et al. reported the results of 2 randomized controlled trials in which a greater proportion of patients reported satisfaction with the sensory profile of budesonide aqueous nasal spray than fluticasone propionate nasal spray. The sensory attributes included in these studies were smell, taste, aftertaste, feel of spray in nose/throat,
and amount of spray running out of nose or running down throat. Attributes were assessed using the Sensory Perceptions Questionnaire, which has 23 items, 7 of which solicit patient preferences. In analyses that included all responding patients, 54.4% of patients in the first study preferred budesonide and 37.8% preferred fluticasone (P < 0.022). In the second study, 47.4% preferred budesonide and 41.1% preferred fluticasone (difference was not significant).

In a randomized, double-blind, crossover trial, Bachert and El-Akkad reported that patients preferred the odor of triamcinolone acetonide aqueous nasal spray and judged it to be less strong compared with fluticasone propionate or mometasone furoate nasal sprays, and the taste of triamcinolone acetonide aqueous nasal spray was preferred to mometasone furoate. Patient preferences were rated on a 14-item nasal spray evaluation questionnaire, which evaluates the acceptability of the drug and associated sensory perceptions immediately (10 items) and 2 minutes after (4 items) drug administration, using a 100-point rating scale. Both Bachert and El-Akkad and Shah et al. assessed patients’ preferences of and preferences for certain INS sensory attributes, but they did not assess the strength of patient preferences in terms of their willingness to pay for an INS with the sensory attributes they prefer or would like to avoid.

Reissman et al. conducted a cost-efficiency study to determine the relative prescribed dosages of 4 INSs and compare economic differences resulting from these prescribing behaviors. In their study, using data from the IMS National Disease and Therapeutic Index for calendar year 2002, Reissman et al. found differences in the average number of sprays prescribed daily and, therefore, differences in the average cost per prescribed day of therapy among budesonide, fluticasone, mometasone, and triamcinolone nasal sprays.

Keith et al. conducted a cost-benefit study with patients receiving either intranasal budesonide by Turbuhaler or aqueous spray. In this study, patients completed a willingness-to-pay questionnaire to measure treatment benefits; however, adaptive preferences were not assessed. Costs were then compared with the willingness-to-pay data as part of the treatment benefit analysis. Results of this study indicated there was no difference in cost, willingness to pay, or cost-benefit when comparing delivery modes. Additionally, it was suggested that willingness-to-pay questionnaires may be a useful method to assess a therapy’s benefit. These previous cost studies, however, did not incorporate patient preferences for INS sensory attributes.

The aim of the current study was to integrate 2 important concepts: patient preferences for INS sensory attributes and treatment cost. We assessed allergic rhinitis patients’ preferences for various sensory attributes and willingness to pay for products with certain sensory attributes as well as the potential impact of their preferences on self-reported willingness to adhere to prescribed allergic rhinitis therapy. We have reported, in a previous publication, the results of each attribute’s relative importance and patients’ willingness to adhere to prescribed therapy. Here, we quantify the strength of patient preference for INS sensory attributes in a monetary amount defined as the patients’ willingness to pay using discrete choice experiment methodology, a form of conjoint analysis, which accommodates the integration of preference and cost. This information may inform both physician prescribing and formulary decision making. Because allergic rhinitis is a common disorder that is associated with decreased quality of life and lower worker productivity, understanding strength of preferences may lead to a more informed selection of INS therapy, which, in turn, may improve patient satisfaction, adherence to therapy, and possibly lower economic burden.

**Methods**

**Study Design and Participants**

We conducted a two-part cross-sectional study of 120 patients with allergic rhinitis in 4 allergy and immunology clinics across the United States (n = 30 at each site in Georgia, Pennsylvania, Texas, and Utah) in November and December 2003. Participant inclusion/exclusion criteria are listed in Table 1. Investigators at the 4 allergy clinics were instructed to recruit patients through medical chart review or other relevant patient databases. The Essex Institutional Review Board (Lebanon, NJ) approved the study. This is the second part of a 2-part cross-sectional study of these 120 patients. In the first part of the study, the patients

### Table 1: Study Inclusion/Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Confirmed diagnosis of allergic rhinitis (seasonal or perennial) for at least 1 year made by a medical professional</td>
<td>- Self-reported smell or taste disturbance judged by site investigator to be clinically important</td>
</tr>
<tr>
<td>- Use of intranasal corticosteroids in last month based on medical records or patient self-report</td>
<td>- Established medical history of severe chronic sinusitis and nasal polyposis as judged by site investigator</td>
</tr>
<tr>
<td>- Age ≥ 18 years</td>
<td>- Presence of active, acute upper respiratory infection</td>
</tr>
<tr>
<td>- Ability to understand the survey as judged by the site investigator</td>
<td>- Presence of acute illness, cognitive or other impairment (e.g., visual) that in the opinion of the site investigator would interfere with study requirements</td>
</tr>
<tr>
<td>- Ability to complete evaluation exercise and protocol requirements</td>
<td></td>
</tr>
<tr>
<td>- Willingness and ability to participate and provide written informed consent</td>
<td></td>
</tr>
</tbody>
</table>

*Acute illness was defined as an illness that would impact the patient’s participation. Patients stated that they felt ill; conditions included febrile illness, exacerbation of allergic rhinitis or sinusitis, or a generalized illness.*
chose between pairs of hypothetical INS products that differed in the intensity of 6 sensory attributes (smell, taste, aftertaste, throat rundown, nose runout, and feel of spray in nose/throat; results were reported in the Annals of Allergy, Asthma & Immunology [2004;93:345-50]). In the second part of the study, reported here, discrete choice experiment methodology was used in which the patients chose among hypothetical INS products that differed in the intensity of the 6 sensory attributes and monthly copayments of $15, $30, and $50.

**Discrete Choice Experiment Survey**

Patients were administered an interactive computerized survey that elicited preferences using a discrete choice method, a form of conjoint analysis. Conjoint analysis methods elicit preferences by showing respondents various hypothetical treatment options or health states that differ in terms of their core attributes and estimate strength of preference based on choice selection.

We described the 6 sensory attributes in detail to patients: smell, taste, aftertaste, amount of spray running down throat (throat rundown), amount of spray running out of nose (nose runout), and feel of spray in nose/throat. These 6 sensory attributes were selected based on focus groups and cognitive debriefing studies that have shown them to comprehensively capture salient sensory perceptions of INSs. Questionnaires using these attributes, such as the Sensory Perception Questionnaire, have shown good preliminary construct and content validity, and they have been used successfully in clinical trials of INSs.

By including different amounts of money as an attribute in a conjoint analysis study design, estimates of willingness to pay for changes in the levels of the attributes of importance can be derived. Therefore, a seventh attribute, monthly copayment amount, was added to determine how much patients would trade-off sensory attributes for a monthly cost burden. In our study, all attributes were described in terms of 3 mutually exclusive intensity levels: mild, moderate, and severe (Table 2). The levels described the varying quality of the attribute.

In the discrete choice section of the survey, participants were shown questions that consisted of 3 sets of hypothetical products. Each hypothetical product included 1 level from each attribute and a monthly copayment amount (see Table 3 for an example question). The participant was asked to choose between the hypothetical products by indicating which product profile was preferable and the strength of their preference. Because all possible combinations of attribute levels cannot feasibly be shown to each respondent, the computer program randomly generated 8 choice sets for each participant from a design matrix that was sampled to ensure an orthogonal and balanced study design. Patients were reminded that each hypothetical product had the same efficacy and adverse event profile, information consistent with that stated in allergic rhinitis consensus guidelines and reviews. The site coordinators were instructed to tell each participant prior to the start of the survey: “Please assume that the products [intranasal steroid sprays] you are asked about all work the same and have the same side effects. The only differences between the products are the ones asked about in the survey.” Patients were also reminded to consider the long-term impact of costs when considering the monthly copayment amounts presented in each question.

The survey concluded with demographic (age, gender, income) and clinical questions that included frequency of INS use, number of prior INS medications used, and coexisting comorbidities.

**Pilot Study**

Before initiating the full study, a 5-patient pilot study was conducted to determine if the survey was easy to understand and feasible. Results of the pilot study indicated that patients were able to understand the survey and found it easy to complete. There was no evidence of respondent fatigue.

**Logic Check**

To determine whether respondents were logically considering each choice set, we showed them 2 identical fixed choice sets that contained hypothetical products containing all mild, all moderate, or all severe levels of each attribute. Logically, respondents would be expected to select the “superior” choice set, in this case, the set with all attributes set at their mildest level and the lowest copayment. Respondents who did not choose the hypothetical INS with all mild attributes and the lowest copayment amount were assumed to be making inconsistent choices and were excluded from the analysis.
Outcomes and Statistical Analyses

Study outcomes were marginal willingness to pay for moderate or severe intensity levels compared with mild intensity levels of each attribute, share of preference (frequency that products containing a particular level of an attribute were chosen over the number of times that level was shown), and the effect of income on product selection. Using multinomial logistic regression, we estimated the marginal effect sizes of all levels and effect size per monthly dollar spent. Dividing the marginal effect size of a level with the marginal effect of a dollar change in copay (obtained in the univariate analyses), we estimated the marginal willingness to pay for each level of each attribute. Because income level can affect willingness to pay, we examined preferences for sensory attributes stratified by annual household income category. All statistical analyses were conducted using Sawtooth Software (Sequim, WA). Ninety-five percent confidence intervals that did not include 0 were considered to be statistically significant. If a level was statistically significant based on logistic regression, we rejected the null hypothesis that that level was equal to the lowest attribute level.

Results

Of 120 patients who met the study criteria, approximately two thirds were women, the mean age was 39 years, and the majority were white (Table 4). A little fewer than half reported using INS products regularly (patients were required to choose either "regularly," "only sometimes," or "other"; the definition of these terms was left to each patient's interpretation) and more than half had experience with 3 or more INS products. We excluded 7 patients from the analysis due to inconsistent responses to the aforementioned logic checks, leaving 113 patients for analysis. These patients provided responses to 904 choice sets and selected from 2,712 hypothetical INS products.

This table was modified and reprinted with permission from reference 8.

* Demographics are reported for the entire study sample (N=120). Seven patients were excluded after enrollment because of inconsistent responses identified during the logic checks; therefore, 113 patients were included in the analysis.

† 1 patient responded “other.”

INS = intranasal corticosteroid.

This table was modified and reprinted with permission from reference 8.

* Demographics are reported for the entire study sample (N=120). Seven patients were excluded after enrollment because of inconsistent responses identified during the logic checks; therefore, 113 patients were included in the analysis.

† 1 patient responded “other.”

INS = intranasal corticosteroid.

Outcomes and Statistical Analyses

Study outcomes were marginal willingness to pay for moderate or severe intensity levels compared with mild intensity levels of each attribute, share of preference (frequency that products containing a particular level of an attribute were chosen over the number of times that level was shown), and the effect of income on product selection. Using multinomial logistic regression, we estimated the marginal effect sizes of all levels and effect size per monthly dollar spent. Dividing the marginal effect size of a level with the marginal effect of a dollar change in copay (obtained in the univariate analyses), we estimated the marginal willingness to pay for each level of each attribute. Because income level can affect willingness to pay, we examined preferences for sensory attributes stratified by annual household income category. All statistical analyses were conducted using Sawtooth Software (Sequim, WA). Ninety-five percent confidence intervals that did not include 0 were considered to be statistically significant. If a level was statistically significant based on logistic regression, we rejected the null hypothesis that that level was equal to the lowest attribute level.

Results

Of 120 patients who met the study criteria, approximately two thirds were women, the mean age was 39 years, and the majority were white (Table 4). A little fewer than half reported using INS products regularly (patients were required to choose either “regularly,” “only sometimes,” or “other”; the definition of these terms was left to each patient’s interpretation) and more than half had experience with 3 or more INS products. We excluded 7 patients from the analysis due to inconsistent responses to the aforementioned logic checks, leaving 113 patients for analysis. These patients provided responses to 904 choice sets and selected from 2,712 hypothetical INS products.

Previous publication of results from this study reported the patient preferences for the 6 attributes.* These results showed that the most important attribute in selecting a product was aftertaste (in 28% of patients), taste (in 19%), throat rundown (in 18%), nose runout (in 12%), smell (in 11%), and feel of spray (in 7%). Results from the current willingness-to-pay analysis depict the strength of preference for product attributes through monetary units. Based on the univariate analyses, the marginal effect sizes of copayment or cost was -0.06 utility score per dollar. For every $1 increase in price, there was a downward utility trend in preference. Table 5 shows the

### Table 3: Example of a Choice Set

<table>
<thead>
<tr>
<th>Product 1</th>
<th>Product 2</th>
<th>Product 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spray has strong smell</td>
<td>Spray has no smell</td>
<td>Spray has weak smell</td>
</tr>
<tr>
<td>Spray has strong taste</td>
<td>Spray has no taste</td>
<td>Spray has weak taste</td>
</tr>
<tr>
<td>Spray has strong aftertaste</td>
<td>Spray has no aftertaste</td>
<td>Spray has weak aftertaste</td>
</tr>
<tr>
<td>No spray dripping down back of throat</td>
<td>Some spray dripping down back of throat</td>
<td>A lot of spray dripping down back of throat</td>
</tr>
<tr>
<td>No spray running out of nose</td>
<td>Some spray running out of nose</td>
<td>A lot of spray running out of nose</td>
</tr>
<tr>
<td>Spray feels moist</td>
<td>Spray feels dry</td>
<td>Spray feels neither moist nor dry</td>
</tr>
<tr>
<td>$15 per prescription</td>
<td>$50 per prescription</td>
<td>$30 per prescription</td>
</tr>
</tbody>
</table>

Please think how these costs affect you over the entire time of treatment.
Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis

marginal willingness to pay to avoid certain sensory attributes of INS products. Comparing the severest intensity level of each sensory attribute with the mildest, patients were willing to pay more per month for an INS with no smell instead of strong smell, no taste instead of strong taste, no aftertaste instead of strong aftertaste, no throat rundown instead of a lot of throat rundown, no nose runout instead of a lot of nose runout, and a wet feel instead of a dry feel. Comparing the moderate intensity levels of each sensory attribute with the mildest, only aftertaste, throat rundown, and nose runout had statistically significant monthly willingness to pay (Table 5). When examined independently, preferences usually declined with increasing intensity levels of sensory attributes and with the increased amount of copayment. However, when copayment was incorporated into the model by examining patients’ selection of products by differing amounts of copayment, a different pattern emerged. In this case, product selections for mild and moderate levels of individual sensory attributes at almost any level of copayment were similar (Figures 1A-F), whereas product selection for severe levels of sensory attributes at the lower levels of copayment were markedly different.

Higher annual household income level did not change the share of preference for smell, taste, aftertaste, and feel of spray. However, patients with a higher income were willing to pay more to avoid a lot of throat rundown and nose runout than those with a low income (Figures 2A-B; \( P < 0.01 \)). Subgroup willingness-to-pay analysis of other demographic groups (frequent vs. intermittent INS users, age groups, gender, comorbid conditions) did not appreciably differ from our main findings (data not shown).

### Table 5: Patients’ Marginal Monthly Willingness to Pay* to Avoid Certain INS Sensory Attributes

<table>
<thead>
<tr>
<th>Attributes and Their Intensity Levels</th>
<th>Marginal Effect (95% CI†)</th>
<th>Patients’ Marginal Willingness to Pay to Avoid Certain INS Sensory Attributes (95% CI†)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smell (reference: no smell)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak smell</td>
<td>-0.04 (-0.15, 0.08)</td>
<td>$0.60 (-$1.27, $2.47)</td>
</tr>
<tr>
<td>Strong smell</td>
<td>-0.66 (-0.77, -0.55)</td>
<td>$10.93 ($9.06, $12.80)</td>
</tr>
<tr>
<td>Taste (reference: no taste)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak taste</td>
<td>0.04 (-0.07, 0.16)</td>
<td>-$0.73 (-$2.62, $1.16)</td>
</tr>
<tr>
<td>Strong taste</td>
<td>-0.74 (-0.85, -0.63)</td>
<td>$12.22 ($10.33, $14.11)</td>
</tr>
<tr>
<td>Aftertaste (reference: no aftertaste)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weak aftertaste</td>
<td>-0.13 (-0.24, -0.01)</td>
<td>$2.08 ($0.21, $3.95)</td>
</tr>
<tr>
<td>Strong aftertaste</td>
<td>-1.20 (-1.31, -1.08)</td>
<td>$19.79 ($17.92, $21.66)</td>
</tr>
<tr>
<td>Throat rundown (reference: no rundown)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some rundown</td>
<td>-0.22 (-0.33, -0.11)</td>
<td>$3.63 ($1.76, $5.50)</td>
</tr>
<tr>
<td>A lot of rundown</td>
<td>-0.63 (-0.75, -0.52)</td>
<td>$10.48 ($8.60, $12.35)</td>
</tr>
<tr>
<td>Nose runout (reference: no runout)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some runout</td>
<td>-0.14 (-0.25, -0.03)</td>
<td>$2.32 ($0.44, $4.19)</td>
</tr>
<tr>
<td>A lot of runout</td>
<td>-0.67 (-0.78, -0.55)</td>
<td>$10.89 ($8.92, $12.87)</td>
</tr>
<tr>
<td>Feel of spray in nose/throat (reference: moist)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neither moist nor dry</td>
<td>-0.08 (-0.19, 0.03)</td>
<td>$1.31 (-$0.56, $3.18)</td>
</tr>
<tr>
<td>Dry</td>
<td>-0.36 (-0.47, -0.24)</td>
<td>$5.92 ($4.05, $7.79)</td>
</tr>
<tr>
<td>Cost (per dollar)</td>
<td>-0.06 (-0.06, -0.06)</td>
<td>–</td>
</tr>
</tbody>
</table>

*As calculated by univariate analysis, the marginal effect size of copayment or cost was -0.06 utility score per dollar, i.e., for every $1 increase in price, there was a downward utility profile in preference. The willingness to pay was obtained by dividing the marginal effect size per attribute level with the marginal effect of cost per dollar.
†95% CIs (confidence intervals) that did not include 0 were considered to be statistically significant.

INS = intranasal corticosteroid.

### Discussion

Marginal willingness to pay depicts the strength of preference for product attributes through monetary units and has the advantage of providing easy-to-understand comparisons. Attribute levels with greater willingness to pay are more preferable than those with less willingness to pay. We found that patients with allergic rhinitis are willing to pay higher monthly copayments for products with mild intensity levels of each sensory attribute than those with higher intensity levels; that is, patients were willing to pay from $6 (spray with a wet feel) to $20 (for no aftertaste) to avoid the more severe intensity levels of a given attribute. Patients selected products with mild attribute intensity levels between 60% and 70% of the time when those products were presented. Aftertaste, throat rundown, and nose runout seemed to have higher willingness to pay to avoid both
Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis

**FIGURE 1** Impact of Monthly Copayment Amount on (A) Smell, (B) Taste, (C) Aftertaste, (D) Throat Rundown, (E) Nose Runout, and (F) Feel of Spray*

* Frequencies represent the proportion of times that a product containing that sensory attribute intensity level was chosen divided by the number of times it was shown to patients. Only 3 copay amounts were presented to patients: $15, $30, and $50.

---

**A. Effect of Copay on Smell**
- No Smell
- Weak Smell
- Strong Smell

**B. Effect of Copay on Taste**
- No Taste
- Weak Taste
- Strong Taste

**C. Effect of Copay on Aftertaste**
- No Aftertaste
- Weak Aftertaste
- Strong Aftertaste

**D. Effect of Copay on Throat Rundown**
- No Amount
- Some Amount
- A Lot

**E. Effect of Copay on Nose Runout**
- No Amount
- Some Amount
- A Lot

**F. Effect of Copay on Feel of Spray**
- Moist
- Neither Moist nor Dry
- Dry
Willingness to Pay for Sensory Attributes of Intranasal Corticosteroids Among Patients With Allergic Rhinitis

moderate and severe intensity levels. Smell, taste, and feel of spray had higher willingness to pay to avoid only the severe intensity level. This information may inform prescribing and formulary decisions. Based on results reported by the authors previously, individual preferences for INS sensory attributes had some variation, e.g., some patients placed strong emphasis on aftertaste only, while others rated aftertaste and smell as equally important.

Other investigators have shown that patients perceive differences in INS sensory attributes and have preferences for certain attributes. Meltzer et al. conducted a double-blind, crossover study of 100 patients with symptomatic allergic rhinitis randomized to receive mometasone furoate nasal spray (MFNS) 200 mcg followed by fluticasone propionate nasal spray (FPNS) 200 mcg, or vice versa, after which they rated the drugs using a sensory attribute questionnaire. The investigators reported that fewer patients perceived scent, immediate taste, and aftertaste with MFNS compared with FPNS; in addition, more than half of the patients expressed a preference for MFNS and stated that they would be likely to comply with this treatment (i.e., use it daily as directed).

Kaliner conducted 2 telephone surveys—1 with 100 family practitioners, general practitioners, and internists and 1 with 503 patients with seasonal and perennial allergic rhinitis—and found that 95% of physicians thought that their patients would prefer an INS with no aftertaste and no smell. However, the author noted that 47% to 60% of patients reported that their physicians had not asked them about their satisfaction with the sensory attributes of the INS they were using, and only 7% of physicians mentioned that they chose an INS because of patient preferences. In addition, 86% of patients reported that they had not complained to their physician about a sensory attribute of their INS treatment. These study results suggest that improved physician-patient communication about sensory attributes could improve selection of INSs. However, a description of sensory attributes is not part of current product labeling.

In the present study, monthly copayment amounts reduce product attribute preference and attenuate the differences between intensity levels. However, even at the highest monthly copayment of $50, patients had a higher share of preference for product attributes with milder intensity levels, suggesting that sensory attributes are important in patient decision making. We also found that income level affects willingness to pay, but this was not a consistent finding. Patients with incomes >$80,000 per year were willing to pay more to avoid excess throat rundown than those with incomes <$40,000 per year.

Choosing INS products that better fit patients’ INS sensory attribute preferences may increase adherence. In his telephone survey of 503 patients with seasonal and perennial allergic rhinitis, Kaliner noted that 45% of patients stated that sensory attributes do influence how often they use INSs.

Limitations

Foremost among the limitations of this study is its small sample size, involving only 113 patients distributed among 4 states. The population was also largely white and middle class, which limits the ability to generalize the results without further replication in more diverse samples.

Second, we did not identify, analyze, or report whether the study patients had seasonal or perennial rhinitis, and severity of symptoms has been found to be much higher among patients with perennial allergic rhinitis who are more likely to take an oral antihistamine than are patients with seasonal allergic rhinitis.

Third, patients may not indicate consistent preferences if they have little experience with INS products. We sought to address this limitation by enrolling patients with allergic rhinitis...
who had been diagnosed at least 1 year before and had used an INS within the last month. Our sample had been diagnosed with allergic rhinitis for a mean duration of 17.2 years with 86.7% of the patients having experience with 2 or more INS products.

Fourth, marginal willingness to pay may not necessarily predict real-life purchasing decisions.

Fifth, our analysis was limited to INS products and did not consider oral antihistamines and other therapeutic options in the treatment of allergic rhinitis.

Our study findings on patients’ willingness to pay might be added to the information already available regarding barriers to informed patient decision making such as the lack of knowledge about treatment options, reluctance to discuss treatment with physicians, no inquiry by physicians about patients’ preferences, or time constraints in physician schedules. Routine patient-physician discussions could improve INS selection and should be encouraged.

Conclusion

We found that patients are willing to pay significant higher monthly copayments to avoid certain sensory attributes of INSs. Given the high prevalence of allergic rhinitis, its adverse effects on quality of life, and sizable social and economic costs, methods to promote physician-patient dialogue about sensory attributes are advisable. Personal preferences may also be important in selecting INS agents for drug formulary placement in copayment tiers. Understanding the strength of patient preferences for INS sensory attributes may lead to more informed selection of pharmacotherapy for allergic rhinitis.

ACKNOWLEDGMENT

The authors acknowledge the contributions of Jeanne McFadden, publications associate, AstraZeneca LP, Wilmington, Delaware, in the preparation of this manuscript.

DISCLOSURES

Funding for this research was provided by AstraZeneca LP, Wilmington, DE, and was obtained by author Christopher Leibman, who was an employee of AstraZeneca LP at the time of this study; author Lisa O’Dowd is currently an employee of AstraZeneca LP. The authors disclose no potential bias or conflict of interest regarding to this article. Parthiv Mahadevia served as principal author of the study. Study concept and design were contributed primarily by Mahadevia, O’Dowd, and Leibman, with input from authors Shailen Shah, Sally Mannix, Jessica Brewer-Jordan, and Leah Kleinman. Data collection was the work of Mahadevia, Shah, Mannix, and Brewer-Jordan, with input from O’Dowd and Leibman; data interpretation was the work of Mahadevia and Shah, with input from the coauthors. Drafting of the manuscript and its revision was the work of Mahadevia, Kleinman, O’Dowd, and Leibman, with input from Mannix and Brewer-Jordan.

REFERENCES


Suboptimal Pneumococcal Pneumonia Vaccination Rates Among Patients at Risk in a Managed Care Organization in Israel

NATAN R. KAHAN, RPh, MHA; DAN-ANDREI WAITMAN, MD, MPH; SHIMON BLACKMAN, BScPharm; and DAVID P. CHINITZ, PhD

ABSTRACT

OBJECTIVE: Pneumococcal pneumonia is a vaccine-preventable disease that poses a significant threat to immunocompromised patients. Vaccination rates tend to be low despite recommendations for vaccination in several groups of high-risk patients including any person aged 65 years or older. The purpose of this study was to (a) evaluate the vaccination rates among high-risk patients in a managed care setting in Israel and (b) gain a better understanding of the factors associated with suboptimal use of this vaccine.

METHODS: Data were extracted from the electronic medical records of the managed care organization for patients with dates of service from January 2000 to December 2004 for whom the vaccine is recommended. Patients were identified via diagnosis codes according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Vaccination rates were calculated for patients in each disease category. These high-risk patients were contacted in a telephone survey to evaluate the variance in knowledge and awareness levels of the disease between the vaccinated and unvaccinated patients.

RESULTS: A total of 672 patients were identified by the ICD-9-CM codes; 140 (20.8%) had been vaccinated and 532 (79.2%) were unvaccinated. Vaccination rates were highest among patients with solid organ transplants (33.3%), followed (20.8%) had been vaccinated and 532 (79.2%) were unvaccinated. Vaccination rates were highest among patients with solid organ transplants (33.3%), followed by nephrotic syndrome (29.4%), bone marrow transplants (10.2%), and human immunodeficiency virus (HIV), for an overall rate of 20.8%. Of these patients, survey responses were obtained from 364 (54.2%). Respondents who were unvaccinated tended to be less well informed about which patient populations are at risk for the disease and the availability of the vaccine.

CONCLUSION: The pneumococcal vaccination rate among immunocompromised patients in this managed care organization was found to be inadequate, at just 29.8% of the target population. Approaches based on direct contact with the patient, such as by a case manager, may be more successful in the future.

KEYWORDS: Pneumococcal pneumonia vaccine, Vaccination rates, Managed care, Insular populations, Immunocompromised

J Manag Care Pharm. 2006;12(2):152-56

Pneumococcal disease, particularly pneumonia, bacteremia, and meningitis, is a vaccine-preventable disease that is an important cause of mortality and morbidity, especially in vulnerable groups such as the elderly, very young, patients with chronic disease, and the immunocompromised. High-risk groups include persons with human immunodeficiency virus (HIV); patients with chronic renal insufficiency, including nephrotic syndrome; individuals with anatomic asplenia; and solid organ transplant recipients being treated with immunosuppressive drugs. The vaccine has been recommended for anyone aged 65 years and older as well as patients aged 2 years and older who have the following high-risk medical conditions: chronic heart, kidney, or lung disease (except asthma); cirrhosis of the liver; alcoholism; diabetes mellitus; chronic cerebrospinal fluid leak; other diseases that suppress the immune system; and sickle cell disease.

In the United States, pneumococcal disease has been estimated to account for 3,000 cases of meningitis, 50,000 cases of bacteremia, 500,000 cases of pneumonia, and 7 million cases of otitis media annually. Furthermore, it has been estimated that pneumococcal infection causes approximately 40,000 deaths annually in the United States, accounting for more deaths than any other vaccine-preventable bacterial disease.

Efficacy rates of the vaccine in immunocompetent adults for the prevention of pneumococcal bacteremia and meningitis have been reported to be from 65% to 75%. However, despite this reported efficacy and although pneumococcal vaccination has been recommended for immunocompetent patients with indications for its administration, vaccination rates in the United States among persons aged 18 to 64 years with one or more risk conditions in 2002 continued to be low (19.1%). Furthermore, despite these recommendations, pneumococcal vaccination has only been included as a Health Plan Employer Data and Information Set (HEDIS) performance measure for patients aged >65 years. Consequently, managed care organizations (MCOs) are presently lacking a benchmark to monitor vaccine performance rates among patients in risk groups other than older age.

The present study was conducted in the Leumit Health Fund, one of the 4 MCOs in Israel, which provides the government-mandated national health package to approximately 650,000 members throughout the State of Israel, representing about 10% of the population. In addition to adopting the vaccination policy for pneumococcal vaccine common to other Western countries, Leumit management has targeted high-risk patient populations to receive the vaccine without having to pay
Methods

Data were extracted from the electronic patient records of the Leumit Health Fund of Israel. All patient records were identified with one or more of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes for a condition for which the vaccine is recommended (Table 1). The vaccination rates were calculated for patients in each disease category. Asplenic patients were not included in the study since this group includes patients who underwent emergency splenectomy and were then vaccinated in the hospital.

A telephone survey was conducted among these patients, both vaccinated and unvaccinated, to evaluate the variances in knowledge and awareness levels of the disease between the vaccinated and unvaccinated groups. The telephone survey was conducted during the month of February 2005. Survey questions (Table 2) included the identification of risk factors and access to the vaccine. Since this group of patients includes large subpopulations of recent immigrants from Ethiopia and the former Soviet Union, interviewers (employees of a commercial survey firm) fluent in Russian or Amharic in addition to Hebrew conducted the survey. In their opening remarks to the patients, the interviewers stated that the survey was being conducted by the Leumit Health Fund among its patients.

Results

A total of 672 patients were identified (532 unvaccinated and 140 vaccinated). Vaccination rates were highest among patients who had undergone solid organ transplants (33.3%), followed by nephrotic syndrome (29.4%), bone marrow transplants (10.2%), and HIV (9%), for an overall rate 20.8% (Table 3).

The interviewers attempted to contact the households or place of work of these patients (21 patients did not have telephones or the telephone number on file was incorrect). Of these, 364 (54.2%) agreed to participate, 87 (12.9%) refused to participate, and 221 (32.9%) were not available. The disease distribution and vaccination rates among the surveyed population appear in Table 4. The overall vaccination rate was observed to be higher among the surveyed population than in the target population (26.1% vs. 20.8%). However, this difference was not statistically significant because of the small sample size.

The results of the survey appear in Table 2. Among the non-immunized patients, 45% of the respondents replied that they did not know what groups of people are at risk of developing pneumonia; 29.9% of those who were immunized (P = 0.06) responded similarly. Only 15.7% of the immunized patients claimed that they themselves are not at risk compared with 39.8% among the nonimmunized respondents (P <0.001). Concerning awareness of the availability of the vaccine, 59.5% of the immunized patients responded that they were aware of its availability compared with 26.9% of the nonimmunized (P <0.001). A total of 57.6% of the immunized patients knew

TABLE 1 ICD-9-CM Diagnosis Codes Used to Identify High-Risk Patients

<table>
<thead>
<tr>
<th>ICD-9-CM Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>042</td>
<td>HIV disease, AIDS</td>
</tr>
<tr>
<td>33.6</td>
<td>Combined heart-lung transplantation</td>
</tr>
<tr>
<td>37.5</td>
<td>Heart transplantation</td>
</tr>
<tr>
<td>41.0</td>
<td>Bone marrow or hematopoietic stem cell transplant</td>
</tr>
<tr>
<td>41.00</td>
<td>Bone marrow transplant, not otherwise specified</td>
</tr>
<tr>
<td>41.01</td>
<td>Autologous bone marrow transplant without purging</td>
</tr>
<tr>
<td>41.02</td>
<td>Allogeneic bone marrow transplantation with purging</td>
</tr>
<tr>
<td>41.03</td>
<td>Allogeneic bone marrow transplantation without purging</td>
</tr>
<tr>
<td>41.04</td>
<td>Autologous hematopoietic stem cell transplant without purging</td>
</tr>
<tr>
<td>41.05</td>
<td>Allogeneic hematopoietic stem cell transplant without purging</td>
</tr>
<tr>
<td>41.08</td>
<td>Allogeneic hematopoietic stem cell transplant with purging</td>
</tr>
<tr>
<td>41.09</td>
<td>Autologous bone marrow transplant with purging</td>
</tr>
<tr>
<td>50.5</td>
<td>Liver transplant</td>
</tr>
<tr>
<td>52.8</td>
<td>Transplantation of pancreas</td>
</tr>
<tr>
<td>55.6</td>
<td>Kidney transplantation</td>
</tr>
<tr>
<td>581</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>581.0</td>
<td>Nephrotic syndrome with lesion of proliferative glomerulonephritis</td>
</tr>
<tr>
<td>581.1</td>
<td>Nephrotic syndrome with lesion of membranous glomerulonephritis</td>
</tr>
<tr>
<td>581.2</td>
<td>Nephrotic syndrome with lesion of membranoproliferative glomerulonephritis</td>
</tr>
<tr>
<td>581.3</td>
<td>Nephrotic syndrome with lesion of minimal change glomerulonephritis</td>
</tr>
<tr>
<td>581.8</td>
<td>Nephrotic syndrome with other specified pathological lesion in kidney</td>
</tr>
<tr>
<td>581.81</td>
<td>Nephrotic syndrome in diseases classified elsewhere</td>
</tr>
<tr>
<td>581.9</td>
<td>Nephrotic syndrome with unspecified pathological lesion in kidney</td>
</tr>
<tr>
<td>V08</td>
<td>Asymptomatic HIV infection status</td>
</tr>
<tr>
<td>V42</td>
<td>Kidney replaced by transplant</td>
</tr>
<tr>
<td>V42.01</td>
<td>Pancreas replaced by transplant</td>
</tr>
<tr>
<td>V42.1</td>
<td>Heart replaced by transplant</td>
</tr>
<tr>
<td>V42.6</td>
<td>Lung replaced by transplant</td>
</tr>
<tr>
<td>V42.7</td>
<td>Liver replaced by transplant</td>
</tr>
</tbody>
</table>

HIV = human immunodeficiency virus; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.
that the vaccine is available free of charge compared with 24.7% of those not immunized (P <0.01), and 57.0% of the immunized patients claimed that they were recommended to receive the vaccine compared with 23.8% among the nonimmunized (P <0.001).

### Discussion

The day after the survey began in February 2005, patients started to appear in Leumit clinics requesting to be immunized. Unfortunately, at that time, stock levels of the vaccine in Israel had been depleted. On the third day of the survey, the public health nurse in charge of the HIV outpatient clinic of one of the country’s major medical centers contacted us, stating that, during the past few days, many of the center’s Ethiopian immigrant HIV patients had come to the center to tell him that an Amharic-speaking women had called them and asked “all kinds of questions.” These patients turned to the health nurse in search of an explanation for what they perceived to be a very unusual and mysterious incident.

We explained the purpose of the study to the nurse and elaborated on the challenges involved in reaching out to this particular group. The nurse suggested that, since these patients come to his clinic on a monthly basis to receive their antiretroviral medications, he could vaccinate the necessary patients if we supplied him with a list of eligible patients and the quantity of vaccines needed. When the vaccine later became available, this procedure was adopted in HIV outpatient clinics throughout Israel. Thus, although this survey was not intended to be a quality improvement intervention per se, it did, in fact, yield favorable QI results.

This study suggests that this MCO must pursue alternative methods for the dissemination of information regarding pneumococcal vaccination that may be vital to the health of particularly vulnerable patients. This point is underscored by the observation of low vaccination rates coupled with the approximately 78% rate of unvaccinated patients who were unaware of the existence of the vaccine. The serendipitous outcome reported here in which evaluative research generated interest both among patients to receive the vaccine and ancillary care givers to pursue administrative solutions is therefore interesting. These results may indicate that future programs to improve vaccination rates may, in fact, emanate from the awareness created by the initiation of benchmarking and performance measure evaluations in particular patient groups.

It has been suggested that the suboptimal adult immunization rates in the United States may not be attributable to lack of interest among primary care physicians and that most physicians would indeed adopt evidence-based strategies to improve immunization delivery. Additionally, it has been established that physician-practice environments that are conducive to patient education and immunization-promotion activity do achieve higher vaccination rates. Accordingly, improved vaccination rates may be achieved

### Table 2

<table>
<thead>
<tr>
<th>1. What groups of people do you think are at higher risk of developing pneumonia?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Don’t know</td>
<td>45.0</td>
<td>29.9</td>
<td></td>
</tr>
<tr>
<td>b. Elderly</td>
<td>14.8</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td>c. Asthmatics</td>
<td>3.3</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td>d. Infants</td>
<td>2.5</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>e. Immunodeficients</td>
<td>26.2</td>
<td>33.3</td>
<td></td>
</tr>
<tr>
<td>f. Heart disease</td>
<td>0.0</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>g. Other</td>
<td>8.2</td>
<td>10.2</td>
<td></td>
</tr>
<tr>
<td>Total (P =0.06)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. To what degree do you believe that you are at higher risk?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Highest</td>
<td>28.5</td>
<td>28.9</td>
<td></td>
</tr>
<tr>
<td>b. Very high</td>
<td>7.8</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>c. Medium</td>
<td>7.4</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>d. Slightly</td>
<td>3.9</td>
<td>20.5</td>
<td></td>
</tr>
<tr>
<td>e. Not at all</td>
<td>39.8</td>
<td>15.7</td>
<td></td>
</tr>
<tr>
<td>f. Other</td>
<td>12.6</td>
<td>10.8</td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Do you know of any measures that can be taken to reduce the risk of pneumonia?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Vaccination</td>
<td>22.4</td>
<td>47.3</td>
<td></td>
</tr>
<tr>
<td>b. Drug</td>
<td>9.2</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>c. Other</td>
<td>8.4</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>d. Don't know</td>
<td>60.0</td>
<td>42.8</td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Are you aware that there is a vaccine for pneumonia?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Yes</td>
<td>26.9</td>
<td>59.5</td>
<td></td>
</tr>
<tr>
<td>b. No</td>
<td>65.2</td>
<td>36.0</td>
<td></td>
</tr>
<tr>
<td>c. Don't know/not sure</td>
<td>7.9</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Were you recommended to receive this vaccine?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Yes</td>
<td>23.8</td>
<td>57.0</td>
<td></td>
</tr>
<tr>
<td>b. No</td>
<td>76.2</td>
<td>43.0</td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Are you aware that you can receive the vaccine free of charge at your MCO clinic?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Yes</td>
<td>24.7</td>
<td>57.6</td>
<td></td>
</tr>
<tr>
<td>b. No</td>
<td>61.5</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td>c. Not sure</td>
<td>13.8</td>
<td>10.9</td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. Why did you not receive the vaccine?</th>
<th>Immunized</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Unaware of availability</td>
<td>76.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. I am not in a risk group</td>
<td>5.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Lack of time</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. No need due to medical care</td>
<td>7.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Don’t believe in effectiveness of vaccines</td>
<td>4.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. I scheduled an appointment for next month</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Other</td>
<td>3.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (P &lt;0.001)*</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* P values were calculated using the chi-square statistical test.
† n =269.
MCO = managed care organization.
in the future through multifaceted programs composed of evidence-based delivery strategies implemented in conjunction with organizational changes that create practice environments more suitable for promotion of vaccination. Similarly, administrative and/or financial support may be necessary in some settings to change current policy environments. Likewise, the recent failure of a media campaign in the United States to promote pneumococcal vaccination reinforces this premise that future efforts should be targeted to the clinical practice setting. The results presented here suggest additional approaches to inducing compliance with vaccination programs.

The present study raises the issue of expanding the HEDIS performance measures to include vaccination rates among immunocompromised patients. Such a measure could constitute a benchmark that MCOs could use to improve pneumococcal vaccination rates among this vulnerable population. The general paucity of studies evaluating factors associated with suboptimal vaccination rates in this population may have contributed to the lack of attention paid by policy makers to this issue. Alternatively, financial considerations or a belief that a vaccine policy would be too difficult to administer may have impeded the inclusion of relevant performance measures. In this context, HEDIS performance measures could be utilized in the future as evaluation tools of processes in which evidence-based guideline formulation and propagation and environmental changes coalesce into an integrative QI program.

The success of the survey itself in generating interest in the community among individual patients and then, consequentially, among other health care providers may provide insight into potential avenues with which to approach this challenge. The postcards sent to high-risk health plan members had small apparent impact on the pneumococcal vaccination rates among high-risk patients. Direct contact with the patients, with or without a survey, appears to be necessary, particularly among more insular immigrant populations from the developing world, without a survey, appears to be necessary, particularly among those who are unfamiliar with Western medical care. Evaluation of vaccination plans in other countries such as the United States.

The present study raises the issue of expanding the HEDIS performance measures to include vaccination rates among immunocompromised patients. Such a measure could constitute a benchmark that MCOs could use to improve pneumococcal vaccination rates among this vulnerable population. The general paucity of studies evaluating factors associated with suboptimal vaccination rates in this population may have contributed to the lack of attention paid by policy makers to this issue. Alternatively, financial considerations or a belief that a vaccine policy would be too difficult to administer may have impeded the inclusion of relevant performance measures. In this context, HEDIS performance measures could be utilized in the future as evaluation tools of processes in which evidence-based guideline formulation and propagation and environmental changes coalesce into an integrative QI program.

The success of the survey itself in generating interest in the community among individual patients and then, consequentially, among other health care providers may provide insight into potential avenues with which to approach this challenge. The postcards sent to high-risk health plan members had small apparent impact on the pneumococcal vaccination rates among high-risk patients. Direct contact with the patients, with or without a survey, appears to be necessary, particularly among more insular immigrant populations from the developing world, such as the Ethiopians in this study, who must cope with the complexities of modern Western medical care that are non-existent in their country of origin.

In addition to telephone contact, case mangers may need to assume responsibility for pneumococcal vaccination of high-risk patients. Since many of these patients receive chronic care in non-MCO facilities, there will be challenges in coordinating care among a multitude of providers, making intervention by the case manager particularly important. Lastly, we learned from the public health nurse that some solutions might be easily implemented through cooperation with junior-level staff of non-MCO facilities.

# Conclusion

The pneumococcal vaccination rates among immunocompromised patients in this MCO in 2005 were found to be inadequate. A more effective approach, such as direct contact with the patient through a case manager, is necessary to increase vaccination rates. It will be necessary to pay particular attention to insular immigrant populations, especially among those who are unfamiliar with Western medical care. Evaluation of vaccination programs based on member surveys has emerged as a potentially effective tool in this respect, which may be considered by health plans in other countries such as the United States.

**TABLE 3** Study Population (n = 672)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonimmunized</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
<td>62 (89.9)</td>
</tr>
<tr>
<td>HIV</td>
<td>242 (91.0)</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>60 (70.6)</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>168 (66.7)</td>
</tr>
<tr>
<td>Total</td>
<td>532 (79.2)</td>
</tr>
</tbody>
</table>

HIV = human immunodeficiency virus.

**TABLE 4** Disease Distribution and Rate of Pneumococcal Immunization of Surveyed Population (n = 364)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonimmunized</td>
</tr>
<tr>
<td>Bone marrow transplant</td>
<td>31 (88.6)</td>
</tr>
<tr>
<td>HIV</td>
<td>99 (86.8)</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
<td>40 (71.4)</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>99 (62.5)</td>
</tr>
<tr>
<td>Total/average</td>
<td>269 (73.9)</td>
</tr>
</tbody>
</table>

CI = confidence interval; HIV = human immunodeficiency virus.

**REFERENCES**


The Estimated Impact of Drug Importation, Mandatory Mail Service, and Medicaid Fee Reduction on Community Pharmacies in Michigan

One common characteristic of the trend toward increased use of mail-service pharmacy services and personal importation of pharmaceuticals is the shift of prescription sales from Michigan pharmacies to out-of-state pharmacies. The absolute and relative economic impact of these developments affecting Michigan community pharmacists are of interest: (1) the adoption of mandatory mail-service requirements in pharmacy benefit programs of Michigan employers, (2) the hypothetical legalization of consumer importation of pharmaceuticals including cross-border shopping, and (3) the recent Michigan Medicaid pharmacy dispensing fee reduction.

A hypothetical community pharmacy unit was constructed using aggregate statistics to investigate the estimated outcomes of these 3 policy changes. Estimates of the magnitude of mandatory mail-service pharmacy and drug importation were developed from data from the Congressional Budget Office (CBO) and from a 2003 report from Milliman USA (consultants and actuaries) funded by the Pharmaceutical Care Management Association (PCMA). These estimates were applied to the hypothetical community pharmacy unit and to the total Michigan community pharmacy market, yielding macroeconomic measures of lost sales, profits, and salaries.

Assuming importation of pharmaceuticals is legalized, the total pharmacy and manufacturer loss is 1,778 jobs in Michigan, and lost sales to out-of-state and out-of-country pharmacies is $450 million. Mandatory mail-service pharmacy shifts $750 million to out-of-state pharmacies, and the equivalent of $81 million is lost in annual employee salaries in Michigan. The Medicaid fee reduction reduced community pharmacy revenue by $16 million. The 3 policy developments combined result in total community pharmacy lost sales of $1.216 billion (20% of a $6 billion market) and $280 million in lost payroll and net profits to owners of Michigan pharmacies. Therefore, mandatory mail service in employer health plans had the most significant impact of the 3 policy changes, accounting for 62% of the total financial impact. Unlike the broad effects of drug importation on drug manufacturers and pharmacy wholesalers as well as community pharmacies, mandatory mail service primarily affects Michigan community pharmacies. The reduction in the Medicaid dispensing fee impacted the profit margin for pharmacy owners but had little if any impact on salaries.

The background for this analysis includes a Michigan community pharmacy market that faced the prospect of significant private policy changes by major employers mandating mail-service pharmacy services and the state of Michigan reducing the Medicaid dispensing fee by 34%, from $3.77 to $2.50 beginning January 1, 2004. Along with these 2 proposed policy changes, there was significant interest in legalizing importation of pharmaceuticals because personal importation also shifts prescription sales to out-of-state pharmacies. These 3 public and private policy developments provided an opportunity to examine the economic impact on Michigan community pharmacies. The objective of the present analysis was to measure the collective and relative economic impact of the shift to employer-mandated mail-service pharmacy services, personal importation of pharmaceuticals, and the Medicaid pharmacy dispensing fee reduction. The economic impacts are estimated per pharmacy and extrapolated for the entire state of Michigan.

The pharmacy unit used for illustrations represents an amalgamation of all Michigan community pharmacies. Using published values for total and median prescription drug sales from the 2004 NCPA-Pfizer Digest,† a hypothetical prescription drug pharmacy unit was constructed. It was assumed that Michigan residents consumed $6 billion in prescription drugs in 2003, based upon published estimates of expenditures in the range of $5.9 billion to $8.4 billion. The number of community pharmacy licenses in Michigan exceeds 2,000,‡ but there are multiple licenses for the same location in some cases. For the

Note: A commentary on the subject of this article appears on pages 164-67 of this issue.

### Table 1: Assumptions Employed in These Economic Estimates*

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of Rxs dispensed per year per pharmacy (in 2003)*</td>
<td>56,399</td>
</tr>
<tr>
<td>Average sales price per Rx*</td>
<td>$51.44</td>
</tr>
<tr>
<td>Estimated annual prescription (Rx) sales [$2,606,479*] per pharmacy</td>
<td>$3,000,000</td>
</tr>
<tr>
<td>Estimated cost of goods sold (77.0%) [$2,009,161 or 77.1%]* per pharmacy</td>
<td>$2,310,000</td>
</tr>
<tr>
<td>Gross margin (23.0% vs. 22.9% [597,318]*) per pharmacy</td>
<td>$690,000</td>
</tr>
<tr>
<td>4.0% [$114,319, 4.4%]* per pharmacy</td>
<td>$120,000</td>
</tr>
<tr>
<td>Number of Michigan community pharmacies</td>
<td>2,000</td>
</tr>
<tr>
<td>(000)-$6 billion in annual Michigan community pharmacy Rx sales</td>
<td>$6,000,000</td>
</tr>
<tr>
<td>Number of Michigan residents§</td>
<td>10,002,379</td>
</tr>
<tr>
<td>Number of Michigan residents subject to employer health plan mandates</td>
<td>5,000,000</td>
</tr>
<tr>
<td>Number of mail-service Rxs per year per affected beneficiary†</td>
<td>1.0</td>
</tr>
<tr>
<td>Number of community pharmacy mail-service Rx equivalents‡</td>
<td>3.0</td>
</tr>
</tbody>
</table>

* These are median values in this table except for the average number of Rxs and the average price per Rx. The average number of Rxs and the average price per Rx and all data presented in brackets [ ] were obtained from the National Community Pharmacists Association, 2004 NCPA-Pfizer Digest, October 2004, for data reported for 2003.

† Derived from the Milliman USA report prepared for the Pharmaceutical Care Management Association.

‡ Derived from the Milliman USA report prepared for the Pharmaceutical Care Management Association.

Rx = prescription.
purpose of convenience and simplification, 2,000 pharmacies are accepted as the approximate number of chain and independent pharmacies in Michigan. The 2004 Digest shows a national average of $2.9 million in prescription drug sales in 2003, and the number of full-time equivalent (FTE) employees per pharmacy was 9.5, including 1.4 employee pharmacists plus 1.1 owner pharmacists, bringing the total to 10.5 FTE pharmacy personnel per pharmacy. Chain and food-market pharmacy statistics vary a bit, but assuming 2,000 Michigan pharmacies each filling 56,000 prescriptions annually and averaging $3 million in prescription drug sales per unit makes it easier to illustrate the impact on a typical Michigan community pharmacy unit. The assumptions are forced to fit a $6 billion Michigan pharmaceuticals market. The assumptions used in these economic estimates are shown in Table 1, including the median prescription sales statistics for a single community pharmacy.

**Policy Change #1: Employer-Mandated Mail-Service Pharmacy**

At the time of these analyses, Michigan pharmacies were prohibited from dispensing mail-service prescriptions. Consequently mandatory mail-service requirements in employee drug benefit plans resulted in prescriptions being shifted to out-of-state pharmacies. Mandatory mail-service volume was extrapolated from the Milliman USA study commissioned by PCMA to study the impact of Michigan House Bill 4987.1 HB 4987 was advanced in 2004 as "any-willing-provider" legislation and would have reduced the ability of health plan sponsors to discriminate between mail-service and community pharmacy. The objective of this bill was to require drug benefit programs to allow community pharmacies to dispense quantities similar to those dispensed by mail-service pharmacies. The conclusion from the Milliman-PCMA study was that Michigan employers would pay $30 (7.9%) more per capita in 2004 dollars if community pharmacies were provided access to the share of the market being channeled to mail-service pharmacies, derived 86% from $26 per capita increased cost due to the loss of discount pricing leverage for pharmacy benefit managers (PBMs) and 14% ($4 per capita) from the difference in community versus mail-service pharmacy pricing.

Assuming that each mail-service prescription (90-day supply) is roughly equivalent to 3 community pharmacy prescriptions (30-day supply each), a simple calculation using 5 million eligible members each receiving 1 mail-service prescription represents 15 million prescriptions per year lost from community pharmacies. If the average community pharmacy prescription price is about $50, the result is $750 million in lost sales (12.5%) by Michigan pharmacies.

The 2.37 million affected persons in Michigan in the Milliman-PCMA analysis resulted from the exclusion of approximately 45% of the Michigan population, including the Blues, self-funded plans, cash (self) pay, and Medicaid consumers. In this Milliman-PCMA analysis, there were 3 primary assumptions that contributed to the estimated $30 per capita savings ($71 million divided by 2.37 million persons): (a) $10 savings (from the elimination of 2 community pharmacy dispensing fees for each mail-service prescription, (b) a larger discount off average wholesale price (AWP), and (c) implied impact from rebates from mail-service pharmacies shared with drug plan sponsors.

The Milliman-PCMA report does not specify the details for the derivation of the $30 per-capita savings, and this report was not published in a peer-reviewed journal. In making the unsupported assumptions, the authors included caveats such as "actuarial modeling is not a precise science and involves judgment-based estimates." Regardless of the caveats regarding the unsupported assumptions, the conclusions, as is often the case, were embraced by many Michigan legislators, employer groups, and the media. If this statistic is extrapolated to half the Michigan population, or 5 million lives, the results would suggest $145 million in annual "savings." This extrapolation in the present analysis assumes that employers, in addition to the 2.37 million covered population identified in the Milliman-PCMA study, would adopt or have adopted similar policies requiring mandatory mail-service pharmacy dispensing.

**Policy Change #2: Legalization of Drug Importation**

Of the 3 policy developments examined, drug importation assumed that there would be enabling federal legislation. The current social/political climate bodes well for the advancement of importation legislation for several reasons. In this author's opinion, there is spillover from the corporate scandals in the tobacco, energy, and telecommunication industries for investors, voters, and consumers, contributing to an anticorporation sentiment. Any hint of corporate deception or ill-gotten profits is an opportunity for front-page journalism.

Additionally, those responsible for managing health care expenditures have little enthusiasm for more expensive pharmaceutical innovations. Given the anticipated 10.7% annual expenditure growth for pharmaceutical expenditures for the time period 2004-2013,7 expensive innovations may be especially unwelcome. Most observers don't believe that spending on pharmaceuticals and pharmaceutical care is offset by reductions in other health care expenditures. The importation debate has also sometimes characterized the U.S. Food and Drug Administration (FDA) as the vanguard of the pharmaceutical industry.

Drug importation has evoked concerns about product integrity and patient safety, but there are also cost considerations. Potential savings from drug importation are undermined by the availability of cheaper generic drugs in the United States compared with Canada8 and the fact that biologicals tend to be excluded from proposed legislation that would permit drug importation. These factors are joined by changes in the U.S. Department of Health and Human Services (HHS) and FDA leadership and recent public attention focused on pharmaceutical product recalls and safety concerns for commonly used drugs.
such as Vioxx. One consequence is an increased enthusiasm for greater drug safety surveillance, probably at the expense of future speedy drug approvals. It is possible that increased budget allocation for the FDA would include funding for surveillance, perhaps making more likely legalization of drug importation (with FDA surveillance).

In the political mix is the question of why the United States should bear the cost burden of global pharmaceutical research and development (R&D) in a global pharmaceutical market, perhaps increasing the probability of ultimate legislative success for drug importation. The HHS Task Force on Drug Importation estimates the 2003 import volume at $1.4 billion. This represents 0.6% of the U.S. $221.4 billion sales reported by IMS Health, which includes some over-the-counter sales. Legalization could have at least a 10-fold increase on drug importation. Convenient access, price differentials, and well-integrated economies, especially in the geographic areas of Michigan with the densest populations, are 3 factors contributing to the higher cross-border shopping in Michigan. Markets outside the United States experience volume slippage due to parallel imports—the amount of products imported to a country that is not consumed in that country. Based on estimates of slippage experienced in other countries, the U.S. Congressional Budget Office (CBO) estimates that the import volume of legalized importation would be 10% to 15% of the U.S. market if drug importation is legalized, increasing the volume of imported drugs.

 Since the CBO report, storefront pharmacies have been established to facilitate importation so the higher end of the range was used. I estimate 7.5% of total prescription volume in Michigan to be the current level of personal importation by Internet, mail service, storefront Canadian pharmacies, and cross-border shopping. The remaining 7.5% are excluded from this analysis because commercial importation would be transmitted through wholesalers and community pharmacies and would not result in lost prescription sales. Senate Bill (SB) 2328 called for both commercial and personal importation, and 7.5% represents half the volume assumed by the CBO in concluding that a $4 billion expenditure reduction, approximately 1% of expected Medicare expenditures, would be realized over the next 10 years. Legalizing importation will be a stimulus to Internet pharmacy sales if consumers interpret legalization as government-assured product integrity. The hypothetical impact of legalized importation is a little more than half the impact of mail service, 7.5% versus 12.5%, or about $450 million. The impact on profits and employee payroll on community pharmacies is illustrated later, along with impact on manufacturing pharmacy since both are affected.

Drug reimportation and importation have grown gradually over several years, and the effects are not immediately visible to community pharmacists. Consequently, the potential business impact on community pharmacy is not as obvious as mandatory mail service or a service fee reduction from a payer (Medicaid). Second, drug importation impacts both community and manufacturing pharmacy, but some may erroneously see drug importation as primarily a pharmaceutical industry issue.

### Estimating the Impact of the Reduction in Medicaid Dispense Fee

The impact of the Medicaid fee reduction is approximately $8,000 per Michigan pharmacy, but, of course, the financial impact is not uniform across pharmacy types or individual pharmacies because of differences in the relative proportion of total pharmacy sales volume accounted for by Medicaid (i.e., payer mix). This estimate is the result of dividing the number of Medicaid prescriptions in 2003 by the estimated 2,000 licensed Michigan pharmacies and multiplying this number by $8,000 per Michigan pharmacy, but, of course, the financial impact is not uniform across pharmacy types or individual pharmacies because of differences in the relative proportion of total pharmacy sales volume accounted for by Medicaid (i.e., payer mix). This estimate is the result of dividing the number of Medicaid prescription in 2003 by the estimated 2,000 licensed Michigan pharmacies and multiplying this number times the $1.27 dispensing fee reduction (34%) from $3.77 to $2.50. Only fee-for-service Medicaid prescriptions are used in the estimate. Unlike mail-service pharmacy and personal drug importation, the Medicaid fee reduction does not result in significantly lower pharmacy sales—$8,000 (1.2%) of $608,000 total lost sales (Table 2).

The impact of the Medicaid fee reduction appears small in relation to mandatory mail service because the workload and investment does not change. Pharmaceutical products must be purchased and dispensed at a lower profit. Assuming pharmacies realize a 4% net profit (Table 1), the $8,000 loss of dispense

### Table 2: The Impact of Mandatory Mail Service, Importation and Medicaid Fee Cut on a Single Michigan Community Pharmacy

<table>
<thead>
<tr>
<th>Rx Sales</th>
<th>Hypothetical Michigan Average ($)</th>
<th>7% COGS ($)</th>
<th>4% Net Profit ($)</th>
<th>Total Effect of Policy ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,000,000</td>
<td>2,310,000</td>
<td>690,000</td>
<td>120,000</td>
<td>-32,000</td>
</tr>
<tr>
<td>2,625,000</td>
<td>2,021,250</td>
<td>603,750</td>
<td>105,000</td>
<td>-375,000</td>
</tr>
<tr>
<td>2,775,000</td>
<td>2,136,750</td>
<td>638,250</td>
<td>111,000</td>
<td>-225,000</td>
</tr>
<tr>
<td>2,992,000</td>
<td>2,310,000</td>
<td>690,000</td>
<td>102,000</td>
<td>-8,000</td>
</tr>
<tr>
<td>77% COGS</td>
<td>120,000</td>
<td>105,000</td>
<td>111,000</td>
<td>-8,000</td>
</tr>
<tr>
<td>4% Net Profit</td>
<td>-15,000</td>
<td>-9,000</td>
<td>-8,000</td>
<td>-8,000</td>
</tr>
</tbody>
</table>

* COGS is 77% of $3,000,000 since there is no change in the volume (number) of Rxs with the Medicaid fee reduction, and the $8,000 effect of the fee reduction drops to the net profit line since overhead is also unchanged.

† Median net profit (4.0%) from National Community Pharmacists Association, 2004 NCPA-Pfizer Digest, October 2004, multiplied by the "net sales."

‡ Net profit compared with hypothetical average ($120,000) prior to effect of policy.

COGS = cost of goods sold, Rx = prescription.

[Table 2: The Impact of Mandatory Mail Service, Importation and Medicaid Fee Cut on a Single Michigan Community Pharmacy](#)
fee revenue would require a $200,000 increase in pharmacy sales revenue to offset the impact on pharmacy net profit.

**Estimating the Relative Business and Social Impact of the 3 Policy Changes**

In Table 2, the values are presented for the hypothetical individual pharmacy unit created earlier. The impact of the mandatory mail-service is to reduce community pharmacy sales by 12.5% or $375,000 ($3 million x 0.125), and corresponding adjustments are made to all other values, using the same 12.5% multiplier. The importation policy reduces annual sales 7.5% or $225,000, and the Medicaid fee reduction affects only the net profit, reducing the hypothetical $120,000 by $8,000 but leaving other values essentially the same, with the $8,000 reduction being constant. For example, under the mail-service policy change, annual sales are reduced by $375,000, gross margin is reduced by $86,250, and net profit is reduced by $15,000.

The bulk ($924 million or 76%) of the aggregate $1.216 billion annual lost sales (Table 3) is the cost of goods sold (COGS) for prescriptions not dispensed from Michigan pharmacies. More significant to the Michigan economy are the lost salaries and net profits that would have been generated and spent again in the community economy.

The impact on prescription sales per community pharmacy was estimated to be 12.5% for mandatory mail service, 7.5% for personal importation, and $8,000 (0.27%) for the 34% reduction in the Medicaid dispense fee. The hypothetical benchmark pharmacy with $3 million in annual prescription drug sales has 10.5 FTEs and 4% net profit. The per-pharmacy impact on net profits from fee adjustment (-$8,000) is approximately equal to the estimated impact of personal importation (-$9,000) but considerably less than the impact of mandatory mail service (-$15,000).

In Table 4, the losses in sales and profits are restated at both the individual pharmacy and aggregate level for the state of Michigan.

The lost Michigan payroll is estimated by using Digest median values to calculate revenue lost for salaries by multiplying the lost sales times 9%, which is the median proportion of sales dedicated to salaries. Consequently, at the pharmacy level, the $375,000 lost sales attributable to mandatory mail service results in a loss of $33,750 ($375,000 x 0.09). Further, dividing the lost salary revenue by the median expenses per employee—$36,000—results in 0.94 FTE lost per pharmacy. As illustrated in Table 5, extending this loss to 2,000 pharmacies results in a loss of 1,880 FTEs in Michigan. This analysis is extended to losses attributable to personal importation if and when it is legalized. The presumed across-the-board reduction proportional to decreased revenue is a general assumption applied to the aggregate. Individual pharmacies may or may not reduce personnel proportional to the decreased revenue.

Unlike mandatory mail service, personal importation, if legalized, could result in an additional loss of pharmaceutical R&D and manufacturing jobs. The U.S. Bureau of Labor Statistics (Wage and Salary Distribution by Industry—Michigan) reported a total of 8,700 Michigan pharmaceutical manufacturing jobs in 2000. The 12.5% reduction in pharmaceuticals sold would result in a corresponding loss of manufacturing jobs. However, lost sales to Michigan pharmacies are offset by increased sales to Canadian pharmacies albeit at lower prices. The lost COGS are reduced by 50% (15% + 2 = 7.5%) and the loss of manufacturing jobs is 653 (8,700 x 0.075).

The direct economic effect of mandatory mail service, importation, and the Medicaid fee cut is the loss of 3,658 jobs (1,880 due to mail service, 1,125 due to importation in community pharmacies, and 653 due to importation for pharmaceutical manufacturers) and $306 million, including the corresponding reduction in employee payroll, employer payroll, and net profits to the community businesses (Table 6). This exercise examines the negative impact on the Michigan community pharmacies, but Michigan pharmaceutical manufacturers are also “losers.”

“Savings” from mandatory mail service is $145 million if the Milliman-PCMA projected savings are extrapolated to half the Michigan population (Table 6). The $180 million in savings to consumers from drug importation assumes a 40% price differential. A comparison using top-selling brand-name products representing nearly 45% of the U.S. market in 2002 showed that Canadian prices were approximately 60% of the U.S. selling price in 2003.12

Foremost among the limitations of this analysis is the estimate of cost savings contained in the Milliman-PCMA report. This report estimated that Michigan employer-sponsored, non-Blues Association, non–self-funded prescription drug benefit plans using PBM services would spend $379 per capita in 2004 for drug benefit coverage, before member cost-share. The

| TABLE 3 Aggregate Michigan Pharmacy Sales and Profit Losses ($ Millions) |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Effect of policy* | Mandatory Mail Service ($) | Importation ($) | Medicaid Fee Cut ($) | Total ($) |
| Michigan Rx sales loss | 6,000 million x 12.5% | 6,000 million x 7.5% | – | – |
| Lost Michigan Rx cost of goods (77%) | 750 | 450 | 16 | 1,216 |
| Lost Michigan Rx gross margin (23%) | 577.5 | 346.5 | 0 | – |
| Lost Michigan Rx net profits (4%) | 172.5 | 103.5 | 16 | – |
| Lost Michigan Rx net profits (4%) | 30 | 18 | 16 | 64 |

* $6,000 million is derived from $3 million per pharmacy x 2,000 community pharmacies.
† National Community Pharmacists Association, 2004 NCPA-Pfizer Digest, October 2004, for 2003 community pharmacy data.
Commentary

Milliman-PCMA report estimated that eliminating the ability of PBM mail-service pharmacies to provide financial incentives for members to use mail service and permitting community pharmacies to dispense mail-service quantities (e.g., 90-day supply) would result in $30 per capita higher costs in 2004, comprising $26 per capita (86%) of lost price leverage that PBMs have with community pharmacies and $4 (14%) from “disallowing differentiated mail-service pricing and removing enrollees’ financial incentive for using mail order.” Neither of these estimates are developed or supported in the Milliman-PCMA report, and others have found that mail-service pharmacy can cost more than community pharmacy dispensing after consideration of the financial incentive provided to drug plan members to use mail order (e.g., only 1 or 2 copayments for a 90-day supply).

A recent analysis by Carroll et al. found 7.0% higher cost for mail-service pharmacy compared with community pharmacy for drug plan sponsors after considering the effect of lower copayments for mail service.17

Second, there was no attempt in this analysis to assess the costs associated with inconvenience or disruption from forcing drug benefit plan members to use mail service. There was also no attempt to estimate any quality-of-care outcomes that might arise from current policy versus proposed policy.

Third, a sophisticated assessment of the economic impact should include the secondary (induced) effects such as lost jobs, supplier business, feeder industries, etc. However, to simplify this analysis, none of the indirect and induced effects included in usual and customary economic impact analyses are applied. The data presented in tables 4 through 6 assume 653 manufacturer jobs lost and $58.7 million lost in manufacturer payroll. These are conservative estimates in the context of economic impact studies. Professor Dean Smith, at the University of Michigan, was commissioned by drug manufacturer Pfizer to estimate the impact of importation on the Michigan economy. Employing assumptions used by economists, there is a 6.2 multiplier effect for each industry job lost. In an unpublished analysis, Smith estimated that 74,000 Michigan lost jobs are industry-related, after applying this multiplier effect on 12,000 jobs compiled by him using 2003 data from the Michigan Economic Development Corporation.18 His estimates for the 2005 economic impact of importation in Michigan include $987 million in lost payroll in 2005. Smith’s analysis produces a larger financial impact because of the assumption of the substantial negative effect on R&D investment because of the role the U.S. market has traditionally played in funding a disproportionate share of global pharmaceutical research. Comparing Smith’s $987 million with the $58.7 million in this analysis illustrates the relationship of direct and induced effects.

| TABLE 4 | Salary and Employee Losses Attributable to Mandatory Mail Service and Importation |
|----------|---------------------------------|---------------------------------|---------------------------------|
|          | Mandatory Mail Service @ 12.5% | Importation at 7.5% (Pharmacy and Manufacturing) | Importation @ 7.5% (Pharmacy Only) |
| Individual pharmacy sales loss | -$375,000 | -$225,000 | -$225,000 |
| Lost employee payroll (9% of sales) | -$33,750 | -$20,250 | -$20,250 |
| FTE job loss per pharmacy* | - 0.94 | -0.56 | -0.56 |
| Statewide loss of jobs for 2,000 pharmacies | -1,880 | -1,125 | -1,125 |
| Owner profit loss (8.1% of lost sales) | -$30,375 | -$18,225 | -$18,225 |
| Aggregate lost Rx sales | -$750 million | -$450 million | -$450 million |
| Lost Michigan COGS at 77% of lost Rx sales | -$577.5 million | -$346.5 million | -$346.5 million |
| Manufacturer FTE job loss† | – | -652.5 | – |
| Lost manufacturing payroll in Michigan‡ | – | -$58,725,000 | – |
| Manufacturing and pharmacy employee loss (652.5+1,125) | – | -1,778 | – |
| 8.1% owner discretionary profits§ | -$60.75 million | -$36.45 million | -$36.45 million |
| Aggregate lost Michigan pharmacy payroll || | -$67.5 million | -$40.5 million | -$40.5 million |
| Employee and owner loss (2 rows above) | -$128.25 million | -$135.675 million | -$76.95 million |

* Lost employee payroll divided by average annual salary of $36,000.
† 8,700 manufacturing jobs (extracted from the U.S. Bureau of Labor Statistics [Wage and Salary Distribution by Industry—Michigan] combining employees from 4 industry codes, including medicinal and botanical manufacturing, pharmaceutical preparation manufacturing, in vitro diagnostic substance, and biological [excluding diagnostics]), multiplied by 0.075% reduction.
‡ Lost FTE jobs (652.5) multiplied by annual estimated salary of $90,000.
§ 8.1% multiplied by aggregate lost Rx sales.
‖ 9% of aggregate lost Rx sales.
COGS = cost of goods sold; FTE = full-time equivalent; Rx = prescription.
These estimates rely exclusively on statistics reported by others, and the author had to make reasoned assumptions. Further, the impact of personal drug importation could be exaggerated if final regulations nudge consumers toward commercial importation through existing distribution channels. However, given 4 gateways to personal drug importation and the probable costs of commercial importation, it is reasonable to assume that the volume of personal importation will be significant. These estimates are limited to the single state of Michigan, which prohibits mail-service pharmacies from having dispensing operations inside the state. Obviously, those states with mail-service pharmacies servicing Michigan will benefit from the shift. The negative impacts on state tax revenues are not included.

This exercise may help highlight some of the factors that determine the relative importance of alternate policy developments on the economy of the state and various stakeholders, including individual community pharmacies, pharmacy owners, and consumers. The Medicaid dispensing fee reduction has a small effect on community pharmacy sales relative to the legalization of prescription drug importation and an even smaller effect compared with mandatory mail-service requirements in drug benefit plans. However, the effect on community pharmacy net profit from the Medicaid fee reduction is approximately equivalent to drug importation and about half the effect of mandatory mail service.

**TABLE 5**

<table>
<thead>
<tr>
<th>Mandatory Mail Service</th>
<th>Importation</th>
<th>Medicaid Fee Reduction</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales</td>
<td>-$750</td>
<td>-$16</td>
<td>-$1,216</td>
</tr>
<tr>
<td>Jobs</td>
<td>-$1,880</td>
<td>-</td>
<td>-3,658</td>
</tr>
<tr>
<td>Payroll</td>
<td>-$67.5</td>
<td></td>
<td>-$166.7</td>
</tr>
<tr>
<td>Net profits</td>
<td>-$60.75</td>
<td>-$16</td>
<td>-$97.3</td>
</tr>
<tr>
<td>Total payroll and profits</td>
<td></td>
<td></td>
<td>-$264</td>
</tr>
</tbody>
</table>

**TABLE 6**

<table>
<thead>
<tr>
<th></th>
<th>Savings * in Millions ($)</th>
<th>Losses* in Millions ($)</th>
<th>Winners</th>
<th>Losers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mailing mail</td>
<td>145††</td>
<td>(154)</td>
<td>Nonpharmacy employers</td>
<td>Local pharmacy employees and owners</td>
</tr>
<tr>
<td>Importation</td>
<td>180††</td>
<td>(136)</td>
<td>Payers and consumers</td>
<td>Manufacturers and local pharmacies</td>
</tr>
<tr>
<td>Medicaid fee reduction</td>
<td>16</td>
<td>(16)</td>
<td>State of Michigan</td>
<td>Owner pharmacists</td>
</tr>
<tr>
<td>Total</td>
<td>341</td>
<td>(306)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* See Table 3.
† Milliman-PCMA report: $71 million extrapolated to half the Michigan population.
‡ 40% price differential on $450 million in diverted U.S. sales.

DISCLOSURES

Some statistics in this article were discussed by the author in his presentation, “Consumer Importation of Pharmaceuticals,” at the opening general session at the Michigan Pharmacists Association Annual Convention and Exposition, February 19, 2005, Dearborn, MI. He discloses no potential bias or conflict of interest relating to this article.

REFERENCES


Mail-Service Pharmacy Savings: A Conclusion in Search of Evidence

Mail-service pharmacy has experienced substantial growth over the last several years, from 5.9% of the total pharmacy market in 1991 to nearly 16% in 2003. Fuel for this growth has come, in part, from mandatory mail-service pharmacy provisions in pharmacy benefits adopted by employers, including the United Auto Workers (UAW) mandate in 2003. The mandate on member benefits is based on the belief that costs for mail-service pharmacy are lower than for community pharmacy.

There is surprisingly little, if any, evidence of the alleged savings from mail-service pharmacy. A number of reports and studies have purported to demonstrate that plan sponsors can realize substantial savings by using mail-service rather than community pharmacy. However, none of these studies actually provides evidence of cost savings.

A study that provides evidence of mail-service savings should have a number of characteristics. It should be based on an analysis of claims data rather than a comparison of contract prices. Such an analysis would show realized savings rather than projected or simulated savings. If not based on all incurred pharmacy claims, the study should be based on an adequate sample of products, prescriptions, and health plans. Ideally, the study should address the issue of wastage. Given that mail-service prescriptions are typically dispensed with quantities 3 times larger than those dispensed by community pharmacies, one would expect a greater wastage rate in mail-service pharmacies. With the increasing prices and high dollar cost of many prescription drugs, the importance of wastage has and will continue to increase. Consequently, wastage should be a major component of the comparison of costs between mail-service and community pharmacies.

If these conditions are met for the comparison of mail-service and community pharmacy, the study should be published in a journal with a reputation for high-quality peer review. This would be necessary for 2 reasons. First, publishing in a journal with the reputation for high-quality peer review ensures that the results of the study are widely available. This speaks to the issues of transparency (not in the usual pharmacy benefits manager [PBM]-related sense of the word) and accessibility (e.g., MEDLINE indexed) of the information. There must be transparency in how the authors came to their results and conclusions. Making analyses transparent guards against bias. Second, peer review ensures that the results of the study are examined by experts before being published. Peer review is not a guarantee that the results are valid, but it serves as an additional check on the quality of a study.

Any study that met all of these criteria could be found in either MEDLINE or International Pharmaceutical Abstracts. A search of these databases turned up only one study that compared the costs of mail-service and community pharmacy based on analysis of claims data. The results of this study indicated that mail-service pharmacy generates savings for patients but results in higher costs for plan sponsors. This occurred because the copay reductions that drug plan sponsors provided to induce patients to use mail-service pharmacy were greater than the savings that were generated from mail service. Importantly, this study did not look at wastage but did comment that the probable effect of wastage would be to decrease the savings generated through mail-service dispensing. This study is further limited in that it only considered one mail-service pharmacy, a pharmacy not owned by a PBM, and it was based on claims from only one health plan. Yet, it is the only study, to date, published in the peer-reviewed literature that provides a comparison of mail-service and community pharmacy costs based on actual claims data.

There is additional literature, which is neither peer reviewed nor published in recognized journals, that compares the cost of mail-service and community pharmacy. A major part of this fringe literature is composed of reports conducted by consulting companies for trade groups, particularly the Pharmaceutical Care Management Association (PCMA), which represents PBMs that own mail-service pharmacies. An example is the Lewin study, published in 2005 for PCMA. This study estimated that, if mail-service pharmacy were used to its full potential, it would result in savings of $178 billion over the next 10 years. A critical assumption in this analysis was that use of mail-service pharmacies provides a savings of 10% compared with community pharmacies. The 10% savings estimate was based on estimates from 3 sources. The first source was a Merrill Lynch investment report that estimated mail-service savings of 5% to 10% for plan sponsors. That is, mail-service pharmacy produced savings for sponsors after taking into account the lower copays typically associated with mail-service dispensing. The Lewin report does not explain how Merrill Lynch arrived at its estimate. Neither a Google search nor a search of the Merrill Lynch Web site was able to locate the report, so it is not possible to comment on the quality of the estimate.

The second source of Lewin's estimate of mail-service pharmacy savings was a 2004 report prepared for PCMA by PricewaterhouseCoopers. This report estimated that mail-service discounts were about 11% greater than community discounts. The report does not explain how this discount was estimated other than saying that “these figures are based on reports and testimony from the General Accounting Office, Congressional Research Service reports, financial reports from PBMs, discussion with industry consultants, conversations with PBMs, and other private research.” As with the Merrill Lynch estimate, one is unable to judge the quality of the estimate because the methods and analyses are not transparent.

The third and final source in the Lewin estimate of mail-service pharmacy savings compared with community pharmacy is a report by the General Accounting Office (GAO). The GAO report estimated that mail-service dispensing provides savings
of 11.5% on brand-name drugs and 9.9% on generic drugs compared with community pharmacy. These results were based on price comparisons on 14 brand-name and 3 generic products. Importantly, the comparisons were based on negotiated prices rather than on actual claims payments. While this report explained how saving estimates were generated and based those estimates on an actual comparison of products, the results are not compelling. Price comparisons based on only 17 products are not likely to give a reliable view of the total mix of products actually dispensed in mail-service and community pharmacies.

There may be substantial differences between actual savings and those suggested by comparison of contract prices. The issue of differential wastage rates between mail-service and community pharmacies has not been adequately addressed. Further, reports in the trade and business press have suggested that PBM mail-service pharmacies engage in a number of practices that result in higher prices to sponsors. These include dispensing products that have been rebalanced and priced higher than the original manufacturer's average wholesale price (AWP), basing formulary decisions on maximizing rebates over net plan sponsor cost, manipulating generic prices to increase PBM profit at the expense of plan sponsors, and switching patients to higher-priced products that maximize PBM rebates. To the extent that these reports are true and common practices, contract prices may not accurately reflect mail-service–community pharmacy cost differences.

These and other allegations regarding the business practices of a PBM with an owned mail-service pharmacy operation were evaluated by a state court jury in Cincinnati, Ohio. In a December 19, 2005, decision, the jury found that the PBM was guilty of "constructive fraud," including shifting generic prescriptions from community pharmacy to higher cost at mail-service pharmacy while claiming lower cost at mail service. The Ohio State Teachers Retirements System, the plaintiff in the case, was awarded $915,000 for breach of fiduciary duty and $6.9 million for fraud.

Finally, it is worth considering that GAO studies are not subject to peer review. Consequently, misleading results and conclusions are more likely to be reported than they would be if the study were subjected to blinded, independent, expert review.

The Lewin report is perhaps correct in concluding that the available evidence indicates a 10% savings rate for mail-service pharmacy. However, the available evidence on which this conclusion is based is not sound.

Kaye, in a 2003 article that was not peer reviewed, provides reasonable advice for preventing mail-service pharmacy from becoming an added expense rather than producing cost savings. In addition to at least 2 community pharmacy (30-day) copayments per mail-service pharmacy prescription, Kaye recommends (a) restriction of mail-service coverage and dispensing to maintenance drugs and (b) the application of the same maximum allowable cost (MAC) pricing to mail-service pharmacy prescriptions that is applied to community pharmacy prescriptions in order to avoid paying more for generic drugs from mail-service pharmacy.17

In this issue of JMCP, McKercher examines the effects of 3 policy changes proposed in the state of Michigan, including mandatory mail-service pharmacy. The basis for the cost estimates in the proposal for mandatory mail-service was a report from Millman USA that was funded by PCMA. This report suffers from limitations common to other unsubstantiated reports of mail-service pharmacy savings. The Milliman report estimated the cost to the state of Michigan of implementing legislation to regulate the operation of PBMs and mail-service pharmacies. The estimates related to mail-service savings appear to be based on statistics reported in the Takeda Prescription Drug Benefit Cost and Plan Design Survey Report. These statistics, according to the Milliman report, indicate that the average reimbursement paid to community pharmacies for brand-name products was 85% of AWP while that paid to mail-service pharmacies was 79.2% of AWP.

These figures may be true, but they are inadequate for a comprehensive estimate of the savings (or not) attributable to mail-service pharmacy dispensing compared with community pharmacy. In addition to suffering from limitations of comparing contract prices rather than actual payments, the contract rate (estimates) ignore mail-service versus community pharmacy differences in generic prices. The Milliman report also indicates that the results were based on their proprietary Health Cost Guidelines. The guidelines are not publicly available, because Milliman sells them by subscription, and the report did not indicate how the guidelines were used. In fact, the Milliman report provides little explanation or detail about the basic assumptions that underlie their estimates, what these estimates were, or how they were developed.

A recent Federal Trade Commission (FTC) study that examined conflict of interest attributable to ownership of mail-service pharmacies appears, at first glance, to provide evidence of mail-service savings. The FTC compared prices among PBM-owned mail-service pharmacies, non-PBM owned mail-service pharmacies, and community pharmacies. The comparisons were based on claims data from December 2003 and compared like quantities of the same drugs. The results indicated that mail-service pharmacies yielded savings for both consumers and plan sponsors.

A close reading of the report reveals some important anomalies. Specifically, the comparisons conducted by the FTC may not give an accurate view of true cost differences between mail-service and community pharmacy because they were based on samples that may not have been representative of the mix of prescriptions actually dispensed. The FTC compared 30-unit prescriptions dispensed at community pharmacies with 30-unit prescriptions for the same mix of products dispensed through mail-service pharmacies. This analysis is only reasonable if one
believes that 30-unit prescriptions dispensed through mail-service pharmacies are an adequate representation of all prescriptions dispensed in mail-service pharmacies. But given that mail service is used predominantly for chronic medications and that the copay discounts that PBMs offer to encourage drug plan beneficiaries to use mail service would not apply to most 30-unit prescriptions, it seems unlikely that patients would use mail service for 30-unit prescriptions.

The FTC also compared 90-unit prescriptions dispensed through the mail with 90-unit prescriptions dispensed in community pharmacies for the same products. As with the 30-unit comparison, this analysis is only reasonable if one believes that 90-unit prescriptions dispensed through community pharmacies are an adequate representation of all prescriptions dispensed in community pharmacies. Few community pharmacies are allowed by their PBM contracts to dispense 90-day supplies, so how representative of community pharmacy could a sample of 90-unit prescriptions be? It seems more likely that 90-unit prescriptions dispensed through community pharmacies and 30-unit prescriptions dispensed by mail-order are oddities. Consequently, it is unlikely that the comparisons conducted by the FTC were valid measurements of mail-service–community pharmacy cost differences.

The FTC report provides some evidence that these samples were unrepresentative. For example, the number of mail-service prescriptions in the sample of 30-unit prescriptions was very small compared with the number of 30-unit community pharmacy prescriptions. Similarly, the sample of community pharmacy 90-unit prescriptions was very small compared with the sample of 90-unit mail-service prescriptions. This indicates that the FTC study compared prescription samples that were special cases rather than adequate representations of the actual market.

The FTC study also did not consider waste. This may be reasonable in that the major purpose of the FTC study was to examine conflicts of interest arising from ownership of mail-service pharmacies. However, it is a significant limitation if the FTC study is used to compare the costs of community and mail-service pharmacy.

In addition to the issue of whether or not mail-service pharmacy produces savings in the aggregate (i.e., the total cost for mail-service pharmacy is lower than the total cost for community pharmacy), there is the issue of whether or not mail-service pharmacy produces savings for plan sponsors. Industry experts have observed, correctly, that the rise in the dollar amount of member copayments makes the practice of providing the mail-service pharmacy option of a 90-day supply of medication for the equivalent of 2 community pharmacy copayments an increasingly expensive proposition for the drug plan sponsor.22,23

All of this raises the question of why there are not more high-quality, peer-reviewed, claims-based studies comparing the costs of mail-service and community pharmacy. PBMs have access to the data that are needed to conduct valid and reliable studies. Many PBMs also have well-qualified researchers capable of conducting such studies, so the absence of this valuable information in the peer-reviewed literature is curious.

This is not to say that mail-service pharmacy does not produce savings or that it does not produce savings for individual plan sponsors. Mail-service pharmacy has the potential to produce savings for some sponsors, but it also has the potential—and has been shown by at least one study—to produce losses for others. What is known is that there is presently little objective, unbiased evidence that mail-service pharmacy produces savings compared with community pharmacy. It’s a shame that plan sponsors do not demand such evidence before attempting to stem the seemingly incessant rise in pharmacy benefit costs by forcing drug plan beneficiaries to use mail-service pharmacy.

Norman V. Carroll, PhD
Professor, Division of Pharmacy Administration
School of Pharmacy
Virginia Commonwealth University
410 N. 12th St.
PO Box 980533
Richmond, VA 23298-0533
nvcarroll@vcu.edu

DISCLOSURES
The author discloses no potential bias or conflict of interest relating to this article.

REFERENCES
Measuring Value in the Treatment of Symptoms of Allergic Rhinitis With Nasal Steroids

Patients’ willingness to pay (WTP) is a subject of interest, particularly in these times of consumer-directed health care and benefit designs that involve multiple copayment tiers. Since tiered copayment products have been found to reduce premium costs, the continued proliferation of tiered copayment benefits can be expected.

Wasserfallen et al. found that parents were willing to pay up to 0.71% of monthly income to avoid the pain experienced by their children in the medical procedure of blood sampling, with a median WTP of 25 CHF (Swiss francs) for a prescription drug to reduce the stress of this experience. These researchers found that it was difficult to assess parents’ WTP in an outpatient setting. Economists Whynes, Frew, and Wolstenholme studied the elicitation formats used in WTP research, finding that the technique is controversial and the relative merits of rival interventions will be predicted, in part, by the elicitation format used in the WTP research. Other researchers have suggested that the WTP method may not be capable of determining precise WTP because of the prominence effect in which subjects may select prominent values (e.g., $5, $10, $20, $50), while others have combined WTP with quality-adjusted life-year (QALY) to ascertain if current proposed cost-effectiveness ratios (e.g., $50,000 per QALY) overstate the willingness of society to pay for medical interventions.

The WTP method seems to be ideal for demonstrating that most patients are willing to pay something to obtain a desirable attribute or to avoid an undesirable attribute. The controversy appears to surround the degree to which the WTP method can produce reliable WTP amounts. In this context, the results of WTP research can often appear to be intuitive. For example, Guerilard et al., in a telephone survey of 562 parents of children who had been treated for an episode of acute otitis media (AOM), found that they had a median WTP in 2002 dollars of Can $31.66 for a single dose of an antibiotic to resolve the AOM or Can $26.63 for a once-daily dosing regimen for 3 days to resolve the AOM. Regression analysis showed that the amount parents were willing to pay increased with the amount of household annual income, the number of AOM episodes experienced in the previous year, and if adverse effects were experienced from antibiotic treatment. Also not surprising, patients with diabetes expressed a WTP about 3 times more out of pocket for inhaled antibiotic treatment. Also not surprising, patients with diabetes who had been treated for an episode of AOM, found that they had a median WTP in 2002 dollars of $12.95 per week. This research performed by Mahadevia et al. Keith et al. reported, in 2004, that patients who received intranasal budesonide delivered by Turbuhaler (i.e., dry as 400 mcg) or aqueous spray (256 mcg) once daily for 4 weeks were willing to spend an average of $15.89 (in 1999 dollars) to alleviate the problems of seasonal ragweed rhinitis. The mean WTP for the drug used during a subsequent ragweed season was $12.95 per week. This research did not assess sensory attributes specifically but found no difference in WTP between the dry versus aqueous delivery methods for budesonide nasal spray.

The present study by Mahadevia et al. in this issue of JMCP...
affirms our intuition that (a) patients can discern among specific sensory attributes of intranasal steroid products, (b) some attributes have higher economic value in their avoidance (e.g., no aftertaste versus strong aftertaste), and (c) the absolute WTP amount is higher for some attributes (i.e., a lot of throat rundown and nose runout) for persons with higher household income. It may also be reasonable to extrapolate these findings to the conclusion that physicians and patients should be discussing product attributes, particularly for patients who will be using intranasal steroids on a regular basis due to persistent symptoms.

The implications of the research on WTP for sensory attributes beyond these conclusions are less clear. The graphs (Figure 1) in the article by Mahadevia et al. are remarkably similar in slope and clustering except for aftertaste (Figure 1C). Second, at $50 per prescription, the sensory attributes have little differentiation. (Readers are encouraged to examine the Choice Set in Table 3 of the article to make their own inferences.) Based upon the actual costs of the 7 therapeutic alternatives in 2005 (Table 1 page 168), there is only an absolute difference of $5 per month between budesonide, mometasone, triamcinolone, and fluticasone.

Members of pharmacy and therapeutics (P&T) committees are challenged in decision making by the absence of information about sensory attributes in the labeling for intranasal steroids. But, Kaliner found, in a telephone survey of 503 patients with seasonal and perennial allergic rhinitis, that 86% of the patients reported that they had not complained to their physician about sensory attributes in the labeling for intranasal steroids.13 Since the work by Kaliner was performed 6 years ago, this research, if conducted today, may find that patients are more outspoken. On the other hand, perhaps sensory attributes of intranasal steroids are important to only a small proportion of the population that suffers from allergic rhinitis. One wonders how important the sensory attributes of intranasal steroids should be in clinical and P&T committee decision making. The one apparent opportunity for quality improvement is in increasing, to more than 7%, the proportion of physicians that base their choice of a nasal steroid on patient preference14 for sensory attributes.

What Is the Future of Thiazolidinediones (TZDs) After Market Introduction of Inhaled Insulin?

The U.S. Food and Drug Administration (FDA) approved inhaled insulin (INH) under the trade name Exubera on January 27, 2006, for use in adult patients with type 1 and type 2 diabetes.15 Exubera is an inhalable, powdered form of insulin delivered by a device developed by Nektar Therapeutics. Earlier in January 2006, Pfizer agreed to acquire the world-wide rights to Exubera from sanofi-aventis for $1.3 billion.16

One of the clinical trials that favored FDA approval of INH was a multicenter clinical trial that randomized 145 persons with uncontrolled type 2 diabetes (with glycosylated hemoglobin [A1c] in the range of 8%-11%) to either INH before meals or rosiglitazone (Avandia) 4 mg twice daily.17 The mean A1c values at baseline were 9.5% in the INH group versus 9.4% for the rosiglitazone group. After 12 weeks of the therapy, the INH group (71 of 76 randomized patients completed the trial) achieved a mean A1c of 7.2% versus 8.0% for the 63 of 69 patients who completed the rosiglitazone treatment arm, yielding 64% greater reduction in A1c (-2.3 absolute points vs. -1.4 absolute points) for INH compared with rosiglitazone, with an adjusted treatment group difference of -0.89, 95% confidence interval [CI], -1.23 to -0.55.18 At 12 weeks of treatment, 82.7% of the INH group achieved A1c of 8% or less versus 58.2% for rosiglitazone, adjusted odds ratio (OR), 7.14; 95% CI, 2.48-20.58; P <0.001. By the American Diabetes Association standard of <7.0% A1c, the proportion achieving the primary end point was more than twice the proportion for rosiglitazone, 44.0% for INH vs. 17.9% for rosiglitazone, (adjusted OR, 4.43; 95% CI, 1.94-10.12). According to the guidelines of the American Association of Clinical Endocrinologists (A1c ≤6.5%), the success rate was even higher for INH versus rosiglitazone, 28.0% vs. 7.5% (OR, 5.34; 95% CI, 1.83-15.57).

Pharmacy and therapeutics (P&T) committees have an interesting question to debate in 2006: the relative value and need for the thiazolidinediones (TZDs) rosiglitazone (Avandia and Avandamet) and pioglitazone (Actos) now that clinicians and patients have access to INH, which has been found to be superior to rosiglitazone in the intermediate outcome of A1c. TZDs have a larger hole to crawl out of when relative safety is considered by P&T committees and clinicians. More than 2 years ago, at the end of 2003, the American Heart Association and the American Diabetes Association released a joint consensus statement warning that patients with moderate-to-severe congestive heart failure (CHF) should not be prescribed either rosiglitazone or pioglitazone.19 Analysis of administrative claims data reported in November 2003 by Delea found a 55% higher incidence of heart failure for 5,441 TZD patients compared with 28,103 control patients with diabetes (hazard ratio = 1.7, P <0.001); the adjusted incidence of heart failure at 40 months was 8.2% for TZD patients and 5.3% for control subjects (absolute difference 2.9%, relative difference 55%).20 The TZDs have a tendency to cause fluid retention and edema, particularly of the feet, a hallmark of CHF. The incidence of fluid retention and edema appear to be exacerbated by concomitant use of insulin and dose-related for both rosiglitazone21 and pioglitazone.22 23

The black cloud over TZDs does not end with fluid retention, edema, and heart failure. The first TZD, troglitzone (Rezulin), approved by the FDA for marketing in the United States in January 27, 1997,24 was withdrawn in March 2000 after its association with hepatotoxicity was no longer in doubt. By year-end 1998, the FDA had record of a total of 32 reported deaths and 4 liver transplants associated with the use of troglitzone.25 Prior to the market withdrawal of troglitzone, the manufacturer had distributed 2 warning letters to physicians, including a notice to...
monitor liver enzymes monthly, and the United Kingdom had withdrawn troglitazone from the market more than 2 years earlier, in November 1999. For pioglitazone, introduced to the U.S. market in July 1999, the first death from liver failure associated with its use was reported in 2004. A “Dear Prescriber” letter dated April 26, 2002, highlighted changes in the precautions section of labeling of rosiglitazone regarding the potential for hepatic effects, even a rare case of hepatic failure, and, in other parts of product labeling, a possibility of weight gain.

Add to peripheral edema, weight gain, and possible hepatotoxicity an apparent increased risk of macular edema. In January 2006, the FDA notified health care professionals of reports of both new-onset and worsening cases of diabetic macular edema associated with the use of rosiglitazone, albeit reversible and apparently dose related.

With an apparent black eye for safety and inferior to INH in efficacy for lowering A1c, the cost outcomes for the TZDs may offer a refuge in the storm. Kalsekar et al., in this issue of JMCP, found, from administrative claims data in a Medicaid fee-forservice population, that patients who started TZD therapy incurred 35% lower costs in a 12-month follow-up period in 2000-2001 for emergency room (ER) visits and hospitalization compared with patients who initiated therapy with insulin, an average of $3,727 versus $5,793, respectively (P < 0.01). For diabetes-related costs only, the 53% higher pharmacy costs in the TZD patients ($1,678) versus insulin patients ($1,096, P < 0.01) was offset by lower costs for emergency room (ER) visits and hospitalization ($2,855 vs. $5,090, P < 0.01), resulting in 25% lower total diabetes-related costs for the TZD group compared with the insulin group ($5,425 vs. $7,255, P < 0.05).

Limitations in the study by Kalsekar et al. are significant. Important among these limitations was the inability to measure disease severity. Lacking clinical values for A1c and blood glucose, the researchers attempted to assure the comparability of the 2 groups through the use of propensity matching. However, the propensity matching technique would tend to exclude patients with more-severe diabetes who were, therefore, using insulin and could not be matched to TZD patients. The magnitude of this limitation can be gleaned from the authors’ Table 1, which shows that 65% (n = 1,271) of otherwise study-eligible patients were excluded in the process of propensity matching, leaving only 690 patients in the final analyses: 345 patients with type 2 diabetes in the TZD group and 345 patients in the insulin group.

Second, Medicaid patients, particularly those not enrolled in managed Medicaid, are most likely not representative of the general population of patients with type 2 diabetes, and discontinuous eligibility contributes to discontinuous care in this population. A hint of the problem of discontinuous care might be found in the 75% of patients identified with a diagnosis of type 2 diabetes who were excluded from the study because of the absence of a pharmacy claim for TZD or insulin plus another 12% of patients who did not have continuous eligibility during the study period. LaFleur, in a previous issue of JMCP, provided a comprehensive and useful review of the limitations of administrative claims data specific to the measurement of costs of care for patients with type 2 diabetes.

Third, the time period for the administrative claims used in the analyses by Kalsekar et al. is confounded by the TZD market disruption caused by the withdrawal of troglitazone in March 2000, in the middle of their 1999-2001 study period. While troglitazone patients were excluded from the 12-month follow-up period, 12.8% of the TZD patients and 13.0% of the insulin patients in the final analysis received troglitazone in the preperiod (Table 3 in Kalsekar et al.). One wonders why the outpatient costs, which included office visits and laboratory tests for liver enzymes, were not higher in the preperiod for both groups and why the outpatient costs were similar ($177 mean difference, $1,070 for the insulin group compared with $893 for the TZD group, P = 0.458 for the comparison) in the postperiod, particularly since there was considerable media attention to the market withdrawal of troglitazone at the time. Consumer groups, represented by Public Citizen, petitioned the FDA in early 2000 to revise the product labeling for all 3 TZDs to describe the adverse effects that include liver toxicity and heart failure.

Fourth, a threat to validity seems inherent in the premise that higher drug costs for TZDs are offset by lower costs for ER visits and hospitalizations, in only 12 months of administrative claims data. For diabetes-related costs, the insulin group had a higher average number of physician office visits, but the average outpatient costs (including physician office visits) were not different between the 2 groups over 12 months of follow-up. However, the contribution of the $1,830 difference ($1,070 for the insulin group vs. $893 for the TZD group, P = 0.458 for the comparison) may have contributed to the $1,830 difference ($153 per month) in total diabetes-related costs ($7,255 for the insulin group vs. $5,425, P = 0.022 for the comparison). Stephens et al. provide a useful context for interpreting these absolute and relative values in their summary of the literature on economic studies in this issue of JMCP, including their Table 1, showing the breakdown of total direct costs for managed care organization (MCO) enrollees with diabetes.

The place in therapy for TZDs in type 2 diabetes is summarized clearly and succinctly in the NICE (National Institute for Clinical Excellence) appraisal released in November 2002. TZDs are third-line therapy in type 2 diabetes after sulfonylureas and metformin have proved unsuccessful when used as monotherapy and in combination to achieve glycemic goals. NICE concluded that “the use of glitazone combination therapy with either metformin or sulphonylurea is not likely to be cost effective when compared with the combination of metformin and sulphonylurea.”

So, much of the market future of TZDs may have to do with
relative cost. In previous research reported in JMCP, Shetty et al. found that patients with type 2 diabetes maintained at target A1c (≤7%) had 24% lower total diabetes-related medical costs compared with patients who were above target A1c (>7%). The actual daily direct drug costs for INH are not yet known. What is known is that the TZDs are not inexpensive. Based upon MCO pharmacy claims for the fourth quarter of 2005, the average direct drug cost, including pharmacy dispensing fees, was $4.34 per day ($130 per month) for Avandia, $4.55 per day ($136 per month) for Avandamet, and $5.13 ($154 per month) for Actos. The evidence presents a classic conundrum for P&T members: a product—INH—with superior efficacy and safety but (probable) higher direct drug cost compared with TZDs. Still, the market introduction of INH in February 2006 seems likely to knock pioglitazone and rosiglitazone from their status in the top 12 drugs by expenditure at year-end 2005.

Frederic R. Curtiss, PhD, RPh, CEBS
Editor-in-Chief
fcurtiss@amcp.org

REFERENCES


Letters to the Editor

JMCP welcomes letters that serve to clarify subjects published in previous issues of the Journal or regarding subject matter of interest to managed care pharmacists. Letters in JMCP are not peer reviewed but are subjected to editorial review. Letters should be prepared in a word processing program, preferably Microsoft Word, and submitted electronically at jmcp.msubmit.net. See www.amcp.org for details.
Abstracts From Professional Poster Presentations at AMCP’s 18th Annual Meeting & Showcase

The following poster presentations have been prepared for the Academy of Managed Care Pharmacy’s 18th Annual Meeting & Showcase, April 5-8, 2006, in Seattle, Washington. Poster presentations are selected by the Program Planning Committee from proposals that are submitted to AMCP. Authors of posters are responsible for the accuracy and completeness of the data presented in the posters and in the abstracts published here.

For more information about the studies described below, please contact the corresponding authors, indicated by an asterisk (*), whose addresses are listed in full; e-mail addresses and telephone numbers have also been provided by some authors. The names of individuals who are scheduled to present at the meeting are underlined.

A COMPARISON OF AVERAGE ANNUAL MEDICAL SERVICES FOR COMORBID CONDITIONS ASSOCIATED WITH METABOLIC SYNDROME FOUND IN EMPLOYEES WITH GOUT VERSUS THOSE WITHOUT GOUT

Novak S.* TAP Pharmaceuticals, Inc., 1600 Flintridge Rd., Austin, TX 78746

OBJECTIVE: To compare the average annual medical services associated with metabolic syndrome among employees with gout and without gout.

METHODS: A retrospective analysis of the Human Capital Management Services Research Reference Employer database was employed. Utilization of services for the 261 specific diagnostic categories designated by the Agency for Healthcare Research and Quality (AHQR) were compared among individuals with gout and without gout, using specific categories of International Classification of Diseases, Ninth Revision (ICD-9) codes during 2001 through 2004. Because gout was one of the 261 specific categories, it was excluded from the analysis. Satterthwaite T tests were used to assess cost differences between employees with gout and a 50:1 propensity score matched sample of employees without gout. Matching was done on age, years with employer, gender, marital status, race, exempt status, full-time/part-time status, annual salary, and first-digit zip code.

RESULTS: Data were available for 1,171 employees with gout and a matched control group of 58,550 employees without gout. Within the top 10 categories of diagnoses, significant differences between the 2 groups in average number of services for diagnostic categories associated with metabolic syndrome included hyperlipidemia (2.19 vs. 0.95, P < 0.001); essential hypertension (1.97 vs. 0.75, P < 0.001); and diabetes mellitus without complications (1.14 vs. 0.42, P < 0.001). These categories ranked 2, 3, and 6, respectively.

CONCLUSIONS: The cohort of employees with gout had a higher incidence of hypertension, diabetes, and hyperlipidemia, which resulted in an increased use of medical services. The study supports the hypothesis that gout may be a signal to alert clinicians of both symptomatic and asymptomatic metabolic disease.

A COST-EFFICACY ANALYSIS MODEL FOR ANTI-TNF AGENTS USED IN THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS

Arjunji RV*, Dabbous OH, Rahman MI. Centocor, Inc., 800 Ridgeview Dr., Horsham, PA 19044

PURPOSE: To provide a cost-efficacy (CE) analysis from a third-party payer perspective of etanercept and infliximab + methotrexate combination therapy when compared with methotrexate (MTX) alone in rheumatoid arthritis (RA) patients with a disease duration of less than 3 years.

METHODS: An Excel-based CE model was developed to estimate the number needed to treat (NNT) and cost per successful outcome using published, 52-week CE data for etanercept and infliximab. Dosing information was obtained from product labels. Plan-specific costs and the cost of adverse events were utilized in the model. The NNT and cost per successful outcome were estimated using American College of Rheumatology scores (ACR 20, 50, 70), and structural damage measures (joint space narrowing [JSN], erosion, and total Sharp score [TSS]).

RESULTS: Based on the ACR scores, the NNT ranges were 7.4 to 11.4 for infliximab + MTX and 14.3 to 20 for etanercept. Utilizing structural damage measures, the NNT for infliximab + MTX therapy was 1.9, 0.4, and 0.3 using JSN, erosion, and TSS, respectively. For etanercept, NNT was 1.8 and 1.7 using erosion and TSS, respectively. For etanercept, NNT was undefined for the JSN measure because of insignificant differences between the treatment and the control groups. Using published average wholesale price minus 15% (AWP-15%), the cost per successful outcome based on the ACR scores ranged from $117,582 to $180,381 for infliximab + MTX and from $227,270 to $318,178 for etanercept. Using AWP-15%, the cost per successful outcome for infliximab + MTX was $30,526, $5,967, and $4,839, respectively, for JSN, erosion, and TSS scores, and for etanercept, it was $28,409 and $26,964 for erosion and TSS, respectively.

CONCLUSIONS: This Excel-based CE model enables payers to perform CE analyses for anti-TNF agents used in the treatment of early rheumatoid arthritis, utilizing plan-specific cost and utilization data.
ADHERENCE AND PERSISTENCE WITH ANTIPSYCHOTIC THERAPY AMONG SCHIZOPHRENIA PATIENTS IN A STATE MEDICAID POPULATION

Hassan M.* AstraZeneca Pharmaceuticals, Brandywine 3B-711B, 800 Concord Pike, PO Box 15437, Wilmington, DE 19850

INTRODUCTION: Successful therapeutic outcome in patients with schizophrenia depends on adherence and persistence with therapy; medications used to treat this population may differ in their adherence and persistence profiles. This study compared adherence and persistence among schizophrenia patients initiated on risperidone, olanzapine, quetiapine or typical antipsychotics in a state Medicaid system.

METHODS: A retrospective, cohort study, using de-identified Medicaid claims data identified adult schizophrenia patients (based on International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes) assigned to quetiapine, olanzapine, risperidone, or typical antipsychotic cohorts, based on first prescription filled between January 1, 1999, and December 31, 2001. Adherence was measured as a medication possession ratio (MPR), calculated as days supply of antipsychotic divided by number of days between prescription fills. Persistence was defined as total number of days from initiation of antipsychotic to its modification (discontinuation, switching, or combination with another antipsychotic). Adherence and persistence were compared between cohorts over a 12-month follow-up period, controlling for confounders using ordinary least squares (OLS) and Cox proportional hazard (PH) regressions.

RESULTS: Mean MPRs were 0.78 ± 0.25 for quetiapine (N = 149), 0.75 ± 0.27 for risperidone (N = 201), 0.77 ± 0.26 for olanzapine (N = 346), and 0.55 ± 0.32 for typical antipsychotics (N = 303). Compared with the quetiapine cohort, patients initiated on typical antipsychotics were 22% less adherent to therapy (P < 0.001, OLS regression). Mean persistence was 228.5 days for quetiapine, 208.2 days for risperidone, 201.8 days for olanzapine, and 192.8 days for typical antipsychotics. Compared with the quetiapine cohort, patients initiated on risperidone or typical antipsychotics were 1.5 and 2.5 times, respectively, more likely to modify treatment (P < 0.001, Cox PH regression).

CONCLUSIONS: Patients with schizophrenia initiated on quetiapine showed significantly greater adherence than the typical antipsychotic cohort and greater persistence than patients receiving risperidone and typical antipsychotics. These findings are in contrast to recent large prospective studies that did not find substantial differences in adherence between these agents.

ANALYSIS OF ORAL ANTIPLATELET DRUG USE IN OUTPATIENT SETTINGS

Bae JP.* Global Health Outcomes, Eli Lilly and Company, Lilly Corporate Center, DC1833, Indianapolis, IN 46285; jpbac@lilly.com

INTRODUCTION: This study examined characteristics of managed care patients taking antiplatelet medications in outpatient settings and analyzed patterns of use using a national claims database over a 3-year period.

METHODS: This retrospective study identified patients with oral antiplatelet claims in a large national managed care claims database (Pharmetrics) between January 2001 and December 2003 (n = 20,387). The entire medical and pharmacy claims history was followed for 3 years. Analysis focused on outpatient use pattern of antiplatelet medications, particularly clopidogrel, and patient characteristics, e.g., demographics, comorbidities, inpatient history, and other cardiovascular medication use. Aspirin therapy was not available in the prescription claims data.

RESULTS: Clopidogrel was the most widely prescribed antiplatelet, representing 88.6% of all prescriptions, followed by cilostazol (7.1%) and dipyridamole + aspirin (4.1%). Most frequent diagnoses included hypertension, chest pain, hyperlipidemia, and coronary arteriosclerosis. On average, users of clopidogrel had 4.71 prescriptions/month in 2003 at a health plan cost of $315.12/month. Average length of therapy for clopidogrel ranged from 213 days for patients who underwent percutaneous coronary intervention (PCI) to 345 days for stroke patients. However, 35% of PCI patients took clopidogrel for ≤30 days. Overall, patients received clopidogrel for 300 days (± 302.7) in the 3-year period. During the use period, patients filled 89% of the days supply needed to maintain their daily regimen. Frequent concomitant cardiac medications included statins (62.4%), beta-blockers (55.5%), angiotensin-converting enzyme (ACE) inhibitors (52.1%), and diuretics (18.4%). Data show that 40% to 50% of patients also discontinued another concomitant cardiac medication upon discontinuing clopidogrel.

CONCLUSIONS: Clopidogrel was the dominant oral antiplatelet by market share, and these patients also used significant pharmacy resources on other medications. While average duration was largely consistent with treatment guidelines, we found wide variations in individual treatment length. This suggests inconsistencies in utilization versus treatment guidelines. High rates of discontinuation of cardiac medications also raise some concern.

ANNUAL TOTAL MEDICAL COSTS FOR BIPOLAR DISORDER PATIENTS TREATED WITH ANTIPLATFORMICS

Brook RA.* The JestaRx Group, 18 Hirth Dr., Newfoundland, NJ 07435-1710

INTRODUCTION: This study examines annual direct medical and prescription drug costs per patient among bipolar disorder (BPD) patients treated with different classes of medications.
METHODS: A retrospective administrative claims database study of BPD patients (International Classification of Diseases, Ninth Revision [ICD-9] codes 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, or 296.8x) from January 2001 through December 2004. Patients with at least 6 months of insurance coverage prior to their first index prescription and 12 months afterwards were grouped into 3 cohorts based on treatment patterns: (1) atypical antipsychotic medication only (APM); (2) other bipolar medication only (BPM)—defined for the study as conventional antipsychotics, primary mood stabilizers, potential mood stabilizers, and the anticonvulsants zonisamide and tiagabine; (3) a combination of both treatments (COMBO). A control cohort of untreated bipolar patients (NM—no treatment medication) with a similar insurance coverage period was used for comparisons. Regression models, controlling for potential demographic, severity, and comorbidity confounders were used to compare annual direct medical and drug costs.

RESULTS: Analysis of the 1,211 patients revealed the following annual direct medical costs per patient: (1) APM only = $7,775 (n = 51); (2) BPM only = $7,029 (n = 522); (3) COMBO = $9,175 (n = 366); (4) NM = $6,042 (n = 272). Patients who used COMBO therapy had significantly higher medical costs (P < 0.05) than both patients who used BPM only and patients receiving no treatment medications (NM). They also reported the highest mental-health-related emergency department visit and inpatient admission rates of any of the treatment groups.

CONCLUSION: Patients on both atypical antipsychotics and other bipolar medications (COMBO) have significantly higher medical costs as compared with the BPM and NM cohorts. Further research is needed to determine if this increased cost is a marker of underlying disease severity and the number of comorbidities, both BPD-related and non–BPD-related.

ANTIHYPERTENSIVE DRUG USE BEHAVIOR ASSOCIATED WITH STEP EDITS FOR ANGIOTENSIN RECEPTOR BLOCKERS IN MANAGED CARE PLANS

Yokoyama K.*, WellPoint Pharmacy Management, 8407 Fallbrook Ave., MS AF-7, West Hills, CA 91304; Krista.Yokoyama@wellpoint.com, (818) 313-5082

INTRODUCTION: Step-edit programs on angiotensin receptor blockers (ARBs) requiring failure of angiotensin-converting enzyme inhibitors (ACEIs) is a common cost containment strategy in managed care.

METHODS: Rejected and paid pharmacy claims from 3 managed health plans with a step edit in place for ARBs were evaluated. Patients who encountered a claim reject for ARB within the first 6 months of edit implementation and have no ARB claim in the previous 3 months were followed for 1 year. Types of index antihypertensive drug(s) utilized after the rejected claim were characterized. Rate of switch to an ARB (for those who did not receive an ARB as index therapy) or discontinuation (for those who received an ARB as index therapy) were calculated at 3 months and 1 year. Rate of initiation of ARB versus ACEI was also compared with a health plan that does not have such an edit in place.

RESULTS: A total of 1,708 patients had a rejected ARB claim during the selection period. Overall, 718 (42%) received an ARB, 802 (47%) received other antihypertensives as index therapy, and 11% of the patients did not show any antihypertensive utilization. Within 3 months of follow-up, 282 (35%) patients who had received other antihypertensives as index therapy were switched to an ARB. At 1 year, 1,114 (65%) of patients either received an ARB as initial therapy or had switched to an ARB. Rate of initiation of ARB versus ACEI in new-start patients was lower in the study group than the control (19% vs. 25%, P < 0.0001).

CONCLUSIONS: A step-edit program on ARBs reduced the number of patients who were prescribed and received ARBs. While a large portion of attempted ARB patients utilized other types of antihypertensives as index therapy, effectiveness of the program was reduced as patients were switched back to ARBs during the 1-year follow-up.

ASSESSING THE IMPACT OF NEUTRALIZING ANTIBODIES ON THE COST EFFICACY OF MULTIPLE SCLEROSIS THERAPIES

Dunn J.*, IHC Health Plans, 4646 West Lake Park Blvd., Suite N3, Salt Lake City, UT 84120; jeffrey.dunn@ihc.com, (801) 442-7984

INTRODUCTION: To determine the impact of neutralizing antibodies (NAbs) on the cost efficacy of multiple sclerosis (MS) therapies in a managed care context.

METHODS: A cost-effectiveness model was developed using relapse rate and disability progression data from the pivotal phase III clinical trials of currently approved MS therapies (interferon [IFN] beta-1a IM [intramuscular Avonex], IFN beta-1a SC [subcutaneous] [Rebif], IFN beta-1b [Betaseron], and glatiramer acetate [GA, Copaxone]). The analyses were conducted from a managed care perspective with time horizons of 24 and 48 months. Treatment-related costs were obtained from the clinical literature and third-party databases. Cost efficacy is expressed as a ratio of total utilization costs per percentage of relative risk reduction. Estimates of “deflation” in efficacy due to NAbs were based on prescribing information and data comparing performance of NAb-positive and NAb-negative patients in open-label extension studies of IFN beta products. Assumptions included the following: comparison of similar end points across different clinical trials, adverse event rates constant across products, constant burden of relapse over time, persistence/compliance rates constant across products, and similar laboratory testing/frequency across IFN beta products. The robustness of the model to changes in incidence of NAbs was tested by 1-way sensitivity analysis.

RESULTS: At 24 months, the cost efficacy for disability progression was $824 ($1.13/day), $1,224 ($1.68/day), $1,075 ($1.47/day), and $2,567 ($3.52/day) for IFN beta-1a IM, IFN beta-1a SC, IFN beta-1b, and GA, respectively. At 48 months, after the development of NAbs, cost efficacy was $1,660 ($1.14/day), $2,537...
Asthma-Related Costs and Resource Utilization Associated with Fluticasone Propionate/Salmeterol Versus Inhaled Corticosteroid in Mild Asthma Patients

Friedman H.* Friedman Analytic Solutions, Inc., 26 Prince St., Suite 2B, New York, NY 10012; howard@analytic-consulting.com, (917) 576-4927

INTRODUCTION: Despite National Asthma Education and Prevention Program (NAEPP) recommendations to begin mild asthma patients on a low-dose inhaled corticosteroid (ICS), many patients start on combination therapy; thus, this research assesses 12-month health care utilization patterns and asthma-related outcomes for patients with mild asthma who begin on fluticasone propionate/salmeterol (FPS) or ICS alone.

METHODS: A continuously benefit-eligible cohort of asthma patients newly initiated on FPS or ICS was identified from a large, geographically diverse administrative claims database (MarketScan) and followed for 1 year. Analyses were based on a subcohort of mild asthma patients as defined: 6 months prior to therapy initiation, (1) no exacerbations requiring hospitalization, emergency room (ER), or outpatient visits resulting in nebulization or prescription for oral steroids and (2) use of any asthma-related medication but no more than 2 short-acting beta-agonist (SABA) canisters. Between-group differences in clinical characteristics were adjusted using propensity score matching. Resource use was determined for asthma-related outpatient visits, ER services, hospitalizations, and medications.

RESULTS: Mean age (40.6 years FPS, 40.9 years ICS) and gender distribution (females: 64.3% FPS, 66.4% ICS) were similar between cohorts (FPS, n = 1,888; ICS, n = 1,888). In the pre-index period, no significant difference was observed in treatment costs, sinusitis or rhinitis history, and average number of SABA canisters. During the 12-month follow-up period, total treatment costs were significantly (P < 0.0001) higher for FPS vs. ICS ($1,206 vs. $804), due primarily to significantly (P < 0.0001) higher drug costs for FPS vs. ICS ($577 vs. $357). Nondrug asthma costs were $529 (FPS) vs. $447 (ICS). The percentage of patients experiencing an exacerbation (14.0% FPS, 13.5% ICS) and the average number of exacerbations in each cohort (0.175 FPS, 0.164 ICS) were similar.

CONCLUSIONS: Initiating mild asthma patients with ICS, as recommended by the NAEPP, can reduce costs of asthma care due to lower drug costs in ICS patients and exacerbation rates comparable to FPS therapy.

Burden of Illness for Patients with New and Recurrent Acute Coronary Syndrome

McCollam P.* Global Health Outcomes, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285

INTRODUCTION: The economic burden of acute coronary syndrome (ACS) continues long after the acute event has resolved. Assessing the impact of new versus recurrent ACS on patients’ burden of illness may help improve patient management. This study compared ACS-related costs between new and recurrent ACS subjects using retrospective medical and pharmacy claims data from a large U.S. health plan.

METHODS: Patients with ACS (defined as unstable angina or acute myocardial infarction [AMI]) were identified using International Classification of Diseases, Ninth Revision (ICD-9) codes between January 1, 2001 and June 30, 2003; the first diagnosis was the “index event.” Patient claims were examined the year before and up to a year after the index event. Hospitalizations, revascularizations, and costs for “new” (no ACS diagnosis before index event) and “recurrent” (previous evidence of ACS) cohorts were compared and analyzed descriptively. Multivariate regression was used to examine cost predictors.

RESULTS: 15,508 patients were identified; 82% had new ACS, 18% had recurrent ACS. The new ACS cohort was more likely to have AMI and be hospitalized for the index event, leading to higher index event costs versus the recurrent cohort. The recurrent ACS cohort, however, had more rehospitalizations, longer lengths of inpatient stay, and a higher probability of a revascularization procedure during follow-up compared with new ACS subjects. After adjusting for confounding factors, multivariate cost models revealed that annualized follow-up medical costs were 11.6% higher and annualized follow-up pharmacy costs were 8.0% higher for the new ACS cohort compared with the recurrent ACS cohort. All the above differences were significant (P < 0.05).

CONCLUSION: Newly diagnosed ACS subjects had significantly higher adjusted costs compared with recurrent subjects 1 year following the index event, but recurrent ACS patients still experienced high medical costs. Future research that incorporates longer follow-up periods would be useful in determining patterns of ACS-related costs and utilization over time.

Burden of Illness in a GI Managed Care Population

Shaya FT.* School of Pharmacy, Pharmaceutical Health Services Research, University of Maryland, 515 West Lombard St., Baltimore, MD 21201

INTRODUCTION: The impact of adherence to gastrointestinal (GI) drug therapy on patients’ GI-related medical costs was determined, from the payer’s perspective, through retrospective analysis of pharmacy and medical claims.
METHODS: Retrospective database analysis of CareFirst BlueCross BlueShield medical and pharmacy claims for the period January 1, 2002-December 31, 2004. Inclusion criteria: continuously enrolled patients who had at least 1 prescription claim for balsalazide disodium, mesalamine, olsalazine sodium, and sulfasalazine. Exclusion criteria (to obtain incident cohort): patients who had at least 1 claim before April 1, 2002. Nonadherence was defined as a failure to refill a prescription claim. Multivariate logistic regression analysis was used to determine the impact of adherence to GI pharmacotherapy on the GI medical costs by type of health care service after adjusting for age, gender, and comorbidities, by constructing a Charlson Comorbidity Index.

RESULTS: Total of 4,947 patients, 45% male, 64% older than 40 years. Patients who adhere to their GI pharmacotherapy incur 69.89% (P < 0.0001; 95% CI, 0.40, 0.63) more GI-related prescription cost than those who did not. Those who are persistent incur 62.15% (P < 0.0001; 95% CI, -1.18 to -0.76) and 13.12% (P = 0.056; 95% CI, -0.28 to 0.003) less GI-related admission, outpatient, and office visits costs, respectively, than those who are not. Compared with nonadherent patients, those who adhere incur 49.81% (P = 0.019; 95% CI, -23.70 to -2.29) fewer total medical costs.

CONCLUSION: On average, nonadherence to GI pharmacotherapy results in higher costs across all types of GI-related health care services as well as total medical costs. Those results may be of interest to managed care organizations.

CLINICAL MEDICATION REVIEW BY A PHARMACIST IN PATIENTS ENROLLED IN DIABETES MELLITUS AND HEART DISEASE MANAGEMENT PROGRAMS

Neafus KL, Prime Therapeutics, Inc., PO Box 64812, St. Paul, MN 55164

OBJECTIVE: To determine whether a complete medication review of members enrolled in a disease management program by a clinical pharmacist would increase appropriate medication use in those members.

METHODS: 264 members enrolled in both diabetes mellitus and heart disease management programs had their medication profiles, including self-reported and pharmacy claims database, evaluated by a clinical pharmacist. Recommendations to change medication therapy in accordance with national guidelines for treatment of diabetes mellitus and heart disease were documented. Letters were sent to treating physicians with suggested changes to prescription-drug therapy regimens. Recommendations were categorized as overutilization, underutilization, contraindications, and drug interaction potential. In addition, electronic notes were left for disease management nurses with recommendations for changes in over-the-counter (OTC) medications and for compliance issues. The nurses then discussed the recommendations with the members directly.

RESULTS: 76 letters were sent to treating physicians, containing 93 identified drug therapy problems. Of the members still enrolled 90 days after letters were sent, 19% of treating physicians had implemented the prescribing recommendations. Most common recommendations for drug therapy changes included statins, angiotensin-converting enzyme inhibitors, beta-blockers, and anticoagulation therapy. In addition, the pharmacist documented 63 electronic alerts to disease management nurses who then contacted the member regarding OTC agents and compliance issues. This resulted in an additional 26% actions taken by members based on the pharmacist’s recommendation.

CONCLUSIONS: Both quality-of-care and medication safety issues were addressed in this program. Recommendations by the pharmacist led to increased adherence to national guidelines for treatment of diabetes mellitus and heart disease in this group of high-risk members. In addition, recommendations to discontinue contraindicated medications were accepted and implemented.

CMS CURRENT DRUG PAYMENT COMPUTATIONS: IMPACTING FUTURE MCO PROCESSES?

Baker J, The Resource Group, PO Box 70, Pickton, TX 75471

INTRODUCTION: This case study details recent Centers for Medicare and Medicaid Services (CMS) program changes in computing drug payments to providers and explores the potential impact on managed care organization (MCO) processes.

METHODS: The primary objective of the case study was 2-fold: (1) develop a step-by-step process model of the CMS average sales price (ASP) + 6% computations for Part B drugs as they relate to providers and (2) conclude whether the model has potential to impact future MCO program processes. Government legislative and regulatory sources were utilized to create the drug computation process model. Published sources were consulted as indicators of awareness about MCO impact.

RESULTS: The case study’s process model identified 4 sequential steps in the CMS computation of ASP + 6%, 7 steps required in ASP data reporting to CMS by manufacturers, and 5 steps in CMS release of quarterly payment data to providers. The computation process, when deconstructed, revealed that (1) ASP is legislatively required to be calculated as the manufacturer’s sales to all purchasers in the United States for that particular 11-digit National Drug Code (NDC), divided by the total number of units sold by the manufacturer in that quarter (certain provisions apply); (2) sales exempt from the Medicaid best-price calculation must be excluded; and (3) 5 types of transactions and items must be deducted, including volume discounts, prompt pay discounts, cash discounts, free goods that are contingent on any purchase requirement, and chargebacks and rebates other than rebates under the Medicaid drug rebate program.

CONCLUSIONS: Even though ongoing questions continue about whether managed care discounts should be included in the ASP computation, there is a paucity of published sources on the
subject. This case study's model indicates that such technical issues within governmental computations may well have an indirect impact on MCO processes. MCO decision makers should be aware of such implications and any potential impact on their processes and programs.

**COMPARING METHODS FOR MEASURING MEDICATION PERSISTENCE AND ADHERENCE IN RETROSPECTIVE CLAIMS ANALYSES: THE CASE OF TREATMENTS FOR OVERACTIVE BLADDER (OAB)**

Patel BV* MedImpact Health Care Systems, Inc., 10680 Treena St., San Diego, CA 92131

**INTRODUCTION:** The objective of this evaluation is to compare various methods of measuring persistence with medication and adherence to overactive bladder (OAB) treatments.

**METHODS:** Continuously eligible patients newly started on OAB treatments during 2002 were identified and followed for 1 year in a pharmacy claims analysis. Four methods of measuring persistence and adherence were evaluated. Method 1 measured persistence as the time from treatment initiation on any of the 4 OAB therapies (“Any OAB”) to a gap in therapy of 30 days or more; Method 2 was analogous to the first but only included time on initial OAB therapy (“Initial OAB”); Methods 3 and 4 measured adherence based on annual medication possession ratio (MPR) for “Any OAB” and “Initial OAB.”

**RESULTS:** Of 24,594 patients identified, 10% were initially prescribed tolxerodine, 35% long-acting tolxerodine (tolterodine LA), 36% oxybutynin, and 18% extended-release oxybutynin (oxybutynin XL). Rank ordering of persistence in days from highest to lowest for Methods 1 and 2 was tolxerodine LA (137 and 131), oxybutynin XL (136 and 127), tolxerodine (126 and 105), and oxybutynin (95 and 89). All pairwise differences except tolxerodine LA versus oxybutynin XL were statistically significant for both methods. Method 3 resulted in an MPR of 0.43 for tolxerodine LA, oxybutynin XL, and tolxerodine, followed by 0.32 for oxybutynin. Rank ordering of MPR with Method 4 showed results similar to Methods 1 and 2: tolxerodine LA (0.40), oxybutynin XL (0.39), tolxerodine (0.34), and oxybutynin (0.29).

**CONCLUSIONS:** When comparing medication persistence and adherence studies, methodological differences must be considered. Given that changes in treatment can affect bladder control and treatment costs, calculating adherence and persistence based on the initial treatment is recommended.

**COMPARING THE COST-EFFECTIVENESS OF THE INTERFERONS (IFNS) UTILIZED IN THE MANAGEMENT OF CHRONIC HEPATITIS C VIRUS (HCV): A MODEL EVALUATING THE CLINICAL AND ECONOMIC IMPACT OF CURRENT TREATMENT OPTIONS**

Goldberg LD,* Goldberg, MD & Associates, 2210 W Main St., Suite 107-384, Battle Ground, WA 98604

**OBJECTIVE AND PERSPECTIVE:** The interferons (IFNs) currently indicated for the treatment of chronic hepatitis C virus (HCV) have been shown to exhibit varying responsiveness in terms of achieving a sustained viral response (SVR); therefore, it is the objective of this model to be used as a tool to compare the relative cost-effectiveness of these agents from the health system perspective.

**METHODS:** An Excel-based model was developed to compare the relative cost of managing chronic HCV infection in terms of both treatment naive and pegylated-IFN nonresponders. The rate of achieving an SVR was the key clinical outcome measure. The perspective of analysis was that of a health system. Drug effectiveness with respect to the SVR rate was based on the published literature for therapy in combination with weight-based ribavirin. Annual therapeutic price (ATP) based on the average wholesale price (AWP) (with consideration of contractual discounts) was used to model the cost of pharmaceutical treatment. The primary economic end point was the drug cost per SVR obtained. Results were displayed for treatment naive, pegylated-IFN nonresponders, and combined cases, respectively. Multifactor sensitivity analyses were conducted.

**RESULTS:** In a typical managed care population, with an estimated prevalence of chronic HCV of 1.4% and with 5% of patients being treated with an average early viral response (EVR) in treatment naïve patients of 80% and 95% in Genotype 1 and Genotypes 2/3, respectively, the projected total impact of HCV drug treatment is $1.22 per member per month (PMPM). For treatment naïve patients, Genotype 1, the cost per SVR obtained is $31,356, $51,152, and $19,113 for Pegasys, Peg-Intron, and consensus interferon (CIFN), respectively. For treatment naïve patients, Genotype 1, the cost per SVR obtained is $287,516, $325,515, and $68,880 for Pegasys, Peg-Intron, and CIFN, respectively. For pegylated-IFN nonresponders, the cost per SVR obtained is $24,890, and $12,305 for Peg-Intron, and CIFN, respectively. For pegylated-IFN nonresponders, the cost per SVR obtained is $18,030, $31,356, $51,152, and $19,113 for Pegasys, Peg-Intron, and CIFN, respectively. Sensitivity analysis across the range of inputs, including member demographics, genotype mix, drug pricing, and “12-week rule” compliance, demonstrate the superior cost-effectiveness of consensus interferon (CIFN) in terms of the primary economic end point of the drug cost per SVR obtained. Modeling of treatment pattern assumptions moving from current national market share figures to higher weighting of CIFN demonstrates significantly reduced drug costs with no decrease in the nominal number of SVR events obtained.

**CONCLUSION:** Treatment of chronic HCV infection with CIFN is
the most cost-effective approach in terms of minimizing both drug costs and the cost per SVR obtained. This economic modeling tool helps demonstrate the value of using evidence-based data to link costs to outcomes and how the available IFNs vary significantly in their cost per SVR obtained.

**COMPARISON OF DIRECT COSTS OF TNF ANTAGONISTS IN UNITED STATES HEALTH PLANS**

Chiou CE, Amgen Inc, One Amgen Center Dr, Mail Stop 28-3-A, Thousand Oaks, CA 91320; cchiou@amgen.com, (805)447-6342

**OBJECTIVE:** To compare the direct costs of tumor necrosis factor (TNF) antagonists for the treatment of rheumatoid arthritis (RA).

**METHODS:** Commercial claims from U.S. health plans were retrospectively analyzed for the TNF antagonists (etanercept [ETA], infliximab [INF], and adalimumab [ADA]). Eligible claims were those submitted for patients diagnosed with RA who were between 18 and 64 years of age and had continuous medical and pharmacy insurance. RA-related health care resource utilization costs (unadjusted costs for health plan + patient) for the 10 months following the initiation of ETA were compared with the RA-related costs after initiating ADA or INF using nonparametric tests. A generalized linear model (with log-link function and gamma distribution) was used to adjust for covariates including age, sex, chronic disease score, prior disease-modifying antirheumatic drug use, comorbidities, and monthly health care costs.

**RESULTS:** Patients receiving ETA (N = 817), INF (N = 613), or ADA (N = 217) had similar baseline characteristics, except for the Deyo-Charlson Comorbidity Index, which was lower for INF patients (ETA 1.54, INF 1.37, ADA 1.49; P = 0.001). Mean monthly RA-related costs were lower for ETA compared with ADA and INF for drug costs (ETA $1,121, INF $1,673, ADA $1,304; P < 0.0001), outpatient costs (ETA $68, INF $193, ADA $84; P < 0.001), and total costs (ETA $1,267, INF $1,949, ADA $425; P < 0.0001). After adjustment for covariates, INF was associated with 55% higher RA-related monthly total health plan costs compared with ETA (P < 0.0001), and ADA was associated with 12% higher costs compared with ETA (P = 0.003). Similar results were obtained for the patient-paid costs.

**CONCLUSIONS:** Etanercept was associated with significantly lower total RA-related direct costs compared with treatment with adalimumab or infliximab. This finding persisted after adjustment for multiple covariates.

**COMPARISON OF HEALTH CARE RESOURCE UTILIZATION COSTS BEFORE AND AFTER INITIATION OF INSULIN GLARGINE FOR THE TREATMENT OF TYPE 2 DIABETES**

Simons WR, Global Health and Economic Outcomes Research, 41 River Rd, Summit, NJ 07901; rsimons@globalhealtheconomics.com, (908) 598-1144

**INTRODUCTION:** Prompted by a study that reported increased health care costs following initiation of insulins (Rosenblum MS, Kane MP, J Manag Care Pharm. 2003;9(4):309-16), we retrospectively compared health care resource utilization costs before and after initiation of treatment with insulin glargine in patients with type 2 diabetes.

**METHODS:** Using a managed care claims database, we identified 1,216 patients with type 2 diabetes who were initiated on glargine as their first insulin and had continuous eligibility 1 year preglargine and 1 year postglargine initiation. Total and diabetes-related pharmacy, medical, and facility costs were compared for the 9-month and 12-month periods before and after glargine initiation. Preglargine and postglargine medical and facility resource utilization costs were also compared by type of service, and a cost trend analysis was performed comparing postglargine costs by 2-month increments with the 2-month period prior to glargine initiation. To avoid bias toward zero due to nonuse of services, Tobit regression was used to determine medical and facility costs. T tests were used for all comparisons.

**RESULTS:** Total and diabetes-related pharmacy costs significantly increased after glargine initiation (P < 0.001): by $715 and $198, respectively, for the 9-month comparison and by $1,030 and $232, respectively, for the 12-month comparison. However, aggregated total and diabetes-related health care resource utilization costs were significantly reduced postglargine (P < 0.001), by $1,499 and $1,248, respectively, for the 9-month period and by $1,313 and $1,409, respectively, at 12 months. Per-patient costs were lower by $148 and $135, respectively, for the 9- and 12-month postglargine periods, driven by fewer consultations, inpatient visits, and office visits. Cost reductions were observed by 2-months after initiation of glargine and were maintained during each of the 2-month periods.

**CONCLUSION:** Initiation of insulin glargine for the treatment of type 2 diabetes may be of economic benefit to the health care system by decreasing diabetes-related and total resource utilization and costs.
COMPARISON OF LDL-C REDUCTION WITH COMMONLY USED DOSES OF ROSUVASTATIN (10 MG) VERSUS SIMVASTATIN (10 MG, 20 MG, AND 40 MG) IN A USUAL CARE SETTING

Bullano MF.* HealthCore, Inc., 800 Delaware Ave., Fifth Fl., Wilmington, DE 19801

INTRODUCTION: To compare low-density lipoprotein cholesterol (LDL-C) reduction with a 10 mg dose of rosuvastatin versus 10 mg, 20 mg, and 40 mg doses of simvastatin in a nonclinical trial setting (observational, usual care setting).

METHODS: In this retrospective longitudinal cohort study, patients newly initiated on rosuvastatin and simvastatin between August 1, 2003, and September 30, 2004, were identified from an administrative claims and lab results database of a Southeastern health plan. Patients with at least 1 prestatin/poststatin initiation lipid panel were followed until they switched, supplemented, or discontinued their initial statin. Mean percentage LDL-C reduction with 10 mg rosuvastatin was compared with simvastatin 10 mg, 20 mg, and 40 mg. Adjusted mean percentage LDL-C reductions were calculated using multivariate regression approach.

RESULTS: A total of 2,379 patients receiving rosuvastatin 10 mg (n = 666) or simvastatin 10 mg (n = 168), 20 mg (n = 787), or 40 mg (n = 758) were included in the study. In this study, rosuvastatin patients were younger (P < 0.05) compared with patients on simvastatin 10 mg, 20 mg, and 40 mg (mean age: 53 years versus 60, 57, and 56 years, respectively). Patients on rosuvastatin 10 mg had significantly higher (P < 0.05) preindex LDL-C (160 mg/dL) compared with simvastatin 10 mg (131 mg/dL), 20 mg (140 mg/dL), and 40 mg (143 mg/dL) groups. Significantly greater LDL-C reductions (P < 0.05) were observed with rosuvastatin 10 mg (34%) compared with simvastatin 10 mg (13%), 20 mg (19%), and 40 mg (23%), respectively. After adjusting for age, gender, and preindex LDL-C, reductions in percentage LDL-C continued to be significantly greater (P < 0.05) for patients on rosuvastatin 10 mg (30%) compared with simvastatin 10 mg (17%), 20 mg (21%), and 40 mg (23%).

CONCLUSION: Rosuvastatin 10 mg was more effective in reducing LDL-C compared with simvastatin 10 mg, 20 mg, and 40 mg in this nonclinical trial, observational (usual care) setting.

COST COMPARISON FOR SPECIALTY INJECTABLE MEDICATIONS USED FOR TREATING OSTEOARTHRITIS BILLED THROUGH MEDICAL OR PHARMACY CLAIMS

Khandelwal NG.* Walgreens Health Initiatives, 1417 Lake Cook Rd., Deerfield, IL 60015; khanndhi@auburn.edu, (334) 329-0098

INTRODUCTION: The purpose of this study was to investigate and compare the average amounts charged for specialty injectable medications used for treating osteoarthritis from medical and pharmacy claims databases.

METHODS: Specialty medications used for treating osteoarthritis are injectable medications that may be administered and billed through the medical benefit or dispensed through specialty pharmacy. We hypothesized that the amounts charged by a specialty pharmacy would be lower than the amounts charged by health care professionals through the medical benefit. This study was conducted using retrospective databases from a large pharmacy benefits management company. All medical and pharmacy claims for Synvisc (hylan G-F 20) and Hyalgan (hyaluronan) medications filled between July and December 2004 were identified and included in the study. The average medical and pharmacy amounts charged per syringe for the 2 specialty medications were computed and compared separately by independent sample t tests using SAS version 9.1.

RESULTS: The average cost per syringe obtained from medical claims for Synvisc (N = 361) was $230.70, while the average cost per syringe obtained from pharmacy claims (N = 193) was $208.30. Similarly the average medical (N = 354) and pharmacy (N = 53) costs per syringe for Hyalgan (N = 361) were $139.90 and $125.40, respectively. The differences between the amounts charged from medical and pharmacy claims for both the specialty medications were found to be statistically significant (P < 0.0001, at alpha 0.05).

CONCLUSION: The amounts charged per syringe through specialty pharmacy for osteoarthritides medications was found to be about 11% lower than the amounts that were charged through the medical benefit. Thus, higher cost savings may be achieved if specialty medications are dispensed through specialty pharmacies.

COST CONSEQUENCES OF APPLYING APPROPRIATE-USE CRITERIA TO DERMATOLOGIC IMMUNOMODULATORS: A PRECOMPARATIVE/POSTCOMPARATIVE ANALYSIS

Chiefari DM.* NMHCRx, 87 Old Coach Rd., Clifton Park, NY 12065

INTRODUCTION: To determine the economic impact of appropriate-use criteria placed on dermatologic immunomodulators for a health maintenance organization (HMO) client.

METHODS: On July 1, 2004, pimecrolimus cream and tacrolimus ointment were designated as formulary, with prior authorization required for a 600,000 life commercial HMO, and criteria requiring a trial of topical corticosteroids for patients older than 5 years was implemented in an effort to increase appropriate drug use while reducing costs. Clinical literature justified the criteria, and the process allowed for special-use considerations on a case-by-case basis. Pharmacy claims data were used to evaluate the effect of the intervention by identifying the number of prescriptions filled, the number of members filling these prescriptions, the total plan cost, and the average cost per prescription for the time frames 4-month preformulary designation (preperiod: March 1, 2004, to June 30, 2004) and postformulary designation (postperiod: July 1, 2004, to October 31, 2004).

RESULTS: The total number of prescriptions filled for the agents
was 1,561, representing 1,308 members preperiod versus 883 prescriptions, representing 757 members postperiod, with total plan costs of $114,451 preperiod versus $73,535 postperiod. The blended average cost per prescription was $73.32 preperiod and $76.36 postperiod. The total cost avoidance achieved was nearly $47,000 for 4 months, with a realized annualized cost avoidance of $140,000.

CONCLUSION: Clinically based appropriate-use criteria administered by the pharmacy benefits manager can achieve significant cost-avoidance outcomes for HMO clients.

■■ COST-EFFECTIVENESS OF A GLAUCOMA SCREENING PROGRAM: A MODEL EVALUATING THE RELATIVE CLINICAL AND ECONOMIC IMPACT IN COMMERCIAL VERSUS SENIOR MEMBER POPULATIONS

Goldberg LD,* Goldberg, MD & Associates, 2210 W Main S., Suite 107-384, Battle Ground, WA 98604

OBJECTIVE AND PERSPECTIVE: Positive return on investment (ROI) for disease management (DM) programs has been limited to those directed at congestive heart failure (CHF) or multiple disease conditions; therefore, it is the objective of this model to be used to evaluate the cost-effectiveness of a glaucoma screening program in commercial versus senior member populations.

METHODS: An Excel-based 14-year economic model previously developed to assess the expected payer costs associated with screening and early treatment of glaucoma patients versus nonscreening of asymptomatic progressive disease was extended to dynamically model the drug treatment cost component (where the prior model was limited to a fixed blended figure based on data from Lee and colleagues). Total costs included screening costs, drug costs, office visits, and surgical treatments associated with glaucoma. Treatment costs and disease progression rates were taken from recently published literature. The cost of screening, drugs, and medication compliance were modeled discretely in the commercial versus senior member populations. Annual therapeutic price (ATP) based on average wholesale price (AWP), with consideration of contractual discounts, was used to model the cost of pharmaceutical treatment. Nonscreened patients were assigned no screening costs and no progressive increase in baseline treatment costs for 7 years, followed by treatment costs for mild disease for 7 years. Screened patients were assigned every-other-year screening cost for 14 years, with a proportion of screened patients at risk assigned early/mild glaucoma treatment costs. Patient epidemiology rates were based on members aged 40 to 64 years for the commercial population and members aged 65 years and older for the senior population. The primary economic end point was the ratio of reduced annual treatment costs compared with the annual program costs. Multifactor sensitivity analyses were conducted.

RESULTS: In a commercial population, total annual costs to “screen and treat” versus a strategy of “no screening” was estimated to be $0.62 per member per month (PMPM) versus $0.80 PMPM, respectively (a difference of $0.12 PMPM in favor of screening). In the senior population, these costs were estimated to be $6.66 PMPM versus $7.94 PMPM, respectively (a difference of $1.28 PMPM in favor of screening). With estimated program costs of $0.009 PMPM and $0.167 PMPM in the commercial versus senior populations, respectively, the calculated potential ROI was estimated to be 2.6 and 1.7, respectively, for these programs.

CONCLUSION: The early identification and treatment of glaucoma in accordance with established evidence-based clinical practice guidelines represents a more cost-effective strategy as compared with nonscreening of at-risk populations. Total annual costs for a glaucoma-screening disease management program are estimated to demonstrate a positive ROI in both commercial and senior populations. These findings may help promote the interest of payers in implementing pertinent quality improvement and Health Plan Employer Data and Information Set (HEDIS)-related efforts.

■■ COST-EFFECTIVENESS OF RECOMBINANT-ACTIVATED FACTOR VII IN THE TREATMENT OF INTRACEREBRAL HEMORRHAGE: A U.S. MANAGED CARE PERSPECTIVE

Earnshaw SR,* RTI Health Solutions, PO Box 12194, Research Triangle Park, NC 27709

INTRODUCTION: To estimate cost-effectiveness of recombinant factor VIIa (rFVIIa) compared with standard care in treating intracerebral hemorrhage (ICH) from a managed care perspective.

METHODS: We developed a decision-analytic model estimating cost-effectiveness of rFVIIa 40 mcg/kg, 80 mcg/kg, and 160 mcg/kg compared with standard care in treating ICH from a managed care perspective. Costs and outcomes were measured at 90 days and annually thereafter for the remainder of a patient’s lifetime. Mortality and disability at 90 days was obtained from a Phase IIb clinical trial. Direct medical costs and resource use for the first 90 days following ICH were estimated from the clinical trial, managed care claims data, and published literature. Costs related to pharmacotherapy, hospitalization, outpatient visits, durable medical equipment, home health care, and rehabilitation/skilled nursing facility were included. Costs for rFVIIa were based on wholesale acquisition cost. Mortality corresponding to the modified Rankin Scale scores derived from published literature were applied to measure cost-effectiveness beyond the first 90 days. Expert clinical opinion was used to support assumptions. Costs and outcomes are reported in 2005 U.S.$ and discounted at 3% annually. One-way and probabilistic sensitivity analyses were performed on key variables and assumptions.

RESULTS: Treatment with rFVIIa 40 mcg/kg as compared with placebo resulted in 1.38 additional life-years and an incremental cost-effectiveness ratio (ICER) of $14,920 per additional life-year. Treatment with rFVIIa 80 mcg/kg reduced total costs by $3,649...
per patient versus placebo and increased life expectancy by 1.59 life-years. 160 mcg/kg dose resulted in an additional 1.46 life-years and an ICER of $11,204 per additional life-year compared with placebo. Results were robust to sensitivity analysis.

CONCLUSIONS: Treatment of ICH with rFVIIa mcg/kg and 160 mcg/kg appears to be cost effective compared with standard care. Because of greater improvements in patient outcomes, treatment with 80 mcg/kg dose of rFVIIa was not only cost effective, but cost saving compared with standard care.

DOSING DISTRIBUTION PATTERNS AND ASSOCIATED COSTS OF ERYTHROPOIETIC AGENTS IN A NATIONWIDE SAMPLE OF ANEMIC PATIENTS WITH PREDIALYSIS CHRONIC KIDNEY DISEASE

Mody SH * Ortho Biotech Clinical Affairs, LLC, 430 Route 22 East, Bridgewater, NJ 08807

INTRODUCTION: To better understand real-world dosing patterns of epoetin alfa (EPO) and darbepoetin alfa (DARB) in patients with predialysis chronic kidney disease (pCKD), a retrospective, observational study was conducted to analyze dosing patterns and associated treatment costs of EPO and DARB in an outpatient setting.

METHODS: Adult, anemic pCKD patients who had ≥2 EPO or DARB claims and were newly initiated on erythropoietic therapy between April 2003 and February 2005 were identified from a nationwide sample of outpatient medical claims from hospital clinics and office practices. EPO and DARB use was identified via HCPCS (HCFA Common Procedure Coding System) codes in medical claims with dose calculated using billed units. Dosing frequency, mean weighted weekly dosing, the dose-only ratio between the 2 agents (units EPO: mcg DARB), and drug costs (using 2005 wholesale acquisition prices) were calculated.

RESULTS: 1,750 EPO and 1,089 DARB patients met the inclusion criteria. Mean age (years, EPO 69 ± 13, DARB 70 ± 12, P = not significant [NS]) and gender distribution (EPO 49% male, DARB 49% male, P = NS) were similar between groups. Weekly and extended dosing (≥ every 2-week [Q2W]) frequencies were utilized in patients receiving EPO (once per week [QW]: 58%, Q2W: 35%, ≥ every 3 weeks [Q3W]: 7%) and DARB (QW: 19%, Q2W: 65%, ≥ Q3W: 16%). The average weighted weekly dose was 12,560 units for EPO and 48.5 mcg for DARB, which corresponded to a dose-only ratio of 259:1 (units EPO: mcg DARB). These doses resulted in estimated mean weekly costs of $153 for EPO and $211 for DARB. Similar dosing patterns and cost differences were observed for patients completing 4, 8, 12, and 24 weeks of therapy as well as when assessing Medicare and commercially insured patients.

CONCLUSIONS: Extended EPO and DARB dosing (≥ Q2W) was common among anemic pCKD patients. However, overall DARB treatment costs were consistently higher than EPO treatment costs regardless of dosing frequency, length of therapy, and insurer.

DOSE-ONLY RATIO BETWEEN EPOETIN ALFA AND DARBEPOETIN ALFA FROM A POOLED ANALYSIS OF THREE MEDICAL CLAIMS DATABASES

McKenzie RS * Ortho Biotech Clinical Affairs, LLC, 4441 Walnut Hill La., Dallas, TX 75229

INTRODUCTION: Epoetin alfa (EPO) and darbepoetin alfa (DARB) are 2 agents approved for the treatment of anemia in cancer patients receiving chemotherapy; however, data are needed to describe the relative dosages of these 2 erythropoietic agents in real-world practice settings.

METHODS: To determine the dose-only ratio (units of EPO: mcg of DARB), a pooled analysis was conducted using 2002-2004 medical claims data from 3 different managed care databases (DBs). Data from patients who were ≥18 years old, had ≥1 claim for cancer, were newly initiated on an erythropoietic agent, and had ≥2 claims of EPO or DARB were included in this analysis. DB heterogeneity was evaluated using both fixed-effects and random-effects models in sensitivity analyses. The dose-only ratios and 95% confidence intervals (CIs) from the individual DB were pooled, and the weight given to each DB was based on the inverse of the variance, with the variance estimated using the Delta method.

RESULTS: A total of 18,564 (EPO: n = 13,688, DARB: n = 4,876) patients were analyzed (DB 1: n = 7,805, DB 2: n = 4,405, DB 3: n = 6,354). Mean cumulative EPO doses were 252,856, 357,836, and 280,588 units for DB 1, DB2, and DB3, respectively, while the mean cumulative DARB doses were 1,072, 1,366, and 1,000 mcg, resulting in dose-only ratios of 236:1, 262:1, and 281:1, respectively. The heterogeneity test indicated that the 3 study results were significantly different (P < 0.0001). The pooled dose-only ratio using the random-effects model was 259:1 (95% CI, 230:1-289:1). A sensitivity analysis using the fixed-effects model rendered a dose-only ratio of 260:1 (95% CI, 253:1-266:1).

CONCLUSION: Based on the cumulative doses of more than 18,000 patients treated with these 2 erythropoietic agents, this research indicated that the dose-only ratio (units of EPO: mcg of DARB) is approximately 260:1.

DRUG PERSISTENCY PATTERNS OF TREATMENT FOR OVERACTIVE BLADDER—EVIDENCE FROM A LARGE MEDICAID POPULATION

Singh G * Stanford University, 100 Hamilton Ave., Suite 22, Palo Alto, CA 94301

INTRODUCTION AND OBJECTIVE: Overactive bladder (OAB) is a common disorder affecting more than 33 million people in the United States. Anticholinergic therapy is the mainstay of medical
therapy for OAB. We compared the persistence of treatment in patients taking oral medical therapies for OAB in a large Medicaid population.

METHODS: Longitudinal data on pharmacy claims from a California Medicaid program (Medi-Cal: January 1, 1995, to January 31, 2004) were used to study OAB patients (aged 18 years or older) newly initiated on oral pharmacotherapy (treatment-free period of 3 months prior to initial prescription, average length of follow-up after start of therapy was 1,228 days). Medi-Cal is the largest state Medicaid program in the United States, with more than 7 million participants. Drug discontinuation was defined as a drug switch to another OAB drug or no prescription refill within 30 days of estimated completion of prior prescription. Time to treatment discontinuation was analyzed using Kaplan-Meier survival plots.

RESULTS: Of all newly treated subjects (N = 119,589), 73.1% were females, and mean age was 66 years. Medication use was stratified into the following 5 categories: 49,866 patients on generic oxybutynin immediate release (IR), 2,046 on branded oxybutynin IR, 25,178 on tolterodine IR, 21,036 on branded oxybutynin extended release (ER), and 21,463 on tolterodine ER. Of the subjects newly started on oral pharmacotherapy, 88.8% discontinued their therapy, while 6.6% switched to another treatment. Kaplan-Meier analysis showed the median days on therapy to be 43, with a significant difference between all 5 strata (P <0.001). Patients on generic oxybutynin IR had the highest rate of discontinuation at 93.1% and the lowest median time on therapy at 33 days. In general, older patients (≥60 years) stayed on their therapy longer than younger subjects (median length of therapy 45 days vs. 37 days, P <0.05).

CONCLUSION: These results show that, in a Medicaid population (where barriers to access are reduced), patients with OAB have poor persistence with medical therapies. Patients started on generic oxybutynin IR discontinue at very high rates; therefore, starting patients on this product may not be an efficient use of health care resources.

ECONOMIC BENEFITS OF ACAMPROSATE THERAPY IN ALCOHOL-DEPENDENT PATIENTS: AN UPDATE

Weycker D.* Four Davis Ct., Brookline, MA 02445; dweycker@pai2.com, (617) 232-4400

INTRODUCTION: Acamprosate therapy has been reported to be cost effective in maintaining abstinence in alcohol-dependent patients who are initiating psychosocial rehabilitation. This study was undertaken to update estimates of the economic benefits of such therapy.

METHODS: Estimated costs were compared over 1 year between patients who received acamprosate as an adjunct to psychosocial rehabilitation versus psychosocial rehabilitation alone. Costs included acamprosate therapy, psychosocial rehabilitation services, and alcohol-related hospitalizations and physician visits. Estimates of resource use were obtained from a German prospective open-label cohort study (Rychlik et al., 2003). Unit costs were estimated using U.S. secondary data sources (2004 Drug Topics Redbook, 2004 Resource-Based Relative Value Scale, 2002 Health Care Cost and Utilization Project Nationwide Inpatient Sample), and expressed in 2004 U.S.$s. One-way sensitivity analyses were conducted to assess the robustness of findings to changes in unit-cost estimates.

RESULTS: The cost of acamprosate therapy over 1 year was estimated to be $62,600 per 100 patients (mean duration of treat-
CONCLUSION: Results demonstrate a positive relationship between copay differential and GFR and FC, controlling for utilization. This suggests members are increasingly likely to evaluate alternatives to expensive medications as their costs increase.

■ EFFECTIVENESS OF A CONTROLLED SUBSTANCES RETROSPECTIVE DRUG UTILIZATION REVIEW INTERVENTION

Hartwig SC,* Prime Therapeutics, Inc., 1020 Discovery Rd., No. 100, Eagan, MN 55121

INTRODUCTION: We developed a retrospective drug use review (RDUR), examining controlled substance (CS) use patterns. Member CS claims were screened using a proprietary scoring method identifying possible CS misuse. Intervention letters were sent to the prescribers. A quasi-experimental cohort study using intervention and concurrent control populations to measure the effectiveness of this intervention was performed.

METHODS: On February 15, 2005, a 52,000 member BlueCross BlueShield plan mailed the CS RDUR intervention letter to 302 prescribers for 168 members (CS use score ≥12). A precomparison and postcomparison was performed to assess changes in per-member CS claims, CS use score, and costs per member per month (PMPM). Of the 168 original members, 128 were continuously enrolled. The control group had 595 continuously enrolled members with a CS use score ≥12, and prescribers did not receive intervention. Claims were analyzed in the preperiod (November 1, 2004, to January 31, 2005) and postperiod (March 1, 2005, to May 31, 2005) for both groups.

RESULTS: Average CS use score decreased in the intervention group from 14.7 to 7.0 (7.7 absolute decrease) and in the control group from 14.9 to 8.3 (6.6 absolute decrease), absolute 1.1 point difference between groups (P = 0.06). In the postperiod, there was an absolute 10.6% difference (P = 0.03) in members still qualifying for an intervention letter (CS score ≥12), intervention 27 (21.0%) members compared with control 188 (31.6%). Intervention group costs PMPM increased 14.1% (preperiod $188.20, postperiod $219.00). Within the intervention group preperiod, there were 7 Actiq claims (13.9% of total CS costs) and 17 in the postperiod (34.3% of total CS costs). The control group costs PMPM decreased 11.8% (preperiod $208.06, postperiod $179.29), with Actiq claims stable.

CONCLUSIONS: This successful CS RDUR program was associated with an additional 1 member no longer qualifying for an intervention for every 9 members who received an intervention. Anticipated decreases in CS expenses were not seen primarily due to increased Actiq utilization.
ESTIMATING THE IMPACT OF A
CONSUMER CHOICE PHARMACY PROGRAM ON
MEDICATION COMPLIANCE AND PERSISTENCY

Jiang JZ.* 1417 Lake Cook Rd., Deerfield, IL 60015;
Jenny.jiang@walgreens.com, (847) 964-6926

INTRODUCTION: The objective of this study is to investigate the impact of a 3-level consumer choice pharmacy (CCP) benefit design on medication compliance and persistency. This program provides patients with an employer-funded pharmacy account, which covers 100% of their prescription medication costs. If the account is depleted, patients pay 100% out of pocket up to a predefined limit. If the limit is met, a traditional benefit design is implemented.

METHODS: A retrospective preperiod and postperiod cohort study was conducted using a large employer-based pharmacy claims data. The preperiod was before the program initiated in January 2005 and the postperiod was the 6-month follow-up. Newly treated patients with maintenance medications from July 1, 2004, to October 31, 2005, were identified. The study group was patients enrolled in the CCP program, and the comparison group was patients not enrolled in the CCP program. Compliance, measured by the medication possession ratio, and persistency, defined as the proportion of individuals remaining on the therapy, were evaluated for both groups at the end of the preperiod and postperiod. A t test was used for continuous variables, and a chi-square test was used for proportions.

RESULTS: Of 1,009 patients available for this study, 78 were included in the study group and 931 were included in the comparison group. Overall, compliance decreased from the preperiod to the postperiod for both groups (0.307 to 0.107 for the study group and 0.359 to 0.146 for the comparison group). Similar trend was observed in persistency rate assessment. The persistency rate in the study group reduced from 41.03% to 21.91% and from 42.31% to 24.36% in the comparison group. The differences were statistically not significant between the 2 groups at both preperiod and postperiod.

CONCLUSIONS: The study indicates that the CCP program does not have a significant impact on compliance and persistency within the first 6 months of program implementation. Further analysis, using a 1-year follow-up period, would fully capture the impact of the 3-level design on medication compliance and persistency.

EVALUATION OF PERSISTENCY AND OUTCOMES IN PATIENTS ON SU COMBINATION THERAPY WITH TZDS OR METFORMIN

Brixner DI.* Department of Pharmacotherapy, University of Utah,
30 South 2000, East Room 258, Salt Lake City, UT 84112-5820

INTRODUCTION: Patients receiving dual therapy with a sulfonylurea (SU) plus metformin (MET) or a thiazolidinedione (TZD) were compared to assess trends in therapy persistency and outcomes over 12 months.

METHODS: A quasi-experimental study design using LabRx data, a 10 million-member research database with claims and clinical data, was used to examine the clinical (fasting blood glucose, low-density lipoprotein [LDL], glycosylated hemoglobin [A1C]), behavioral (time to combination discontinuation) and economic outcomes (costs) for SU plus pioglitazone (SUP), SU plus rosiglitazone (SUR), and SU plus MET (SUM).

RESULTS: 9,481 patients were identified on a combination of SU + TZDs or METFORMIN or a thiazolinedione (TZD) were evaluated for both groups at the end of the preperiod and postperiod. A test was used for continuous variables, and a chi-square test was used for proportions. The study indicates that the CCP program does not have a significant impact on compliance and persistency.

CONCLUSIONS: The differences were statistically not significant between the study groups. Although differences in persistency were not significant, PPPM costs were significantly lower for SUP overall and for SUR among the 2 TZDs. Differences in adjusted per-patient-per-month (PPPM) pharmacy costs were significant ($248) versus SUP ($296) and between SUP and SUR ($276) and between SUP and SUR ($201).

FACTORS PROMOTING FORMULARY SOFTWARE ACCEPTANCE IN THE SAFETY NET PROVIDER COMMUNITY

Banks PW.* L.A. Care Health Plan, 555 W Fifth St., Los Angeles, CA 90013; pbanks@lacare.org, (213) 694-1250, ext. 4251

INTRODUCTION: This study examined factors promoting the adoption and effective use of drug reference software on handheld computers to reduce formulary burden and enhance clinical practices among safety net providers.

METHODS: We surveyed providers serving low-income patients at safety-net clinics in Los Angeles County, California. A convenience sample of 26 clinics served as clusters, covering diverse populations in the urban core; 215 providers were canvassed, answering 96 questions about provider workload, prescribing activity, formulary concerns, and experience using drug reference software on personal digital assistants (PDAs).

RESULTS: 1. Nearly three fifths of providers identified formularies as a
moderate-to-major problem. This perception was empirically consistent, worsening with higher numbers of formularies and longer lookup times.

2. PDA use is common in local safety net clinics and is well-regarded but not yet prevalent—a ready target for process improvement, if follow-on studies confirm effectiveness. Two fifths of providers already owned PDAs; half of providers had used drug reference software. No clinic with PDA users had fewer than one third of providers using PDAs—suggesting that critical mass is vital in technology adoption.

3. More than two thirds of providers indicated that PDA drug reference tools would benefit clinical practice through efficiency and fewer adverse drug events.

4. Targeting resources. Safety-net doctors are frequently new: nearly half had less than 5 years experience; 65% of young doctors saw formularies as a problem compared with 47% of doctors in practice 15+ years. Less-experienced doctors exhibited more variability in time spent on formulary issues. For them, PDA tools may reduce the learning curve.

CONCLUSIONS: The findings predict substantial acceptance of PDA drug reference tools by safety-net providers to reduce formulary burden and adverse drug events. The results are being used to design a randomized control study, placing PDAs in safety-net clinics to test effectiveness.

### HEALTH PLAN ATTRITION AMONG TYPE 2 DIABETES PATIENTS RELATIVE TO NONDIABETES PATIENTS IN A COMMERCIALLY INSURED POPULATION

**Koo Y.** *Pfizer, Inc., 235 E. 42nd St., New York, NY 10017*

**INTRODUCTION:** Health plan attrition rates for type 2 diabetes patients relative to nondiabetes controls were examined.

**METHODS:** Patients initiating health plan enrollment between January 1, 1998, and September 30, 1999, who were enrolled for at least 6 months were identified from a large administrative claims database. Patients with evidence of type 2 diabetes during the first 6 months of health plan enrollment were selected for study and followed for 5 years. These patients were matched on a 1:1 basis to a nondiabetes control group based on age, gender, geographic region, health plan type, and comorbidity profile (dyslipidemia, hypertension, obesity, coronary artery disease/atherosclerosis). A second nondiabetes control group was also randomly selected for comparison. Rates of nonmortality disenrollment were evaluated and compared for diabetes patients versus controls with a chi-square test of significance.

**RESULTS:** Of the 9,878 type 2 diabetes patients identified, 9,811 were matched to nondiabetes controls, and a random control group of 29,634 was drawn. Mean age was 51 years among the diabetes patients and matched controls and 38 years for the random controls. Females comprised 46% of diabetes patients and matched control group and 53% of the random control group. Rates of health plan disenrollment among diabetes patients (37.1%) were lower than those of matched controls (38.7%, \( P = 0.0171 \)) and random controls (47.7%, \( P < 0.0001 \)).

**CONCLUSIONS:** These data indicate that diabetes patients may exhibit lower rates of health plan disenrollment than patients without diabetes. This finding suggests that if the diabetes population is not properly managed over the long term, they may contribute to higher rates of resource utilization as a consequence of their longer affiliation with the health plan. Therefore, factors associated with health plan disenrollment should be taken into account in the development of risk stratification and disease management strategies.

### HEMOGLOBIN LEVELS ASSOCIATED WITH DIAGNOSIS OF ANEMIA

**Lawless G.** *Amgen Inc., One Amgen Center Dr., MS 37-2-C, Thousand Oaks, CA 91320-1799; glawless@amgen.com, (805) 447-8024*

**INTRODUCTION:** The association between hemoglobin level and a diagnosis of anemia in oncology patients was evaluated through a retrospective claims database analysis, as was the hemoglobin level most likely to “trigger” diagnosis.

**METHODS:** Members of a large U.S. health plan with an oncology diagnosis and chemotherapy claims between January 1, 2000, and February 28, 2002, were included. Medical and laboratory claims were examined to identify chemotherapeutic episodes, *International Classification of Diseases, Ninth Revision* (ICD-9) codes for anemia, and hemoglobin values within each episode and immediately preceding new anemia diagnoses. Descriptive statistics and multivariate regression were used to examine the relationship between anemia diagnosis and hemoglobin values.

**RESULTS:** A total of 3,180 chemotherapeutic episodes corresponding to 2,717 oncology patients were identified. In episodes in which the hemoglobin dropped below 12 g/dL (1,689 episodes; 53%), an anemia diagnosis occurred in only 733 episodes (45%). Additionally, an anemia diagnosis was found in only 66% of the episodes where hemoglobin fell below 10.0 g/dL. Being older than 50 years, having non-Hodgkin’s lymphoma, and having fatigue or renal disease were observed to increase the odds of diagnosis, after controlling for hemoglobin nadir values and chemotherapeutic agent. Adjusting for age older than 50 years, sex, and breast cancer diagnosis, the mean hemoglobin value before anemia diagnosis was 11.2 g/dL (95% confidence interval, 11.0-11.3).

**CONCLUSION:** Among oncology patients with hemoglobin values below 12 g/dL in this database, there is a gap between those who receive a diagnosis of anemia and those who do not. At hemoglobin values below 10 g/dL, the anemia level at which the National Comprehensive Cancer Network most strongly recommends considering aggressive treatment, only two thirds of patients are diagnosed with anemia. Our findings provide evidence that identifying patients with ICD-9 codes for anemia
from claims data may be misleading and can significantly underestimate the true number of patients with anemia.

### IMPACT OF A STATIN MEDICATION COMPLIANCE PROGRAM IN A MANAGED CARE SETTING

**Thaker DL, WellPoint Pharmacy Management, 8407 Fallbrook Ave., MS AF-7, West Hills, CA 91304**

**PURPOSE:** Previous studies suggest medication compliance of statin therapy is suboptimal. The goal of this study was to evaluate the impact of a nonbranded compliance program designed to improve patient adherence to statin therapy in a managed care setting.

**METHODS:** Members who were more than 28 days late in refilling their medication within the first 3 months of statin therapy or had a medication possession ratio (MPR) < 80% over 6 months were identified weekly from a large managed care plan of more than 2 million members through pharmacy claims review. The program included member-refill reminders and physician faxes notifying them of their nonadherent patients to encourage prescription refill. Targeted patients were tracked to evaluate confirmed refill rates at 3 months. Medication compliance of those who received the intervention was measured by MPR within 6 months post-intervention. Program impact was estimated by comparing refill rates and medication compliance of patients with similar characteristics that did not have such a program in place.

**RESULTS:** A total of 5,627 members were targeted for the intervention, and successful contact was made in 96% of targeted members. Among successful contacts, confirmed refills were observed in 77% of the patients, as compared with 72% in the control group (P < .01). Overall, the study group showed 33% improvement in the mean MPR versus the control, which demonstrated a reduction in mean MPR at 6 month follow-up. In addition more than 59% of previously noncompliant patients displayed improvement in adherence rate, with MPR exceeding 80% within 6 months post-intervention.

**CONCLUSIONS:** Early aggressive member and physician intervention can improve member adherence to statin therapy. Administrative claims surveillance offers a convenient means for managed care plans to design and implement programs that impact member drug use behavior.

### IMPACT OF PHONE INTERVENTION THROUGH COMMUNITY PHARMACY ON MEDICATION PERSISTENCY AND INITIAL REFILL RATE

**Meller CP, Walgreens Health Initiatives, 1417 Lake Cook Rd., Deerfield, IL 60015; Chris.meller@walgreens.com, (847) 964-6931**

**INTRODUCTION:** The objective of this study was to evaluate the impact of a phone intervention made by a local community pharmacy on medication persistency in patients taking long-term chronic medications.

**METHODS:** Patients taking chronic medications were targeted if they were at least 7 days late on getting their refill. The data was collected between May 2004 and August 2005 from national retail pharmacy chain stores based in the Midwest. The patient's community pharmacy was alerted and directed to contact the patient by phone within 72 hours to remind the patient and gather information about the missed prescription. Patients who had a valid contact from their pharmacy were placed in the intervention group while patients unable to be contacted were treated as controls. We hypothesized that because of the positive
relationship between a community pharmacy and its patients, the intervention group would have higher persistency and an initial refill rate than the control group. Persistency was defined as the number of months that patients continued to refill their medications within 7 days of their refill date, and initial refill rate was defined as the proportion of patients refilling their medications within 17 days of the refill due date. The difference in initial refill rate and persistency was estimated by using a chi-square test and log-rank test, respectively. Additional analysis was done to control for age and gender.

RESULTS: An initial refill rate of 55% (N = 4649) was observed in the intervention group compared with 40% (N = 7949) in the control group (P < 0.0001). On average, patients in the intervention group continued refilling their medications for 1.41 months compared with 1.02 months in patients in the control group (P < 0.05).

CONCLUSIONS: A telephone intervention call made by a local community pharmacy to patients on chronic medications had a positive impact on initial refill rate and medication persistency.

IMPLEMENTING THE PENNSYLVANIA MEDICATION ALGORITHM PROJECT: AN INNOVATIVE PARTNERSHIP

Strouss LA,* Community Care Behavioral Health Plan, 112 Washington Pl., One Chatham Center, Suite 734, Pittsburgh, PA 15219; stroussl@ccbh.com, (412) 402-8719

INTRODUCTION: Consumer-centered treatment approaches that emphasize recovery, rehabilitation, and empowerment can improve mental health outcomes for people with severe and persistent mental illness. The Pennsylvania Medication Algorithm Project in Schizophrenia (PennMAPS) is a consumer-centered approach to client recovery that focuses on medication adherence and education. PennMAPS was previously employed only within the state hospital system. This demonstration outlines its implementation by a behavioral health managed care organization (BH-MCO) in the outpatient setting.

METHODS: Several consultations with experts from the Texas Medication Algorithm Project and Ohio Medication Algorithm Project were conducted with the BH-MCO leadership team. Needs and feasibility assessments served as a foundation for implementation of PennMAPS. Staff and peer (consumer) facilitators were interviewed. Physician education was provided by the leadership team and local experts. Individual physician discussions were provided by the BH-MCO behavioral health pharmacist. The PennMAPS program was funded solely by the behavioral health organization.

RESULTS: The PennMAPS was implemented in 2 sites—outpatient and partial hospitalization. A total of 12 staff facilitators were trained (6 at each site) as well as 4 peer facilitators (2 at each site). Training was conducted by program coordinators (psychiatric nurse and behavioral health pharmacist) during the period from September 2004-December 2004. Final implementation began in February 2005. Preliminary trends of changes in consumer responses pre-PennMAPS implementation and post-PennMAPS implementation demonstrate increases in medication knowledge (20%); feeling comfortable communicating with the physician (20%); and agreement that the patient is a worthwhile person (30%).

CONCLUSION: Based on expert experience and a detailed implementation plan, a consumer-centered, multidisciplinary behavioral health intervention was successfully initiated and demonstrates initial success in clinical outcomes. The PennMAPS demonstrates a unique collaboration of BH-MCO and consumer-focused intervention. This intervention is one of the first such efforts to be evaluated. Due to enthusiastic responses by staff and consumers, program expansion is being investigated.

INAPPROPRIATE ORAL TRANSMUCOSAL FENTANYL (ACTIQ) UTILIZATION AND MANAGEMENT OPPORTUNITIES

Gleason PP,* Prime Therapeutics, Inc., 1020 Discovery Rd., No. 100, Eagan, MN 55121; pggleason@primetherapeutics.com, (651) 286-4190

INTRODUCTION: Actiq is indicated only for management of breakthrough pain in cancer patients already receiving ≥60 mg morphine/day or the equivalent for a week or longer. Actiq’s prescribing information (PI) states, “patients should limit consumption to 4 or fewer units per day.” Actiq use outside labeling and utilization management opportunities were assessed by a retrospective pharmacy and medical claims analysis.

METHODS: All Actiq claims were identified during the period from April 1, 2005, to June 30, 2005, from a 1.8 million-member BlueCross BlueShield plan. The date of each member’s initial Actiq claim was used to create a 30-day look-back window. An assessment for a long-acting opioid sustained-release (SR) morphine, oxycodone, hydromorphone, or fentanyl patch) claim in the 30-day look-back window was performed. Actiq utilizing medical claims were queried for at least 1 cancer or acquired immune deficiency disease (AIDS) International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis in any of 5 diagnostic fields during the 365 days prior to their initial Actiq claim.

RESULTS: 95 members utilized Actiq during second quarter 2005. There were 284 Actiq claims with the following per-claim averages: plan payment $1,187, quantity dispensed 70, days supply 17, and daily quantity consumed 4.1. There were 44 of 284 (15.5%) claims with quantities greater than 120; 53 of 95 (55.8%) members had no long-acting opioid claims within the 30-days prior to their Actiq claim. Of the 87 members with at least 1 medical claim, 21 (24.1%) had a cancer or AIDS diagnosis.

CONCLUSIONS: Considerable Actiq use is outside PI labeling. Fewer than half of Actiq users received long-acting opioids; 1 of every 7 Actiq claims exceeded recommended consumption limits (limiting the quantity to 120 per claim could save the plan $108,296 per quarter), and only 1 of 4 members had a cancer or
AIDS diagnosis. Health plans should consider utilization management tools to improve appropriate Actiq use and decrease costs.

**LIPID TREATMENT AND LDL-C GOAL ATTAINMENT AMONG HIGH-RISK PATIENTS IN A MANAGED CARE SETTING**

Nag SS, * Outcomes Research and Management, Merck & Co., Inc., 770 Broad St. of Sumneytown Pike, WP39-166, West Point, PA 19486

**BACKGROUND:** We used managed care administrative data to examine lipid testing, treatment, and likelihood of low-density lipoprotein cholesterol (LDL-C) goal attainment (<100 mg/dL) among 11,552 newly diagnosed high-risk patients (coronary heart disease [CHD] or diabetes [DM]) not previously prescribed lipid treatment.

**METHODS:** Patients were retrospectively identified (1999-2000) 1-year prior to lipid treatment (baseline) and followed up (F/U) for up to 3.5 years (mean 2.15 years; range 1.0-3.5 years). We estimated the proportion tested, treated, and treated-to-goal within 6 months. Among those not at goal within 6 months, we estimated the proportion treated-to-goal within 12 months and over the mean F/U. Logistic regression estimated the likelihood of goal attainment within 12 months and over the mean F/U among patients who were not at goal within the first 6 months and continued to be treated.

**RESULTS:** Of the 11,552 patients, 40.5% had a lipid test within 6 months of diagnosis. Of those tested, 26.6% were treated and 39.0% of those treated attained goal. Goal attainment improved to 50.1% (within 12 months) and 58.4% (over mean F/U). Only 17.4% of those treated were initiated on aggressive lipid therapy (expected LDL-C reduction ≥40.0%). Among those not at goal within 6 months (61.0%; n = 760) and who continued to be treated over mean F/U (n = 496), 33.7% were titrated up and 38.7% were switched to other agents. Goal attainment among those titrated and switched was 48.5% and 48.4%, respectively. Patients not attaining goal within 6 months and who continue to be treated over mean F/U (n = 200), anxiety (n = 153), insomnia (n = 149), bipolar mania (n = 127), and agitation (n = 119). “Other” includes any diagnosis excluding insomnia, anxiety, bipolar mania, agitation, schizophrenia, psychosis not otherwise specified. A follow-up mailing containing survey results and prescriber information was sent to all participating physicians to increase awareness and education.

**CONCLUSION:** The utilization of LD quetiapine is common for off-label indications, particularly as a hypnotic or anxiolytic. Prescriber education was provided through survey results and information on appropriate use of quetiapine. Future interventions include intensive educational outreach to high physician utilizers to influence prescribing pattern, and cost analysis.

**MODELED ACHIEVEMENT OF OPTIMAL LIPID VALUES WITH EXTENDED-RELEASE NIACIN/LOVASTATIN IN ELDERLY PATIENTS BY CENTERS FOR MEDICARE AND MEDICAID SERVICES DIAGNOSIS CLUSTERS**

Charland SL, * Kos Pharmaceuticals, Inc., 1 Cedar Brook Dr., Cranbury, NJ 08512; scharland@kospharm.com

**INTRODUCTION:** As Medicare Part D is enacted, therapy decision makers will require information about specific medication use in the elderly within new Centers for Medicare and Medicaid Services (CMS) diagnosis clusters. The purpose of this study is to model the effect of extended-release niacinLovastatin (ERNL) and individual components on the achievement of combined optimal low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) values in cardiovascular-related CMS RxHCC diagnostic clusters.

**METHODS:** Patients older than 65 years were selected from a 2.1 million record managed care database if they had a lipid panel between January 1, 2000, and December 31, 2001; no concomitant

---

**LOW-DOSE QUETIAPINE UTILIZATION WITHIN A LARGE AMBULATORY POPULATION**

Strouss LA, * Community Care Behavioral Health Plan, 112 Washington Pl., One Chatham Center, Suite 734, Pittsburgh, PA 15219; stroussla@ccbh.com, (412) 402-8719

**INTRODUCTION:** Recent data demonstrate frequent utilization of low-dose (LD) quetiapine (≤200 mg) for psychiatric symptoms other than psychosis. The goal of this study was to assess use of LD quetiapine in patients enrolled in a commercial, Medicare, and Medicaid managed care organization.

**METHODS:** Pharmacy claims data were analyzed from January 1, 2005, through March 31, 2005, to identify patients receiving LD quetiapine. Prescribing physicians were then faxed a standardized survey to evaluate indication for LD quetiapine use. The primary objective was to assess indications for LD quetiapine use. The secondary objective was to educate prescribers regarding the appropriate use of LD quetiapine. Data were stored in an Access database and assessed using descriptive statistics.

**RESULTS:** A total of 3,055 members had a paid claim for quetiapine. Of those, 82% (n = 2526) were Medicaid members. 1,084 members (35%) received a prescription for LD quetiapine. The majority of LD quetiapine recipients (76%) were Medicaid members, followed by commercial (21%) and Medicare (3%). Of the LD quetiapine claims, 345 prescribers were identified, and 1,322 patient-specific surveys were prepared. However, 222 surveys could not be sent because of insufficient contact information, reducing the total number to 1,100. 542 surveys were returned (49% response rate). The top 5 indications for use were: other (n = 200), anxiety (n = 153), insomnia (n = 149), bipolar mania (n = 127), and agitation (n = 119). “Other” includes any diagnosis excluding insomnia, anxiety, bipolar mania, agitation, schizophrenia, psychosis not otherwise specified. A follow-up mailing containing survey results and prescriber information was sent to all participating physicians to increase awareness and education.

**CONCLUSION:** The utilization of LD quetiapine is common for off-label indications, particularly as a hypnotic or anxiolytic. Prescriber education was provided through survey results and information on appropriate use of quetiapine. Future interventions include intensive educational outreach to high physician utilizers to influence prescribing pattern, and cost analysis.
lipid therapy; and continuous eligibility for 24 months. Patients were grouped by *International Classification of Diseases, Ninth Revision* (ICD-9) codes into CMS diagnosis clusters: lipid disorders (RXHCC19), acute myocardial infarction and unstable angina (RXHCC92), cerebral hemorrhage and effects of stroke (RXHCC102), vascular disease (RXHCC106), and diabetes (RXHCC176&18DM). Using each patient's initial lipid values, treatment effects were modeled upon product labeling for ERN/L (1,000/40 mg, 2,000/40 mg), ERN (1,000, 2,000 mg) and L (40 mg). Optimal lipid values were defined per National Cholesterol Education Program Adult Treatment Panel III, American Heart Association, and American Diabetes Association guidelines, as appropriate, and achievement of combined optimal lipid values across treatments was compared by Pearson's chi-square.

**RESULTS:** We analyzed 24,172 elderly patients: 55% were female, and the mean age for females/males was 75 ± 7/74 ± 6 years, respectively. Baseline lipids (females/males): LDL-C (136 ± 36/123 ± 32 mg/dL); HDL-C (55 ± 15/44 ± 12 mg/dL); TG (155 ± 71/150 ± 75 mg/dL). At baseline, only 6% to 16% of females and 8% to 18% of males achieved combined optimal lipid values across the RXHCC clusters. Modeled treatment significantly increased (P <0.05) optimal lipid value achievement in females: ERN/L 1,000/40 mg: 41%-59%; ERN/L 2,000/40 mg: 48%-63%; ERN 1,000 mg: 16%-33%; ERN 2,000 mg: 24%-45%; and, L 40 mg: 28%-42%. Males demonstrated similar modeled treatment responses.

**CONCLUSIONS:** Based upon product labeling, a greater proportion of elderly males and females across various CMS diagnosis clusters would achieve optimal lipid values with ERN/L compared with individual components.

*MULTIPLE LIPID ABNORMALITIES AS A TARGET FOR INTERVENTION IN PATIENTS UNDER MANAGED CARE*

**Stanek EJ** * Kos Pharmaceuticals, Inc., 1 Cedar Brook Dr., Cranbury, NJ 08512, estanek@kospharm.com, (609) 495-0645

**INTRODUCTION:** Recent data reveal that low achievement of combined optimal low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TGs) due to undertreatment is associated with a 45% increase in cardiovascular events. Although strongly suggestive that a combination lipid-altering therapy approach would be useful, it is unclear how many patients would benefit from this in a managed care setting. Our purpose was to examine the prevalence of multiple lipid abnormalities (MLAs) and the need for combination therapy in a predominantly elderly population.

**METHODS:** Patients were selected from a 2.1 million record managed care database if they had a lipid panel between January 1, 2000, and December 31, 2001; no concomitant lipid therapy; and continuous plan eligibility for 24 months. Optimal lipid values per National Cholesterol Education Program Adult Treatment Panel III, American Heart Association, and American Diabetes Association guidelines: LDL-C <100 or <130 mg/dL per risk level, HDL-C >40 men/50 mg/dL women, TG <150 mg/dL. Four study groups were identified by combined optimal values achieved and manifest suboptimal lipids: Group I–all optimal; Group II–LDL-C suboptimal (lone high LDL-C); Group III–HDL-C and/or TG suboptimal with optimal LDL-C (abnormal HDL-C/TG axis); Group IV–LDL-C plus HDL-C and/or TG (MLA). Group frequencies were determined for the overall, primary, and secondary prevention populations, and these cohorts were compared by chi-square.

**RESULTS:** We analyzed 44,351 patients: 23,403 primary prevention; 20,948 secondary prevention; median age 67 years; 55% ≥65 years; male 50%. Group I-IV frequencies for overall/primary prevention/secondary prevention populations: Group I–11%/13%/9%; Group II–25%/15%/37%; Group III–24%/34%/12%; Group IV–40%/38%/42%, within all groups significant (P <0.05) for primary versus secondary prevention.

**CONCLUSIONS:** The MLA phenotype, consisting of nonoptimal LDL-C plus nonoptimal HDL-C and/or TG, was the most prevalent in this predominantly elderly managed care population. Combination therapy using ≥2 available drugs with diverse effects on LDL-C, HDL-C, and TG appears needed to optimize lipids.

*OBERSATIONAL STUDY OF HYPERTENSION DIAGNOSIS IN PATIENTS NEWLY INITIATED ON SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs) OR SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)*

**Gleason PP** * Prime Therapeutics, LLC, 1020 Discovery Rd., No. 100, Eagan, MN 55121; pgleason@primetherapeutics.com, (651) 286-4190

**INTRODUCTION:** Serotonin norepinephrine reuptake inhibitors (SNRIs, duloxetine, venlafaxine) are associated with dose-dependent increases in the incidence of elevated blood pressure. We compared the risk of a new hypertension diagnosis among SNRI- and selective serotonin reuptake inhibitors (SSRI)-naive members in an observational cohort study.

**METHODS:** Medical and pharmacy administrative claims data from a 1.8 million-member BlueCross BlueShield plan from January 1, 2003, to March 31, 2005, were used to identify SNRI- and SSRI-naive new-start cohorts of members from January 1, 2004, to March 31, 2004 (1Q2004). Using the 1Q2004 SNRI/SSRI initial claim date, treatment-naive was defined as lacking any supply of SNRI/SSRI in the prior 120 days. Additionally, members had no hypertension medical claim in the prior 365 days. All SNRI/SSRI claims from the initial claim forward 365 days were assessed for day-supply gap using a 1.5 days supply multiplier. Each member's SNRI/SSRI duration of therapy was terminated on the first gap date. Development of hypertension was defined as a medical claim with an *International Classification*
INTRODUCTION: The research seeks to characterize the extent to which concomitant drugs are used in the treatment of ADHD. METHODS: Data were drawn from a national medical and pharmacy claims database covering more than 80 managed care organizations and 60 million lives. Patients (75,963) were included if they had continuous enrollment from January 1, 2003, to July 31, 2004; a diagnosis of attention-deficit/hyperactivity disorder (ADHD); and at least 1 claim for an ADHD medication during the study period (July 2003 to June 2004). Patient-level drug claims were assigned to calendar months, and months with usage from multiple classes were identified. To focus on long-term polypharmacy rather than transitional management, the first month of each treatment episode with a given drug was excluded. ADHD drugs were categorized into 6 classes: long-acting stimulants (LASs): 262,818 months of use, atomoxetine (ATX): 72,325 months, intermediate-acting stimulants (IAS): 33,613 months, short-acting stimulants (SASs): 99,305 months, bupropion (BUP): 41,195 months, and alpha-2 agonists (A2A): 27,931 months.

RESULTS: Combination months comprised the following proportions of all non-first months on therapy: 14.2% for patients on LAS, 16.2% on ATX, 25.2% on IAS, 26.7% on SAS, 40.3% on BUP, and 64.7% on A2A. The drug had been initiated in combination or initiated earlier and supplemented with other medications 10.9% of the non-first months on LAS, 6.1% on ATX, 19.3% on IAS, 15.1% on SAS, 25.4% on BUP, and 42.5% on A2A.

CONCLUSION: LASs and ATX are the most likely ADHD medications to be used as monotherapy. While they have similar overall levels of combination use, combination use with ATX is more likely to have arisen from adding it onto another drug than is the case for LASs. This may, in part, reflect the more recent appearance of ATX on the market compared with stimulants.

POLYPHARMACY IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A RETROSPECTIVE CLAIMS ANALYSIS

POLYPHARMACY IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A RETROSPECTIVE CLAIMS ANALYSIS

Omar MA, Novartis Pharmaceuticals Corporation, One Health Plaza, E. Hanover, NJ 07936

INTRODUCTION: We evaluated the extent of postfracture follow-up for osteoporosis after a fracture as well as adherence and persistence of patients with a fracture on any of the following osteoporosis medications:

- SASs (Selegiline, Pargyline, and Tranylcypromine)
- SSRI (Citalopram, Paroxetine, Fluoxetine, Sertraline, and Fluvoxamine)
- SNRI (Venlafaxine and Duloxetine)
- ATX
- BUP
- A2A
- LASs
- IAS

We used a national medical and pharmacy claims database covering more than 80 managed care organizations and 60 million lives. Patients (75,963) were included if they had continuous enrollment from January 1, 2003, to July 31, 2004; a diagnosis of osteoporosis or a fracture (ICD-9-CM codes: 820.08, 824.0, 827.2), and at least 1 claim for a bone-related medication during the study period (July 2003 to June 2004). Patient-level drug claims were assigned to calendar months, and months with usage from multiple classes were identified. To focus on long-term polypharmacy rather than transitional management, the first month of each treatment episode with a given drug was excluded. Osteoporosis medications were categorized into 6 classes: SASs: 262,818 months of use, SSRI: 72,325 months, SNRI: 33,613 months, ATX: 99,305 months, BUP: 41,195 months, and A2A: 27,931 months.

RESULTS: Combination months comprised the following proportions of all non-first months on therapy: 14.2% for patients on SAS, 16.2% on SSRI, 25.2% on SNRI, 26.7% on ATX, 40.3% on BUP, and 64.7% on A2A. The drug had been initiated in combination or initiated earlier and supplemented with other medications 10.9% of the non-first months on SAS, 6.1% on SSRI, 19.3% on SNRI, 15.1% on ATX, 25.4% on BUP, and 42.5% on A2A.

CONCLUSION: SASs and ATX are the most likely osteoporosis medications to be used as monotherapy. While they have similar overall levels of combination use, combination use with ATX is more likely to have arisen from adding it onto another drug than is the case for SASs. This may, in part, reflect the more recent appearance of ATX on the market compared with stimulants.

POSTFRAC TURE FOLLOW-UP AND MEDICATION UTILIZATION PATTERN OF PATIENTS WITH OSTEOPOROTIC FRACTURES IN A MANAGED CARE HEALTH CARE SYSTEM

Omar MA, Novartis Pharmaceuticals Corporation, One Health Plaza, E. Hanover, NJ 07936

INTRODUCTION: We evaluated the extent of postfracture follow-up for osteoporosis after a fracture as well as adherence and persistence of patients with a fracture on any of the following osteoporosis medications:

- SASs (Selegiline, Pargyline, and Tranylcypromine)
- SSRI (Citalopram, Paroxetine, Fluoxetine, Sertraline, and Fluvoxamine)
- SNRI (Venlafaxine and Duloxetine)
- ATX
- BUP
- A2A
- LASs
- IAS

We used a national medical and pharmacy claims database covering more than 80 managed care organizations and 60 million lives. Patients (75,963) were included if they had continuous enrollment from January 1, 2003, to July 31, 2004; a diagnosis of osteoporosis or a fracture (ICD-9-CM codes: 820.08, 824.0, 827.2), and at least 1 claim for a bone-related medication during the study period (July 2003 to June 2004). Patient-level drug claims were assigned to calendar months, and months with usage from multiple classes were identified. To focus on long-term polypharmacy rather than transitional management, the first month of each treatment episode with a given drug was excluded. Osteoporosis medications were categorized into 6 classes: SASs: 262,818 months of use, SSRI: 72,325 months, SNRI: 33,613 months, ATX: 99,305 months, BUP: 41,195 months, and A2A: 27,931 months.

RESULTS: Combination months comprised the following proportions of all non-first months on therapy: 14.2% for patients on SAS, 16.2% on SSRI, 25.2% on SNRI, 26.7% on ATX, 40.3% on BUP, and 64.7% on A2A. The drug had been initiated in combination or initiated earlier and supplemented with other medications 10.9% of the non-first months on SAS, 6.1% on SSRI, 19.3% on SNRI, 15.1% on ATX, 25.4% on BUP, and 42.5% on A2A.

CONCLUSION: SASs and ATX are the most likely osteoporosis medications to be used as monotherapy. While they have similar overall levels of combination use, combination use with ATX is more likely to have arisen from adding it onto another drug than is the case for SASs. This may, in part, reflect the more recent appearance of ATX on the market compared with stimulants.
medications: risedronate, alendronate, or raloxifene.

METHODS: Health care claims from January 1998 to December 2001 were used to select patients who were older than 55 years; identified as having a pelvis, wrist, or vertebral fracture; and continuously enrolled for at least 1 year prior and 3 years post-fracture. We excluded patients with prescription claims for the above-mentioned drugs or medical claims for previous fracture during 1 year prior to index fracture. Outcome measures included percentage of patients with at least 1 postfracture claim for osteoporosis or bone density scan as well as adherence and persistence for those on osteoporosis therapy. Adherence was assessed using the medication possession ratio and persistence defined as the percentage of patients continuing therapy for 12 months with <30 days gap from end of drug supply of the previous refill.

RESULTS: Records indicated that 1,576 patients met the index fracture criteria. After excluding those with a claim for osteoporosis diagnosis and/or bone scan (n = 335) prior to the date of index fracture, we found that within 2 months of fracture, 9.5% had a claim for either osteoporosis or bone scan or both (3.6% diagnosis only, 3.6% bone scan only, 2.3% both). Of the patients with a fracture, prescription records for 194 patients taking one of the drugs of interest were available. Adherence was determined to be 51.8%. Average persistence was 163 days, with 19% of patients persistent at the end of month 12.

CONCLUSIONS: Despite increased risk of second fractures and recommendations for evaluation for osteoporosis, we found that health care claims for osteoporosis diagnoses and bone density scans were not routinely found for patients with fractures, and adherence and persistence with therapy was poor.

PRESCRIBING STIMULANTS FOR CHILDREN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: IMPACT OF PHYSICIAN VISIT CHARACTERISTICS

Unni SK * University of Louisiana at Monroe, 700 University Ave., Monroe, LA 71209; sudhirunni@hotmail.com, (727) 518-4317

INTRODUCTION/PURPOSE: The study objective was to examine the influence of physician visit characteristics on prescribing of stimulants in attention-deficit/hyperactivity disorder (ADHD) among children in the United States.

METHODS: Data from the U.S. National Ambulatory Medical Care Survey was used. Office-based physician visits documenting diagnosis of ADHD (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 314.00 or 314.01) were extracted for 1998 to 2002, for children up to 18 years. Data were collected on length of time (in minutes) spent in physician's office (TIMEMD), counseling provided by physician during the visit (THERPREV), and type of physician office (RETYPOFF) as the predictor variables. The dependent variable was whether or not stimulants were prescribed during that visit (MEDTOT). A logistic regression model was used to analyze the data using SAS version 8.2.

RESULTS: A total of 896 records were identified for analysis. The model was found to be significant (P value of likelihood ratio = 0.0002). The variables TIMEMD and THERPREV were significant (P = 0.0001, 0.0008), whereas RETYPOFF was nonsignificant. The adjusted odds of prescribing stimulants in ADHD decreased by 0.983 for every additional minute spent with the physician (95% CI, 0.975-0.992). Adjusted odds of prescribing stimulants was 1.417 times when counseling was provided by physicians compared with no counseling (95% CI, 1.032-1.945).

CONCLUSION: The prescribing of stimulants in ADHD appears to be related to time spent with and counseling provided by the physician, perhaps due to a better and more accurate diagnosis. The type of office setting was not significant, probably because of a lack of variation in the data for type of office settings.

PRESCRIPTION COMPLIANCE AND PERSISTENCY WITH IMATINIB IN PATIENTS WITH CML AND GIST

Tsang I-P*, Rudychev I. Bayser Consulting, 4709 Golf Rd., Suite 803, Skokie, IL 60076

INTRODUCTION: Compliance and persistency of patients prescribed imatinib (Glivec/Gleevec), an oral molecularly targeted anticancer therapy for the treatment of chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors (GIST), was measured through analysis of patient-level pharmacy claims data.

METHODS: Compliance and persistency were established by analyzing the drug-filling activity of patients compared with the prescribing activity of their physicians using patient pharmacy records (N = 4,043) over a 14-month period (January 2003 through February 2004). Observed daily average consumption (DACON) and average prescribed days of therapy were derived and compared. Compliance and persistency were also established for segments of the population based on their age, gender, and initial imatinib dose prescribed.

RESULTS: Overall, the compliance rate (defined as medication possession ratio) was 75% and persistency (time on therapy without significant gaps in refills) averaged 256 days of therapy over 12 months. Among patients who filled 2 or more imatinib prescriptions, compliance was ≥80%. Forty-one percent of patients were more than 90% compliant. Patients with initial doses of 400 mg/day were found to be the most compliant. The most persistent were those with initial dosages of 400 or 800 mg/day. The DACON fluctuated above and below the recommended dose in approximately 73% of patients.

CONCLUSIONS: This is the first assessment of patient compliance and persistency with prescribed imatinib therapy. While better than most nononcology products, suboptimal compliance and persistency with imatinib poses a threat as doses <300-400 mg may result in lower plasma concentrations than needed to
eliminate malignant cells. Patient compliance and persistency may be compromised by responses to the initial imatinib prescription, poor side-effect management, and patient- or physician-initiated treatment interruptions. Patient support programs and improved communication on treatment expectations could potentially optimize outcomes.

**PRESCRIPTION DRUG COPAYMENTS AND ADHERENCE AND PERSISTENCE TO STATIN THERAPY**

**INTRODUCTION:** To assess the effects of statin copayments at the index prescription (initial prescription for new/incident patients) and the increase in copayments over time on statin adherence and persistence among individuals with employer-based insurance.

**METHODS:** A retrospective study based upon medical and pharmacy claims for continuously enrolled statin users from the 2001-2003 Medstat MarketScan database. Generalized estimating equation logit models were used to estimate the effects of changes in copayments on statin adherence (derived from the medication possession ratio) using a panel data framework. Cox proportional hazards models were used to study the effects of copayments on persistence (time until discontinuation). Separate estimates were produced for patients with no prior use of statins (new patients, n = 142,341) and patients with prior use of statins (continuing patients, n = 92,344).

**RESULTS:** Higher copayments were associated with reductions in adherence and persistence to statin therapy. New patients were more price sensitive than continuing patients (odds ratio [OR]: 0.911, P < .01 new patients; 0.996, P = .45 continuing patients). The size of the index or starting copayment had a larger effect on adherence (OR: 0.814, P < .01) than the increase in copayments over time (OR: 0.919, P < .01) and higher statin copayments were also associated with a significant increase in the hazard of statin discontinuation (hazard ratio: 1.58, 95% confidence interval, 1.525-1.632) for new patients.

**CONCLUSIONS:** Higher copayments serve as a financial barrier to compliance with statin therapy for new and continuing statin users. The copayment size at initiation of statin therapy can play a significant role in statin compliance. Adherence to a statin regimen has been associated with a reduction in cardiovascular events and procedures; therefore, the implications of higher copayments on compliance to statin therapy should be considered by policy makers and plan managers.

**PROPRIETY SCORE MATCHING AND MULTIVARIATE ANALYSIS: COMPLEMENT OR SUBSTITUTE?**

**INTRODUCTION:** Since, in observational studies, assignment of subjects to the treatment and control groups is not random, the estimation of effects of treatment may be biased by the existence of confounding factors. Propensity score matching and multivariate analysis are 2 common approaches to remove heterogeneity by controlling for observables. This study assesses whether multi-variate analysis should be used as a complement or a substitute to propensity score to isolate treatment effect.

**METHODS:** A retrospective database analysis was done using Medstat’s Market Scan Commercial Claims and Encounters database. In particular, asthma and nonasthma cohorts are selected to estimate burden of illness by using propensity score matching and multivariate analysis. We examined 2-to-1 matching, nearest-neighborhood matching (NNM) with replacement, Mahalanobis matching (MM), MM with calibers, stratification method, kernel matching, and radius matching. Then we used multivariate analysis as a complement and ran general linear models over the matched group. We also used multivariate analysis as a substitute and ran GLM models over the unmatched group. Burden of illness results were then compared.

**RESULTS:** Asthma patients have higher expenditures than control groups. Using multivariate analysis as a complement, estimated expenditures ranged from $3,754 to $5,157, with standard errors ranging from $994 to $1,232, depending on the type of matching techniques used prior. Multivariate analysis as a substitute yields an expenditure of $4,247 with the smallest standard error ($489).

**CONCLUSION:** The growing attention on Phase IV studies increased the popularity of the propensity score matching technique, which created a quasi-randomized experiment from the retrospective data set. This study showed that multivariate analysis could be a good substitute for the propensity score matching technique with good controls and flexible functional forms.

**PSORIATIC ARTHRITIS PATIENTS TREATED WITH ETANERCEPT HAVE REDUCTIONS IN CAREGIVER BURDEN, HEALTH CARE RESOURCE UTILIZATION, AND ABSENTEEISM**

**INTRODUCTION:** To evaluate the effect of etanercept on health care resource utilization (HRU), caregiver burden, and absenteeism in psoriatic arthritis patients in a multicenter, open-label study.

**METHODS:** Patients received etanercept 50 mg weekly for 24 weeks. At each visit, patients described the number of sick days, health care resource utilization, changes in job responsibilities because of psoriatic arthritis, paid assistance with housework, and assistance from friends or family since the last visit. HRU was
Abstracts From Professional Poster Presentations at AMCP's 18th Annual Meeting & Showcase

compared using the Wilcoxon signed rank test as were mean sick days per month for patients working ≥20 hours per week at baseline; the percentage requiring assistance was compared using the McNemar test.

**RESULTS:** 1,122 patients with active psoriatic arthritis enrolled. The mean number of sick days per month decreased from 0.8 at baseline to 0.6 at week 24 (P = 0.0002) as did the proportion of patients reporting a change in job responsibilities because of psoriatic arthritis (3% at baseline, 2% at week 24; P < 0.0001). At week 24, fewer patients (11%) reported having paid someone to help with housework than at baseline (21%; P < 0.0001). The percentage of patients who reported a friend or family member taking time off from work to provide care or transportation decreased from 8% at baseline to 3% (P < 0.0001) at week 24. Reductions were seen in all categories of HRU. Mean emergency room or urgent care visits, mean physician's office visits, mean nurse practitioner or physician assistant visits, and mean psychologist, naturopath, acupuncturist or chiropractor visits over the past 6 weeks all declined from baseline to week 24 (P < 0.0001). Mean visits by a health professional in the subject's home over the previous 3 months declined from 0.04 at baseline to 0.01 at week 24 (not statistically significant).

**CONCLUSIONS:** Psoriatic arthritis patients have substantial disease burden, including caregiver burden, absenteeism, and HRU, which is meaningfully reduced by etanercept treatment.

***PSYCHOSOCIAL CORRELATES OF PERSISTENCE WITH STATIN THERAPY WITHIN A MANAGED CARE SETTING***
Arjuni RV,* AstraZeneca, 5521 Reseda Blvd., Suite 202, Tarzana, CA 91356

**OBJECTIVE:** To document medication-related knowledge, attitudes, and practices of health maintenance organization (HMO) members recently prescribed a statin and to assess if these constructs are predictive of medication persistence.

**METHODS:** HMO members identified as “statin new starts” (a pharmacy claim for a statin with no prior claims for lipid therapy during the previous 12-month period) were invited to participate in a telephone survey. Interviews were successfully completed on 150 health plan members, with no systematic differences detected between survey respondents and nonrespondents. The survey included sociodemographic background characteristics; National Cholesterol Education Program risk classification items; constructs from the Health Belief Model, including patients’ perceived susceptibility/severity of heart disease; perceived benefits and barriers of taking cholesterol-lowering medication; and the 4-item Morisky medication compliance scale.

**RESULTS:** At 6 months postinitiation of therapy, follow-up pharmacy claims data were available for 133 patients, of which 42.1% were classified as persistent (never experiencing a gap of greater than 59 days between refills for a 30-day supply of medication). A step-wise logistic regression identified 5 statistically significant predictors of 6-month persistence, including: (1) Morisky compliance scale, (2) concerns about medication side effects, (3) age, (4) perceived susceptibility, and (5) gender. The odds of being classified as nonpersistent were higher among respondents endorsing one or more of the 4 items in the Morisky scale, those who “strongly agreed” that they were concerned about side effects from the statin, younger patients, those who “strongly agreed” that they were much less likely than similarly aged individuals to develop heart disease, and females.

**CONCLUSIONS:** A small number of psychosocial correlates obtained in close proximity to initiation of statin therapy can accurately identify the subset of patients who are at high risk of nonpersistence. Implementation of a simple survey can be an effective strategy to implement within the context of a comprehensive disease management program.

***REAL-WORLD DOSING PATTERNS FOR SELF-ADMINISTERED ANTI-TUMOR NECROSIS FACTORS***

**PURPOSE:** The purpose of this analysis was to assess real-world dosing patterns for self-administered anti-tumor necrosis factors (TNFs).

**METHODS:** Retrospective analyses of National Data Corporation's (NDC's) database were conducted. Patients with a pharmacy claim for etanercept (25 mg, 50 mg) or adalimumab (40 mg) for various therapeutic areas, including rheumatology, gastroenterology, and dermatology, from November 2004 through June 2005 were analyzed. Prescription claims were stratified into 3 cohorts: new, continuing, or switched. Patients in the new prescription cohort were those without a claim and patients in the continuing cohort were those with a claim 3 months preceding the study period. Patients in the switched prescription cohort were defined as those switched from 25 mg to 50 mg etanercept. Average dose per patient and percentage deviation from reference dosing were calculated for etanercept (25 mg, 50 mg) and adalimumab for each cohort and therapeutic area.

**RESULTS:** For both drugs, patients in the new cohort had greater dose deviations and higher average doses than those in the continuing cohort across all therapeutic areas. Among patients in the new cohort, both agents had doses well above the reference dose. Dermatology patients utilized the highest average dose for both drugs. Among dermatology patients in the new cohort receiving the etanercept 50 mg formulation, the average dose was 97% higher than the once-weekly reference dose. Etanercept patients in the 25 mg-continuing cohort received doses that were slightly below the twice-weekly reference dose, and those in the 50 mg-continuing cohort received doses that were 10% above the once-weekly reference dose. In the adalimumab-continuing cohort, doses were 11% above the 40 mg every-other-week reference dose.
CONCLUSIONS: Overall, in the cohorts examined through a retrospective review of 8 months of claims data, this study illustrates that doses well above reference dose are commonly prescribed for the self-administered anti-TNFs.

■ REDUCING POLYPHARMACY IN A MEDICAID POPULATION

Bae SU. * CalOptima Department of Pharmacy, 1120 W La Veta Ave., Orange, CA 92868; sbae@caloptima.org, (714) 246-8471

INTRODUCTION: This study investigates the impact of intervention via drug profile review letters written by a clinical pharmacist as a part of the ongoing effort to reduce polypharmacy in an outpatient Medicaid population.

METHODS: Drug profiles of members requesting an exemption from the monthly limit of 8 prescriptions were reviewed by a clinical pharmacist to assess drug appropriateness, potential interactions, and compliance with evidence-based treatment guidelines. A drug profile review letter along with recommendations was sent to the prescriber of members identified with polypharmacy. Acceptance rate of recommendations and cost impacts of changes made in drug therapy are reported.

RESULTS: During the 1-year period from January 1, 2004, to December 31, 2004, we reviewed drug profiles for 1,512 members requesting exemption from the monthly medication limit, and 116 polypharmacy review letters were sent to prescribers. From the 116 review letters sent, 70 prescribers (60%) discontinued one or more medications as per recommendations made in the review letters, and 37 prescribers (32%) did not take the recommendations. Nine members (8%) were not included or were no longer eligible for the plan. Cost savings based purely on monthly cost of discontinued medications was estimated at $89,700. Estimated average cost saving was $770 per member per year.

CONCLUSIONS: The polypharmacy review letters for targeted members resulted in a reduction of polypharmacy, based solely on drug cost savings. The full impact of drug therapy management such as in terms of avoidance of potential adverse drug reactions, increasing awareness of polypharmacy among our prescribers, and possible enhancement on adherence to compliance are difficult to assess.

■ REDUCTION OF INAPPROPRIATE DRUG USE THROUGH FORMULARY MANAGEMENT

Eletrcby JM*, Santoro JE. CalOptima Department of Pharmacy Management, 1120 W La Veta Ave., Orange, CA 92657

OBJECTIVE: To measure the impact of formulary management on inappropriate use of propoxyphene or propoxyphene combinations in the elderly population.

METHODS: A Medi-Cal managed care plan in California, after submission to and approval from the Pharmacy & Therapeutics (P&T) Committee sought to remove propoxyphene or propoxyphene combinations from the approved drug list for patients aged 65 years and older. Approximately 1 month after P&T approval, prior authorization was required for new prescriptions of propoxyphene or propoxyphene combinations for members aged 65 years and older, and effective 4 months after P&T approval, a prior authorization was required for existing prescriptions of generic Darvocet N for members aged 65 years and older. This recommendation was a result of findings widely published in medical literature that propoxyphene is potentially inappropriate for the elderly due to central nervous system-related side effects.

RESULTS:

<table>
<thead>
<tr>
<th>Date Range</th>
<th>No. of Unique Members</th>
<th>No. of Rxs Filled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of propoxyphene or propoxyphene combinations at baseline (3-month duration)</td>
<td>1,136</td>
<td>1,905</td>
</tr>
<tr>
<td>Use of propoxyphene or propoxyphene combinations after prior authorization requirement for new prescriptions (3-month duration)</td>
<td>549</td>
<td>1,055</td>
</tr>
<tr>
<td>Use of propoxyphene or propoxyphene combinations after prior authorization requirement for existing prescriptions (3-month duration)</td>
<td>164</td>
<td>308</td>
</tr>
<tr>
<td>Decrease (overall)</td>
<td>972</td>
<td>1,597</td>
</tr>
<tr>
<td>% decrease (overall)</td>
<td>86%</td>
<td>84%</td>
</tr>
</tbody>
</table>

Rx = prescription.

CONCLUSIONS: Numerous studies have been published about the extent of inappropriate drug use in the elderly population. Exploring the use of effective formulary management to reduce inappropriate drug use is an important step toward improving quality of care in the elderly population.

■ TIMELINESS OF CHILDHOOD IMMUNIZATIONS AMONG CHILDREN EXPOSED TO COMBINATION VACCINES AND SINGLE-AGENT VACCINES IN A MANAGED CARE HEALTH PLAN

Happe L. * Applied Health Outcomes, 4114 Woodlands Pkwy., Suite 500, Palm Harbor, FL 34685

INTRODUCTION: Coverage rates for childhood vaccinations are at an all-time high of 81% (National Immunization Survey, 2004); however, only 26% of children receive all vaccinations on time or acceptably early, based on the ACIP/AAFP/AAP Recommended Childhood and Adolescent Immunization Schedule. Delayed vaccinations not only contribute to children not completing the recommended schedule, but may also place children at risk for vaccine-preventable diseases. The DTaP-HepB-IPV combination vaccine has the potential to positively impact immunization timeliness.

METHODS: Children who were enrolled for 24 months following birth were identified from administrative claims of IHC Health...
Plans, Inc., an integrated nonprofit health plan, from January 2003 to September 2005. Children receiving at least 1 dose of a single-agent vaccine and not receiving a combination DTaP-HepB-IPV vaccine were assigned to the “single-agent” cohort, while children receiving at least 1 dose of combination DTaP-HepB-IPV vaccine were assigned to the “combination” cohort. Timeliness of DTaP, HepB, and IPV administration over 24 months was evaluated by comparing actual vaccination dates with the recommended schedule (Luman et al. JAMA. 2005;293:1204-11). RESULTS: A total of 3,407 children were identified (combination cohort, n = 1,135; single-agent cohort, n = 2,272). Overall, 48.4% of children experienced delays in 4-dose series DTaP, 17.9% in 3-dose series HepB, and 18.6% in 3-dose series IPV. The comparable rates reported by Luman et al. were 47.9%, 28.0%, and 32.5%, respectively. In the combination cohort, significantly fewer children experienced delayed vaccination compared with the single-agent cohort: 4-dose series DTaP (36.0% vs. 54.6%, P <0.001) and 3-dose series DTaP (22.3% vs. 51.8%, P <0.001), HepB (9.6% vs. 22.0%, P <0.001), and IPV (13.1% vs. 21.3%, P <0.001).

CONCLUSIONS: Combination DTaP-HepB-IPV use was significantly associated with fewer vaccination delays compared with single-agent use. Coverage rates are widely recognized as a quality indicator; however, timeliness of childhood vaccinations may have important implications in reducing the risk of vaccine-preventable disease.

### TITRATION AND PERSISTENCE WITH TAMSULOSIN AMONG MEN WITH BENIGN PROSTATIC HYPERPLASIA IN A LARGE MANAGED CARE POPULATION

**Davis KL, RTI Health Solutions, 200 Park Offices Dr., #218, Research Triangle Park, NC 27709; kldavis@rti.org, (919)541-1273**

**INTRODUCTION:** This study assessed patterns of titration and persistence with tamsulosin, the first U.S. Food and Drug Administration-approved selective alpha-adrenergic blocker indicated for the treatment of benign prostatic hyperplasia (BPH) in a managed care population.

**METHODS:** This retrospective analysis evaluated dosing and refill patterns from medical claims of 33,671 men in the PharMetrics database with a BPH diagnosis and treatment with tamsulosin between October 8, 1999, and January 31, 2005. The rate and magnitude of titrations, medication possession ratio (MPR), and time to discontinuation (defined as a refill gap of >60 days) were estimated. Use of other medications and prostate surgeries following initial prescription were also documented.

**RESULTS:** Among patients with at least 2 valid tamsulosin doses (N = 27,350), 3,522 (12.5%) titrated upward following initial dose, while 946 patients (3.5%) had at least 1 downward titration. Of those with an upward titration, 3,330 (94.5%) had at least 1 doubling of dose. The average dose at first titration was 0.90 mg/day, compared with an average starting dose of 0.44 mg/day across all prescriptions observed. The first upward titration for 1,946 patients (55.3%) occurred within 6 months of initial prescription. Among all patients, 17,158 (50.9%) discontinued tamsulosin, with an average time to discontinuation of 187 days. The average MPR for tamsulosin was 0.42. Among all patients, 6,492 (19.3%) had at least 1 claim for another BPH medication while 2,618 (7.8%) required prostate surgery following initial tamsulosin prescription. Transurethral resection of the prostate was the most common, representing 77.6% of all surgeries received.

**CONCLUSIONS:** Results indicate that more than 10% of BPH patients who start on tamsulosin require an upward dose titration, and approximately half appear to take a drug holiday at some point during treatment. Cost of therapy and potential side effects that result from dose escalation should be considered in a drug with high utilization.
and its partner have instead elevated the communication process to a valuable teaching tool. Providers better understand the plan's clinical guidelines, and future prescribing patterns are impacted. **CONCLUSIONS:** An important part of the plan's Health Plan Employer Data and Information Set (HEDIS) scores reflected in their accreditation outcome is a measurement of access to the care and services members need. Through automation of the process, access to care is enhanced by more timely approvals as well as through enhanced provider education.