Weight Uniformity of Split Tablets Required by a Veterans Affairs Policy

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Do Decision-Analytic Models Identify Cost-Effective Treatments? A Retrospective Look at Helicobacter Pylori Eradication

Evaluation of Personal Digital Assistant Drug Information Databases for the Managed Care Pharmacist
C O N T E N T S

■ ORIGINAL RESEARCH
401 Weight Uniformity of Split Tablets Required by a Veterans Affairs Policy
James E. Polli, PhD; Sharon Kim, BA; and Brian R. Martin, PharmD

408 Selected Characteristics of Senior Citizens’ Prescription Drug Payment and Procurement in 1998 and 2001
Jon C. Schommer, PhD; David A. Mott, PhD; Richard A. Hansen, PhD; and Richard R. Cline, PhD

416 Physician Perceptions of the Use of Medications for Attention Deficit Hyperactivity Disorder
Karen M. Stockl, PharmD; Tom E. Hughes, PhD; Manal A. Jarrar, BA; Kristina Scenik, RPh, PhD; and Amy R. Perwien, PhD

424 Patient Adherence With Amlodipine, Lisinopril, or Valsartan Therapy in a Usual-Care Setting
Jenifer Wogen, MS; Charles A. Kreilk; Richard C. Livornese, MS; Krista Yokoyama, PharmD; and Feride Frech, MPH, RPh

■ FORMULARY MANAGEMENT
430 Do Decision-Analytic Models Identify Cost-Effective Treatments? A Retrospective Look at Helicobacter Pylori Eradication
Kathleen A. Fairman, MA, and Brenda R. Motheral, PhD

■ CONTEMPORARY SUBJECT
441 Evaluation of Personal Digital Assistant Drug Information Databases for the Managed Care Pharmacist
Colleen M. Lowry, PharmD; Maria D. Kostka-Rokosz, PharmD; and William W. McCloskey, PharmD

■ DEPARTMENTS
385 Publisher’s Letter
Judith A. Cahill, CEBS

386 Cover Impressions
Ebbescent Blush (1995)
Lissa Perkins
Shelia Macho

449 Editorial
● Using Decision-Analytic Models Wisely
Fzar Hakim, PhD

451 Editorial Subjects—In This Issue
● Pharmacoconomics—Determination of the Cost-Effectiveness of Helicobacter Pylori Eradication
● Formulary Management Methods and Pharmacoconomics

457 Letters

460 Abstracts From Professional Poster Presentations at AMCP’s 2003 Educational Conference

481 Managed Care Pharmacy Residency and Fellowship Programs
EDITORIAL MISSION

JMCP publishes peer-reviewed original research manuscripts, subject reviews, and other content intended to advance the use of the scientific method, including the interpretation of research findings in managed care pharmacy. JMCP is dedicated to improving the quality of care delivered to patients served by managed care pharmacy by providing its readers with the results of scientific investigation and evaluation of clinical, health, service, and economic outcomes of pharmacy services and pharmaceutical interventions, including formulary management. JMCP strives to engage and serve professionals in pharmacy, medicine, nursing, and related fields to optimize the value of pharmaceutical products and pharmacy services delivered to patients.

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**JMCP Achieved a Significant Milestone in July 2003—**
**MEDLINE Indexing**

I am pleased to announce that the Journal of Managed Care Pharmacy has been approved for Index Medicus and MEDLINE indexing, including articles, editorials, letters to the editor, and supplements. Indexing in MEDLINE, the major component of the National Library of Medicine's (NLM's) PubMed and the online counterpart to Index Medicus, has been a long-time goal for JMCP and AMCP because MEDLINE indexing will allow JMCP's original research, subject reviews, and other relevant content to be disseminated to a much wider, international audience. Since MEDLINE indexing is accorded only to those publications adhering to the most rigorous standards of content validity and originality and editorial and production integrity and quality, it is AMCP's distinct honor to have its official publication share this noteworthy status with the best periodicals in the pharmacy and medical fields.

NLM, on the campus of the National Institutes of Health in Bethesda, Maryland, is the world's largest medical library. A national resource for all U.S. health science libraries through a National Network of Libraries of Medicine, it collects materials in all areas of biomedicine and health care as well as works on biomedical aspects of technology, the humanities, and the physical, life, and social sciences. The collections include more than 6 million items—books, journals, technical reports, manuscripts, microfilms, photographs, and images.

The MEDLINE database contains more than 12 million journal article references and abstracts from about 4,500 journals, going back to the early 1960s. Through the Web site (http://www.nlm.nih.gov), some 400 million searches of the MEDLINE database are done each year by health professionals, scientists, librarians, and the public. JMCP strives to provide timely, reliable information to its approximately 15,000 readers—including managed care pharmacists who are tasked with making important decisions that affect clinical, service, and cost outcomes of patients who are health plan members; educators; clinicians; and researchers. That information will now be searchable via Index Medicus and MEDLINE.

Credit goes to everyone who over the years has contributed to bringing JMCP to the point that it qualified for this distinction. As readers of the publication, you can appreciate how the Journal has evolved. The Academy began the publication in 1995 as the first peer-reviewed journal that documented the practice and principles of managed care pharmacy. Over the years, its format has changed to accommodate the needs of busy readers, who are already overwhelmed by the exploding volume of literature in medicine and clinical pharmacy. The content has improved in quality as well as a result of the thorough peer-review process, which uses a selective assignment of each article to no fewer than three experts in the principal subject matter of the manuscript. Special kudos go to Editor-in-Chief Frederic R. Curtiss, PhD, RPh, CEBS, and his staff—Tamara Faggen, managing editor; Jennifer Booker, peer review administrator; and Laura Mahoney, graphic designer—who have developed and perfected many of these enhancements.

We anticipate that MEDLINE indexing will make JMCP an even more attractive medium for authors in the academic/research community to submit their manuscripts because of the greater availability of their research to those interested in managed care pharmacy worldwide.

This milestone caps a significant amount of work that has been going on for a number of years, but it’s not the end of our journey—it’s only the beginning. Our objective is to continue to nurture JMCP’s reputation as the premier source of information on the methods and outcomes of managed care pharmacy interventions.

Judith A. Cahill, CEBS
Publisher
Montreal artist Lissa Perkins has a talent for creating images that somehow make sense, even though they defy rational explanation. Her fascinating painting, *Ebbescent Blush*, is a colorful example of fantasy art.

The Art of Fantasy Web site provides the answer to the question, “What is fantasy art?” The word “fantasy” means “unrestrained imagination and fancy (from the Greek phantasia). . . . Fantasy art can appear in many forms—limited only by the imagination. Whether it’s sword-wielding barbarians, mice that dance and talk, fairies, elves, or angels, fantasy art is all around us. It has a long history, from Classical Greek and Roman times through the Renaissance and up through the present day. Fantasy paintings have always been recognized as fine art. In fantasy art, you might find humor, romanticism, adventure, terror, insight, or inspiration, but you will always find imagination!”

Perkins definitely used her vivid imagination when she created *Ebbescent Blush*—and its title. She explained that “‘ebbescent’ has to do with the ebb of the tide and the scent and blush (colors) of the flowers. I make up words for most of my fantasy art.”

*Ebbescent Blush* is very lively and charming—it seems as if Perkins has invited us to share a glimpse of a secret netherworld. Subtle distortions of perspective and whimsical creatures serve to transform the scene into a land of make-believe. A waterfall tumbles toward a narrow stream, which flows past the likes of a blue elephant and a bright pink rabbit. The stream spills into a tide pool containing brightly colored, fanciful fish that can be seen below the surface of the water. Near the top of the painting, the moon and sun are both visible in the night sky, as are a few distant planets. Or perhaps the sun is really a planet as well? Either way, it doesn’t seem to matter in this particular case. Perkins has left plenty of room for interpretation in her composition.

Exotic plants and birds add to the nearly endless detail found in *Ebbescent Blush*. In fact, Perkins has stated that the painting is still a work in progress. She said, “This painting is the most complex I’ve ever done. I started it in ’95, and I’m still touching it up—it’s one of those that never seem to end. It’s half sold to a person who paid half the price, then promptly, and mysteriously, disappeared. I’ve held on to it in the hopes that I might find that person again.”

Perkins said that she had been interested in art since childhood and, after high school, decided to pursue formal training. She enrolled in painting and drawing classes at Dawson College, along with computer art and graphic design classes at Le Centre des Arts Visuels in Montreal. She remarked, “I originally worked with colored pencil and ink but fell in love with acrylics after my first painting class. I still like to draw very detailed illustrations in pencil but focus mainly on acrylic painting and papier-mâché sculpture.”

Perkins has created her own Web site, named Shmooglepuss Design. It’s a delightful smorgasbord of her paintings, murals, sculptures, digital art, and drawings. She mentioned that her murals are the latest addition to her artistic repertoire. She said that, “…since I’ve found it difficult to cram all these beasties onto one canvas, I’ve started doing whole walls.”

Perkins’s future plans include researching the possibility of illustrating children’s books and exhibiting her work in a solo show. Some of her paintings are currently on display and available for purchase at the Crossroads bistro in Montreal. She said that exhibiting her paintings at Crossroads has been a mixed blessing because they’re selling so well she doesn’t have enough of them left for a solo show at a gallery.

A framed print of *Ebbescent Blush* will be on display in the AMCP conference registration area of the Montreal Convention Center at AMCP’s 2003 Educational Conference in Montreal, October 15-18, 2003.

Be sure to visit Perkins’s Web site at www.shmooglepuss.com to see her other distinctive artwork. She also has a virtual guest book on the site for visitors to sign and leave messages. One visitor’s comment reads, “What I have witnessed so far [of your artwork] is intriguing … keep shooting for the moon, and when you get there send me a postcard.” And chances are he will receive a lunar postcard from Lissa Perkins someday.

Sheila Macho
JMCP Contributing Editor

**Cover Impressions**

**About our cover artist**

*Lissa Perkins, Ebbescent Blush, acrylic on canvas. Montreal, Quebec, Canada. Copyright 1995.*

**Cover Credit**


**Sources**

Interview with the artist.
www.shmooglepuss.com
www.bnr-art.com/fantasy.htm
www.canadiancreative.com/ccsite/visualarts/lissa-perkins.shtml
**Editorial Content and Peer Review**

All articles in *JMCP* undergo 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
- Letters

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

**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**

Editorials should be relevant to managed care pharmacy and address a topic of contemporary interest; these submissions are peer reviewed.

**Letters**

These submissions may be peer reviewed for accuracy. If the letter addresses a previously published article, an author response may be appropriate.

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*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.
JMCP Author Guidelines

**JMCP** accepts for consideration manuscripts prepared according to the Uniform Requirements for the Submission of Manuscripts to Biomedical Journals.1

### Manuscript Preparation

Manuscripts should include, in this order, a title page; an abstract of no more than 400 words; text, references, tables, figures, and graphs; and financial disclosures and conflicts of interest (see Submission Checklist for details).

**JMCP** abstracts should be written narratives that contain the information described for each type of article shown below, where applicable. For descriptions of editorial content, see “JMCP Editorial Policy” in this journal or at www.amcp.org/jmcp/ep.pdf.

**Original Research**

An abstract is required in the format of:
- Objective
- Methods
- Results

**Subject Reviews**

An abstract is required, generally in the format of:
- Objective
- Conclusion
- Summary
- Keywords

**Formulary Management**

An abstract is required in the format of Original Research or Subject Reviews, depending upon the subject matter.

**Contemporary Subjects**

An abstract is required in the format of Original Research or Subject Reviews, depending upon the subject matter.

**Editorials**

These submissions require no abstract.

**Letters**

These submissions require no abstract or title page.

### Reference Style

References should be prepared following modified **AMA** style. Shown below are examples of common types of references:

1. Standard journal article
   (List all authors when 6 or less; if more than 6, list only the first 3 and add et al.)
   Lennard EL, Feinberg PE. Overview of the New York State program for prescription drug benefits. 

2. No author given
   Managed Healthcare. 1994(Sep);4(9):64.

3. Journal paginated by issue
   Corrigan PW, Luchins DJ, Malan RD, Harris J. 
   Managed Healthcare. 1994(Sep);4(9):64.

4. Book or monograph by authors

5. Book or monograph with editor, compiler, or chairman as author
   Chernow B, ed. Critical Care Pharmacotherapy. 
   Baltimore, MD: Williams & Wilkins; 1995.

6. Chapter in a book
   Pharmacotherapy: A Pathophysiologic Approach. 
   Norwalk, CT: Appleton & Lange; 1992:1811-12.

7. Government agency publication
   NIH NHLI-60-2185-84.

8. Dissertation or thesis

9. 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.

### Submission of Manuscripts

A paper copy of the manuscript, including origination of figures and tables, should be submitted to the **JMCP** Peer Review Administrator at the Academy of Managed Care Pharmacy at 100 North Pitt Street, 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 send an electronic version of the manuscript, either on a disk or via e-mail to jmcp@jabong.org. All text should be in a word processing program (preferably Microsoft Word). Tabular material also should be 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. We cannot accept PowerPoint graphics. Please identify the format (PC or MAC), all programs used, and all file names.

**Cover letter:** the corresponding author should
- briefly describe the importance and scope of the manuscript,
- certify that the paper has not been accepted for publication or published previously and that it is not under consideration by any other publication, and
- identify the nature and extent of any financial interest or affiliation that any author has with any company, product, or service discussed in the manuscript.

All manuscripts are reviewed prior to peer review. Manuscripts may be returned to authors prior to peer review for clarification or other revisions. Peer review generally requires 4 weeks but may extend as long as 8 weeks in unusual cases. Solicited manuscripts are subject to the same peer-review standards and editorial policy as unsolicited manuscripts.

### Submission Checklist

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

- **Cover letter**
  - Manuscript: prepared in 10- or 12-point type, double-spaced (on disk or sent via e-mail to jmcp@jabong.org), including
    - title page with identification of all authors (with academic degrees and preferred credentials, position title, name of employer, city and state) and complete contact information for the corresponding author (mailing address, telephone and fax numbers, and e-mail address)
  - abstract: no more than 400 words
  - keywords: follows the abstract
  - references: cited in numerical order as they appear in the text and prepared following modified **AMA** style
  - 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); match symbols in tables and figures to explanatory notes, if included
  - Disclosures and conflict of interest: completed and signed author attestation forms (available at www.amcp.org/jmcp/ep.pdf); clearly indicate source(s) of funding and financial support.

**REFERENCE**

Overview of Chronic Obstructive Pulmonary Disease: New Approaches to Patient Management in Managed Care Systems

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ABSTRACT

OBJECTIVE: To split several tablet products relevant to the Veterans Affairs (VA) Maryland Healthcare System and assess whether the resulting half tablets provide equal doses.

METHODS: From a VA list of products that are required to be split, 7 products were evaluated, along with 5 other commonly split tablet products. A trained pharmacy student split tablets using a tablet splitter provided by the VA. Half tablets were assessed for weight uniformity.

RESULTS: Of the 12 products subjected to splitting, 8 products (atorvastatin, citalopram, furosemide, glipizide, metoprolol, paroxetine, sertraline, and warfarin) yielded half tablets that passed the weight-uniformity test. The 4 failing products were lisinopril, lovastatin, rofecoxib, and simvastatin. Unusual tablet shape and high tablet hardness predisposed products to failing the weight-uniformity test. The 4 failing products resulted in half tablets that were generally within 20% of their target weight range, suggesting that splitting these specific products would not result in adverse therapeutic effects due to dose variation created by tablet-splitting.

CONCLUSION: Split-tablet results were relatively favorable and generally support a VA practice to split specific tablets. Public quality standards for half tablets, including their content uniformity, are needed to better delineate the policies for acceptable tablet splitting.

KEYWORDS: Tablet splitting, Weight uniformity, Tablet-weight uniformity, Veterans Affairs

J Managed Care Pharm. 2003;9(5):401-07

Weight Uniformity of Split Tablets Required by a Veterans Affairs Policy

JAMES E. POLLI, PhD; SHARON KIM, BA; and BRIAN R. MARTIN, PharmD

In recent years, the U.S. Department of Veterans Affairs (VA) has been faced with escalating pharmacy costs. These increased costs are the result of increased enrollment, an aging patient population that requires more prescription medicines, and increased acquisition costs of prescription medicines. The VA has turned to tablet-splitting programs as one approach to contain costs. Several pharmacoeconomic studies have indicated that splitting certain tablets can produce significant cost savings.1-3

A tablet-splitting program was implemented 2 years ago at the VA Maryland Health Care System, which is part of the Veterans Integrated Service Network 5 (VISN 5) region. VISN 5 provides care for veterans in Maryland; Washington, D.C.; eastern West Virginia; Northern Virginia; and south central Pennsylvania.

Candidate drugs were considered for this tablet-splitting initiative if they had a relatively high cost, tablet splitting was not considered to be detrimental to drug release, and the tablets were easily split with a standard tablet-splitting device. VISN 5 now mandates tablet splitting of 8 tablet products for outpatients: atorvastatin, citalopram, lovastatin, paroxetine, rofecoxib, sertraline, sildenafil, and simvastatin. New prescriptions for these products are filled with a tablet that contains twice the prescribed dose, and patients are instructed to take 1 half tablet. A standard tablet-splitting device is also dispensed with the prescriptions. A patient may opt out of the tablet-splitting program if the splitting of tablets proves to be difficult. Also, several other tablets are frequently split, due to cost and therapeutic reasons. Between May 2001 and April 2002, the tablet-splitting initiative directly saved the VA Maryland Healthcare System about $560,000; approximately 41,000 patients received pharmacy services from the health care system during this time.

Equal splitting is presumably necessary for weight uniformity from half tablet to half tablet. We previously found that several commonly split tablets, when split by a razor blade or by hand, usually did not produce evenly split tablet halves.6 We observed that no visible tablet features (e.g., tablet scoring) predisposed a product's half tablets from passing or failing the uniformity test. Rosenberg et al. found tablet splitting to yield half tablets that generally did not meet an expectation for dose uniformity.7 They determined the weights and weight uniformity of tablet halves dispensed by pharmacists. Rosenberg et al. found that only 7 of the 22 dispensed prescriptions met an expectation of accurate tablet halves (defined as less than 15% error) with acceptable weight uniformity (i.e., less than 6% relative standard deviation).

www.amcp.org  Vol. 9, No. 5  September/October 2003  JMCP  Journal of Managed Care Pharmacy  401
From these recent studies, we hypothesized that tablet splitting following practices of the VA Maryland Health Care System would result in half tablets that generally fail to provide acceptable dose uniformity. Specifically, the objective of our study was to split several tablet products relevant to the VA Maryland Healthcare System and assess whether the resulting half tablets provided equal weights. Seven of the 8 mandatory split products in the VISN 5 region (all but sildenafil) were evaluated, along with furosemide, glipizide, lisinopril, metoprolol, and warfarin, which are commonly split at the VA Maryland Healthcare System. Although not mandatory, splitting of these latter 5 products is permissible, at the discretion of the prescriber. Splitting tablets allows for more precise dosage adjustment and greater patient convenience, for example, by eliminating the need for 2 separate prescriptions to achieve a desired dose. For instance, a patient prescribed lisinopril 30 mg daily can take a 20 mg and a 10 mg tablet, which would require 2 copayments since a 30 mg tablet is not commercially available. Alternatively, the patient could be prescribed one and one-half 20 mg tablets daily, which requires only 1 prescription and only 1 copayment.

**Methods**

The following products were donated by either the VA Maryland Healthcare System or the University of Maryland School of Pharmacy: atorvastatin 40 mg (Lipitor, Pfizer, Lot #053X0V), citalopram 40 mg (Celexa, Forest, Lot #M0114M), furosemide 40 mg (Geneva, Lot #114028), glipizide 10 mg (Geneva, Lot #126235), lisinopril 40 mg (Prinivil, Merck, Lot #L14686; generic lisinopril was not available at the time of this study but is now purchased by the VA), lovastatin 40 mg (Mevacor, Merck, Lot #L1143; generic lovastatin was not available at the time of this study but is now purchased by the VA), metoprolol tartrate 50 mg (Caraco, Lot #1333A), paroxetine (Paxil, GlaxoSmithKline, Lot #400019813), rofecoxib 25 mg (Vioxx, Merck, Lot #L1030), sertraline 100 mg (Zoloft, Pfizer, Lot #9JP018A), simvastatin 20 mg (Zocor, Merck, Lot #L1016), and warfarin 5 mg (Coumadin, DuPont Pharmaceuticals, Lot #SP094A).

The previously described tablet-splitting method and acceptance criteria were followed, with the exception that a tablet splitter (ACE-LIFE Pill Splitter model PS12E; Health Enterprises Inc., North Attleboro, MA) was used. This tablet splitter consists of upper and lower platforms, which are connected by a hinge. The lower platform provides for the placement of the tablet within a V-shaped region. A razor blade is centered on the upper platform. A tablet is split by pressing the upper platform onto the lower platform (Figure 1). This model of tablet splitter is distributed to VA patients who are instructed to split tablets. For this study, one trained, supervised pharmacy student (tester) performed all tablet splitting in a controlled laboratory environment. This study design did not employ patients; rather, it employed a trained tester to split tablets, since individual patients are known to vary in their ability to split tablets. In evaluating the hypothesis that tablet splitting would result in half tablets that generally fail to provide acceptable dose uniformity, our methodology represents a best-case approach.

Each tablet was carefully placed in the designed split area of the splitter; in all cases, the aim was to obtain evenly split tablet halves. The tester split Zestril 40 mg tablets to affirm the ability of the tester to obtain the favorable tablet-splitting results reported previously (i.e., weight uniformity that passes the acceptance criteria). If a tablet was scored, the tablet was situated in the splitter such that the blade would cut within the score groove. However, for warfarin and furosemide, splits were also performed when the tablet was randomly placed in the splitter (i.e., random orientation of the tablet score relative to the blade). Also, because of its trapezoid shape, lisinopril (Prinivil) could be placed into the splitter with 2 different orientations; both orientations were evaluated.

The previously applied criteria were followed in assessing whether the resulting half tablets split uniformly. The criteria were adapted from the U.S. Pharmacopeia’s (USP) <905> “Uniformity of Dosage Units” test for whole tablets. Briefly, the test entailed subjecting 30 tablets of each product to the following:

- 30 tablets were weighed. The mean weight per tablet was calculated. The acceptable 85% to 115% range for a perfectly split tablet was determined from this mean weight. All weight measures employed a Mettler AE 100 analytical balance (Mettler Toledo, Inc., Columbus, OH).
- 10 of the 30 tablets were individually weighed. Each tablet was split, resulting in 20 half tablets. Each half tablet was weighed.
- From the 20 half tablets, the number of tablet halves outside the 85% to 115% range was counted. The number outside the 75% to 125% range was also counted. The relative standard...
deviation (RSD) of the half-tablet weights was calculated. If, at most, 1 half tablet was outside the 85% to 115% range, but within the 75% to 125% range, and if the RSD was \( \leq 10.0\% \), the half tablets passed this uniformity test.

- If 2 half tablets were outside the 85% to 115% range (but within 75% to 125% range) or if RSD > 10.0%, the additional 20 tablets were split. To pass, none of the additional 40 half tablets could be outside the 85% to 115% range, and the RSD for all 60 half tablets needed to be \( \leq 10.0\% \).
- If 3 or more of the 20 half tablets were outside the 85% to 115% range, the half tablets failed this uniformity test. Also, if any half tablets were outside the 75% to 125% range, the half tablets failed this uniformity test.

Hence, like the USP “Uniformity of Dosage Units” test for whole tablets, half tablets could fail because of too many half tablets outside the 85% to 115% range, too many half tablets outside the 75% to 125% range, or too high an RSD. However, the criteria applied here are more liberal than the USP test for whole tablets, since the USP test allows an RSD of a maximum 6%. Also, half-tablet weight, rather than chemical assay of actual drug, was evaluated. These 2 aspects facilitate tablet halves to pass the uniformity test. The percent-dose loss due to the splitting process was also monitored. The percent-dose loss was the relative difference between the weight of the original tablet and the combined weight of its 2 half tablets.

### Results

Of the 12 products subjected to splitting, 8 products (67%) yielded half tablets that passed the weight uniformity test. These results generally contrast with previous results where 8 of 11 razor-blade-split products provided half tablets that failed.\(^6\) Tables 1 and 2 list the products that passed and failed, respectively. Using a tablet splitter in this study, all 6 scored tablets passed, while most un-scored tablets failed (4 of 6 failed). This tendency conflicts with a previous observation that no visible tablet features (e.g., tablet scoring, tablet shape) predisposed a product’s half tablets from passing or failing the uniformity test.\(^6\) Among the 3 products included in both our previous and the present study, paroxetine and sertraline each passed in both studies, while atorvastatin failed previously but passed here.

Warfarin and furosemide passed, regardless of how the tablet score was oriented relative to the splitter’s blade (Table 1). For each of these products, results from the random orientation were slightly less desirable than the results from the nonrandom orientation. Lisinopril failed, regardless of how the tablet score was oriented relative to the splitter’s blade (Table 2).

Rofecoxib and simvastatin (Table 2) failed the uniformity test for every reason: too many half tablets outside the 85% to 115% range, too many half tablets outside the 75% to 125% range, and too high an RSD. Lovastatin and lisinopril in one orientation (i.e., the orientation that provided a more stable fit of the Prinivil tablet within the tablet splitter) failed for 2 of these 3 reasons. Lisinopril in the other orientation (i.e., the orientation that provided a poor fit of the tablet within the tablet splitter) failed for all 3 reasons.

### Discussion

**Favorable Tablet-Split Results**

The objective of this report was to split several tablet products relevant to the VA Maryland Healthcare System and assess
whether the resulting half tablets provided equal doses. Our findings here are surprisingly favorable. Using the same criteria applied here, our previous observations from razor-blade splitting showed that a majority of tablets did not split evenly and visible tablet features did not predict a product’s half tablets from passing or failing the uniformity test. Using similar criteria, Rosenberg et al. also observed tablet splitting that resulted in half tablets that generally did not exhibit half-tablet uniformity. Hence, our expectations for this study were low. However, the results are relatively favorable and generally support the mandatory tablet-split policy of the VISN 5 region. Of the 12 products subjected to splitting, 8 products yielded half tablets that passed the weight-uniformity test. For these 8 products, including warfarin, it would appear that motivated and capable patients, under the direction of a pharmacist, would not experience any adverse therapeutic effects due to dose variation from tablet splitting. This conclusion is based on the half tablets of these 8 products exhibiting weight uniformity to whole tablets.

One possible explanation for the differences between this study, where a majority of tablets passed, and our previous results, where a majority of tablets failed, is that the use of a specific model of tablet splitter provided better tablet splitting. However, Sedrati et al. identified several tablet products that, when split using a tablet splitter, resulted in half tablets with doses outside a 85% to 115% range of the target half-tablet dose. Using similar criteria, Rosenberg et al. also observed tablet splitting that resulted in half tablets that generally did not exhibit half-tablet uniformity. Hence, our expectations for this study were low. However, the results are relatively favorable and generally support the mandatory tablet-split policy of the VISN 5 region. Of the 12 products subjected to splitting, 8 products yielded half tablets that passed the weight-uniformity test. For these 8 products, including warfarin, it would appear that motivated and capable patients, under the direction of a pharmacist, would not experience any adverse therapeutic effects due to dose variation from tablet splitting. This conclusion is based on the half tablets of these 8 products exhibiting weight uniformity to whole tablets.

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Possible Role of Tablet Shape and Hardness in Less-Favorable Tablet-Split Results

The 4 products that failed the weight-uniformity standard were lovastatin, lisinopril, rofecoxib, and simvastatin. In contrast to our previous observations that scoring, or any other visible characteristic, could not predict uniformity test results, a tablet score here tended to explain whether a tablet passed or failed the uniformity test. However, we suspect that shape and tablet hardness, and not scoring, were perhaps the true determinants of acceptable uniformity. Relative to the products that split evenly (Table 1), 3 of the 4 failed products (Table 2) have unusual shapes. Lisinopril (Prinivil) is trapezoidal in shape, with no central axis that could provide an even split. Additionally, lisinopril, in either orientation, did not sit well within the tablet splitter; the tablet did not match the angle of the tablet splitter and rocked as the blade cut through the tablet, particularly for the second orientation. Simvastatin’s positioning within the splitter was unstable because of the tablet’s shield shape. In contrast to the unusual shapes of lisinopril and simvastatin, the roundness of glipizide facilitated its favorable positioning within the tablet splitter.

The hardness and spherical shape of rofecoxib resulted in difficult, unreliable splitting. (Tablet hardness was assessed by the tester’s perception of the force required to split the tablets; rofecoxib tablets were deemed the hardest tablets.) Rofecoxib’s extreme hardness required that the tablet-splitter’s blade be firmly pressed into the tablet. Subsequently, this great force caused the tablet to uncontrollably rock as the tablet was cut. Rofecoxib also lost the most tablet residue (i.e., “crumbs”), because of the need to press hard on the tablet splitter.

### Table 2 - Performance of Tablets That Did Not Split Successfully

<table>
<thead>
<tr>
<th>Product</th>
<th>Percent Outliers Beyond 89%-111% (and Beyond 79%-129%)</th>
<th>Percent Dose Loss (a Max)</th>
<th>Observations</th>
<th>Scored (Y/N)</th>
<th>Flat (Y/N)</th>
<th>Tablet Shape</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mevacor 40 mg</td>
<td>15 (0)</td>
<td>10.4</td>
<td>0.9 (3.2)</td>
<td>Failed by a small margin</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Prinivil 40 mg (orientation 1)</td>
<td>20 (0)</td>
<td>13.4</td>
<td>1.5 (7.2)</td>
<td>This orientation provided a good fit of the tablet within the tablet splitter</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Prinivil 40 mg (orientation 2)</td>
<td>40 (10)</td>
<td>15.8</td>
<td>0.6 (1.0)</td>
<td>This orientation provided a poor fit of the tablet within the tablet splitter</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Vioxx 25 mg</td>
<td>50 (20)</td>
<td>21.1</td>
<td>1.9 (6.2)</td>
<td>Thick and hard tablet; most difficult to split since the blade is able to move tablet during splitting</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Zocor 20 mg</td>
<td>20 (10)</td>
<td>15.0</td>
<td>0.00 (1.30)</td>
<td>Difficult to position the tablet in the splitter</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Lovastatin did not exhibit any apparent shape or hardness difficulties, but it marginally failed. Lovastatin is a relatively thick tablet for its small size.

Interestingly, all 4 products from Merck failed, and all non-Merck products passed. These Merck products—lisinopril, lovastatin, rofecoxib, and simvastatin—do not appear to share any one common physical characteristic, except that each has an unusual shape to some extent.

**Lovastatin and Lisinopril: Clinical Considerations**

For lovastatin, 15% of the half tablets exhibited weights greater than ±15% of target. For one orientation of lisinopril within the tablet splitter (i.e., orientation 1, where the top of this trapezoidal-shaped tablet was placed toward the splitter's blade), 20% of the half tablets exhibited weights greater than ±15% of target. The percent RSD for lovastatin and lisinopril half-tablet weights was just over 10%. A similar degree of failure was previously observed with several other products. Cohen has indicated that this degree in half-tablet weight variability is acceptable since therapeutic outcomes would likely be unchanged.

Given the wide therapeutic index of lovastatin and lisinopril, it would appear that splitting these 2 products is acceptable. Gee et al. found that splitting HMG Co-A reductase inhibitors such as lovastatin had no negative effect on lipid panels or liver enzyme tests. Laboratory lipid and liver enzyme tests were conducted before and after 512 patients were enrolled in an HMG Co-A reductase inhibitor tablet-splitting program. Among the patients, 85% of the patients were treated with simvastatin, 15% were taking lovastatin, and 1 patient was administered atorvastatin. Patients were maintained on the same HMG Co-A reductase inhibitor and dose before and after implementation of the program. Laboratory results comparing whole- and half-tablet performance from all 512 patients indicated that there was no change in total cholesterol and triglycerides. Statistically, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) changed favorably, and liver enzymes AST and ALT each increased, although these changes were apparently not clinically significant. These results suggest that a split-tablet program had no effect of HMG (e.g., lovastatin) clinical outcomes.

Rindone found that splitting lisinopril did not change control of stable hypertension. Rindone randomized 28 patients with hypertension, who were on stable doses of lisinopril, into a crossover clinical trial. Patient blood pressures were measured when they were taking whole tablets and split tablets. No statistically significant differences in systolic or diastolic blood pressures were observed between whole-tablet and split-tablet groups.

**Simvastatin: Clinical Considerations**

Relative to lovastatin and lisinopril, tablet-splitting results for simvastatin were less satisfactory (Table 2). Twenty percent of the half tablets fell outside the ±15% target weight range, with half of those half tablets falling outside the ±25% target weight range. However, 3 studies have assessed the clinical performance of split simvastatin tablets and found favorable results. Using retrospective chart review, Duncan et al. evaluated the effect of splitting simvastatin on patient LDL cholesterol and total cholesterol. Patients were taking simvastatin whole tablets and obtained regular lipid management and cholesterol measurements. Patients were converted to split tablets and maintained the same milligram-per-day dose. There was no statistically significant increase in either LDL or total cholesterol after conversion to split tablets; in fact, each laboratory value decreased. Duncan et al. conclude that half-tablet dosing of simvastatin was as effective as whole-tablet dosing. They also found similar findings for atorvastatin.

In a similar study, Rindone and Arriola converted hyperlipidemic patients from fluvastatin to simvastatin, where patients were instructed to use a tablet splitter to split simvastatin tablets in half. In the 56 patients who completed the study, total cholesterol, triglycerides, and high-density lipoprotein were unchanged, with LDL statistically decreasing. Rindone and Arriola indicate that this substantial cost-savings approach, which, in part, relied on splitting simvastatin tablets, exhibited lipid control in the majority of patients. Most recently, Gee et al. measured laboratory lipids and liver enzyme levels in 512 patients who were enrolled in a HMG Co-A reductase inhibitor tablet-splitting program, where 85% of the patients were treated with simvastatin, as described above. These 3 studies, along with the present split-tablet results and wide therapeutic index of simvastatin, support the mandatory tablet-split policy for simvastatin.

**Rofecoxib and Sildenafil: Clinical Considerations**

Rofecoxib tablets provided the least desirable half tablets. Fifty percent of the half tablets fell outside the ±15% target weight range, 40% of those half tablets fell outside the ±25% target weight range. Since rofecoxib has a high therapeutic index, we anticipate that these rofecoxib dose variations will not result in adverse clinical outcomes. The effective daily dose of rofecoxib ranges from 12.5 mg to 50 mg, but the drug is not particularly sensitive to dose. Further, when healthy volunteers were administered up to 5 times the maximum recommended dose for a period of 14 days, no serious toxicities were observed; hence, dose variations from rofecoxib half tablets do not present a toxicity problem.

While sildenafil tablets were not split here and are on the VISN 5 mandatory split list, a clinical study supporting VA policy by Orrico et al. found that the dose of sildenafil citrate could be titrated to the lowest effective dose while incorporating tablet splitting as a method to reduce drug cost. In 96 patients, 58% responded to 50 mg (half tablet) of the drug.

**Further Managed Care Considerations**

To date, the mandatory tablet-splitting program continues to
offer a substantial costs savings to the VA, both on a local and a
national level. Results here support this program, as weight uni-
formity was generally accepted for these products. Tablet-
splitting initiatives offer the VA, and potentially other managed
care organizations, an attractive cost benefit, while maintaining
good health care for health plan members.

As demonstrated here with the several nonmandatory split
products tested, other prescription medications may be suitable
for a tablet splitting program. For a product to be an appropriate
candidate for splitting, several factors should be consid-
ered.1 Sustained-release, enteric-coated, and other dosage forms
where tablet splitting would compromise the products intended
release mechanism should not be considered. The product
should be relatively flat-priced across dose or have an acqui-
sition cost to the organization that would offer a savings by splitt-
ing the higher doses. To maximize savings, tablet splitting
should be preferentially considered for more expensive medica-
tions. Using these criteria, VA and other health care organiza-
tions may prospectively identify prescription medications
where mandated tablet splitting will reduce prescription costs
without compromising patient care.

It should be noted that the VA tablet-splitting program is
cost-neutral to patients. The patient copayment is $7 for a
30-day supply, although some patients are exempt from providing
a copayment because of financial status or service-con-
ected disabilities. Since copayments are based on days of ther-
apy and not drug costs, VA patients do not have a financial
motivation to split tablets. However, patients in other health care
systems, particularly those patients who pay out-of-pocket
for medications, would likely have a greater incentive to utilize
tablet splitting. This motivation would be most pertinent to
those products that are flat-priced, enabling patients to pur-
chase twice the drug supply for a given cost.

■ Limitations

The results of this study generally support the mandatory
tablet-splitting policy of the VISN 5 region but are subject to
limitations. One limitation is that there are no publicly defined
acceptance criteria for half-tablet weight uniformity. Hence,
alternative criteria can be considered and applied to our results.
In our consideration of the data, we applied criteria that we have
used previously.6 These criteria are more liberal than the
USP test for whole tablets, in part since the USP test allows only
an initial RSD of no more than 6%, while the criteria that we
applied allowed 10% RSD. If an initial 6% RSD limit were
applied, several of the products in Table 1 that we found to pass
would require further evaluation (i.e., “Stage 2” testing) and
could possibly fail. Additionally, half tablets were assessed for
dose uniformity immediately after being split; half tablets were
not placed back into a prescription vial, where they may be
subjected to attrition. At this time, we know of no specific evi-
dence to favor any particular acceptance criteria for weight uni-
formity of half tablets. It has been suggested that patients, care-
givers, and health systems would benefit from public quality
standards for half tablets.6,7

A second potential limitation of this study is the use of a
trained pharmacy student to perform the tablet splitting. It is
possible, and even likely, that different outcomes would result,
depending on who performed the splitting. It would be perhaps
desirable to evaluate the ability of various individuals and
patients to split tablets and to elucidate the individual patient
factors that contribute to successful tablet splitting. Given the
positive results of our study, further research would be desirable
to determine if VA patients can obtain similar favorable weight
uniformity to better replicate the real-world environment.
Other studies have assessed the ability of patients to split
tables. McDevitt et al. evaluated the ability of healthy volun-
teers to split hydrochlorothiazide tablets by hand.23 Gender,
age, education, or tablet-splitting experience were not found to
be predictive of the ability of individuals to split tablets. Peek
et al. evaluated the ability of patients to split simvastatin, meto-
prolol, warfarin, and lisinopril tablets.24 Individual patients
were assigned to one of 4 groups that differed in brand of tablet
splitter and whether patients were instructed in the method of
tablet splitting. Peek et al. found that both the brand of the
tablet-splitting device and instruction improved tablet-splitting
accuracy. Patient experience also resulted in more accurate
splitting of warfarin tablets.

A third potential limitation was our use of a specific device
to split tablets. Peek et al. found that one splitter performed
better than another splitter.23 The suggestion that different
tablet-splitting devices can yield markedly different uniformity
results reflects our previous anecdotal experience with a tablet-
splitting device different from the device used in the present
study. In our previous experience, the commercially available
tablet splitter appeared to be of lower quality and poor design;
a razor blade was simply glued onto a plastic housing at an
angle not perpendicular with the plastic housing, resulting,
commonly, in properly centered tablets splitting into approxi-
mately one third/two third “halves.” The poor design and per-
formance of this earlier device caused us to abandon the use of
a tablet splitter and rely on splitting tablets with a simple razor
blade, by hand.6 Hence, we suspect that the quality of the tablet
splitter can directly affect half-tablet weight uniformity, and our
results using the ACE-LIFE Pill Splitter model PS12E may not
be applicable to all tablet-splitting devices.

We also did not measure patient outcomes. Tablet splitting
could have an adverse effect on patient compliance. Several
studies have examined the influence of patient tablet splitting
on compliance and generally indicate that most patients accept
tablet splitting. For example, Carr-Lopez et al. studied 233
patients, aged 35 to 87 years, who were prescribed 40 mg
tables of lovastatin and instructed to split them into two 20 mg
doses.25 Most patients reported that the tablet splitter was easy

406 Journal of Managed Care Pharmacy JMCP September/October 2003 Vol. 9, No. 5 www.amcp.org
to use and did not affect their compliance. However, 6% reported that the tablet splitter was difficult to use, and they would not split tablets even to save money. Mendez et al. found similar results for patients taking half tablets of simvastatin, although 40% of patients believed that splitting would influence compliance.26 Fawell et al. studied the relationship of tablet splitting and compliance, drug acquisition cost, and patient acceptance for fosinopril sodium.27 Patients accepted tablet splitting, and the splitting of fosinopril sodium tablets reduced the drug acquisition costs in the health system without affecting patient compliance.

Another potential limitation is the unknown clinical significance of dose variability in half tablets. The focus of our work was on products relevant to the VISN 5 region. Other products of interest may include drugs with a narrower therapeutic index. Dose variability is expected to be of greater potential importance for drugs with a narrow therapeutic index. Warfarin was evaluated here and is considered a narrow therapeutic index drug. Given the small dose variations observed here for warfarin half tablets and the lack of evidence to suggest any adverse clinical effects of such small dose variations, we anticipate tablet splitting of warfarin to have no clinical consequence.

Conclusion

Previous observations from experience with razor blade tablet splitting showed that a majority of tablets did not split evenly and that visible tablet features did not predict success or failure of the half tablets to pass the weight-uniformity test. However, our results for weight uniformity in the current study were favorable and generally support the mandatory tablet-splitting policy of the VISN 5 region. We interpret our results to indicate that a tablet-splitting policy is a viable approach to provide patients with dosage forms with acceptable weight uniformity. There is, however, a need for quality standards for half tablets to permit health care providers to better delineate the acceptability of tablet-splitting policies.

ACKNOWLEDGMENTS

We thank Alfred Abramson (University of Maryland School of Pharmacy) and Pharmacy Services of the VA Maryland Healthcare Systems for providing tablets for this investigation.

DISCLOSURES

No outside funding supported this study. Author James E. Polli served as principal author of the study. Study concept and design were contributed primarily by Polli and author Brian R. Martin. Analysis and interpretation of data were contributed by Polli and author Sharon Kim. Drafting of the manuscript was the work of Polli and Martin, and its critical revision was the work of Polli and Kim. Statistical expertise was contributed by Polli. Polli has been principal investigator for grants from Forest Laboratories.

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www.amcp.org  Vol. 9, No. 5 September/October 2003  JMCP  Journal of Managed Care Pharmacy 407
Selected Characteristics of Senior Citizens’ Prescription Drug Payment and Procurement in 1998 and 2001

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ABSTRACT

BACKGROUND: People without prescription drug coverage face greater financial burdens and may sometimes be unable to follow the courses of treatment prescribed by their physicians. The U.S. legislature is considering Medicare coverage for prescription drugs and the use of managed care approaches for containing costs associated with senior citizens’ prescription drug therapy.

OBJECTIVE: The purpose of this study was to describe selected characteristics of senior citizens’ prescription drug payment and procurement.

METHODS: Data were obtained via mailed survey from national random samples of senior citizens in 1998 and in 2001. Descriptive statistics and regression analyses were used to describe relationships among study variables.

RESULTS: Of 2,434 deliverable surveys, 946 (39%) were returned. Of these, 700 (29%) respondents provided usable data for analysis. Results showed that in 2001, compared with 1998, the proportion of senior citizens without any prescription insurance coverage did not change significantly, 29% and 32%, respectively. However, the proportion of respondents with prescription drug coverage who had to share costs of prescriptions through copayments and coinsurance rose significantly, from 69% in 1998 to 89% in 2001. Between 1998 and 2001, the proportion of senior citizens using mail-order pharmacies rose significantly, from 17% to 27%, and the proportion who reported financial hardship also rose, from 19% in 1998 to 31% in 2001. Controlling for year, prescription drug use, and income, logistic regression analysis showed that respondents without any prescription insurance coverage were about 5 times more likely to report financial hardship compared with those having coverage.

CONCLUSIONS: The proportion of senior citizens without any prescription drug insurance coverage did not change significantly between 1998 and 2001, but cost sharing in terms of the proportion that had cost-sharing requirements and the amount of the cost sharing through copayments and coinsurance rose significantly. Self-reported financial hardship and the use of mail-order pharmacies among seniors increased between 1998 and 2001.

KEYWORDS: Senior Citizens, Medicare, Prescription drugs, Insurance, Financial hardship, Utilization

J Managed Care Pharm. 2003;9(5):408-15

Researchers have described the financial burden of prescription drug costs for senior citizens (aged 65 years and older)^1^-^1^ and examined the association between prescription drug insurance coverage and patterns of drug use and associated drug expenditures.^2^ The results of this work suggested that insurance coverage for prescription drugs makes a difference in the amount of drugs people obtain, how much they spend on drugs out-of-pocket, and how much is spent in total on their behalf. People with insurance coverage not only obtain more prescriptions than those without coverage, but they also are likely to have access to a broader array of therapies, including more costly therapies. People without prescription drug coverage face greater financial burdens and may sometimes be unable to follow the courses of treatment prescribed by their physicians.

In response to the increased burden of prescription drug costs over time, senior citizens have turned to mail-order pharmacies, prescription drug discount cards, use of generic drugs, purchase of less-expensive prescription drugs from other countries such as Canada, and changed their patterns of drug taking to help decrease the costs of the drugs they use.^1^-^1^ The U.S. Congress is considering Medicare coverage for prescription drugs and the use of managed care approaches for containing costs associated with prescription drug therapy.

Our overall goal for this study was to investigate trends in how senior citizens pay for their prescription medications and how they procure them. To identify emerging trends, we described selected characteristics of senior citizens’ prescription drug payment and procurement in 1998 and again in 2001. Regarding payment for prescription drugs, we compared the proportion of senior citizens who had some type of prescription drug coverage and, for those who reported some type of prescription drug coverage, we compared the proportion that had a cost-sharing component for their coverage and described out-of-pocket copayment amounts and coinsurance amounts for brand and generic prescriptions. Regarding procurement of prescription drugs, we described sources for purchasing prescription drugs with a specific focus on the use of mail-order pharmacy. Also, we estimated and compared the proportion of respondents reporting financial hardship due to procuring prescription drugs.

To add to the existing literature^ using a complementary method of data collection and analysis, we chose to employ multivariate models to assess the association of year (1998, 2001) and respondent demographics with having prescription drug insurance. For respondents with some type of prescription drug insurance, descriptive statistics were used to describe the
addresses were obtained from KM Lists, Inc., a company that randomly in the same manner. The sampling frame and mailing in 2001, 864 individuals aged 65 years and older were selected ed in a systematic random fashion from the U.S. population. In and in 2001 from national random samples of senior citizens. Data were obtained via mailed survey methodology in 1998

Data Collection

Methods

Data Collection

Data were obtained via mailed survey methodology in 1998 and in 2001 from national random samples of senior citizens. In 1998, 1,570 individuals aged 65 years and older were select ed in a systematic random fashion from the U.S. population. In 2001, 864 individuals aged 65 years and older were selected randomly in the same manner. The sampling frame and mailing addresses were obtained from KM Lists, Inc., a company that compiles a complete listing for the United States from publicly available sources, including telephone directories, drivers’ license databases, and other public records. The company continually updates its lists and tests them for validity.

Data collection followed Dillman’s mailed survey method.20,21 The Dillman method is based on the development of survey procedures that create respondent trust and perceptions of increased rewards and reduced costs for being a respon dent, take into account features of the survey situation, and have as their goal the overall reduction of survey error (sam pling error, coverage error, measurement error, and non response error).21 Each sampled person was mailed a survey packet containing a cover letter requesting participation, the survey form, a postage-paid return envelope, and a $1 bill as incentive to participate. A follow-up postcard was mailed 1 week after the first mailing to increase response rate.

Based on the relatively low response rate we achieved in 1998 (29%), we decided to add a tracking number to surveys in order to identify nonresponders in 2001. For those who had not yet responded, a follow-up mailing was sent 3 weeks after the initial mailing to increase the response rate. Thus, our 2001 survey utilized fewer initial sample members but a more thor ough follow-up with nonresponders.

Another addition to the 2001 survey was a question on the cover of the survey instrument in which we asked the recipient of the survey to report the primary reason a person was not able to complete the survey if the sample member was not able to respond. The response categories to this question were: (1) person is physically or mentally no longer able to complete the sur vey, (2) person is now living in a nursing home or other assist ed-living facility, (3) person is deceased, (4) person is no longer at this address for some other reason, or (5) other (please specify). This question allowed us to better understand reasons for nonresponse and the potential for nonresponse bias.

Study Variables

To measure variables related to prescription drug payment (existing prescription drug coverage, cost sharing, and out-of pocket payment levels per prescription), each respondent was asked to report what type of prescription drug insurance (if any) he or she had and associated out-of-pocket costs per pre scription using 6 scenarios (Survey Question). For prescription drug procurement variables, respondents were asked to report their primary source for obtaining prescription drugs. Responses were categorized as (1) large chain (traditional chain pharmacy, mass merchandiser pharmacy, grocery store pharmacy), (2) mail order (mail-order or Internet pharmacy), (3) independent (independent pharmacy), or (4) other (clinic pharmacy or other). Also, respondents were asked to answer yes or no to the following question: “Does obtaining prescription medications cause you any financial hardships?” This deliberately was a sub jective question that allowed us to capture respondents’ perceptions about financial hardship they experienced in purchasing prescription medications.
Selected Characteristics of Senior Citizens’ Prescription Drug Payment and Procurement in 1998 and 2001

For comparison purposes, respondents were asked a series of demographic-related questions. These questions related to the respondents’ age, gender, education, employment status, marital status, income, number of people living at home, race, health insurance coverage for physician visits, number of prescription drugs taken daily, number of over-the-counter (OTC) drugs taken daily, and whether or not they had high blood pressure, arthritis, or a heart condition. These demographic variables were included based on a review of the literature that suggested that these variables could influence the other variables in our study. It should be noted that no adjustments for inflation were made when comparing the 1998 and 2001 data.

For the 2001 survey, we added questions related to out-of-pocket costs for 30-day supplies of medications, deductibles, caps (annual benefit maximums), and tiered copayments that were associated with prescription drug insurance plans. Responses to these additional questions in the 2001 survey could, of course, not be compared with survey responses in 1998 but add information to help interpret our survey findings.

Data Analysis
Descriptive comparisons were made between respondents in 1998 and respondents in 2001 for demographic, drug payment, and drug procurement variables using the Independent Samples t test and chi-square test statistic. Then, to control for any differences in the demographic profile of respondents in 1998 and 2001, a multivariate approach was employed for analysis. Linear regression and logistic regression analyses were used to test the relationships between the independent variables (year and demographic variables) and dependent variables. Goodness of fit for competing linear regression models was assessed based on change in R². Goodness of fit for competing logistic regression models was assessed based on the change in –2 log likelihood and model improvement chi-square statistics. For each regression method, the best-fitting model was chosen based on goodness of fit and parsimony of interpretation. Based on the findings of the multivariate analyses, descriptive statistics were computed to help interpret the results.

Results
Of 2,434 deliverable surveys, 946 (39%) were returned. In 1998, 463 (29%) out of 1,570 surveys were returned, and in 2001, 483 (56%) out of 864 were returned. It should be noted that the discrepancies in rate of return are likely due to our more thorough follow-up in 2001. Of the 946 responses overall, 365 contained usable responses in 1998 (98 had no usable responses) and 335 contained usable responses in 2001 (148 had no usable responses).

Due to the relatively large number of surveys we received with no usable responses in 1998, we added a question on the cover of the 2001 survey asking the recipient of the survey to report the primary reason why a person was not able to complete the survey if the sample member was not able to respond. A total of 132 out of the 148 individuals who were not able to provide usable data provided a reason. Twenty percent reported that the person to whom the survey was addressed was now deceased, 17% reported that the person was physically or mentally no longer able to complete the survey, 7% reported that the addressee no longer lived at the address, 5% reported that the addressee was now living in a nursing home or other assisted-living facility, and the remaining 51% checked “other.” Most of those who checked “other” reported that they were not interested in completing surveys or did not think that the survey applied very much to them because they did not take any medications or received their medications through the military.

Initial frequency counts for the data revealed that the income variable exhibited a relatively high number of missing cases: 87 (12%) out of the 700 surveys. To impute values for the missing cases, a logistic regression equation was developed based on the usable data. Then, the equation was used to predict whether a respondent with a missing income value should be coded as “less than $15,000” or “$15,000 or more.” The analysis presented in this article includes the imputed values.

Respondent Demographics
Table 1 presents comparisons between 1998 and 2001 for respondent demographics. The typical respondent in 2001 compared with 1998 had lower education, was less likely to be white, was less likely to have health insurance for physician visits, used more prescription and OTC medications on a daily...
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reported financial hardship rose from 19% in 1998 to 31% in  
2001 (P<0.01). Logistic regression results (Table 3) showed 
that the best predictors of using mail-order pharmacy were 
year, number of prescriptions currently used, prescription 
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For the subset of respondents with prescription drug insurance coverage, year, number of prescriptions used daily, and income were associated with financial hardship (Table 4). For this subset of respondents, 12% reported financial hardship in 1998 compared with 22% in 2001. Also, 13 percent of these respondents with household incomes of $15,000 or more reported financial hardship compared with 33% of respondents with household incomes less than $15,000 per year. For these respondents with prescription drug coverage, those who reported financial hardship used an average of 4.5 prescriptions daily compared with respondents who did not report financial hardship who used 3.1 prescriptions daily (P<0.01).

**Discussion**

In 1998, 68% of the respondents in this study reported having prescription drug insurance coverage, and, in 2001, 71% reported having such insurance coverage. The U.S. Department of Health and Human Services (DHHS) estimated that 69% of Medicare beneficiaries had prescription drug insurance coverage at some time during the year in 1996. Our estimates for 1998 and 2001 are similar to the DHHS estimate for 1996. These findings suggest that the proportion of senior citizens who had some type of prescription drug coverage did not change significantly from 1996 to 2001.

However, the characteristics of that coverage have changed over time. For example, the proportion of respondents who had to share costs of prescriptions through copayments and coinsurance rose significantly between 1998 and 2001. For those with copayments, out-of-pocket amounts increased significantly for brand-name products between 1998 and 2001 as did coinsurance percentages for generic products. Increasing patient cost sharing for prescription drugs is consistent with recent trends showing that employers have and are planning to increase cost sharing in prescription drug coverage offered to retirees. A fundamental change involves the use of 3-tier copayment benefit structures, mainly increasing copayments for brand-name drugs. As health care costs and, specifically, drug costs continue to increase, it is likely that cost sharing will increase for seniors with drug coverage.

A concern with higher drug costs paid out-of-pocket is the financial hardship that it places on seniors. Our results suggest that the proportion of seniors who report financial hardship related to prescription drugs has increased over time (19% in 1998 and 31% in 2001). Lower-income seniors and higher users of prescription drugs were more likely than their counterparts to report hardship associated with drug costs. Our results also show...
Selected Characteristics of Senior Citizens’ Prescription Drug Payment and Procurement in 1998 and 2001

that insured persons are feeling the hardship of drug costs as well, especially high users of prescription drugs. One explanation for the hardship among insured persons is the increase in the likelihood and amount of cost sharing reported by insured persons between 1998 and 2001. Regardless of insurance status, drug costs are a financial hardship for many seniors, especially for high users of prescription drugs.

Our findings related to prescription drug procurement showed that between 1998 and 2001 the proportion of senior citizens using mail-order pharmacies rose significantly from 17% to 27%. The increase in the use of mail order as a primary source for obtaining prescription drugs also likely is a response to increasing insurance costs. For example, more than 90% of employers who offer prescription drug coverage offered a mail-order option in 2002. Employers, directly or through pharmacy benefit managers, can obtain somewhat lower prescription prices through mail-order pharmacies in an attempt to lower costs and premiums, and thus offer mail order as an option for obtaining prescription drugs. Employers and other drug plan sponsors often provide financial incentives to patients to use mail order by allowing them to obtain a larger quantity (days supply) of a drug per copayment dollar.

To verify this trend in our sample, we added a question to the 2001 survey that asked respondents to provide the out-of-pocket cost for a 30-days supply of each drug product they reported taking. In 2001, out-of-pocket copayment amounts per 30-days supply of prescription drugs averaged $10.33 for mail-order patrons compared with $11.95 for patrons of other pharmacies (not significantly different at a significance level of 0.05). We are limited in our analysis because we did not collect this information in 1998. However, we did verify that differences in cost-sharing amounts between mail order and other channels of procurement largely were due to differences in the days supply of the purchases.

Our assessment of changes in cost sharing between 1998 and 2001 did not include other forms of cost sharing found in drug coverage for seniors. For example, deductibles and annual benefit maximums (“caps”) are common components of Medigap plans that cover prescription drugs. Our survey in 2001 included questions about the presence of deductibles and annual benefit caps associated with drug coverage for seniors. We found that 16% of the 335 respondents in 2001 had a deductible and 8% of the 335 respondents had an annual benefit cap. Deductible amounts ranged from $50 to $1,680 (median = $200). Cap amounts ranged from $500 to $5,000 (median = $1,500). A concern with asking respondents about deductibles and benefit caps is whether they know what these components are and the amounts of the deductibles and caps. Future studies assessing out-of-pocket costs for prescription drugs for seniors could begin to examine methods to reliably obtain this information about deductibles and caps since they are important components of some forms of drug coverage and impact out-of-pocket cost and possibly drug access and use.

Income level was associated with having drug coverage: lower-income seniors were less likely to have drug coverage. Income likely is a factor in obtaining coverage since lower-income seniors may be less able to afford insurance premiums for Medigap coverage. Past studies have shown that income level is positively associated with purchasing any Medigap supplement to Medicare. As of 2000, 26 states had planned or implemented state-level drug assistance programs to help seniors cover the cost of prescription drugs. Commonly, income is a method used to establish eligibility for these programs. As these programs are implemented, it is likely that income will become less of a factor associated with not having drug coverage.

The implications of these trends are not fully known and more research is needed to not only track the trends but also to investigate how increased cost sharing and restrictions in sources for procuring prescription drugs might affect access to medications or patterns of using medications. For example, to what extent does the financial hardship of procuring prescription medications affect the use of drugs for treatable chronic conditions? How does financial hardship affect the treatment of acute conditions? Will increased financial hardship reduce adherence with drug regimens? What are the implications of senior citizens using mail-order procurement for their prescriptions? Can mail-order pharmacy increase the ease with which seniors obtain medications? Are seniors able to access the information they seek about their medications through the mail-order distribution channel?

We propose that continued monitoring of the trends we identified can be helpful for understanding how to make changes in prescription drug insurance plans for seniors in the future. Also, the findings can help us understand how to design managed care methods for improving access to and utilization of prescription medications. From the data we collected, it appears that relatively small changes in out-of-pocket expenditures or in the number of medications prescribed for seniors could have a relatively large impact on their financial hardship, especially for lower-income seniors.

Limitations

The results and our interpretation of them should be tempered with the limitations of the study. The results are based on respondents’ self-reports, raising obvious questions of reliability regarding the type and nature of insurance coverage as well as prescription drug use. We believe that the potential issues regarding reliability in self-reported data were addressed by describing drug insurance types explicitly and asking subjects for not only the number of current drugs used but also to list them by name, as a validity check. We plan to use the results to improve our future questions so that participant response burden is minimized. For example, questions that resulted in a relatively high number of unusable responses will be reviewed for readability and clarity.

Other limitations relate to sampling and selection bias. For example, nonresponders to health surveys may be older and in...
poorer health or, in terms of drug use, may use more medications. Thus, our findings may underestimate drug use for the senior citizen population. Conversely, we found evidence in our study that individuals who did not use any medications decided not to participate because they thought that the survey did not apply to them. Also related to nonresponse bias, we used a more thorough follow-up for the 2001 survey compared with the 1998 survey. Thus, our samples in those 2 years might not be as comparable as desired due to the different levels of follow-up that we employed. For example, results in Table 1 suggest that the typical respondent in 1998 held a higher level of education than the typical respondent in 2001.

The sampling frame and mailing addresses for this study were obtained from a company that maintains a commercial mailing list. Their database is updated continually from public sources such as telephone directories and driver’s license databases. However, by the time we mailed our surveys, it is likely that some members of our sample were deceased, physically or mentally no longer able to complete the survey; were no longer at the address, or moved to a long-term care or assisted-living facility. We estimated that about half of nonresponders fit these categories based on the responses received from individuals who provided reasons why a sample member was not able to complete the whole survey (see Results). Based on feedback from sample members, it appears that the other half of the nonresponder group had other reasons for not completing the survey such as: (1) having no interest in completing surveys, (2) thinking that the survey did not apply to them because they did not take any medications, or (3) thinking that the survey did not apply to them because they received their medications through the military.

CONCLUSIONS

The proportion of senior citizens without any prescription insurance coverage did not change significantly between 1998 (32%) and 2001 (29%). However, the proportion that had to share costs of prescriptions through copayments and coinsurance rose significantly, from 69% to 89%. For those with copayments, out-of-pocket amounts increased significantly for brand-name products between 1998 and 2001 but not for generic products. However, the coinsurance percentages for generic drugs increased between 1998 and 2001. The proportion of senior citizens using mail-order pharmacies rose significantly, from 17% to 27% between 1998 and 2001. The proportion that reported financial hardship also rose from 19% in 1998 to 31% in 2001. Controlling for year, prescription drug use, and income, logistic regression analysis showed that respondents without any prescription insurance coverage were 5 times more likely to report financial hardship compared with those having drug coverage. The trends in payment and procurement for prescription drugs that we identified are consistent with trends in characteristics of coverage available to seniors. Also, the results mirror reports in the lay press about the increasing number of senior citizens who are searching for ways to decrease the financial hardship of obtaining prescription drugs.

DISCLOSURES

Funding for this research was provided by the American Association of Colleges of Pharmacy New Investigator Program and by the University of Minnesota Grant-in-Aid of Research Program and was obtained by authors Jon C. Schommer and David A. Mott. Schommer and author Richard R. Cline are employed by the University of Minnesota. Schommer served as principal author of the study. Concept and design were contributed primarily by Schommer and Mott. Analysis and interpretation of data were contributed by Schommer, Mott, and author Richard A. Hansen. Drafting of the manuscript and its critical revision and statistical expertise were contributed by all authors.

REFERENCES


Background: Attention deficit hyperactivity disorder (ADHD) is a prevalent mental health condition, occurring in 3% to 5% of school-aged children. Although stimulant medications are a recommended treatment for this disorder, physicians’ views of these medications have not been systematically evaluated.

Objective: This study examined physician-prescriber perceptions of using medications to treat ADHD symptoms in children or adolescents.

Methods: A survey was developed with 4 physicians expert in treating ADHD in children. The survey was pilot-tested with a sample of 10 practicing physicians. A sample of 1,000 physicians, with a history of prescribing stimulant medications to children or adolescents, was randomly selected and mailed a 30-item survey. Items were rated on a 7-point response scale (strongly agree, agree, slightly agree, undecided, slightly disagree, disagree, strongly disagree).

Results: A total of 365 physicians responded to the survey, for a 37% response rate. More than 92% of respondents strongly agreed or agreed that ADHD symptoms cause problems in pediatric patients and stimulants are effective in treating ADHD. The stimulant drug side effects of decreased appetite or weight loss, sleep disruption, and exacerbation of anxiety were a concern (strongly agree or agree response) for 32%, 50%, and 22% of physicians, respectively. Diversion of ADHD medication was a concern for 19% of respondents. Physicians reported that controlled medications for children or adolescents with ADHD are a burden for themselves (32% strongly agreed or agreed), for their staff (37% strongly agreed or agreed), and for parents (40% strongly agreed or agreed). Approximately 38% of physicians responded that they would prefer prescribing a nonstimulant medication with a U.S. Food and Drug Administration indication for treating children or adolescents instead of a stimulant medication, and 58% would prefer prescribing a nonstimulated medication that does not have evidence of abuse potential versus one that is controlled and has evidence of abuse potential.

Conclusion: Although physicians overwhelmingly perceive stimulant medications as being effective for treating ADHD symptoms in children or adolescents, many would prefer a nonstimulant medication. While many physicians consider the side effects of the stimulants easily managed, others are concerned about prescribing stimulants because of their side effects, risk of diversion, and administrative burden. The majority of physicians would prefer to prescribe a noncontrolled medication without abuse potential instead of a controlled medication to treat children or adolescents with ADHD.

Keywords: Attention deficit hyperactivity disorder, Stimulant medications, Physician survey, Prescribing practices

AbSTRACT

Attention deficit hyperactivity disorder (ADHD), the most commonly diagnosed childhood behavioral disorder, occurs in 3% to 5% of school-aged children. Children with ADHD require more than 1.5 times more primary care visits, 9 times more outpatient mental health visits, and 3 times more prescriptions per year, compared to children without ADHD. The total annual health care costs for children with ADHD are estimated to be more than twice that of children without the disorder, and these costs become significantly larger when a child with ADHD is diagnosed with a comorbid condition. In a study conducted in the United States using data from the 1996 Medical Expenditure Panel Survey, the unadjusted mean health care expenditures for a child with ADHD were $1,151, much higher than the $661 in expenditures incurred by a healthy child in that same year.

The stimulant medications (e.g., methylphenidate, amphetamine, and ephedrine) are the most frequently prescribed treatments for children and adolescents with ADHD. Prescriptions for the stimulant medications have increased dramatically over the past decade. Among children in the United States with ADHD, methylphenidate treatment increased 2.5-fold between 1990 and 1995, so that by 1995, 2.8% of all U.S. youths (aged 5 to 18 years) were receiving this medication. From 1990 to 1993, outpatient visits due to ADHD rose from 1.6 to 4.2 million per year; medications were prescribed to 90% of patients during these visits. Of the medications prescribed, 71% were for methylphenidate. In 1996, an estimated 75% of physician visits for children with ADHD resulted in a prescription for a stimulant medication.

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The stimulants are controlled medications classified as Schedule II substances by the U.S. Drug Enforcement Administration (DEA). The Schedule II designation is assigned to substances with a high abuse potential and severe psychological or physical dependence liability. Each state in the United States has its own laws on how Schedule II substances are to be dispensed. Prescribing Schedule II medications in California has more barriers than in any of the other states because California requires that physicians use a triplicate prescription for all Schedule II medications. The physician keeps one copy of the triplicate prescription, the original copy goes to the pharmacy, and the third copy is sent to the DEA. According to the California Bureau of Narcotic Enforcement, only 61% of physicians licensed in California are able to write prescriptions for Schedule II medications. In a survey conducted by the Southern California Cancer Pain Initiative, 27% of physicians responding that they do not prescribe Schedule II medications because of fear of investigation, and 59% reported substituting a weaker opioid, despite the need for a Schedule II medication, to avoid regulatory scrutiny or investigation.

Physician Selection

Methods

Physician Selection

This survey was a cross-sectional survey of physicians treating children and adolescents with ADHD in California, Arizona, Oregon, and Colorado. Using data obtained from a pharmacy claims system of a large managed care organization based in the Western United States, 1,000 physicians with a history of prescribing stimulant medications to children or adolescents between December 2001 and May 2002 were randomly selected to receive the survey. An equal number of surveys (n=500) were mailed to physicians in a triplicate state (i.e., California) and to physicians in 3 nontriplicate states (i.e., Arizona, Colorado, and Oregon).

Survey Description

In collaboration with 4 physicians expert in treating ADHD in children (i.e., 2 child psychiatrists, 1 pediatrician, and 1 adult psychiatrist), we developed a survey to measure physician perceptions on the use of medications for ADHD. The survey was pilot-tested with 10 practicing physicians to evaluate their comprehension of the items and response choices. Individual interviews were conducted with each of the 10 pretest physicians who focused on the interpretation of each item (e.g., “What does this question mean to you?”), the appropriateness of the response choices (“How well do the response choices capture your thought?”), and the overall content of the survey. This methodology was based on cognitive testing procedures described by Lessler and Forsyth. Minor revisions to the survey were made based on results of the cognitive testing.

The final survey consisted of 30 items. The first 18 items asked physicians to select the response that most accurately described their opinion regarding a statement on the use of medications for ADHD (Table 2). Responses were rated on a 7-point scale: (1) strongly agree, (2) agree, (3) slightly agree, (4) undecided, (5) slightly disagree, (6) disagree, and (7) strongly disagree. Additional survey items asked for demographic information such as age, gender, years in practice, state of practice, practice setting, and medical specialty. Physicians were also asked to estimate the number of children and adolescents they see in their office in a typical week, the number with ADHD in a typical week, the amount of additional time it takes them to manage (e.g., writing, tracking) a controlled versus a noncontrolled prescription, and the additional amount of time it takes their staff to manage (e.g., working with parents, tracking) a controlled versus a noncontrolled prescription.

Each survey was coded with an identification number and mailed with a cover letter and stamped, self-addressed envelope for return mail. A medically related gift with a value of $25 was provided as compensation for completing the survey. A second mailing with a reminder letter and an additional physician survey instrument was sent to those who did not respond within 2 weeks of the initial mailing. Surveys were mailed during September 2002. Surveys received by September 27, 2002, were collected for data entry and analysis. Data were entered initially and then reentered through a verification system to ensure accuracy.

Statistical Methods

All statistical analyses were performed using SAS software, version 8.2. Means and standard deviations were used to describe continuous variables, and percentages were used to describe categorical variables. Survey responses were assigned a numerical value of 1 through 7, with 1 representing strongly agree and 7 representing strongly disagree. The mean survey response was
calculated for each question. F tests or t tests were performed to compare mean survey responses based on specialty and controlled prescription status (i.e., triplicate versus nontriplicate). In addition, the Dunnett-Hsu method was used to address the multiple group comparisons in physician specialty by comparing the mean survey response for child and adolescent psychiatrists to the mean survey response for each of the other specialties.

### Results

Of the 1,000 physicians targeted for the survey, 365 (37%) responded after 2 mailings; 189 (52%) were from the triplicate state and 176 (48%) were from nontriplicate states. The demographics of the survey respondents were stratified by triplicate versus nontriplicate states (Table 1). The distribution of age, gender, years in practice, and specialty were similar for physicians in triplicate versus nontriplicate states; however, the practice setting was significantly different for physicians in triplicate states compared to physicians in nontriplicate states ($P<0.0001$).

An analysis was conducted to examine whether there were any differences in demographics for the survey responders compared to survey nonresponders. Demographic information on the 635 nonresponders was obtained from the pharmacy

<table>
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<td>Partnership</td>
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<td>Single specialty group</td>
<td>118</td>
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<tr>
<td>Multispecialty group</td>
<td>107</td>
</tr>
<tr>
<td>Other</td>
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<td>Specialty</td>
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<td>Pediatrics</td>
<td>223</td>
</tr>
<tr>
<td>Family</td>
<td>46</td>
</tr>
<tr>
<td>Child and adolescent psychiatry</td>
<td>50</td>
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<tr>
<td>Psychiatry</td>
<td>28</td>
</tr>
<tr>
<td>Other</td>
<td>14</td>
</tr>
</tbody>
</table>

* Percentages were calculated using the total number of respondents (N=365) as the denominator. Percentages may not add up to 100% because some physicians did not answer certain questions.

† The state of practice displayed here is based on information reported from the physicians. Triplicate versus nontriplicate status was determined based on the state of practice reported in the pharmacy claims system.

‡ P value is not applicable to state distribution since triplicate versus nontriplicate classification was based on the physician’s state of practice.
### TABLE 2: Responses to Survey Items*

<table>
<thead>
<tr>
<th>Survey Items†</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Slightly Agree</th>
<th>Undecided</th>
<th>Slightly Disagree</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
<td>N %</td>
</tr>
<tr>
<td>1. ADHD symptoms cause problems in school (e.g., classroom, recess).</td>
<td>290 79.5</td>
<td>65 17.8</td>
<td>3 0.8</td>
<td>2 0.6</td>
<td>1 0.3</td>
<td>1 0.3</td>
<td>0 0.0</td>
</tr>
<tr>
<td>2. ADHD symptoms cause problems outside of school (e.g., evenings, weekends).</td>
<td>244 66.9</td>
<td>105 28.8</td>
<td>13 3.6</td>
<td>1 0.3</td>
<td>0 0.0</td>
<td>0 0.0</td>
<td>0 0.0</td>
</tr>
<tr>
<td>3. Stimulants are effective in treating ADHD symptoms for children or adolescents in school (e.g., classroom, recess).</td>
<td>230 63.0</td>
<td>124 34.0</td>
<td>6 1.6</td>
<td>1 0.3</td>
<td>1 0.3</td>
<td>1 0.3</td>
<td>0 0.0</td>
</tr>
<tr>
<td>4. Stimulants are effective in treating ADHD symptoms for children or adolescents outside of school (e.g., evenings, weekends).</td>
<td>196 53.7</td>
<td>138 37.8</td>
<td>23 6.3</td>
<td>1 0.3</td>
<td>3 0.8</td>
<td>2 0.6</td>
<td>0 0.0</td>
</tr>
<tr>
<td>5. Controlled medications for children or adolescents with ADHD are a burden for me.</td>
<td>35 9.6</td>
<td>80 21.9</td>
<td>87 23.8</td>
<td>11 3.0</td>
<td>33 9.0</td>
<td>78 21.4</td>
<td>40 11.0</td>
</tr>
<tr>
<td>6. Controlled medications for children or adolescents with ADHD are an administrative burden for my staff.</td>
<td>40 11.0</td>
<td>94 25.8</td>
<td>88 24.1</td>
<td>10 2.7</td>
<td>19 5.2</td>
<td>83 22.7</td>
<td>30 8.2</td>
</tr>
<tr>
<td>7. Controlled medications for children or adolescents with ADHD are a burden for parents.</td>
<td>33 9.0</td>
<td>114 31.2</td>
<td>93 25.5</td>
<td>25 6.9</td>
<td>23 6.3</td>
<td>53 14.5</td>
<td>23 6.3</td>
</tr>
<tr>
<td>8. When prescribing stimulant medications for children or adolescents with ADHD, drug holidays should be incorporated.</td>
<td>28 7.7</td>
<td>83 22.7</td>
<td>62 17.0</td>
<td>43 11.8</td>
<td>39 10.7</td>
<td>83 22.7</td>
<td>24 6.6</td>
</tr>
<tr>
<td>9. When I prescribe a controlled medication for children or adolescents with ADHD, I am concerned that they will end up in the wrong hands (i.e., be diverted).</td>
<td>11 3.0</td>
<td>57 15.6</td>
<td>125 34.3</td>
<td>23 6.3</td>
<td>50 13.7</td>
<td>88 24.1</td>
<td>8 2.2</td>
</tr>
<tr>
<td>10. I am concerned about sleep disruption when I prescribe a stimulant for children or adolescents with ADHD.</td>
<td>20 5.5</td>
<td>96 26.3</td>
<td>153 41.9</td>
<td>15 4.1</td>
<td>38 10.4</td>
<td>39 10.7</td>
<td>2 0.6</td>
</tr>
<tr>
<td>11. I am concerned about decreased appetite or weight loss when I prescribe a stimulant for children or adolescents with ADHD.</td>
<td>37 10.1</td>
<td>147 40.3</td>
<td>137 37.5</td>
<td>7 1.9</td>
<td>22 6.0</td>
<td>12 3.3</td>
<td>1 0.3</td>
</tr>
<tr>
<td>12. I am concerned that prescribing a stimulant for children or adolescents with ADHD and anxiety will exacerbate their anxiety.</td>
<td>14 3.8</td>
<td>66 18.1</td>
<td>149 40.8</td>
<td>23 6.9</td>
<td>55 15.0</td>
<td>51 14.0</td>
<td>4 1.1</td>
</tr>
<tr>
<td>13. Stimulant side effects are easily managed</td>
<td>13 3.6</td>
<td>122 33.4</td>
<td>135 37.0</td>
<td>28 7.7</td>
<td>44 12.1</td>
<td>20 5.5</td>
<td>2 0.6</td>
</tr>
<tr>
<td>14. I am uncomfortable prescribing a stimulant for children or adolescents to treat ADHD.</td>
<td>2 0.6</td>
<td>12 3.3</td>
<td>15 4.1</td>
<td>5 1.4</td>
<td>18 4.9</td>
<td>132 36.2</td>
<td>180 49.3</td>
</tr>
<tr>
<td>15. I am uncomfortable prescribing a controlled medication with evidence of abuse potential for children or adolescents with ADHD.</td>
<td>15 4.1</td>
<td>43 11.8</td>
<td>49 13.4</td>
<td>8 2.2</td>
<td>46 12.6</td>
<td>126 34.5</td>
<td>76 20.8</td>
</tr>
<tr>
<td>16. The controlled status of stimulants prevents the over prescribing of these medications.</td>
<td>21 5.8</td>
<td>66 18.1</td>
<td>50 13.7</td>
<td>32 8.8</td>
<td>47 12.9</td>
<td>118 32.3</td>
<td>29 8.0</td>
</tr>
<tr>
<td>17. If available and with a FDA indication for treating ADHD in children or adolescents, I would prefer prescribing a medication that is not a stimulant versus a stimulant</td>
<td>31 8.5</td>
<td>106 29.0</td>
<td>63 17.3</td>
<td>112 30.7</td>
<td>13 3.6</td>
<td>28 7.7</td>
<td>8 2.2</td>
</tr>
<tr>
<td>18. If available and with a FDA indication for treating ADHD in children or adolescents, I would prefer prescribing a noncontrolled medication that does not have evidence of abuse potential versus one that is controlled [and has] evidence of abuse potential.</td>
<td>73 20.0</td>
<td>138 37.8</td>
<td>69 18.9</td>
<td>46 12.6</td>
<td>9 2.5</td>
<td>16 4.4</td>
<td>11 3.0</td>
</tr>
</tbody>
</table>

* Percentages were calculated using the total number of respondents (N=365) as the denominator. Percentages may not add up to 100% because some physicians did not answer certain questions.
† Copyright © 2003, Eli Lilly and Company. All rights reserved.
claims system; this information was not complete for all of the demographic characteristics. The pharmacy claims data for nonresponders were compared to the demographic information reported by the survey responders. There were no significant differences between responders and nonresponders when comparing physician age (based on data from 292 nonresponders), gender (based on data from 287 nonresponders), controlled prescription status (i.e., triplicate versus nontriplicate states, based on data from all 635 nonresponders), or state of practice (based on data from all 635 nonresponders). Compared to responders, specialty was significantly different for the 506 non-responders with specialty data (P < 0.0001). Responders were more likely to be psychiatrists (combining psychiatrists and child and adolescent psychiatrists; 21.6% versus 9.1%, respectively), and less likely to be family practice (12.7% versus 28.9%, respectively). However, these data are difficult to interpret because of the large amount of missing data for non-responders in the pharmacy claims system.

Physician responses by survey item are shown in Table 2. Approximately 97% of physicians strongly agreed or agreed that ADHD symptoms cause problems in school, and 96% strongly agreed or agreed that ADHD symptoms cause problems outside of school. Physicians overwhelmingly agreed that stimulant medications are effective in treating ADHD symptoms in children or adolescents both in school (97% strongly agreed or agreed) and outside of school (92% strongly agreed or agreed).

Stimulant side effects such as sleep disruption and decreased appetite or weight loss were a concern (with a strongly agree or agree response) for 32% and 50% of physicians, respectively. Approximately 22% of physicians strongly agreed or agreed that they were concerned that prescribing a stimulant for children or adolescents with ADHD and anxiety will exacerbate their anxiety. However, 37% of physicians strongly agreed or agreed that the side effects of stimulants are easily managed.

Physicians responded that controlled medications for pediatric patients with ADHD are a burden to themselves (32% strongly agreed or agreed), to their staff (37% strongly agreed or agreed), and to parents (40% strongly agreed or agreed). When they were asked to estimate the amount of additional time it takes them to manage (e.g., writing, tracking) a controlled versus a noncontrolled prescription, physicians reported an average of 6.0 ± 5.2 minutes per prescription. When asked to esti-

### Table 3: Survey Responses* according to Specialty

<table>
<thead>
<tr>
<th>Survey Item</th>
<th>Pediatrics N=223 Mean (SD)</th>
<th>Family Practice N=46 Mean (SD)</th>
<th>Child Psychiatry† N=50 Mean (SD)</th>
<th>Psychiatry N=27 Mean (SD)</th>
<th>Other N=14 Mean (SD)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>1.3 (0.6)§</td>
<td>1.4 (0.6)§</td>
<td>1.0 (0.3)</td>
<td>1.0 (0.2)</td>
<td>1.1 (0.4)</td>
<td>.002</td>
</tr>
<tr>
<td>2</td>
<td>1.4 (0.6)§</td>
<td>1.7 (0.6)§</td>
<td>1.1 (0.3)</td>
<td>1.2 (0.4)</td>
<td>1.1 (0.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>3</td>
<td>1.5 (0.7)§</td>
<td>1.6 (0.5)§</td>
<td>1.1 (0.3)</td>
<td>1.1 (0.3)</td>
<td>1.1 (0.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>4</td>
<td>1.7 (0.8)§</td>
<td>1.9 (0.8)§</td>
<td>1.2 (0.4)</td>
<td>1.2 (0.5)</td>
<td>1.3 (0.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>5</td>
<td>3.8 (1.9)§</td>
<td>3.5 (1.7)§</td>
<td>4.6 (2.1)</td>
<td>4.0 (2.3)</td>
<td>4.1 (2.3)</td>
<td>.08</td>
</tr>
<tr>
<td>6</td>
<td>3.5 (1.9)§</td>
<td>3.5 (1.7)§</td>
<td>4.8 (2.1)</td>
<td>3.7 (2.3)</td>
<td>3.4 (1.7)</td>
<td>.0008</td>
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<tr>
<td>7</td>
<td>3.3 (1.7)§</td>
<td>3.4 (1.6)</td>
<td>4.1 (2.1)</td>
<td>3.0 (1.9)§</td>
<td>2.8 (1.5)§</td>
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<tr>
<td>8</td>
<td>3.8 (1.8)§</td>
<td>3.1 (1.7)§</td>
<td>5.1 (1.6)</td>
<td>3.9 (2.1)§</td>
<td>4.6 (2.1)</td>
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</tr>
<tr>
<td>9</td>
<td>4.0 (1.6)</td>
<td>4.0 (1.6)</td>
<td>3.8 (1.6)</td>
<td>3.8 (1.6)</td>
<td>4.4 (1.6)</td>
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</tr>
<tr>
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<td>3.3 (1.4)§</td>
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<td>2.3 (1.2)</td>
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<td>3.4 (1.5)</td>
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<td>3.3 (1.3)§</td>
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<td>2.6 (1.0)</td>
<td>2.9 (1.7)</td>
<td>2.5 (1.2)</td>
<td>.003</td>
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<tr>
<td>14</td>
<td>6.1 (1.2)§</td>
<td>5.5 (1.4)§</td>
<td>6.7 (0.7)</td>
<td>5.9 (1.7)§</td>
<td>6.6 (1.6)</td>
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<tr>
<td>15</td>
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<td>4.0 (1.8)</td>
<td>5.2 (2.1)</td>
<td>4.9 (2.2)</td>
<td>5.9 (1.7)</td>
<td>.23</td>
</tr>
<tr>
<td>16</td>
<td>4.2 (1.9)</td>
<td>4.2 (1.7)</td>
<td>4.6 (1.8)</td>
<td>4.8 (2.1)</td>
<td>5.2 (1.7)</td>
<td>.15</td>
</tr>
<tr>
<td>17</td>
<td>3.3 (1.3)§</td>
<td>2.8 (1.3)</td>
<td>3.5 (1.8)</td>
<td>2.7 (1.6)</td>
<td>4.3 (2.1)</td>
<td>.001</td>
</tr>
<tr>
<td>18</td>
<td>2.6 (1.4)§</td>
<td>2.2 (1.0)§</td>
<td>3.1 (1.8)</td>
<td>2.4 (1.8)</td>
<td>3.8 (2.0)</td>
<td>.002</td>
</tr>
</tbody>
</table>

* Scale = 1-7, with 1 = strongly agree and 7 = strongly disagree.
† Survey item numbers correspond to the items numbered in Table 2.
‡ Child psychiatry = child and adolescent psychiatry.
§ Represents a significant difference (P<0.05) in mean response for physicians in this specialty compared to the mean response for child and adolescent psychiatrists.
|| n = 221; ¶ n = 222; # n = 45; ** n = 49; †† n = 26.
Physician Perceptions of the Use of Medications for Attention Deficit Hyperactivity Disorder

mate the amount of additional time it takes their staff to manage (e.g., working with parents, tracking) a controlled versus noncontrolled prescription, physicians reported an average of 6.8 ± 6.2 minutes per prescription. Approximately 19% of physicians strongly agreed or agreed that they are concerned with diversion when they prescribe a controlled medication for children or adolescents with ADHD.

Approximately 38% of physicians strongly agreed or agreed that they would prefer prescribing a nonstimulant instead of a stimulant if a nonstimulant with a U.S. Food and Drug Administration (FDA) indication for treating ADHD in children or adolescents with ADHD. Since current clinical guidelines recommend that controlled medications are a burden to themselves and to their staff, and psychiatrists and pediatricians were more likely to agree that controlled medications are a burden to parents (survey items 5 through 7 in Table 3).

Compared to other specialties, child and adolescent psychiatrists were more likely to disagree that drug holidays should be incorporated when prescribing stimulants to children and adolescents with ADHD (survey item 8 in Table 3). Child and adolescent psychiatrists were more likely to agree that stimulant side effects are easily managed compared to pediatrics (survey item 13 in Table 3).

Child and adolescent psychiatrists were less likely than other specialists to be uncomfortable prescribing a stimulant for children and/or adolescents with ADHD (survey item 14 in Table 3). Family practice physicians were more likely than child and adolescent psychiatrists to prefer a noncontrolled medication that does not have evidence of abuse potential instead of one that is controlled and has evidence of abuse potential (survey item 18 in Table 3).

Perceptions of Physicians in Triplicate Versus Nontriplicate States

Several survey items had significantly different survey responses among physicians in triplicate states versus physicians in nontriplicate states (Table 4). Physicians in the triplicate state (California) were more likely than those in the nontriplicate states to believe that controlled medications for children or adolescents with ADHD are a burden to themselves (mean survey response of 3.7 versus 4.1, *P*<0.001). More physicians in triplicate states than in nontriplicate states thought that drug holidays should be incorporated when prescribing a stimulant for children or adolescents with ADHD (mean survey response of 3.7 versus 4.1, *P*=0.02). More physicians in triplicate states than in nontriplicate states were uncomfortable prescribing a stimulant for children or adolescents to treat ADHD (mean survey response 5.9 versus 6.4, *P*<0.001).

Discussion

This study was the first to systematically evaluate physicians’ perceptions regarding the use of medications for the treatment of children and adolescents with ADHD. Since current clinical

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Survey Responses* According to Controlled Prescription Status</th>
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</thead>
<tbody>
<tr>
<td>Survey Item No.†</td>
<td>Nontriplicate</td>
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<td>18</td>
<td>173</td>
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</tbody>
</table>

* Scale = 1-7, with 1 = strongly agree and 7 = strongly disagree.
† Survey item numbers correspond to the items numbered in Table 2.
‡ Represents a significant difference (*P*<0.05) in mean response for this survey item among physicians in triplicate versus nontriplicate states.

Preferences of Physicians According to Specialty

Physician responses varied according to specialty (Table 3). Child and adolescent psychiatrists were more likely than pediatricians and family practice physicians to agree that ADHD symptoms cause problems and that the stimulants are effective in treating ADHD (survey items 1 through 4 in Table 3). Compared to child and adolescent psychiatrists, family practice physicians and pediatricians were more likely to agree that controlled medications are a burden to themselves and to their staff, and psychiatrists and pediatricians were more likely to agree that controlled medications are a burden to parents (survey items 5 through 7 in Table 3).

Compared to other specialties, child and adolescent psychiatrists were more likely to disagree that drug holidays should be incorporated when prescribing stimulants to children and adolescents with ADHD (survey item 8 in Table 3). Child and adolescent psychiatrists were more likely to agree that stimulant side effects are easily managed compared to pediatricians (survey item 13 in Table 3).

Child and adolescent psychiatrists were less likely than other specialists to be uncomfortable prescribing a stimulant for children and/or adolescents with ADHD (survey item 14 in Table 3). Family practice physicians were more likely than child and adolescent psychiatrists to prefer a noncontrolled medication that does not have evidence of abuse potential instead of one that is controlled and has evidence of abuse potential (survey item 18 in Table 3).
practice guidelines and clinical studies support the use of the stimulant medications as an effective treatment of ADHD, it is not surprising that physicians believe that the stimulant medications are effective for treating ADHD symptoms in children and adolescents. However, the preferences of some physicians to prescribe a nonstimulant instead of a stimulant medication indicate that the effectiveness of the stimulant medications is not the only factor that physicians evaluate when prescribing a medication to treat ADHD in children and adolescents.

Child and adolescent psychiatrists were more concerned with the stimulant side effects of sleep disruption and decreased appetite or weight loss than were family practice physicians, 50% to 32%, respectively. These results are not surprising considering that the stimulant side effects of insomnia and appetite suppression have been well documented in the literature. Approximately 22% of physicians were also concerned that prescribing a stimulant for children and/or adolescents with ADHD and anxiety will exacerbate their anxiety. Despite concerns regarding the stimulant side effects, 37% of physicians responded that the side effects of the stimulants are easily managed. Physicians were more likely to believe that the side effects are easily managed if they were child and adolescent psychiatrists, which may indicate that physicians who have more experience in treating children and/or adolescents with ADHD are more confident in managing the stimulant side effects.

Approximately 19% of physicians were concerned with diversion when they prescribe a controlled medication for children or adolescents with ADHD. The concerns of these physicians corroborate those of the DEA, which has been supportive of a public education program to decrease the diversion of the stimulant medications. Rates of diversion of the stimulant medications in the United States have not been documented in the literature; however, diversion rates were reported among adolescent students who were prescribed stimulants in Canada, where 14.7% gave away some of their medication, 7.3% sold some of their medication, 4.3% experienced theft, and 3.0% were forced to give up some of their medication. With the recent increase in prescribing of stimulants for treatment of ADHD, additional studies are warranted to evaluate the occurrence of diversion of the stimulants among children and adolescents in the United States.

Prescribing burden was another concern of physicians, with 32% to 40% indicating that controlled medications are a burden to themselves, their staff, and parents. Physicians in triplicate states were more likely to think that controlled medications are a burden to themselves compared to physicians in nontriplicate states. This may be the result of the extra burden (e.g., paperwork and time) involved with writing a triplicate prescription. Compared to some of the other specialties, child and adolescent psychiatrists were less likely to think that controlled medications are a burden to themselves, their staff, or parents. One possible explanation for this is that child and adolescent psychiatrists may treat the most severe cases of ADHD, in which case, they and the parents may be more likely to appreciate the symptom control from the stimulant medications and less likely to be concerned with the burden of administering a controlled medication.

Until recently, for patients who were unable to tolerate a stimulant medication, physicians had to resort to the antidepressants (e.g., tricyclics, bupropion), antipsychotics, clonidine, and guanfacine. While these medications have been studied in small populations of patients with ADHD, there have been mixed results, and none have been FDA-approved for ADHD or for use in children and/or adolescents. Atomoxetine (Strattera), which was approved by the FDA in November 2002, is the first noncontrolled, nonstimulant medication that is FDA-approved for the treatment of ADHD in children, adolescents, and adults. Since this survey was conducted prior to the availability of atomoxetine, it would be interesting to conduct a similar survey of physician preferences now that physicians have clinical experience using this new chemical entity.

**Limitations**

There were several limitations that may prohibit generalizing these results to other populations. Since physicians who prescribe stimulants to children and adolescents were selected for this survey, these results may not be representative of all physicians who treat children and adolescents with ADHD. This study only included physicians practicing in 4 states in the Western United States; therefore, geographic differences in physician preferences must be noted when extrapolating the results of this survey to other regions of the country.

While the 37% response rate is consistent with other physician response rates for studies pertaining to ADHD, the 63% of physicians who did not respond could have different characteristics and different responses to the survey items than the physicians who returned the surveys. The survey asked respondents about their perceptions of the stimulants as a class of medications and did not distinguish among the different stimulant products (i.e., methylphenidate, dextroamphetamine, and amphetamine). Physicians may consider the side effects, abuse potential, and efficacy of one specific stimulant medication different from another. Furthermore, the survey asked about prescribing preferences for both children and adolescents combined and did not allow physicians to indicate if they had differing thoughts about medication prescribing for children versus adolescents.

**Conclusion**

Physicians overwhelmingly perceive stimulant medications to be effective for treating ADHD symptoms in children or adolescents, but many would prefer to prescribe a nonstimulant medication. Even though some physicians consider the side effects of the stimulants easily managed, others are concerned about prescribing stimulants because of their side effects, risk of diversion, or administrative burden. The majority (58%) would prefer to prescribe a noncontrolled medication without abuse.
Physician Perceptions of the Use of Medications for Attention Deficit Hyperactivity Disorder

potential instead of a controlled medication with abuse potential for the treatment of ADHD in children and adolescents.

DISCLOSURES

Funding for this research was provided by Eli Lilly and Company and was obtained by authors Tom E. Hughes, Amy R. Perwien, and Kristina Secnik. Who are employees and stockholders of Lilly. Author Karen M. Stockl served as principal author of the study. Study concept and design were contributed by Stockl, Hughes, Perwien, and Secnik. Analysis and interpretation of data were contributed by Stockl and author Manal A. Jarrar. Drafting of the manuscript was primarily the work of Stockl, and its critical revision was the work of Hughes, Jarrar, Perwien, and Secnik. Statistical expertise was contributed by Jarrar and Perwien, and administrative, technical, and/or material support was provided by Jarrar, Perwien, Secnik, and Stockl. The survey was developed by Hughes, Perwien, and Secnik. This study was presented as an abstract and poster at the International Society for Pharmacoeconomic and Outcomes Research 8th Annual Meeting, Arlington, VA, May 18-21, 2003.

REFERENCES


Patient Adherence With Amlodipine, Lisinopril, or Valsartan Therapy in a Usual-Care Setting

JENIFER WOGEN, MS; CHARLES A. KREILICK; RICHARD C. LIVORNESE, MS; KRISTA YOKOYAMA, PharmD; and FERIDE FRECH, MPH, RPh

ABSTRACT

OBJECTIVE: To compare the persistence and compliance in a usual-care setting with 3 drugs (amlodipine, lisinopril, or valsartan) from 3 different pharmaceutical classes—calcium-channel blocker, angiotensin-converting enzyme inhibitor, and angiotensin receptor blocker, respectively, commonly used to treat hypertension.

METHODS: This retrospective observational study included a cohort of 142,945 continuously benefit-eligible patients from a pharmacy benefit management drug claims database who began therapy with lisinopril, valsartan, or amloidipine. Concurrent use of other cardiovascular medications was assessed as a proxy for cardiovascular disease severity. Chronic Disease Score (CDS), derived from pharmacy claims data, was used to classify patient chronic disease burden as mild, moderate, or severe. Drug utilization measures included compliance, persistence, medication possession ratio (MPR), duration of therapy, and drug discontinuation. Multiple linear regression techniques were used to assess the impact of various predictor variables on study outcomes and to compare compliance among treatment groups, adjusted for age, gender, and CDS.

RESULTS: The mean age of the study cohort was 63.1 years; 53% were female. Just over one half (51%, n=73,148) received amloidipine, 28% (n=40,238) received lisinopril, and 21% (n=29,669) received valsartan. Significantly more valsartan patients (63%) remained persistent on therapy at 12 months past the index date of the first prescription, compared with amloidipine (53%) and lisinopril (50%) patients (P<0.001). Both crude and adjusted compliance rates also were greater for valsartan patients, reflected by an adjusted mean MPR of 75%, compared with 67% for amloidipine and 65% for lisinopril (P<0.0001, both comparisons).

CONCLUSION: These results suggest that, in a usual-care setting, patients receiving valsartan (relative to amloidipine or lisinopril) appear to be more compliant and persistent with pharmacologic therapy, independent of patient chronic disease burden.

KEYWORDS: Antihypertensive therapy, Chronic Disease Score, Compliance, Persistence, Valsartan

J Managed Care Pharm. 2003;9(5):424-29

Objective

Hypertension is a chronic, asymptomatic disease affecting an estimated 25% of the U.S. adult population. It is associated with significant morbidity and mortality as well as considerable consumption of health care resources. Numerous clinical studies have shown that continuous control of arterial blood pressure improves outcomes. Approximately 30% of individuals with hypertension are unaware of their disease status; furthermore, 11% of those diagnosed are untreated, and 58% of those who are treated are not controlled.

Pharmacologic management of hypertension commonly involves the use of multiple therapeutic agents from several classes, including calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, diuretics, and the more recently introduced angiotensin receptor blockers (ARBs). Despite the overwhelming clinical evidence supporting improved outcomes with antihypertensive therapy, compliance and persistence remain poor, as evidenced by high medication discontinuation rates during the first year of therapy.

Medication tolerability problems, such as cough, swelling of the extremities, and fatigue, are associated with the chronic use of many antihypertensive agents. An unfavorable tolerability profile may be an important contributor to poor patient compliance. The ARBs have demonstrated excellent tolerability, with few side effects reported in placebo-controlled trials. In clinical trials, the ARB valsartan demonstrated comparable efficacy to the ACE inhibitors lisinopril and enalapril, with reduced incidence of cough. The side-effect rate for patients treated with the ARB valsartan was lower than that for patients treated with ACE inhibitors or CCBs. In addition, recent data suggest that ARBs are associated with improved patient persistence compared with ACE inhibitors, CCBs, diuretics, and beta-blockers.

Methods

Cohort Construction

This was a retrospective, longitudinal cohort study utilizing an administrative pharmacy claims database from a large pharma-
patients whose pharmacy claims data were available for research purposes were identified (N=46 million). Subjects who were continuously benefit-eligible for both mail-order and community pharmacy prescriptions between August 1, 1997, and July 31, 2000, were identified for preliminary cohort inclusion (n=14.6 million). From this population, the study cohort was identified, consisting of patients who received an initial prescription for valsartan, lisinopril, or amlodipine between August 1, 1998, and July 31, 1999. The study cohort represented patients who were new to therapy within the therapeutic class. Patients who received a prescription for a drug from the same class as the index agent during the 12 months preceding the index prescription were excluded from the cohort. The final study cohort was comprised of 142,945 patients.

All utilization analyses were performed relative to the index agent. The study evaluation included patient data for the 2-year period from August 1, 1998, through July 31, 2000, with each patient contributing 12 months of data following initiation of therapy with the index antihypertensive prescription.

Study Definitions

Study definitions are provided in Figure 1. The “index prescription” was defined as each patient’s first prescription during the study identification period, between August 1, 1998, and July 31, 1999. Patient age was calculated as of the date of the index prescription fill.

The drug utilization parameters that were evaluated included compliance, persistence, medication possession ratio (MPR), duration of therapy, and drug discontinuation. Compliance was calculated for all patients with at least 2 fills of the index antihypertensive agent. Compliance estimates were determined by summing the days’ supply (the number of days the dispensed drug supply should last based on prescriber dosing instructions) for all member prescriptions dispensed from the index prescription date to the last fill date (excluding the days’ supply dispensed at the last fill) divided by the patient’s duration of therapy. Duration of therapy was calculated as the last prescription date within the study window minus the index prescription date. The MPR was defined as the percentage of time that a patient had a supply of the index drug available during the 12 months following the index prescription, based on prescriber dosage instructions and days’ supply of medication dispensed at each fill. A patient may demonstrate high compliance but a lower MPR if that patient discontinues therapy at some point within the 12 months postinitiation of therapy, since the compliance calculation uses each patient’s specific length of drug therapy in days (i.e., the last fill date minus the first fill date) as the denominator, while the MPR calculation uses a fixed denominator of 365 days.

Discontinuation was characterized as stopping therapy with the index antihypertensive agent and not receiving a fill for the index agent within 60 days after exhausting the drug supply from the prior prescription. Patients were classified as remaining persistent with the index agent if they did not discontinue therapy prior to the month in question (% remaining on therapy = 100% – % discontinuing therapy). Time to therapy discontinuation was calculated as the number of days from the index prescription fill date to the date of index agent supply exhaustion preceding the gap of >60 days.

Chronic Disease Burden

Patient chronic disease burden was assessed using a modified Chronic Disease Score (CDS)23 based on the method by Clark et al.24 The CDS utilized the presence of drug markers during the study period to identify the existence of chronic disease states (e.g., coronary/peripheral vascular disease, cardiac disease/congestive heart failure, hyperlipidemia, asthma, and diabetes mellitus). Individual disease states were weighted and summed to derive an overall score for each patient that represented the patient’s total chronic disease burden. Patient chronic disease burden was classified as mild, moderate, or severe based on score thresholds set using clinical criteria: mild = CDS of 0 to 3; moderate = CDS of 4 to 11; and severe = CDS >11.

In addition to the CDS, the use of other drugs for managing cardiovascular disease was evaluated for the entire cohort. Drug classes of interest included beta-blockers, digitalis, nitrates, antihyperlipidemic agents, diuretics, combination diuretic for-
Patient Adherence With Amlodipine, Lisinopril, or Valsartan Therapy in a Usual-Care Setting

Statistical Analysis

All statistical and descriptive analyses were performed using SAS version 8.0 (Cary, North Carolina). Results for continuous variables are presented as means ± standard deviation. Analyses of variance (ANOVA) and covariance (ANCOVA) and t-tests were used for analyzing continuous data, while the chi-square test was used for categorical data. Multiple variable linear regression techniques were used to evaluate the impact of independent variables, such as age, gender, and CDS on compliance and MPR, and least square means were used to adjust outcome variables for effects of independent variables. A Cox proportional hazards regression model was used to evaluate risk of therapy discontinuation.

Results

The new-start antihypertensive medication cohort consisted of 142,945 patients, 53% of whom were female, with a mean age of 63.1 years (Table 1). During the 2-year study period ended July 31, 2000, more than one half (51%) of the cohort initiated therapy on amlodipine, while 28% received lisinopril and 21% received valsartan. The mean CDS for the entire cohort was 10.15 ± 6.00 and essentially was comparable for all groups (Table 1). Valsartan patients had a slightly lower CDS (mean, 9.62 ± 5.66, P <0.0001) compared with lisinopril (mean, 10.19 ± 5.96) or amlodipine (mean, 10.34 ± 6.15) patients, and a significantly smaller proportion of valsartan patients was classified as having a severe chronic disease burden (31% versus 35% for lisinopril and amlodipine, P<0.0001). The most common concomitant cardiovascular medications used during the study period included diuretics in 34.7% of patients, antihyperlipidemic therapy in 31.8%, and beta-blockers in 25.5% (Table 2). Valsartan patients were less likely to be prescribed concomitant cardiovascular medications.

Overall, 54% of the study cohort remained on therapy with their index agent at 12 months following the initial prescription. A significant difference was observed in therapy persistence among the study agents: 63% of valsartan patients compared with 53% of amlodipine patients (P<0.001) and 50% of

TABLE 1 Demographic and Clinical Characteristics of Patient Cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Amlodipine (n=73,148)</th>
<th>Lisinopril (n=40,128)</th>
<th>Valsartan (n=29,669)</th>
<th>Total (n=142,945)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cohort (%)</td>
<td>51.2</td>
<td>28.0</td>
<td>20.8</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>Mean age in years (±SD)</td>
<td>63.9 ± 13.9</td>
<td>62.1 ± 14.4</td>
<td>62.4 ± 13.5</td>
<td>63.1 ± 14.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female (%)</td>
<td>53.0</td>
<td>48.8</td>
<td>56.4</td>
<td>52.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean CDS†</td>
<td>10.34 ± 6.15</td>
<td>10.19 ± 5.96</td>
<td>9.62 ± 5.66</td>
<td>10.15 ± 6.00</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mild (%)</td>
<td>12</td>
<td>11</td>
<td>14</td>
<td>12</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Moderate (%)</td>
<td>53</td>
<td>53</td>
<td>55</td>
<td>53</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Severe (%)</td>
<td>35</td>
<td>35</td>
<td>31</td>
<td>35</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* P value was calculated using analysis of variance for age and mean CDS, using chi-square analysis for gender and mild, moderate, and severe CDS categories.
† CDS = Chronic Disease Score.

TABLE 2 Concurrent Use of Cardiovascular-Related Medications

<table>
<thead>
<tr>
<th>Class of Medication</th>
<th>Amlodipine (n=73,148)</th>
<th>Lisinopril (n=40,128)</th>
<th>Valsartan (n=29,669)</th>
<th>Total (n=142,945)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>36.0</td>
<td>34.7</td>
<td>31.4</td>
<td>34.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antihyperlipidemic agents</td>
<td>32.9</td>
<td>30.7</td>
<td>30.8</td>
<td>31.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>28.0</td>
<td>23.8</td>
<td>21.4</td>
<td>25.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antiplatlet agents</td>
<td>15.1</td>
<td>15.1</td>
<td>11.1</td>
<td>14.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nitrates</td>
<td>17.0</td>
<td>14.3</td>
<td>9.7</td>
<td>14.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Digitalis</td>
<td>7.8</td>
<td>11.5</td>
<td>7.4</td>
<td>8.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diuretic combination†</td>
<td>9.2</td>
<td>6.7</td>
<td>5.3</td>
<td>7.7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* P value calculated using the chi-square test.
† Includes diuretic combined with angiotensin-converting enzyme inhibitor, calcium channel blocker, or beta-blocker.

mulations (e.g., with ACEI or beta-blocker), and antiplatelet agents. Patients were classified as “yes” or “no” based on whether they received medications from any of these classes, in addition to the index agent, during the study period.
Utilization studies,7,22,26 which demonstrated that the choice of antihypertensive agent has an important impact on persistence with antihypertensive therapy by initial study agent demonstrated that throughout the 12-month evaluation period, a higher percentage of patients who were initially prescribed valsartan remained on therapy compared with initial therapy with either amlodipine or lisinopril, the difference was significant at 12 months (63.0% for valsartan versus 52.9% for amlodipine and 50.3% for lisinopril, \( P < 0.001 \) for both) (Table 3).

A multiple linear regression model, controlling for study independent variables, found that treatment group, age, gender, and use of antihyperlipidemic agents (yes/no), beta-blockers (yes/no), and nitrates (yes/no) were all significant predictors of compliance. Use of diuretics and combination diuretic products, antplatelet agents, and digitalis significantly predicted patient MPR. However, when compliance and MPR were adjusted for significant covariates, valsartan patients remained significantly more compliant; the adjusted mean compliance for valsartan was 88.9% compared with 86.6% \( (P < 0.001) \) for amlodipine and lisinopril, while the adjusted MPR for valsartan was 75.3% compared with 67.2% \( (P < 0.001) \) for amlodipine and 64.6% \( (P < 0.001) \) for lisinopril.

A Cox proportional hazards model, with valsartan as the reference agent, was used to assess therapy discontinuation while controlling for gender, age, CDS, and use of other agents for hypertension. Patients who initiated therapy on lisinopril (hazard ratio, 1.45; \( P < 0.001 \)) or amlodipine (hazard ratio, 1.33; \( P < 0.001 \)) were more likely to discontinue therapy within the first 12 months than were valsartan patients (Table 4).

This study has demonstrated that therapy with valsartan was associated with better patient compliance and persistence compared with either lisinopril or amlodipine in a usual-care setting. Improved compliance and persistence with valsartan may be related to better tolerability, as suggested by a lower discontinuation rate during the first year of therapy. In a survey of 2,115 patients and 336 physicians in the United Kingdom, Lip et al. demonstrated that 34% of patients reported unacceptable side effects with hypertension therapy, and physicians reported that 42% of medication switches were due to side effects.21 The data from this study are also consistent with findings from other utilization studies,7,22,26 which demonstrated that the choice of antihypertensive agent has an important impact on persistence rates with a therapeutic regimen. In addition, this research corroborates other studies that have found ARBs to be associated with improved patient compliance and lower discontinuation rates compared to other antihypertensive drug classes including ACEIs and CCBs.7,22,27

Persistence with antihypertensive medications has proven effective for decreasing the long-term consequences of untreated hypertension,28 as well as reducing the consumption of health care resources during the first year of therapy.29 The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7) recommends thiazide diuretics as initial therapy for hypertensive patients without comorbidities.30 However, the benefit of diuretics on morbidity and mortality, as demonstrated by randomized clinical trials, may not be fully realized in the usual-care setting, where compliance and persistence with therapy may not be optimal.

In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), patients using the thiazide diuretic chlorthalidone had similar mortality results as patients prescribed amlodipine or lisinopril and experienced less cardiovascular morbidity.31 In the ALLHAT study, a randomized trial but without the continuous follow-up of a typical randomized clinical trial, 87% of chlorthalidone patients were persistent at 1 year and 81% at 5 years posttherapy initiation. In contrast, other observational studies have shown much lower persistence rates with thiazide diuretics in nonclinical trial settings21,22,27; one study found that at 1 year, only 21% of patients remained on medication, and at 4 years, only 16% were persistent with thiazide diuretics.22 Interestingly, valsartan patients in the present study less frequently used other cardiovascular medications as compared to lisinopril or amlodipine patients. These results suggest that these medications are being used as initial therapy in many patients, in contrast to JNC 6 and JNC 7 guidelines.

**Limitations**

Since this analysis used administrative pharmacy claims, it is important to recognize some study limitations. First, the analy-
s used drug markers to proxy the presence of cardiac disease, should address this limitation; however, using drug markers to identify disease states may not be as accurate as medical record review or prospective data collection.

This study also did not include measures of clinical effectiveness (blood pressure control) or outcomes (morbidity and mortality) for the evaluated cohort of patients. Many of the patients in the current study were using other antihypertensive medications and had other comorbidities according to the CDS; therefore, the results of the current study may not apply solely to patients with simple hypertension. Finally, as in all studies of drug claims data, the study population included only persons with pharmacy benefits coverage, and these study results may not reflect the drug-taking behavior of patients without some form of insurance for prescription medications.

**Conclusion**

This observational study demonstrated that patients in a usual-care setting who receive valsartan therapy, compared to the CCB amlodipine and the ACEI lisinopril, have greater persistence and compliance. These findings suggest that agent selection for chronic pharmacologic management of hypertension has the potential to affect patient drug-taking behavior and perhaps longer-term outcomes in a typical real-world setting.

**DISCLOSURES**

Funding for this research was provided by Novartis Pharmaceuticals Corporation, Inc., via a grant to The Institute for Effectiveness Research, a subsidiary of Medco Health Solutions, Inc., and was obtained by author Jenifer Wogen. Wogen and authors Charles A. Kreilick and Richard C. Livornese are employed by The Institute for Effectiveness Research; author Feride Frech is employed by Novartis. Wogen served as principal author of the study. Study concept and design were contributed primarily by Wogen and Frech. Analysis and interpretation of data were contributed by Wogen, Kreilick, and Livornese. Drafting of the manuscript and its critical revision were the work of Wogen, Frech, and author Krista Yokoyama. Statistical expertise was contributed by Wogen and Kreilick, and administrative, technical, and/or material support was provided by Patti Ann Starzec, The Institute for Effectiveness Research. A poster presentation of this research was presented, in part, at the American Society of Hypertension 16th Annual Scientific Meeting and Exposition, San Francisco, May 18, 2001.

**REFERENCES**


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**TABLE 3** Crude and Adjusted MPR and Compliance Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Amlodipine (n=73,148)</th>
<th>Lisinopril (n=40,128)</th>
<th>Valsartan (n=29,669)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean days to therapy discontinuation (±SD)</td>
<td>241.6 ± 140.2</td>
<td>234.6 ± 141.1</td>
<td>270.1 ± 131.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Crude (unadjusted) mean compliance (±SD)</td>
<td>86.7 ± 20.2</td>
<td>86.3 ± 20.5</td>
<td>88.5 ± 18.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Crude (unadjusted) mean MPR (±SD)</td>
<td>67.5 ± 37.6</td>
<td>64.8 ± 37.3</td>
<td>75.6 ± 35.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted† mean compliance (±SE)</td>
<td>86.6 ± 0.001</td>
<td>86.6 ± 0.001</td>
<td>88.9 ± 0.001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted mean† MPR (±SE)</td>
<td>67.2 ± 0.14</td>
<td>64.6 ± 0.19</td>
<td>75.3 ± 0.22</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

* P value calculated using analysis of variance for comparisons of crude means and least square regression for adjusted means.
† Adjusted for age, gender, and CDS using least square regression.

**TABLE 4** Results of Cox Proportional Hazards Model for Therapy Discontinuation*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cox Proportional Hazards Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.993</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>0.954</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CDS</td>
<td>1.013</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>1.333</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>1.446</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diuretics</td>
<td>1.103</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diuretic combination†</td>
<td>1.544</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>1.131</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nitrates</td>
<td>1.137</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antihyperlipidemic agents</td>
<td>0.743</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Digitalis</td>
<td>1.049</td>
<td>0.0012</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>1.032</td>
<td>0.0118</td>
</tr>
</tbody>
</table>

* Reference agent=valsartan.
† Includes diuretic combined with angiotensin-converting enzyme inhibitor, calcium channel blocker, or beta-blocker.
CDS = Chronic Disease Score.


ABSTRACT

BACKGROUND: Pharmacoeconomic models of Helicobacter (H) pylori eradication have been frequently cited but never validated.

OBJECTIVE: Examine retrospectively whether H pylori pharmacoeconomic models direct decision makers to cost-effective therapeutic choices.

METHODS: We first replicated and then validated 2 models, replacing model assumptions with empirical data from a multipayer claims database. Database subjects were 435 commercially insured U.S. patients treated with bismuth-metronidazole-tetracycline (BMT), proton pump inhibitor (PPI)-clarithromycin, or PPI-amoxicillin. Patients met >1 clinical requirement (ulcer disease, gastritis/duodenitis, stomach function disorder, abdominal pain, H pylori infection, endoscopy, or H pylori assay). Sensitivity analyses included only patients with ulcer diagnosis or gastrointestinal specialist care. Outcome measures were: (1) rates of eradication retreatment; (2) use of office visits, hospitalizations, endoscopies, and anti-secretory medication; and (3) cost per effectively treated (nonretreated) patient.

RESULTS: Model results overstated the cost-effectiveness of PPI-clarithromycin and underestimated the cost-effectiveness of BMT. Prior to empirical adjustment, costs per effectively treated patient were $1,001, $980, and $1,730 for BMT, PPI-clarithromycin, and PPI-amoxicillin, respectively. Estimates after adjustment were $852 for BMT, $1,118 for PPI-clarithromycin, and $1,131 for PPI-amoxicillin. Key model assumptions that proved retrospectively incorrect were largely unsupported by either empirical evidence or systematic assessment of expert opinion.

CONCLUSIONS: Organizations with access to medical and pharmacy claims data should test key assumptions of influential models to determine their validity. Model replication and validation are becoming increasingly common. Pharmacoeconomic decision-analytic studies of the impact of eradicating Helicobacter (H) pylori in ulcer patients provide a good example of models’ influence in clinical and policy literature. In 1994, a National Institute of Health (NIH) Consensus Conference recommended that H pylori infection in peptic ulcer patients be treated with regimens combining antisecretory and antibiotic medications. Practice guidelines published in 1996 advised practitioners that 3-drug regimens containing bismuth, metronidazole, and tetracycline (BMT) had higher bacterial eradication rates than 2-drug regimens containing a proton pump inhibitor (PPI) plus either amoxicillin or clarithromycin. However, the choice between BMT and PPI-based 3-drug combinations (usually PPI-amoxicillin-clarithromycin or PPI-clarithromycin-metronidazole) was less clear. Clinical trials had documented eradication rates of more than 85% to 90% for both BMT and PPI 3-drug combinations. Head-to-head comparison studies of BMT and PPI-based 3-drug regimens used widely varying methodologies and produced mixed results. A 1996 meta-analysis that applied a uniform methodology to multiple clinical trials found that eradication rates for BMT versus PPI-based triple therapies were not significantly different.

While decision-analytic models are a frequently used tool in economic evaluations of drug therapy, skeptical responses to conclusions derived from them are becoming increasingly common. Concerns have been expressed that models rely excessively on assumption, are more susceptible than other types of research to oversimplification and bias, and too often represent a “black box” to decision makers. Are such criticisms justified?

Examination of this question is important because pharmacoeconomic model results are influential. Models are used in the United States for educational and drug promotion purposes and, more recently, have become a required component of the Academy of Managed Care Pharmacy’s guidelines for the submission of clinical and economic data to support formulary listing in health plans. In other countries, economic model results are a required or optional part of the drug reimbursement approval process.

Pharmacoeconomic decision-analytic studies of the impact of eradicating Helicobacter (H) pylori in ulcer patients provide a good example of models’ influence in clinical and policy literature. In 1994, a National Institute of Health (NIH) Consensus Conference recommended that H pylori infection in peptic ulcer patients be treated with regimens combining antisecretory and antibiotic medications. Practice guidelines published in 1996 advised practitioners that 3-drug regimens containing bismuth, metronidazole, and tetracycline (BMT) had higher bacterial eradication rates than 2-drug regimens containing a proton pump inhibitor (PPI) plus either amoxicillin or clarithromycin. However, the choice between BMT and PPI-based 3-drug combinations (usually PPI-amoxicillin-clarithromycin or PPI-clarithromycin-metronidazole) was less clear. Clinical trials had documented eradication rates of more than 85% to 90% for both BMT and PPI 3-drug combinations. Head-to-head comparison studies of BMT and PPI-based 3-drug regimens used widely varying methodologies and produced mixed results. A 1996 meta-analysis that applied a uniform methodology to multiple clinical trials found that eradication rates for BMT versus PPI-based triple therapies were not significantly different.

In light of this history and given that BMT costs considerably less than PPI-based regimens, particularly those including clarithromycin, one would expect that early economic discussions of optimal regimens would have generally favored BMT. Yet, beginning in 1996, reviews and commentaries began arguing that using PPI-based regimens instead of BMT was cost effective. These arguments were based not on direct measurement...
of service costs but on findings of decision-analytic models that had begun appearing in the literature in 1995. 25-30 Two key features of these models explained these conclusions. First, models comparing outcomes for different eradication regimens assumed that BMT's effectiveness in clinical practice would be compromised by noncompliance and metronidazole resistance. 29,30 Second, models assumed that costs associated with disease recurrence (e.g., office visits, laboratory work, and hospitalizations) would far exceed the costs of the regimen drugs themselves, making the recurrence rate “the principal determinant of overall cost”21 in model results. Recurrence-related costs, it was argued, were so high that medication costs were “minor”22 to economic outcome.

A more recent study was the first to measure empirically the retreatment rates and medical service costs for patients treated with different eradication regimens in routine clinical practice. 31 Controlling for patient age, gender, use of gastrointestinal (GI) specialty care, and clinical criteria, retreatment rates were lower for 3-drug than 2-drug therapies and not significantly different for BMT versus PPI 3-drug therapies. 31 Consistent with the view that recurrence resulted in additional medical expense, retreated patients incurred higher medical costs than nonretreated patients. However, in most medical service categories, follow-up costs for patients taking less effective versus more effective regimens were not significantly different.31 These findings raised questions about the degree to which decision analytic models of H pylori eradication had directed decision makers to cost-effective therapeutic choices.

The present study explored that issue, responding to the call to validate and update models using “real life” outcomes data.3,32 The 2 models examined in this study, Model A30,33 and Model B,29 were selected because they are widely cited, well documented, and the only models to compare outcomes for patients treated with different H pylori eradication regimens in the United States. We first replicated the models’ results. Then, in place of model assumptions, we substituted actual service utilization measures derived from a database of integrated medical and pharmacy claims.

Research questions included: (1) To what extent do model-calculated and actual retreatment rates match? (2) To what extent do models’ assumed recurrence-related services match actual medical service-use patterns? (3) When models are empirically adjusted, do conclusions about the cost-effectiveness of different therapeutic choices change?

### Methods

Models were replicated using Data 3.5 for Health Care (TreeAge Software).34 Actual service utilization information came from an integrated medical and pharmacy claims database of commercially insured patients enrolled in several managed care organizations (approximately 70% independent practice association [IPA] and 30% group model) located throughout the United States. The 435 patients included in the present analysis are a subset of a sample used in a previously published study of retreatment rates and medical costs for patients aged >16 years who were treated with H pylori eradication regimens.31 The present study’s patients were treated with one of 3 regimens common to Models A and B: BMT (N = 98), PPI-clarithromycin (N = 207), and PPI-amoxicillin (N = 130). Of BMT-treated patients, 24% filled a prescription for an H2 receptor antagonist (H2RA) along with the eradication regimen medications.

Although Model A did not initially include patients treated with PPI 3-drug regimens, final analyses in the present study included an additional 119 patients treated with the 3-drug combination PPI-clarithromycin-metronidazole. These analyses were performed for 2 reasons. First, PPI-based 3-drug regimens are currently recommended, while PPI-based 2-drug regimens are generally recognized today as ineffective.35 Second, after its initial development, Model A was used to assess the cost-effec-

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**Table 1** Assumptions Used in Original Models of Helicobacter Pylori Eradication Rates

<table>
<thead>
<tr>
<th>Model</th>
<th>Base Case (%)</th>
<th>Lowest (%)</th>
<th>Highest (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model A</strong>29</td>
<td>Metronidazole resistance</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Compliance:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bismuth + metronidazole + tetracycline</td>
<td>65</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Proton pump inhibitor + clarithromycin</td>
<td>95</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Proton pump inhibitor + amoxicillin</td>
<td>95</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Efficacy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bismuth + metronidazole + tetracycline</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Proton pump inhibitor + clarithromycin</td>
<td>78</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Proton pump inhibitor + amoxicillin</td>
<td>55</td>
<td>30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Model B</strong>29</th>
<th>Base Case (%)</th>
<th>Lowest (%)</th>
<th>Highest (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance-adjusted eradication success*:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bismuth + metronidazole + tetracycline</td>
<td>80</td>
<td>78</td>
<td>82</td>
</tr>
<tr>
<td>Proton pump inhibitor + clarithromycin</td>
<td>65</td>
<td>61</td>
<td>68</td>
</tr>
<tr>
<td>Proton pump inhibitor + amoxicillin</td>
<td>58</td>
<td>55</td>
<td>60</td>
</tr>
<tr>
<td>Posteradication recurrence, <em>H pylori</em> negative</td>
<td>3</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Posteradication recurrence, <em>H pylori</em> positive</td>
<td>73</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

*Lowest and highest rates represent the lower and upper limits, respectively, of the 95% confidence interval.
tiveness of PPI-based 3-drug regimens.\textsuperscript{33} The database's and models' study time periods were approximately the same. Database patients were continuously eligible from April 1, 1995, through December 31, 1996, and filled prescriptions for an \textit{H pylori} eradication regimen during the time period June 1, 1995, through May 31, 1996. Each patient's follow-up period began on the date that the regimen prescriptions were filled and ended on the study end date, December 31, 1996. Database patients met one or more of the following clinical criteria during the 60 days + the regimen date: (1) primary, secondary, or tertiary diagnosis (International Classification of Diseases, 9th revision, [ICD-9]) code for ulcer disease (531XX-534XX), gastritis/duodenitis (535XX), stomach function disorder (536XX), abdominal pain (7890X), or \textit{H pylori} infection (041.86), or (2) Current Procedural Terminology (CPT) code for endoscopy (432XX) or \textit{H pylori} assay (86677). To reflect typical clinical practice, all patients meeting these criteria were included regardless of dose or duration of eradication treatment.

Database diagnostic criteria were consistent with those of the models, both of which have been applied to populations treated for \textit{H pylori} infection irrespective of whether the precipitating diagnosis was ulcer disease or another condition (e.g. gastritis or nonulcer dyspepsia).\textsuperscript{29,31} However, because Model A's patient population initially was limited to duodenal ulcer patients with confirmed infection,\textsuperscript{30} we performed sensitivity analyses on a subset of patients with a diagnosis of ulcer disease combined with either diagnosed \textit{H pylori} infection or procedure codes for endoscopy or \textit{H pylori} assay. Additional sensitivity analyses limited the sample to patients with >1 claim from a GI specialist during the time period from 30 days before through 7 days after the initial regimen date because GI specialists are more likely than primary care physicians to treat \textit{H pylori} infection appropriately.\textsuperscript{36}

**Comparison of Models—Calculated With Actual Retreatment Rates**

To replicate Model A's recurrence rates, baseline eradication rates for each regimen were reduced by factors representing assumed noncompliance and, for BMT patients only, assumed metronidazole resistance. The resulting eradication rates were then weighted by assumed recurrence rates for patients with (2%) and without (86%) bacterial eradication.\textsuperscript{54} For Model B patients, baseline eradication rates for each regimen were reduced by assumed noncompliance factors to replicate that model's compliance-adjusted result.\textsuperscript{29}

For database patients, retreatment was defined as filling a second set of eradication regimen prescriptions (for either the same or a different regimen) during the follow-up period. For both database and model patients, “best case” and “worst case” retreatment rates were calculated. For database patients, the best-case and worst-case rates were, respectively, the lower and upper limits of the 95% confidence intervals around actual retreatment rates. Calculation of best-case and worst-case rates for the models were based on model assumptions and sensitivity ranges. Best-case rates used the lower limits of models' sensitivity ranges for metronidazole resistance and recurrence and the upper limits of sensitivity ranges for compliance and eradication rate (Table 1). Worst-case rates used the opposite ends of the sensitivity ranges.

To address the possibility that some patients with recurrent symptoms were treated with antisecretory therapy instead of repeat eradication therapy, a sensitivity analysis defined a patient as having persistent symptoms, albeit not necessarily recurrent infection, if either retreatment or initiation of antisecretory therapy occurred during the follow-up period. This approach might seem counterintuitive since the NIH consensus statement recommended eradication therapy on either initial or subsequent disease presentation.\textsuperscript{9} We made the calculation because Model A assumed that all patients with recurrent disease would be treated with antisecretory therapy alone and that patients without recurrent disease would receive no antisecretory drugs.

Our original analysis plan was to substitute actual retreatment rates into both models and assess the impact on model-calculated total medical cost. However, we were able to replicate costs fully for Model A only. After consultation with one of Model B's authors, further attempts to replicate costs for Model B became infeasible due to author availability problems. Thus, only retreatment rates are presented for Model B.

**Comparison of Models—Assumed With Actual Medical Services**

Model A assumed that all patients would receive initial and final office visits plus the \textit{H pylori} eradication medications and that patients with recurrent disease would receive additional medical and pharmacy services attributable to disease recurrence. We updated Model A with database-derived utilization rates for both retreated and nonretreated patients. (Methodological note: In calculating cost attributable to retreatment, this approach is mathematically equivalent to updating the model with the difference between the utilization rates for retreated and nonretreated patients. For example, if a service is used by 50% of retreated and 30% of nonretreated patients, we could either directly substitute those figures into the model or assume a retreatment-related utilization rate of 20% (with 0% assumed for nonretreated patients). We selected the former approach because it is more straightforward and reflects actual service use.) For each retreated database patient, a medical service (office visit, endoscopy, or hospitalization) was defined as retreatment-related if it occurred during the 45-day period from 14 days prior through 30 days after (~14+30) that patient's retreatment date. To avoid confusing retreatment-related costs with initial treatment costs, we eliminated from the medical service analyses 2 patients whose retreatment occurred fewer than 15 days after the initial treatment. To have 30 days of postretreatment data for all patients, we also eliminated 7 patients whose retreatment occurred fewer than 30 days prior to the end of the study. Thus, of 58 retreated patients, 49 were included in these analyses.
Do Decision-Analytic Models Identify Cost-Effective Treatments? A Retrospective Look at *Helicobacter Pylori* Eradication

**FIGURE 1** Model A Baseline Replication
To obtain comparable data for nonretreated patients, we first calculated the mean number of days from initial treatment to retreatment for retreated patients. That figure—117 days—was added to each nonretreated patient's initial eradication regimen date to produce the nonretreatment-comparison date. The time period from 14 days prior to 30 days after the nonretreatment-comparison date was then used to calculate nonretreatment-comparison utilization and costs. Sensitivity analyses measured the percentages of retreated and nonretreated patients with any GI service use in the follow-up period, regardless of the timing of the service use relative to the retreatment date.

We defined GI costs to include not only ulcer disease but also a wide variety of GI symptoms. Thus, we identified office visit and hospital services as GI-related if they either met the diagnostic or procedural criteria for study inclusion or included any of the following ICD-9 codes: 530XX (diseases of esophagus), 537XX (other gastroduodenal disorder), 787XX (GI system symptoms), 5781X (blood in stool), 564XX (functional digestive disorder), or 5699X (intestinal disorder not otherwise specified). For any hospital stay in which either the primary, secondary, or tertiary diagnosis met these diagnostic criteria, costs for all professional and facility claim lines were summed to calculate hospitalization cost.

Although Model A assumed only use of H2RAs in assessing antisecretory medication use, we also included PPI use to be as consistent as possible with the model assumption of high recurrence-related costs. Antisecretory drugs were identified using a Generic Product Identifier (GPI) code beginning with either “42” (H2RA) or “49” (PPI). The percentages of patients with ≥1 claim for an antisecretory medication at any time following the retreatment date (retreated patients) or retreatment-comparison date (nonretreated patients) were calculated. The percentages of retreated and nonretreated patients still using antisecretory medication as of the study end, defined as having ≥1 claim within 45 days of December 31, 1996, were also calculated. Model A assumed that antisecretory use continued for 18 months for all patients with recurrent disease. To be as consistent as possible with model results, we assumed that all patients still using antisecretory medications at the study end date continued to use them for the full 18 months assumed by Model A. For patients not still using antisecretory medications at study end, we calculated the mean length of actual use and substituted that figure into the model.

We substituted actual allowed billed charge data into Model A instead of the model’s assumed costs. Allowed billed charges exclude noncovered services but do not reflect payers’ discounts off the total billed charge. Thus, results are unaffected by discounts unique to any particular health plans. To assess expenses for initial and final office visits, we calculated the mean charge for all GI-diagnosis office visits occurring on or up to 7 days prior to the regimen date. Mean charges for office visits and endoscopies were calculated for the −14/+30-day period. Mean monthly charges for antisecretory drugs were calculated for all claims after the retreatment date. Mean hospital charges were calculated for the −14/+30-day period. Since only 7 hospitalizations occurred during that time, we also calculated charges for the 70 hospitalizations occurring throughout the follow-up period as a sensitivity analysis. This methodology is similar to Model A’s, which used national average inpatient charges for ulcer diagnoses as the source of its hospital cost figure.

### Cost Per Effectively Treated Patient

For the original Model A, the effective treatment rate was 1 minus the estimated recurrence rate. For the empirically revised model, the effective treatment rate was 1 minus the actual retreatment rate. For both models, cost per effectively treated patient was calculated as total estimated cost per treated patient divided by the effective treatment rate.

### Results

Model A’s reported outcome—total cost associated with each of the 3 regimens—was replicated to within $1 for 2 of the regimens (BMT and PPI-clarithromycin) and to within $3 for PPI-amoxicillin (Figure 1). Model A’s sensitivity analyses were also replicated. Model B’s recurrence rates were replicated exactly.
for PPI-clarithromycin and PPI-amoxicillin, and within 1 percentage point for BMT.

**Retreatment Rates**

Both models’ results overstated actual retreatment rates (Table 2). Across all regimens, model-calculated rates were higher than actual rates of retreatment. The discrepancy between modeled and actual retreatment rates was particularly large for BMT. Model A’s “Base Case” retreatment rates for BMT, PPI-clarithromycin, and PPI-amoxicillin exceeded actual rates by 367%, 57%, and 122%, respectively, and exceeded the upper limit of actual rates’ 95% confidence interval (“Worst Case”) by 155%, 22%, and 60%. For the same regimens, Model B’s Base Case exceeded actual rates by 183%, 100%, and 78% and exceeded the upper limit of actual rates’ 95% confidence interval by 55%, 22%, and 28% respectively.

Results were similar when the sample was limited to patients with (1) diagnosed ulcer disease in combination with an *H pylori* diagnosis, endoscopy, or *H pylori* assay or (2) GI specialty treatment (not shown). When persistent symptoms were defined to include either retreatment or antisecretory therapy, rates were considerably higher for all regimens, as expected, but the pattern of differences among the regimens remained similar.

**Patterns of Care for Retreated and Nonretreated Patients**

Nonretreated patients generally used more services, and retreated patients used fewer services than assumed in Model A (Table 3). The model assumed that 100%, 100%, and 50% of patients
with recurrent disease would use antisecretory medications, office visits, and endoscopies, respectively. The model further assumed use rates of 0% for these services for nonrecurrent patients. Actual respective use rates for these services were 65%, 41%, and 6% for retreated and 46%, 10%, and 2% for nonretreated patients.

Revised per-service charges were somewhat higher than costs originally assumed by Model A for office visits and antisecretory medication but less than half that assumed for endoscopies (Table 3). The model assumed that all hospitalizations were inpatient at $22,809 each, but more than 80% of the 70 hospital episodes during the follow-up period, and 4 of the 7 hospitalizations during the –14/+30-day period were outpatient, making actual charges substantially lower than assumed charges. Mean (median) charges per hospitalization were $5,022 ($1,488) for the 7 hospitalizations occurring during the –14/+30 period and $3,256 ($1,394) for the 70 hospitalizations occurring during the entire follow-up period. To be as consistent as possible with the models’ assumption of high recurrence-related costs, we used the higher $5,000 figure in the revised model.

Sensitivity analyses of service-use rates produced similar findings, whether measuring service use for the entire study period, for ulcer patients, or for patients treated by GI specialists (not shown). For nearly every service category, utilization rates were significantly higher for retreated than nonretrained patients. However, use rates for retreated patients were not as high as assumed by Model A, and nonretrained patients’ utilization rates consistently exceeded 0%.

**Effect of Changed Assumptions on Results**

Revising Model A to reflect actual retreatment rates and service costs produced substantial changes in results (Table 4, Figure 2), with BMT more cost effective and PPI-clarithromycin less cost effective than originally estimated. In the original replicated Model A, costs per effectively treated patient were slightly higher for BMT and much higher for PPI-amoxicillin than for PPI-clarithromycin. After revising Model A for actual retreatment rates, potential limitations should be discussed.

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Changes to Cost-Effectiveness Findings After Modifications to Model A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMT</strong></td>
<td>PPI-clarithromycin</td>
</tr>
<tr>
<td>Total cost per patient ($)</td>
<td>721</td>
</tr>
<tr>
<td>Patients with no retreatment (%)</td>
<td>72.0</td>
</tr>
<tr>
<td>Cost per effectively treated patient ($)</td>
<td>1001</td>
</tr>
<tr>
<td><strong>Final adjusted model</strong></td>
<td></td>
</tr>
<tr>
<td>Total cost per patient ($)</td>
<td>800</td>
</tr>
<tr>
<td>Patients with no retreatment (%)</td>
<td>93.9</td>
</tr>
<tr>
<td>Cost per effectively treated patient ($)</td>
<td>852</td>
</tr>
</tbody>
</table>

Cost-Effective Findings After Including Patients Treated With PPI-clarithromycin-metronidazole

| **PPI-clarithromycin-metronidazole** |
| BMT | PPI-clarithromycin | PPI-amoxicillin |
| Total cost per patient ($) | 795 | 961 | 916 |
| Patients with no retreatment (%) | 93.9 | 86.5 | 81.5 |
| Cost per effectively treated patient ($) | 847 | 1111 | 1123 |

PPI = Proton pump inhibitor. BMT = Bismuth-metronidazole-tetracycline.

This is one of few studies to validate pharmaco-economic decision-analytic models. The findings corroborate the findings of other critical reviews39 and raise questions about models’ role in guiding treatment selection. Before considering these implications, potential limitations should be discussed.

One is the possibility that some nonretreated database patients actually had persistent infections that will result in future recurrences and medical cost. Indeed, if one assumes that 100% of patients with persistent infection seek treatment, database retreatment rates are lower than expected given published efficacy data. However, this study meets a need for outcomes research recognizing that patients with persistent *H pylori* infection are not always sufficiently symptomatic to seek medical attention. Moreover, the follow-up period to identify retreatments in the database study (range 7 to 19, median 12.5 months) was generous compared with model parameters. Under Models A and B, respectively, recurrences were assumed to occur at 6 months and 4 to 7 months.

An additional potential concern is selection bias, i.e., that patients whom physicians knew to be less compliant were prescribed PPI-based regimens because these were considered more tolerable than BMT. This possibility is belied by the similarity between the present study’s results and findings of randomized clinical trials. Specifically, based on the results of randomized clinical trials, one would expect the lowest retreatment rates for BMT and PPI-clarithromycin-metronidazole, higher rates for PPI-clarithromycin, and the highest rates for PPI-amoxicillin, consistent with what was observed in the claims database.
Another potential issue is inaccuracy inherent to use of a claims database, particularly imprecision in diagnostic coding. While this possibility exists, there is no reason to believe it affected patients treated with any particular regimen. Moreover, neither utilization nor retreatment rate findings were sensitive to stringency of diagnostic criteria for study entry or receipt of specialty care.

These findings represent just one database, albeit a geographically diverse and multipayer database. Results for other populations could be different. We urge payers with access to integrated medical and pharmacy data to conduct similar validations of these and other models to test key model assumptions and results against empirical evidence.

A final potential limitation is inherent to all models. We have adjusted a model's 2-year cost projections based on data from a shorter time period. Even an adjusted and more accurate model is still only a model, not a direct cost measurement over the full 2 years. In particular, the true length of antisecretory therapy is unknown. The assumption that all patients still using antisecretory drugs at study end continued to use them for 18 months is somewhat questionable but was made to be as consistent as possible with Model A's original assumptions.

Conclusions

Findings derived from this study's multipayer database suggest that the pharmacoeconomic model results for H pylori eradication did not direct decision makers to cost-effective treatment choices. BMT's retreatment rates were overestimated by both models. Moreover, after adjusting Model A to reflect actual retreatment rates and service-use patterns, BMT was more cost effective and PPI-clarithromycin less cost effective than Model A had originally indicated.

But did the publication of these pharmacoeconomic models actually affect the behavior of decision makers such as physicians and formulary developers? One might argue that, since the limitations of models are widely recognized, the present study's findings are of little import. Research and policy literature published in the years following the models' development refute that view since models were commonly cited to justify use of more expensive drug regimens. For example, in a journal targeted to formulary decision makers, a physician panel member citing Model A concluded in 1998 that "if a regimen costs $100 but fails to cure the patient's disease, then endoscopy will be needed … at a cost of about $1,000." Similarly, a 1998 review article, appearing in a prominent journal targeted to physicians, cited Model A to document that "ineffective treatment regimens increase the costs associated with treatment because they result in the need for continued interaction with health care providers, further procedures, and maintenance therapy." Notably, in both instances, the cited...
Do Decision-Analytic Models Identify Cost-Effective Treatments? A Retrospective Look at Helicobacter Pylori Eradication

Information represented model assumptions, described as if they had been empirically determined.

Consideration of specific problems in the models can guide recommendations to enhance models’ usefulness. Several problems in key assumptions affected model results.

First, the assumption that all successfully treated patients discontinue antisecretory medication, although common to H pylori eradication models at that time, appears to have been incorrect. The present study findings are consistent with more recent assumptions reduced the estimated cost for patients receiving hospital services from more than $24,000 to approximately $6,000.

Second, assumptions about the degree of noncompliance and its impact on patient outcomes played a substantial role in discrepancies between modeled and database outcomes. Model A’s assumed compliance of 65% with triple therapy (bismuth-metronidazole-tetracycline) and 95% with PPI-clarithromycin and PPI-amoxicillin regimens even though in most clinical trials published before 1996, dropout rates for all regimens including triple therapy were less than 5%. The highest dropout rate that had been observed for triple therapy was 20% in a nonrandomized trial with 40 patients. Model B’s compliance assumptions were based on a study of NSAID therapy dosing schedules. Whether NSAID and H pylori therapies are sufficiently comparable to generate similar compliance patterns is open to question.

Third, assumptions about the degree of noncompliance and its impact on patient outcomes played a substantial role in discrepancies between modeled and database outcomes. Model A’s assumed compliance of 65% with triple therapy (bismuth-metronidazole-tetracycline) and 95% with PPI-clarithromycin and PPI-amoxicillin regimens even though in most clinical trials published before 1996, dropout rates for all regimens including triple therapy were less than 5%. The highest dropout rate that had been observed for triple therapy was 20% in a nonrandomized trial with 40 patients. Model B’s compliance assumptions were based on a study of NSAID therapy dosing schedules. Whether NSAID and H pylori therapies are sufficiently comparable to generate similar compliance patterns is open to question.

Fourth, Model A’s sensitivity testing included primarily 1-factor analyses that did not foresee the discrepancies in multiple assumptions observed in our study. The only reported
2-factor analysis included a sensitivity test on metronidazole resistance and compliance in which compliance was assigned an upper limit of 80% for BMT and a lower limit of 75% for the PPI-based regimens.

The choices made by the authors of these models demonstrate the “gray areas” that decision-analytic modelers face when they try to predict outcomes of new treatment approaches. For example, any compliance assumptions made in 1996 were unavoidably speculative because empirical data on compliance rates with *H pylori* eradication in clinical practice were not available. However, publications relying on *H pylori* model results in making cost-effectiveness assessments were appearing in the literature at the same time that some physician letters and commentaries were questioning model assumptions.

These problems demonstrate the value of standard techniques to ascertain expert opinion, such as a Delphi panel. Neither Model A nor Model B used an expert panel in developing compliance assumptions, although Model B used an expert panel in developing utilization assumptions.

An additional important step would be the increased use of sophisticated modeling techniques to reflect more precisely the probabilities of various treatment outcomes. A recent study applying “bootstrapping” methodologies to Model B suggested that the revised method yielded additional insights into *H pylori* eradication. Such techniques might be particularly useful when there is truly no way to predict a clinical outcome such as, for example, the rate at which patients will continue to use antisecretory drugs after successful *H pylori* eradication.

Despite the overall transparency and thorough documentation of these 2 models, replicating them was not an easy task, and we were unable to fully replicate costs for Model B. To facilitate validation efforts of this type, we would echo opinions that electronic versions of models should be made readily available to other researchers after publication and a required part of submission for prepublication peer review.

Our findings raise concerns about peer review of these models. Models are, by definition, heavily reliant on their assumptions. Particularly in Model A, key model assumptions about compliance and recurrence-associated utilization were largely unsupported. Whether models are using the best available information should be a key part of the peer-review process.

One might argue that the need for rapid information about newly introduced drugs is so acute that the use of “common sense,” albeit unstudied, assumptions is sometimes necessary, recognizing that no pharmacoeconomic model is ever 100% accurate. In other words, a balance between speed and accuracy will remain an unavoidable fact of life in pharmacoeconomics. However, when inaccuracies in a model’s assumptions are so inconsistent across treatments that empirical correction of the model changes treatment recommendations, one must question the usefulness of the model. This question, and the more general question of what criteria should be used to assess the validity of pharmacoeconomic models, should receive more serious attention.

While errors in economic modeling may not be as troubling as errors in studies of efficacy or safety, preventing and correcting such errors is in patients’ best interest. Since health care resources are finite, payer funds expended on one treatment are, by definition, unavailable for others. Moreover, since patients commonly pay portions of both monthly premiums and per-prescription costs, promoting cost-effective treatment decisions ultimately controls not only payers’ costs but also patients’ out-of-pocket expenditures.

Our findings reaffirm the oft-expressed need for ongoing examination of the validity of pharmacoeconomic models.

ACKNOWLEDGMENTS
The authors thank Emily Cox, PhD, for comments on the study’s design, C. Daniel Mullins, PhD, for his helpful review of an earlier version of this manuscript, and Zafar Hakim, PhD, for thoughtful comments that made a valuable contribution to the improvement of this manuscript.

DISCLOSURES
Funding for this research was provided by Express Scripts, Inc., employer of authors Kathleen A. Fairman and Brenda R. Mothetal. Fairman served as principal author of the study. Study concept and design, analysis and interpretation of data, drafting of the manuscript and its critical revision, and statistical expertise were contributed by both authors.

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Evaluation of Personal Digital Assistant Drug Information Databases for the Managed Care Pharmacist

COLLEEN M. LOWRY, PharmD; MARIA D. KOSTKA-ROKOSZ, PharmD; and WILLIAM W. McCLOSKEY, PharmD

ABSTRACT

BACKGROUND: Personal digital assistants (PDAs) are becoming a necessity for practicing pharmacists. They offer a time-saving and convenient way to obtain current drug information. Several software companies now offer general drug information databases for use on handheld computers. PDAs priced less than $200 often have limited memory capacity; therefore, the user must choose from a growing list of general drug information database options in order to maximize utility without exceeding memory capacity.

OBJECTIVE: This paper reviews the attributes of available general drug information software databases for the PDA. It provides information on the content, advantages, limitations, pricing, memory requirements, and accessibility of drug information software databases.

SUMMARY: Ten drug information databases were subjectively analyzed and evaluated based on information from the product’s Web site, vendor Web sites, and from our experience. Some of these databases have attractive auxiliary features such as kinetics calculators, disease references, drug-drug and drug-herb interaction tools, and clinical guidelines, which may make them more useful to the PDA user.

CONCLUSION: Not all drug information databases are equal with regard to content, author credentials, frequency of updates, and memory requirements. The user must therefore evaluate databases for completeness, currency, and cost-effectiveness before purchase. In addition, consideration should be given to the ease of use and flexibility of individual programs.

KEYWORDS: Personal digital assistant (PDA), Drug information, Drug information software, Drug information databases, Pharmacist

J Managed Care Pharm. 2003;9(5):441-48

Personal digital assistants (PDAs) have become an indispensable tool for pharmacists practicing in a variety of settings. They promote patient safety and improve quality of care by providing quick access to drug information. PDAs offer a significant advantage over text publications in terms of information currency. Many pharmacy database programs offer monthly, weekly, or even daily information updates. Pharmacists are not only using PDAs to access drug information but also to record activities and interventions, reconcile patient medication histories with medications on admission, and document medication errors. PDAs permit more efficient use of the pharmacist’s time.

Pharmacists join other health care providers in using PDAs in the scope of their daily practice. Approximately 30% of physicians now own a PDA, with the percentage expected to increase to 50% by 2005. Fifty percent of physicians are using PDAs in their clinical practice to access drug and reference information. By 2004, 20% of physicians will be using PDAs for prescription entry, retrieval of lab data, dictation, and medical billing. This percentage may further increase as managed care organizations become involved in electronic prescribing initiatives. A study by Papshev and Peterson in the Journal of Managed Care Pharmacy found that 61% of managed care pharmacy managers felt electronic prescribing implementation was feasible, while only 16% had implemented electronic prescribing. Nurses, too, are finding that PDAs are an efficient way to streamline the patient-information-gathering process and to reduce paperwork.

Health care professionals are reaching for PDA technology not just for convenience but also to combat the number of medication errors that occur each year. A recent study of 1,116 hospitals showed that medication errors occurred in 5% of patients per year, corresponding to approximately 1 error every 23 hours or 1 in 20 hospital admissions. Fortunately, not all of these medication errors adversely affected patient outcomes. Medication errors are not confined to the inpatient setting, and a current study is underway to determine if the use of PDAs reduces medication errors in the primary care setting.

As with all new technologies, PDAs have limitations. Cost, battery life, and memory capacity may place restrictions on their usage. Costs range from $100 to $800 per device, depending on the features of the model selected. Batteries last for up to 15 hours before having to be recharged. Most PDAs are preloaded with one of 2 operating systems, Palm OS or Microsoft Pocket PC, which manage all other software programs installed on the handheld device. Memory capacities range from 2MB to 51MB for Palm OS and 4MB to 128MB for Pocket PC systems, often with the option of adding additional memory via an expansion card, which resembles a tiny disk. Table 1 lists drug

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The A2zDrugs information database is more of the authors.

This article reviews and subjectively analyzes 10 general drug information database options, their potential advantages, possible limitations, pricing information, memory requirements (Table 2), and where they can be accessed via the Internet. Other PDA specialty drug information databases have been reviewed elsewhere.11 The 10 databases evaluated were, to our knowledge, the only general drug information databases available at the time this manuscript was developed. Databases were analyzed using information provided on the product’s Web site, vendor Web sites, and from our experience. An asterisk (*) indicates that a particular product has been tested by one or more of the authors.

<table>
<thead>
<tr>
<th>Database Program Compatibility With Expansion Cards</th>
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<tbody>
<tr>
<td><strong>Database</strong></td>
</tr>
<tr>
<td>A2zDrugs</td>
</tr>
<tr>
<td>AHFS Drug Information</td>
</tr>
<tr>
<td>DrDrugs</td>
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<tr>
<td>ePocrates Rx</td>
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<tr>
<td>ePocrates Rx Pro Premium</td>
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<tr>
<td>Lexi-Platinum</td>
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<tr>
<td>MobileMICROMEDDEX</td>
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<tr>
<td>MosbyDrugs</td>
</tr>
<tr>
<td>PDRDrugs</td>
</tr>
<tr>
<td>Physician’s Drug Handbook</td>
</tr>
<tr>
<td>Tarascon Pocket Pharmacopoeia Deluxe</td>
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</tbody>
</table>

Other PDA specialty drug information databases have been analyzed using information provided on the product’s Web site, vendor Web sites, and from our experience. An asterisk (*) indicates that a particular product has been tested by one or more of the authors.

**Drug Information Database Options**

**A2zDrugs (version 6.0.152)**

**Description:** There are several A to Z Drug Facts products produced by Facts and Comparisons, including A2zDrugs, Drug Facts Silver, Drug Facts Gold, and Drug Facts Platinum.12-14 The A2zDrugs information database has more than 700 drug monographs. These monographs contain information such as brand name, classification, actions, route/dosage, overdose, indications, precautions, contraindications, adverse reactions, lists of interacting agents, pregnancy information, administration/storage, age, patient/family education, assessment/interventions, and lab interference information. Drug Facts Silver offers more drug monographs (more than 850), pronunciation guides, information on dosage form/strength, and how the product is supplied, and auto-updates. Drug Facts Gold includes drug interaction screening technology, which allows the user to input patient medications and “screen” for interactions, in addition to the enhancements made to the Drug Facts Silver database. The drug interaction screening tool iFacts includes interaction significance, principals, drugs, effects, mechanisms, management, and references. Drug Facts Platinum includes all of the information from Drug Facts Gold plus a natural products database with more than 300 monographs taken from The Review of Natural Products, published by Facts and Comparisons. These natural product monographs contain scientific and common names, uses, dosing, lists of drug interactions, side effects, and sections on botany, history, pharmacology, and toxicology.

**Potential Advantages:** A free trial version is available from www.skyscape.com. Patient care and clinical information are separated for ease of use in monographs. In addition to the full monographs provided for approved products, condensed information is also presented for investigational, orphan, and combination drugs. The iFacts tool provides references for interactions. A personalized list of frequently used drugs can be created for faster access to information. Free-text notes can be entered in the note section.

**Potential Limitations:** The A2zDrugs information database is sold separately from the drug interaction screening technology. Drug Facts Silver, Gold, and Platinum are compatible with expansion cards of Pocket PC but not Palm OS devices. There is no information on cost or cost comparisons. The Review of Natural Products received only a fair recommendation as a primary reference in a recent review of herbal-reference literature, based on inconsistencies among monographs.15 A recent study, supported by the St. Louis College of Pharmacy Research Incentive Fund, questioned the clinical usefulness of A to Z Drug Facts.16

**AHFS (American Hospital Formulary Service) Drug Information (version 2003)**

**Description:** The handheld version of AHFS Drug Information has a database of more than 1,200 monographs indexed by therapeutic class, brand name, generic name, and keywords.17 Monographs contain dosage and administration information, uses, cautions, toxicity, drug interactions, pharmacology, pharmacokinetics, stability, and expert analysis. There is also an option to create a personalized formulary through the American Society of Health-System Pharmacists (ASHP) Access System.
**TABLE 2** Summary Description of Drug Information Databases

<table>
<thead>
<tr>
<th>Software Program</th>
<th>Memory Required</th>
<th>Advantages</th>
<th>Limitations</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2zDrugs</td>
<td>3.6MB Palm OS, 7.3MB Pocket PC</td>
<td>• Free trial version&lt;br&gt;• Investigational and orphan drugs&lt;br&gt;• Can create personalized drug lists&lt;br&gt;• Note-entering capability&lt;br&gt;• Monthly updates</td>
<td>• Drug interaction screening software sold separately&lt;br&gt;• Silver, Gold, Platinum products only compatible with Pocket PC expansion cards&lt;br&gt;• No drug cost information</td>
<td>$49.95 per year</td>
</tr>
<tr>
<td>AHFS Drug Information</td>
<td>Multimedia card</td>
<td>• More portable than the text version&lt;br&gt;• Monthly updates</td>
<td>• Updates are not automatic&lt;br&gt;• No free trial version</td>
<td>$100.00 per year</td>
</tr>
<tr>
<td>DrDrugs</td>
<td>2.5MB Palm OS, 5.8MB Pocket PC</td>
<td>• Free trial version&lt;br&gt;• Monographs for 30 alternative agents&lt;br&gt;• Note-entering capability</td>
<td>• No drug cost information</td>
<td>$49.95 per year</td>
</tr>
<tr>
<td>ePocrates Rx</td>
<td>2.5MB Palm OS</td>
<td>• Free download&lt;br&gt;• Formulary information&lt;br&gt;• Automatic updates&lt;br&gt;• MultiCheck drug interaction software</td>
<td>• Not compatible with expansion cards</td>
<td>Free</td>
</tr>
<tr>
<td>ePocrates Rx Pro Premium</td>
<td>3.0MB Palm OS, 4.0MB Pocket PC</td>
<td>• Alternative agent monographs&lt;br&gt;• DocAlert system&lt;br&gt;• MedMath calculator&lt;br&gt;• ePocrates ID</td>
<td>• Not compatible with expansion cards</td>
<td>$49.99 per year</td>
</tr>
<tr>
<td>Lexi-Platinum</td>
<td>2.7 to 5.8MB Palm OS, 3.4 to 5.8MB Pocket PC</td>
<td>• International brand name index&lt;br&gt;• Free trial version&lt;br&gt;• Discounts available for students, faculty and on multiple database purchases</td>
<td>• Each Lexi database is sold separately&lt;br&gt;• No drug cost information</td>
<td>$75.00 per year</td>
</tr>
<tr>
<td>Mobile MICROMEDEX</td>
<td>1.8MB Palm OS, 2.2MB Pocket PC</td>
<td>• Free for individuals/institutions who subscribe to the MICROMEDEX system&lt;br&gt;• Automatic updates&lt;br&gt;• Free trial version</td>
<td>• No drug cost information&lt;br&gt;• Drug interaction screening software purchased separately&lt;br&gt;• No note-entering capability</td>
<td>$74.95 per year</td>
</tr>
<tr>
<td>MosbyDrugs</td>
<td>5.6MB Palm OS, 13.5MB Pocket PC</td>
<td>• Evaluates drug interactions and gives recommendations for clinical management&lt;br&gt;• Free trial version</td>
<td>• Source of drug cost information is not revealed</td>
<td>$64.95 *</td>
</tr>
<tr>
<td>PDRDrugs</td>
<td>2.1MB Palm OS, 5.6MB Pocket PC</td>
<td>• Free trial version&lt;br&gt;• Note-entering capability</td>
<td>• Package insert information only&lt;br&gt;• Drug interaction screening software purchased separately</td>
<td>$49.95 per year</td>
</tr>
<tr>
<td>Physician’s Drug Handbook</td>
<td>2MB Palm OS/Pocket PC</td>
<td>• Does not present any significant advantages over other databases due to dated material</td>
<td>• Corresponds to the 9th edition of the Physician’s Drug Handbook published in 2001 – not current</td>
<td>$75.00 *</td>
</tr>
<tr>
<td>Tarascon Pocket Pharmacopoeia Deluxe</td>
<td>1.5MB Palm OS/Pocket PC</td>
<td>• Prerelease version available as a free download&lt;br&gt;• Referenced drug interaction software&lt;br&gt;• Alternative agent monographs</td>
<td>• Limited drug cost information</td>
<td>$25.00 per year</td>
</tr>
</tbody>
</table>

*Indicates a one-time fee; no updates except with release of new product version.

**Additional Information:** **AHFS Drug Information** is supplied on a multimedia card that is compatible with Franklin eBookman, Palm OS, and Pocket PC devices. The database can also be purchased on CD-ROM and then downloaded onto an expansion card for use on the PDA. The multimedia card and CD-ROM are available for $100 from www.ashp.org.

**Potential Advantages:** The PDA version of **AHFS Drug Information** is a more convenient way to utilize this reference than the print version. The PDA multimedia card version is not abridged and contains all monograph information (approximately 4,000 pages) available in the printed **AHFS Drug Information.** Free monthly online updates are available.

**Potential Limitations:** A free demonstration of the multimedia card is not available, although a 30-day trial of the ASHP Access System, which includes a choice of **AHFS Drug Information** monographs, is available. An automatic update feature is currently unavailable. The user is informed of monthly updates via e-mail and then must download the update from the Internet.
**DrDrugs Davis Drug Guide for Physicians (version 6.0.152)**

**Description:** DrDrugs is a collection of 1,500 drug monographs with concise drug information. Monographs contain the following: U.S. and Canadian drug brand names, classification, action, pharmacokinetics, time/action profile, route and dosage, indications, contraindications and precautions, adverse drug reactions and side effects, lists of interacting agents, pregnancy risk factors, controlled substance schedule, and U.S. and Canadian availability. Monographs are indexed by brand and generic names, therapeutic classification, and pharmacologic classification. In addition to standard drug monographs, there are also monographs for 475 combination products and several commonly used alternative agents.

**Additional Information:** DrDrugs is compatible with Palm OS and Pocket PC. An annual subscription costs $49.95 and can be purchased from www.collectivemed.com or www.skyscape.com.

**Potential Advantages:** This database provides monographs for approximately 30 alternative agents. A free demonstration version is available from www.collectivemed.com or www.skyscape.com. Notes can be entered for each drug monograph.

**Potential Limitations:** No cost information is provided in drug monographs. References are not provided for monographs or drug interactions.

**ePocrates (version 6.0)**

**Description:** The daily-updated drug information program ePocrates is divided into 2 databases: ePocrates Rx and ePocrates Rx Pro Premium. Both databases offer more than 2,800 drug monographs, formulary information for selected health plans, MultiCheck drug interaction technology, and automatic updates when hot syncing, linking the PDA to a desktop or laptop computer that is connected to the Internet. Individual monographs are indexed by brand name, generic name, and drug class, with information on mechanism of action, metabolism, excretion, adult and pediatric dosing, contraindications and cautions, adverse reactions, drug interactions, pregnancy and lactation, DEA schedule, dosage forms, manufacturer, and cost. Monographs for several over-the-counter medications are included. DocAlerts, which provide updated clinical information, are available with both databases.

Additional features of the ePocrates Rx Pro Premium product include alternative agent monographs, an enhanced MultiCheck interaction system, ePocrates ID, a medical calculator, drug-comparison tables, and clinical guideline tables. Alternative agent monographs are taken from the Natural Medicines Comprehensive Database and include information on reported uses, reported dosage, adverse drug reactions, cautions, potential drug interactions, and synonyms. MultiCheck software for Rx Pro Premium scans for both drug-drug and drug-herbal interactions for up to 30 medicinal agents. The infectious disease database ePocrates ID indexes more than 300 diagnoses, 350 microorganisms, and 250 drugs. It gives empirical as well as specific treatment recommendations for adults and children. The medical calculator, MedMath, also available online free of charge, contains medical equations and will calculate patient-specific variables. MedMath provides the equation used in the calculation and a literature reference. Equations include body surface area, ideal body weight, and creatinine clearance, among 34 total equations. There are approximately 45 tables included in Rx Pro Premium, including steroid comparisons, insulin comparisons, therapeutic drug levels, and hypertension treatment guidelines.

**Additional Information:** The ePocrates Rx program is available as a free download from the company's Web site (www.epocrates.com). The enhanced version, ePocrates Rx Pro, is also available at www.epocrates.com for an annual fee of $49.99. Both ePocrates Rx and ePocrates Rx Pro are compatible with Palm OS. Pocket PC is compatible with ePocrates Rx Pro.

**Potential Advantages:** The Natural Medicines Comprehensive Database, which provides the alternative agent monographs, was recently reviewed and highly recommended for clinicians. The editors, authors, and reviewers of the ePocrates database include physicians and pharmacists who obtain monograph information from primary literature, such as clinical trials; drug manufacturers; society; or expert panel recommendations; drug safety alerts; and tertiary literature, such as textbooks and review articles. The DocAlert system is activated by updating ePocrates and enables the clinician to request, by selecting from a topic list on the PDA, additional information on new drugs, clinical trial results, FDA safety alerts, and other medical news. The requested information is then sent to the clinician via e-mail. The free version of ePocrates, which serves as a product demonstration, can satisfy general drug information needs. A note section is available for free text to be entered for each drug monograph. References are provided for MedMath calculations, ePocrates ID monographs, and for some clinical guidelines (e.g., Advance Cardiac Life Support Guidelines). Formulary information is available for more than 130 health plans as well as for many hospitals, pharmacy benefit managers, and other health care groups.

**Potential Limitations:** Drug cost information is estimated from pricing at drugstore.com, which provides costs for many oral and topical products, but few parenterally administered products. ePocrates is currently not compatible with expansion cards.

**Lexi-Comp (version unspecified)**

**Description:** Lexi-Comp is separated into several databases with multiweekly information updates. Lexi-Platinum, the comprehensive drug database, is divided into 3 views: Essential View, Comprehensive View, and Comprehensive Plus Specialty View. The Essential View contains information on brand/generic drug names, drug class, mechanism of action, pharmacokinetics/dynamics, general and special dosing information, approved
and investigational drug uses, contraindications/precautions, adverse reactions, lists of interacting agents, pregnancy/lactation, and dosage forms. The Comprehensive View adds synonyms; Canadian brand names; more detailed pregnancy/lactation information; drug effects when used with ethanol, herbs, or supplements; laboratory test interactions; product stability; administration; reference drug levels; dietary considerations; patient education; nursing information; overdose/toxicity data; monitoring parameters; anesthesia/critical care considerations; and geriatric information. The Comprehensive Plus Specialty View adds cardiovascular considerations, compatibility, mental health considerations, emetic and vesicant potential, bone marrow transplant considerations, and additional monitoring information. An international brand-name index, with medications from 58 countries, can be downloaded for use with the Comprehensive Plus Specialty View.

Potential Advantages: A recent comparison of Lexi-Platinum with other programs found it to be the most comprehensive and dependable drug information database. Speciality databases are available in the areas of infectious disease, pediatrics, poisoning and toxicology, natural products, dentistry, and nursing. A free product demonstration is available for nonsubscribers. The handheld databases are written and peer-reviewed by physicians, pharmacists, nurses, and toxicologists. MobileMICROMEDEX contains monographs for some over-the-counter medications in addition to prescription products. The database is automatically updated when the user hot syncs with a desktop computer. Individual hospitals or other institutions can have their formulary made accessible via PDA or desktop PC by using the MICROMEDEX Formulary Advisor.

Potential Limitations: There is no estimated drug pricing information. The scope of the MobileMICROMEDEX database is narrower than that of the MICROMEDEX system available online. The previously cited study in Pharmacotherapy found MobileMICROMEDEX to be unsuitable for clinical use. Interaction screening technology must be purchased separately. No references are provided for monographs. There is no opportunity to enter free-text notes within drug monographs.

MosbyDrugs (version 2001)*

Description: MosbyDrugs is the handheld version of Mosby's Drug Consult combined with MosbyIx, an interaction screening tool. This database references the Top 200 Drugs, plus other commonly used drugs. The database includes information on domestic and foreign brand names, therapeutic classification, clinical pharmacology, pharmacokinetics, adult and pediatric dosage, indications, contraindications, precautions, adverse effects, lists of interactions, pregnancy/lactation, special considerations, dosage forms, and cost. There are multiple indexes: Main Index (generic name), Brand Index, Chemical Index, Therapeutic Index, Indications Index, and the Index for International Brand Names. The MosbyIx interaction database...
presents the significance, recommended actions, special circumstances, and references for drug interactions. It also analyzes drug-lab interactions.

Additional Information: The PDA database is available from multiple vendors, including www.collectivemed.com and www.skyscape.com, for $64.95. It is compatible with Palm OS and Pocket PC systems.


Potential Limitations: The updated version of MosbyDrugs must be purchased when new editions are made available. The source of drug cost information is not revealed.

PDRDrugs (version 6.0.151)*

Description: This handheld database contains information from the Physicians' Desk Reference. Drug monographs include drug brand and generic names, therapeutic class, adult and pediatric dosing, indications, contraindications, adverse reactions, warnings and precautions, Black Box warnings, lists of interacting agents, pregnancy and nursing information, U.S. Drug Enforcement Administration class, how the product is supplied, and the manufacturer's name.

Additional Information: PDRDrugs is compatible with Palm OS and Pocket PC systems. An annual subscription with quarterly updates can be purchased for $49.95 at www.skyscape.com or www.collectivemed.com.

Advantages: A free product demonstration is available from www.collectivemed.com or www.skyscape.com. Drug monographs include the manufacturer's name. A section for free-text notes is provided.

Limitations: This database does not contain information on herbal products or non-U.S. Food and Drug Administration-approved indications since information is based on manufacturer package inserts for FDA-approved products. The drug interaction screening tool must be purchased separately. Drug cost information is not available.

Physician's Drug Handbook (version 2001)

Description: This product is based on the Physician's Drug Handbook and has 900 generic product monographs. The following information is contained within the monographs: pharmacodynamics and pharmacokinetics, route and dosage, overdosage, geriatric use, pediatric use, indications, contraindications, adverse reactions, interactions, effects on diagnostic tests, breastfeeding, how supplied, special considerations, information for the patient, and summary information of drug use in specific disease states.

Additional Information: This database is compatible with Palm OS and Pocket PC systems.

Potential Advantages: Currently, the Physician's Drug Handbook does not provide any significant advantages over other PDA drug databases because the information may be dated.

Potential Limitations: The Physician's Drug Handbook does not provide information on alternative medicinal agents, drug cost, or a section for individual notations. The database corresponds with the ninth edition of the handbook, published in 2001, and therefore does not provide the most current drug information. A free product demonstration is not available.

Tarascon Pocket Pharmacopoeia Deluxe PDA Edition (beta-test version)*

Description: This second-generation product is currently in development as a replacement for Tarascon ePharmacopoeia, which is no longer available. Drug monographs are indexed by brand and generic names, classification, and indication. They contain mechanism of drug action, metabolism, adult and pediatric dosing guidelines, FDA-approved and -unapproved uses, warnings and cautions, adverse reactions, lists of interacting agents, pregnancy and lactation information, dosage forms, and cost information. Drug interaction screening technology, alternative agent monographs, 47 reference tables, and calculators for 9 medical equations are also included.

Additional Information: A prerelease test version is currently available as a free download from www.tarasconpublishing.com. When the product is officially released, it will require a $25 annual subscription. Tarascon Pocket Pharmacopoeia is compatible with Palm OS and Pocket systems as well as expansion cards of Palm OS devices.

Advantages: Information for the drug interaction screening tool is referenced and taken from The Medical Letter. Alternative agent monographs are incorporated into the database as a separate section. Drug monographs are peer-reviewed by experts. The test version of the product is currently available free of charge. The date of the last update is provided.

Potential Limitations: Drug cost information is provided from www.drugstore.com for many oral and topical products but is often absent for parenterally administered products. Once the product is officially made available, the subscription must be renewed annually.

Discussion

Most of the information on PDA handheld drug information databases is provided on product or vendor Internet sites and is subject to change, potentially on a daily basis. Since Web sites vary with regard to frequency of updates, some vendors may offer older versions of drug information products even though updated versions are available. It is important to check for a version number or a year of publication especially when purchasing electronic versions of products offered in book or handbook format. To make a product more appealing, some vendors report the number of brand-name drugs referenced in
the drug information product instead of the number of monographs (by generic drug name). Since a single product may have multiple brand names, a misleading representation of the breadth of information may be created. Some vendors disclose specific product details, including monograph reviewers, the depth of information provided, and database update information. This information is an indication of the quality of the drug information database. If it is not provided, most sites offer an e-mail address for the purpose of requesting additional information.

Current, complete, flexible, cost effective, accurate, evidence-based, relevant, simple, and verifiable are key characteristics of information databases24,25 and are defined as follows:

- **Current**: One of the merits of handheld electronic databases compared with handbooks and other annually published drug information sources is its ability to be up-to-date. It is important to determine the frequency of updates of the databases—daily, weekly, monthly, quarterly, or yearly—since programs are not all updated with the same frequency.

- **Complete**: Monographs should provide brand and generic names, drug classification, mechanism of action, kinetic information, adult and pediatric dosing information, drug uses and indications, contraindications and precautions, adverse drug reactions, drug interactions, pregnancy and lactation information, DEA schedule, dosage forms, manufacturer, and cost information.

- **Flexible**: The drug information user should be able to adapt drug monographs by entering his or her own notations for a particular drug.

- **Cost effective**: Costs quickly accrue when multiple databases must be purchased in order to attain the desired breadth of information. A single database that provides all the necessary information should be sought. It is important to note that product cost does not correlate with information breadth or dependability.16

- **Accurate**: Programs should be free of typographical errors and information omissions.

- **Evidence-based**: References should be provided for individual monographs and for supplemental features.

- **Relevant**: Information provided in drug monographs should be applicable to clinical practice. For example, programs that include pictures of medicinal plants, while interesting, are not likely to be clinically useful.

- **Simple**: Information should be presented in such a way as to allow a novice to install, update, and access drug information.

- **Verifiable**: Drug information should be consistent with that found in authoritative literature sources.

Databases that meet these criteria can enhance clinical decision making, reduce variability of pharmacist recommendations, and save time in a managed care setting. In addition to drug information, helpful PDA programs may include disease references, medical abbreviations or medical dictionaries, laboratory references, medical or kinetics calculators, and intervention documentation technology. These auxiliary programs can be purchased from multiple vendors, or in some cases, are available free of charge, and have been reviewed elsewhere.11

**Conclusion**

Electronic drug information programs for PDAs are designed to fill in the gaps in human memory, particularly important in light of the volume of new information that is reported each day. Drug information databases are generally abridged and are not a substitute for consulting textbooks, original research, and other appropriate drug information resources.

**DISCLOSURES**

No outside funding supported this evaluation. The authors report that they did not receive funding or gifts from any vendor covered by this review. Author Colleen M. Lowry served as principal author, and she and authors Maria D. Kostika-Rokosz and William W. McCloskey contributed to the concept and design. Drafting of the manuscript was primarily the work of Lowry, and its critical revision was the work of authors Kostika-Rokosz and McCloskey.

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Using Decision-Analytic Models Wisely

In this issue, Fairman and Mothertal address an aspect of validation of decision-analytic models. In their research, Fairman and Mothertal first replicated 2 published decision-analytic models of *Helicobacter pylori* eradication, and subsequently reran the models replacing original model assumptions with empirical data from a multipayer claims database. They found that key assumptions of the original models were not consistent with the empirical data from the database, which consequently led to different conclusions being supported when the models were rerun.

In the face of these results, one might question the value of the original models. Unfortunately, some degree of discordance between the assumptions used to populate decision-analytic models and subsequently collected empirical data is to be expected. In other words, as noted by Sculpher et al., all models developed at time \( t \) will be “wrong” (in terms of their predictions) at time \( t+1 \). This does not mean that original models are of little value. Models are usually constructed in response to a situation where there is incomplete empirical data available at time \( t \) in order to inform a decision that must be made at time \( t \) (i.e., cannot be deferred). And, in doing so, the model that is constructed should make explicit the gaps in the knowledge base at time \( t \) as well as the sensitivity of the model to the assumption(s) made in lieu of the missing empirical data. To the extent that the ensuing model is very sensitive to the value of the assumption(s) made, this suggests the need for follow-up data collection after implementation of the decision at time \( t \).

In clinical practice and health policy settings, decisions will be made regardless of the availability of a model. However, when available, models provide the means “…to structure evidence on clinical and economic outcomes in a form that can help to inform decisions about clinical practices and healthcare resource allocations (p.9).”

In the case of the published models of *Helicobacter pylori* eradication, it is evident that these models were sensitive to the assumptions made about eradication rates and patterns of care for retreated and successfully treated patients. By collecting empirical data on these parameters, Fairman and Mothertal have provided the basis for updating the model parameterization when the time will come to revisit the decision on *Helicobacter pylori* eradication at time \( t+1 \).

A necessary condition for a successful revisitation, however, is the clear and unambiguous construction of the initial models with sufficient transparency for a qualified analyst to replicate the models. Transparency is one of the key attributes of a “good” decision-analytic model, more so than predictive accuracy. Indeed, the Consensus Conference on Guidelines on Economic Modelling in Health Technology Assessment concluded that the main 5 properties of a “good” decision-analytic model were: transparency, internal consistency, reproducibility, interpretability, and exploration of uncertainty.

Decision-analytic models are now a required component of the Academy of Managed Care Pharmacy’s guidelines for the submission of clinical and economic data to support formulary listing in health plans. In evaluating and using such decision-analytic models, it is important for managed care decision makers to consider the following:

(a) Models cannot make a decision—all they can do is provide a structured and explicit look at the costs and consequences that would then need to be considered by the decision maker. Simply put, models inform decision making at a particular point in time by making explicit the relationships between assumptions and outcomes—however, the veracity of the assumptions underlying the model need to be carefully considered by the decision makers in evaluating the trustworthiness of any model.

(b) Models and their results should not be considered as claims about the facts or as predictions about the future; model outputs are always contingent on the inputs, which is why it is imperative that model inputs be as transparent and accessible as possible. This principle is very effectively illustrated by the Fairman and Mothertal article, wherein it was shown that the original models were highly sensitive to the assumptions made about eradication rates and patterns of care for retreated as well as successfully treated patients.

(c) The principle of transparency in modeling suggests that the simpler the model the better it is (all else being equal); “black boxes” are usually less desirable. For instance, the transparency of the original models facilitated their replication by Fairman and Mothertal.

(d) When model predictions are evaluated, it is more important to focus on the modeled relationship between inputs and outputs than on the outputs only. This is also illustrated effectively by Fairman and Mothertal, wherein they show that one of the key assumptions that did not hold in the original models was the one relating to whether patients are treated as inpatients or outpatients for hospital care.

(e) Models should never be regarded as complete, but should be repeatedly updated and/or replaced as new evidence becomes available regarding their structure or inputs. Indeed, as Weinstein et al. note, the ability of models to adapt to new evidence should be regarded as a strength, not as a weakness. The original models of *Helicobacter pylori* eradication can be updated for future use with the data from the Fairman and Mothertal study, at least for the use of the organizations represented in this dataset.

A more detailed list of questions for assessing quality of decision-analytic models is provided by Sculpher et al., while excellent reviews are also provided in references 3 and 4. Decision-analytic models are playing an increasingly important role in health care decision making, and more such research needs to be conducted and published on testing model assumptions, parameters, and structure in the course of determining the quality of decision-analytic models. The work by Fairman and Mothertal provides an important illustration of how such research can proceed in organizations with access to medical information.
and pharmacy claims databases.

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REFERENCES


Pharmacoeconomics—Determination of the Cost-Effectiveness of Helicobacter Pylori Eradication

In 1994, the National Institutes of Health Consensus Panel on *Helicobacter pylori* (HP) in peptic ulcer disease (PUD) recommended HP eradication in patients who test positive for HP and who have new or recurrent gastric or duodenal ulcers or require maintenance acid-suppressive therapy for PUD.¹ The guidelines did not, however, recommend HP eradication in the absence of detection of infection with HP even in patients with persistent symptoms. Also, the role of HP infection in nonulcer dyspepsia (NUD) is controversial. In the middle 1990s, HP infection was blamed for 80% to 90% of the symptoms and “misery” of ulcers.² Some advocated the use of HP eradication therapy without obtaining definitive evidence of HP infection. By 1998-1999, however, the evidence was conclusive that only about 20% to 25% of NUD patients with HP infection when treated with effective HP eradication therapy reported symptomatic relief at 1 year.³⁴

A randomized controlled trial of 337 patients with NUD found that eradication of HP was 90% at 4 to 6 weeks in the treatment group versus 2% in the placebo group.³ The treatment group received a 2-week, twice-daily regimen of 20 mg omeprazole, 1,000 mg amoxicillin, and 500 mg clarithromycin (OAC). At the 12-month follow-up, the rate of successful treatment (defined as no more than mild pain or discomfort centered in the upper abdomen [a score of 0 or 1]) was 50% in the placebo group versus 46% in the treatment group during the 7 days prior to the final 12-month visit. Treatment was considered a failure if the patient had taken medication for dyspepsia, other than antacids, in the 30-day period prior to the last visit. Equally important, there was no significant difference in the rate of successful treatment (relief of symptoms) at 12 months between patients who were HP-negative (48%) versus HP-positive (49%). The accumulated evidence shows that the relationship between symptoms in NUD and HP infection is not predictable, and the eradication of HP does not necessarily cure the disease as measured by symptoms. Complete relief of symptoms occurred in 28% of the oral triple therapy patients and 23% of placebo patients. Perhaps as few as 20% of patients with NUD will benefit from HP eradication.

There is apparently much that we still do not know about NUD, heartburn symptoms, and HP infection. For example, the duration (durability) of symptoms of NUD appears to be a factor in the effectiveness of HP eradication regimens as measured by relief of symptoms. One study found that 27% of NUD patients who had reported symptoms for less than 5 years reported relief of symptoms after HP eradication compared to 12% for the subgroup of NUD patients who had reported having NUD symptoms for 5 years or more.⁵ Some might argue that the truth about the value of HP eradication lies in the definition of the disease—NUD, PUD, or heartburn. Managed care pharmacists who work in disease management will appreciate the observations of gastroenterologists participating in clinical practice improvement projects who describe NUD, heartburn, and gastroesophageal reflux disease as a “brag bag of symptoms.”⁶

The article by Fairman and Motheral in this issue of the *Journal* tackles a difficult and complex subject area, validation of predictive decision-analytical models that are, by definition, models, and not actual observations. As pointed out by Zafar Hakim, PhD, one of the reviewers of this manuscript, models are simplifications of clinical practice and will never be able to capture the richness and diversity of clinical practice.⁷ Models will never yield completely accurate predictions of costs or other outcomes. Equally important, one might question the use of any HP eradication recipe given the apparent fact that HP eradication relieves problematic symptoms in only 1 in 5 NUD patients. This context also includes the predictable rate of HP reinfection and recurrence of dyspeptic symptoms in one fourth to one third of NUD patients at the 2-year follow-up.⁸ Furthermore, heartburn and NUD symptoms are often manageable without drug intervention and the avoidance of symptom triggers such as spicy foods, fatty foods, alcohol, cigarettes, heavy meals, large body mass, or eating too close to bedtime.⁹ Previously in the *Journal*, Kozma, Dickson, Mullenix, and Reeder presented results of pharmacoeconomic (PE) modeling of the relative merit of HP eradication versus usual care (antisecretory therapy) for peptic ulcer disease and suggested that a prior history of ulcer is necessary to make empiric HP eradication cost effective.¹⁰

Readers will note that the article by Fairman and Motheral examines assumptions inherent in early PE models applied to HP eradication recipes, oral triple therapy with BMT (bismuth, metronidazole, tetracycline), and dual therapy comprised of a PPI with either amoxicillin or clarithromycin. Triple and quadruple drug therapies are generally preferred today, often in 1-week regimens rather than the 2-week regimens common in the 1990s. Recipes of 3 antibiotics with a PPI for as few as 5 days (the MACOR study) have been shown to eradicate HP infection in 86% to 89% of patients.¹¹ The purpose of the article by Fairman and Motheral is not evaluation of PE analyses of state-of-the-art HP eradication recipes. Rather, the point is that assumptions employed in PE models require validation using actual health plan data when these data become available. In the case of the 2 PE models evaluated by Fairman and Motheral, the BMT model with lower direct drug cost was found to be the most cost effective using actual health plan data, contrary to the PE model prediction.

When HP eradication is pursued, there may be a role for clinical pharmacists in delivering maximum value. A gastrointestinal clinic operated by clinical pharmacists was shown to attain 100% patient adherence to HP eradication regimens and no patients resumed acid-suppression therapy at 1-month follow-up.¹² A separate study showed that clinical pharmacist intervention with prescribers could increase the utilization of the BMT oral triple therapy regimen with either 2 weeks of a proton pump inhibitor (PPI) or 4 weeks of an H2-receptor antagonist (as recommended in 1998 by the American College of Gastroenterology) from 0% of all HP-eradication regimens to
The pharmacist intervention produced a 31% average savings for all HP eradication by increasing the utilization of the lower-cost BMT regimen and reducing utilization (from 74% to 26%) of the higher-cost OAC (omeprazole, amoxicillin, and clarithromycin) regimen. Cost-effectiveness might also be achieved via 1-week HP eradication recipes with PPI pantoprazole. Seven-day regimens including either twice-daily pantoprazole 40 mg, amoxicillin 1,000 mg, and clarithromycin 500 mg (“PAC7”) or twice-daily pantoprazole 40 mg, bismuth subcitrate 108 mg 4 times daily, tetracycline 500 mg 4 times daily, and metronidazole 200 mg 3 times daily and 400 mg at night (“PBMT7”) produced similar HP eradication rates, 78% and 82%, respectively, both superior in clinical outcome to 69% HP eradication achieved with 14 days of BMT without PPI.

As is often the case in medicine, the challenge is to identify those patients who are most likely to benefit from the intervention (sensitivity) and exclude those unlikely to benefit from the intervention (specificity). Long-term use of acid-suppression therapy, histamine-2 receptor antagonists (H2RAs) in the 1980s to the end of the 1990s and supplanted by PPIs in the middle 1990s, can be expensive and a drain on the financial resources of health plans. Introduction of generic cimetidine, followed by generic ranitidine, famotidine, and nizatidine, reduced the average annual cost of H2RA therapy from nearly $1,000 per patient to less than $250 per patient. The introduction of generic omeprazole at year-end 2002 had not by mid-2003 reduced significantly the average annual PPI cost of nearly $1,500 per patient per year, before copayment.

A study of 1,007 patients on long-term H2RA therapy (defined as 6 months or more) found that PUD was the most common indication for H2RA prescribing (42%). PUD was found in 58% of patients receiving long-term H2RA drug therapy who had their HP serology tested and were HP-positive. While two thirds (67%) of the patients reported improvement in quality of life following HP eradication, and H2RA use was reduced, there is no guarantee that PUD patients treated with an HP-eradication recipe will discontinue use of H2RA or PPI drug therapy. The findings noted above, in which clinical pharmacist intervention in an HP-eradication intervention was associated with no resumption of acid suppression therapy at 1-month follow-up, need validation over a longer follow-up period. It is entirely possible that HP eradication, achieved at any incremental cost as measured in total prescription drug expenditures, results in some relief of symptoms in a majority of patients on long-term acid-suppression therapy.

For managed care organizations in 2003, the direct drug cost at discounted prices, before member copayment or pharmacy dispensing fees, was about $44 for quadruple therapy for 7 days with PBMT7 or $102 for 7 days with triple therapy PAC7, compared with about $250 for the commercial packaging of 14 days of therapy with lansoprazole, amoxicillin, and clarithromycin. Avoidance of even 1 month of therapy with a PPI in 1 of 2 patients treated with PBMT7 or PAC7 would cover the direct drug cost of most HP eradication recipes. For patients with PUD, HP infection is present in 85% to 95% of patients, and eradicating HP is effective in healing the ulcers. For patients with NUD, the relative risk reduction for persistent dyspeptic symptoms (the same or worse) at 3 to 12 months following HP eradication is 9% compared with placebo, and the number needed to treat is 15 NUD patients to obtain 1 case of cured dyspepsia. The cost to obtain 1 dyspeptic-free NUD patient with PBMT7, the lowest-cost therapy, is therefore $660 in 2003 dollars versus $1,530 for PAC7 or $3,750 for the commercial package of lansoprazole, amoxicillin, and clarithromycin.

Formulary Management Methods and Pharmacoeconomics

Twenty years ago, 40% of hospitals stocked a single drug product to represent a therapeutic category, and 31% of hospitals allowed automatic therapeutic interchange performed by pharmacists. In calendar year 2002, 88% of hospitals with greater than 100 beds employed therapeutic interchange as part of formulary management.

Cost-effectiveness analysis is a fundamental part of determining the value of drug therapy compared with the cost, or the value-for-money equation. Yet, most pharmacy and medical directors involved in drug formulary decisions of pharmacy and therapeutics (P & T) committees apparently have an inadequate understanding of basic terms and methods of pharmacoeconomics (PE). A survey conducted in 1999 and reported in the March/April 2000 issue of the Journal found that (a) while most pharmacy and medical directors involved in drug formulary decisions believed that their P & T committees understood pharmacoeconomics, only 17% felt that their committee understood pharmacoeconomics completely and (b) most terms in pharmacoeconomics were not well understood, e.g., 71% of respondents reported inadequate understanding of quality-adjusted life year, 78% conjoint analysis, 88% the Markov model, and 95% league tables. There is also distrust of pharmacoeconomic data, perhaps since most pharmacoeconomic analyses are sponsored by manufacturers of the products that are the subject of the PE analyses.

In addition to apparent poor understanding of PE terms and methods and distrust of PE data among decision makers, bias in PE studies is unavoidable, creating a ripe opportunity for mistrust. PE studies use economic data applied to an inferred association between one or more independent variables and a dependent variable. The PE researcher has control over the selection of economic data, inclusion criteria, range of dependent variables, and the dependent variable. Selection bias is a potential source of error in any study, and a common threat is nonrandom, nonresponse data or otherwise nonrandom missing data. For example, using medical claims data will show a lower incidence of diagnoses of depression than would patient chart data, which would have a lower incidence of diagnoses of...
between 1998 and 2002, 29 and employer-sponsored prescrip-
tion drug coverage (available to about 2.5 million Medicare beneficiaries through a Medicare+Choice plan). But, Medicare+Choice plans (12.8% of all Medicare beneficiaries) had drug coverage in 1999,! rising to 41% in 2003; in 2002, 90% of members with a generic-only benefit had no annual benefit maximum. Among basic Medicare+Choice plans, 60% covered only generic drugs in 2003. Copayments for primary care and specialist office visits also increased, and 82% of members were subject to some type of cost sharing for inpatient hospital admissions in 2003.

Commercial health plans are reluctant to drop coverage of prescription drugs for Medicare beneficiaries for a multitude of reasons, including the perceived value of these benefits among members and the apparent favorable influence that drug coverage has on member satisfaction. A survey in 2001 of 3,457 adults aged 19 years or older, including Medicare-eligible beneficiaries, found that Medicare beneficiaries who had prescription drug coverage were 50% more likely than those without it to rate their insurance as excellent and about one half as likely to report medical bill problems.31 The percentage of Medicare enrollees aged 65 years or older who rated their insurance as excellent was 36% among members enrolled in plans with prescription coverage compared with 22% for members in health plans without prescription drug coverage. The percentage of Medicare enrollees aged 65 years or older who reported any medical bill problem was 15% for plans with prescription drug coverage versus 29% for Medicare members in health plans without prescription drug coverage.

In a previous issue of the Journal, Mc Kercher, Taylor, Lee, Chao, and Kumar found that prescription drugs in elderly families accounted for approximately twice the proportion of total out-of-pocket medical care burden compared with nonelderly families, 45.6% and 23.7%, respectively. The higher proportion of total medical care burden and total economic burden attributable to prescription drugs in the elderly was traced to larger prescription drug expenditures, Financial Burden, and Health Plan Satisfaction Among Medicare Beneficiaries Researchers have for years been studying the milieu of factors associated with the large variation in prescription drug utilization among Medicare beneficiaries. There is potential for greater financial burden imposed by prescription drugs among the elderly who on average use 3 times the number of prescriptions per month compared with persons younger than 65 years.4 But the distribution of drug expenditures and financial burden is not uniform. Seventeen percent of Medicare beneficiaries had no ($0) spending on prescription drugs in calendar year 2001, whereas spending of $1,000 or more was found among 28% of Medicare beneficiaries and accounted for 76% of total expenditures for prescription drugs for this population.27 According to data obtained from the Medicare Current Beneficiary Survey, 76% of all Medicare beneficiaries had some drug coverage at some point in 1999, up from 73% in 1997 and 1998 and considerably higher than the 57% reported in 1992.28 About one third of the supplemental prescription drug coverage among Medicare beneficiaries was employer-sponsored and 17% (12.8% of all Medicare beneficiaries) had drug coverage through a Medicare+Choice plan. But, Medicare+Choice plans became unavailable to about 2.5 million Medicare beneficiaries between 1998 and 2002,29 and employer-sponsored prescription drug benefits for Medicare beneficiaries aged 65 to 69 years declined from 40% in 1996 to 35% in 2000.30

For the 5-year period through 2003, Medicare+Choice plans with any prescription drug coverage declined from 73.4% in 1999 to 66.1% in 2003, and the percentage with an annual maximum drug benefit maximum increased from 23.3% to 70.0%.31 When weighted by enrollment, 83.9% of Medicare+Choice members had a prescription drug benefit in 1999, dropping to 68.9% in 2003. In 1999, only 10.6% of Medicare+Choice members had a limited drug plan benefit with a $500 annual maximum, but by 2003, 53.4% of Medicare+Choice members had an annual drug benefit maximum of $500. In the Commonwealth Fund data, a relatively small portion of Medicare+Choice plans applied the annual benefit maximum through a quarterly cap, affecting 12.2% of members in 1999 and 8.8% of members in 2003, but these data differ from other data sources that show that among HMOs that imposed drug benefit maximums (83% of plans affecting more than two thirds of membership) in 2001, 42% imposed an annual cap (average $1,160), 47% had quarterly caps (average $351), and 11% imposed monthly caps (average $80).32

Cost sharing in the form of copayments per prescription has also increased. The average generic copay was $10 or less for 84% of members in 1999 versus 72% in 2003. The brand copay was $20 or more for 14% of members in 1999, rising to 74% of members in 2003. An emerging trend was found in coverage of generic drugs only, affecting 11% of Medicare+Choice members in 1999, rising to 41% in 2003; in 2002, 90% of members with a generic-only benefit had no annual benefit maximum. Among basic Medicare+Choice plans, 60% covered only generic drugs in 2003. Copayments for primary care and specialist office visits also increased, and 82% of members were subject to some type of cost sharing for inpatient hospital admissions in 2003.

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In a previous issue of the Journal, Mc Kercher, Taylor, Lee, Chao, and Kumar found that prescription drugs in elderly families accounted for approximately twice the proportion of total out-of-pocket medical care burden compared with nonelderly families, 45.6% and 23.7%, respectively. The higher proportion of total medical care burden and total economic burden attributable to prescription drugs in the elderly was traced to larger prescription quantities, price, and utilization, but not more expensive drugs. In this issue of the Journal, Schommer, Mott, Hansen, and Cline found the proportion of senior citizens without any prescription insurance coverage did not change significantly—from 32% in 1998 to 29% in 2001.33 However, the proportion of respondents with prescription drug coverage that had to share costs of prescriptions through copayments and coinsurance rose significantly—from 69% in 1998 to 89% in 2001.

A key question that begs for useful answers is what behaviors result when persons with prescription drug needs encounter financial barriers to access. Schommer, Mott, Hansen, and Cline found that the proportion of senior citizens who used mail-order pharmacies increased from 17% in the 1998 survey to 27% in the 2001 survey. A Harris Interactive
poll of 3,465 Californians aged 18 years or older with chronic illness, conducted in November and December 2002, found that nearly one half (46%) reported doing nothing when faced with an increase in drug cost sharing.38 The specific survey question stated that the survey respondent had prescription drug coverage and the amount paid to fill a prescription increased in the past year. More than one third of respondents (36%) reported that they asked their physician or pharmacist for a generic prescription drug, 21% asked the physician to prescribe a less-expensive alternative drug, 16% did not get the prescription filled, and 18% used mail-order service to fill the prescription.

In a previous issue of the Journal, Cox and Henderson found that Medicare+Choice members with an annual drug benefit maximum relied in part on prescription drug samples to mitigate the financial burden of prescription drug needs.39 This practice is likely to be self-defeating in reducing the financial burden since (a) higher-cost drugs are more heavily sampled and (b) the availability of drug samples may affect physician prescribing practices by reducing the immediate pressure to find lower-cost therapeutic alternatives.37 We await the results of research in which investigators ask the important questions regarding the nature and usefulness of interactions with physicians in offering recommendations for generic drugs and other lower-cost therapeutic alternatives to help reduce out-of-pocket expenditures for the elderly.

- Hypertension, Prescription Drug Copayments, and Drug Therapy Adherence

In this issue of the Journal, Wogen, Kreilick, Livornese, Yokoyama, and Frech found that drug therapy adherence differs by type of drug.38 In this study, a higher rate of adherence to therapy was found for valsartan compared with lisinopril or amiodipine. Several factors can affect adherence to drug therapy aside from the safety and effectiveness of the drug. A factor not addressed in the extant study, but a curious one is the relationship of member cost share to drug therapy adherence. Some drug industry analysts attributed the small increase in U.S. sales of the block-buster drug atorvastatin (Liptor, for hypercholesterolemia) in 2003 Q1 and declines in sales of category leaders sertraline (Zoloft, for depression), and amiodipine (Norvasc, for blood pressure) during this period to rising copayments in drug benefit plans.39 One wonders how formulary status and copay design (e.g., relative copayments) might have influenced the results observed by Wogen, Kreilick, Livornese, Yokoyama, and Frech, particularly since one of their study drugs was amiodipine. Neither formulary status nor copay design was reported, and one of the study medications, lisinopril, became available in generic form during the study period, but not until the 35th month of the 36-month study period. It is reasonable to speculate that adherence with generic lisinopril, with its lower copayment, would have been more resilient over time compared with brand drugs amiodipine and valsartan, both with higher (brand drug) copayments.

There are also data to suggest that pharmacy provider type, mail-service versus community pharmacy, another feature of drug benefit design, may influence drug therapy adherence.40 This variable, certainly relevant in the database employed by Wogen, Kreilick, Livornese, Yokoyama, and Frech (a pharmacy benefit manager database with a high penetration of mail-service prescriptions), was not measured in the current study. Future studies of drug therapy adherence derived from drug claims data might also include a measure of the average member cost share per day of therapy, in dollar amount and percentage, for the target drugs in the study. This variable has become increasingly important with the proliferation of multi-tier copay drug plans and sometimes widely disparate copayments for generic versus preferred brand versus nonformulary drugs. Managed care pharmacists also need to know if and how mail-service pharmacy is a factor in drug therapy adherence, through the simple convenience of a 90-day supply or home delivery versus store purchase or a lower cost-share requirement.41

There are also the important subjects of midpoint and end-point clinical outcomes, none of which were measured in the current study. A study of blood pressure control in a New York health maintenance organization (HMO) in 1998 found that only 35% of patients reached target blood pressure (<140 mm Hg systolic and 90 mm diastolic for the general population and <130/85 mm Hg in diabetics and patients with renal insufficiency).42 An equally important finding in this “real-world” study was that only 68% of patients were treated with drugs recommended in the HMO’s treatment guidelines based upon the Joint National Committee (JNC) recommendations. Others have found that members of HMOs and preferred provider organizations were more likely to use angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) for essential hypertension compared to fee-for-service health insurance and out-of-pocket purchasers who were more likely to use diuretics and beta-blockers, the latter consistent with JNC guidelines.43 A survey of 316 primary care physicians responding to a 26-item questionnaire in the year 2000 found that 41% reported little or no knowledge of JNC guidelines, at that time in its sixth iteration.44 This lack of familiarity was also evidenced in the use of ACEIs as the most common first-line drug of choice for hypertension, contrary to both JNC guidelines dating back to version III (1984) that advocated the use of diuretics and beta-blockers as first-line therapy.45

Examination of the relative value of ACEIs, CCBs and angiotensin receptor blockers (ARBs) in the treatment of hypertension must include the context of the results of the Antihypertensive and Lipid-lowering Trial to Prevent Heart Attack Trial (ALLHAT), released in December 2002. The ALLHAT study results suggest that most of the more than 40 million Americans with hypertension46 could be treated more effectively, more safely, and more cheaply with low-cost diuretics such as chlorthalidone and hydrochlorothiazide at a
fraction of the cost of ACEIs such as ramipril or quinapril and CCBs such as amlodipine, felodipine and long-acting nifedipine and diltiazem.47 The 8-year ALLHAT study, conducted in a real-world environment with a mean follow-up of 4.9 years, produced unequivocal evidence that amlodipine and lisinopril were associated with the same incidence of the primary outcome of combined fatal coronary heart disease or nonfatal myocardial infarction as a diuretic (chlorthalidone); all-cause mortality was also the same among the 3 treatment groups.48 However, the diuretic (chlorthalidone) was superior to CCB (amlodipine) in the 6-year rate of heart failure (HF), 7.7% versus 10.2%, relative risk (RR) 1.38, and chlorthalidone was superior to lisinopril in the 6-year rates of combined cardiovascular disease, 30.9% versus 33.3%, RR 1.10, stroke (5.6% versus 6.3%, RR 1.15) and HF (8.7% versus 7.7%, RR 1.19). Robert Anderson, one of the ALLHAT investigators, had additional observations regarding the ALLHAT study findings in a previous issue of the Journal.49

The study by Wogen, Kreilick, Livornese, Yokoyama, and Frech contains some interesting data in the area of combination drug therapy. More than one third (36.7%) of the patients started on valsartan were already taking a diuretic or diuretic combination. More than 40% of the patients started on amlodipine (45.2%) or lisinopril (42.4%) were taking a diuretic or diuretic combination; 31% to 33% were taking an antilipid drug. Amlodipine and lisinopril patients appeared to be more likely to be on concomitant therapy with nitrates, digitalis, or nitrates. Concurrent use of beta-blockers was more common among first-therapy amlodipine patients (28.0%) compared with lisinopril (23.8%) and valsartan (21.4%). Interesting subanalyses would have determined how many first-therapy patients with amlodipine, lisinopril, or valsartan were also taking both diuretics and beta-blockers or were diabetic patients, as determined by proxy of drug therapy for diabetes.

Managed care pharmacists might also note that Wogen, Kreilick, Livornese, Yokoyama, and Frech found that the study drugs were used as first-line, monotherapy in 30.5% of the cohort of patients, utilization that is contrary to JNC VII guidelines and the evidence produced in the ALLHAT study. Valsartan was most likely to be used as monotherapy (35.5%), followed by lisinopril (32.5%) and amlodipine (27.4%, P<0.001). Also noteworthy in this study is that the valsartan patients were more likely to have a lower Chronic Disease Score (CDS), further distancing these results from current evidence-based treatment guidelines.

Conclusions derived from this current study should be framed in the context of the very large case numbers that tend to make small variation in every value of every independent variable statistically significant. For example, the 3 groups, taking valsartan, amlodipine, or lisinopril, are not homogenous in patient characteristics such as age and gender (Table 1, P<0.0001).50 A mean age of 62.4 years for the 29,669 valsartan patients is practically no different than the 62.1 mean age for the 40,128 lisinopril patients or 63.9 mean age for the 73,148 amlodipine patients. Similarly, the 3 groups are statistically different in mean CDS, with valsartan associated with the lowest CDS. However, while statistically different (P<0.0001), a CDS of 9.62 for valsartan does not seem to be clinically or practically different from the mean 10.15 CDS for lisinopril or 10.34 for amlodipine. The need to evaluate practical significance against statistical significance flows through to the study dependent variables. All measures for drug therapy compliance and adherence were statistically significant (P<0.0001), favoring valsartan, but 88.5% mean compliance for valsartan seems clinically and practically no different than the mean 86.7% compliance with amlodipine or 86.3% for lisinopril.

Frederic R. Curtiss, PhD, RPh, CEBS
Editor-in-Chief

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17. Derived from Average Wholesale Prices (AWP) in Medispan on July 27, 2003, discounted to 85% and common Maximum Allowable Cost (MAC) prices among pharmacy benefit managers for generic bismuth tablets, generic tetracycline 500 mg capsules, and generic metronidazole 250 mg tablets.


Dear Editor,

We are writing to discuss the paper entitled “Patient-Reported Utilization Patterns of Fentanyl Transdermal System and Oxycodone Hydrochloride Controlled-Release Among Patients With Chronic Nonmalignant Pain” in the May/June 2003 issue of the Journal of Managed Care Pharmacy.

We credit the authors in their task of collecting information on chronic pain patients via survey method, as this type of study in chronic nonmalignant pain patients has never been conducted. The results, although intriguing, were based on a single survey with no follow-up survey assessments.

It is interesting to note that the only values that were significant in the multivariate analyses were gender (more females in the fentanyl transdermal system group) and duration on medication (those taking oxycodone hydrochloride controlled-release were taking the medication longer than those on the fentanyl transdermal system). We have several questions and comments that we would like the authors to address in order to provide the readers with a more complete understanding of the results:

1. We recommend providing a complete version of the survey to the readership. The pieces of the survey provided in the article do not permit the reader to make a full assessment of the questions asked. A full version of the survey should be made available so the reader can make a more complete and objective assessments of the findings. Additionally, a complete version of the survey could be helpful to other health care workers interested in this data.

2. We recommend collecting pain scores from a valid and reliable scale when surveying pain patients. This survey examined duration of adequate pain relief based on recall without using a pain scale. We feel the primary endpoint of interest for pain patients should be pain control as measured by a valid reliable instrument.

3. This study focused on pain clinics. It should be noted that patients referred to such practices often are not representative of the general population that has a pain complaint. Thus, there is substantial ascertainment bias in this study, which may reduce the generalizability of the results to a typical primary care setting.

4. Why were differences within the 2 groups not accounted for in the beginning of the analysis? The 2 groups compared appear to be different with regard to gender (more females in the fentanyl transdermal system group), time on therapy (those taking oxycodone hydrochloride controlled-release were taking the medication longer than those on the fentanyl transdermal system), and use of supplemental analgesia (the oxycodone hydrochloride controlled-release group were taking significantly less). There was no control for potential confounding in this analysis.

5. Why was nonparametric analyses employed, and why did the results (morphine equivalents of controlled-release oxycodone was significantly less than the transdermal fentanyl system) change dramatically after controlling for patient characteristics (morphine equivalents of the transdermal fentanyl system was less than controlled-release oxycodone)?

6. In conducting the multivariate analyses, it was mentioned that the sample selection was not normally distributed and therefore the bootstrapping method (repeated samples drawn from a smaller sample to estimate the empirical distribution) was instituted. Why was a complete presentation of the distribution results not available in the manuscript? A complete presentation of the distribution results would assist the readers in understanding what was not normally distributed and would allow the reader to make the judgment if moving on to bootstrapping is appropriate. We feel bootstrapping was not necessary since the population of surveyed patients was 437 for the oxycodone hydrochloride controlled-release group and 253 for the fentanyl transdermal system group.

7. In tables 3 and 4, the mean, standard deviation, and median were provided, which are very helpful in understanding the distribution; however, more information on distribution would be helpful to the reader. We request the authors to provide a minimum and maximum value when the standard deviation is greater than the mean and provide the mode when it is not equal to the median. Providing this information will help the reader assess the distribution within each group.

8. A sensitivity analyses was performed on the morphine equivalents for transdermal fentanyl system but not for controlled-release oxycodone. We request that either a sensitivity analyses be conducted for both agents or a single morphine equivalent dosage be selected for the transdermal fentanyl system. The current approach induces bias on the effective dose of both the transdermal fentanyl system and the controlled-release oxycodone tablet. Whereby the transdermal fentanyl system is given the opportunity to be more or less effective, the controlled-release oxycodone tablet is not given this opportunity.

The method for data collection in these chronic pain patients is unique and provides beneficial information that cannot be captured through either a retrospective database analyses or a randomized clinical trial. We appreciate the publication of this information and hope to have our questions answered by the authors.

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The Authors Respond

We welcome and encourage thoughtful critique of prospective, observational, multicenter studies. The respondent's letter raises several points about our methods, which we attempt to clarify below.

This patient-reported utilization study\(^1\) was conducted to assess the actual daily use of fentanyl transdermal system (transdermal fentanyl) and oxycodone hydrochloride (HCl) controlled-release among patients with chronic nonmalignant pain and to compare these patterns to standard dose administration guidelines recommended in the manufacturers' prescribing information (PI). The focus of this investigation was patient-reported utilization patterns, not pain control. As such, the patient-reported utilization survey (from which questions were included in the manuscript) inquired about the duration of adequate pain relief by using time intervals (refer to Tables 3 and 4) that could then be compared with the standard dose administration guidelines as recommended in the manufacturers' PI. We agree that studies in which the primary outcome measure is pain control should include a validated pain-related instrument.

Seifeldin and Grossman are correct in that this survey was administered to patients with chronic nonmalignant pain referred to clinics that specialize in pain management. As we previously noted in the manuscript, the results of this study may not be generalizable to either malignant pain patients or patients who seek medical care in other settings.

To better describe the distributions, below we have provided the minimum and maximum values for variables where the standard deviation exceeded the mean; we also have provided the mode for variables where the median did not equal the mode. Among oxycodone HCl controlled-release patients, the interval between administrations was 7.8 hours, on average, while the mode was 6 hours (median 7 hours). The mode for daily dose of oxycodone HCl controlled-release was 60 mg (median 80 mg), and the minimum and maximum values were 10 mg and 2,400 mg, respectively. Among fentanyl transdermal system patients, the number of days the current patch will be worn was 2.5, on average, while the mode was 2 days (median 2.5 days). The mode for daily dose of transdermal fentanyl was 50 mcg/hour (median 75 mcg/hour).

Several points raised by the Seifeldin and Grossman are based on a misunderstanding of our methods.

Both unadjusted (Table 5) and adjusted (Table 6) analyses were performed. By definition, the unadjusted analysis did not control for potential confounding factors, whereas the adjusted analysis did control for demographic and clinical characteristics that differed between groups. A patient characteristic that is associated with both the treatment (transdermal fentanyl or oxycodone HCl controlled-release) and the outcome (daily oral morphine equivalents) would be considered a confounding factor and could influence the results and inferences, as we observed in this study.

Because the manufacturer's PI for transdermal fentanyl provides a range of oral morphine equivalents (Table 1), in the "base case" analysis, the average of the range for each dosage strength of transdermal fentanyl was used to calculate daily oral morphine equivalents (Table 5). In addition, sensitivity analyses were conducted by varying the oral morphine equivalents for each dosage strength of transdermal fentanyl between the low and high values (Table 5). A priori, we selected the "base case" oral morphine equivalents of transdermal fentanyl for use in the multivariate analysis, which adjusted for demographic and clinical characteristics that differed between groups.

A nonparametric "bootstrapping" approach was used to estimate the mean difference in daily oral morphine equivalents from oxycodone HCl controlled-release compared with transdermal fentanyl because the dependent variable—oral morphine equivalents—was skewed. Bootstrapping involves "resampling" the data many times (i.e., repetitive computations) to generate an empirical estimate of the entire sampling distribution.\(^3\) A nonparametric bootstrapping procedure allowed development of an asymmetric 95% confidence interval around the mean difference in daily oral morphine equivalents between groups. A parametric bootstrapping approach may have inappropriately developed a symmetric 95% confidence interval. The nonparametric bootstrapping approach also permitted estimation of the probability that the daily oral morphine equivalents from oxycodone HCl controlled-release exceeded the daily morphine equivalents from transdermal fentanyl. The probability that oxycodone HCl controlled-release patients had higher oral morphine equivalents was 82.6%, which suggests a trend toward higher oral morphine equivalents per day in the oxycodone HCl controlled-release group (Table 6).

While the respondents raise certain valid points, we stand by the central finding of our study: transdermal fentanyl and oxycodone HCl controlled-release both appear to be used by patients in a manner that is inconsistent with the standard recommendations in the manufacturers' PI; however, the difference between patient-reported utilization (i.e., average interval between oxycodone HCl controlled-release administrations or number of days the current transdermal fentanyl patch will be worn) and the standard recommendations in the manufacturers' PI (i.e., average interval between oxycodone HCl controlled-release administrations or number of days the current transdermal fentanyl patch will be worn) is more pronounced with oxycodone HCl controlled-release. Among oxycodone HCl controlled-release patients, only 18% of patients were observed to exhibit every-12 hour administration patterns (Table 3), whereas 41% of transdermal fentanyl patients reportedly wore the patch for at least 3 days (Table 4).

These findings contradict a statement in a previous letter to the Editor\(^4\) that stated, "No information exists in the OxyContin package insert with regard to tablet quantity restrictions" While that is true, and the oxycodone HCl controlled-release package insert permits asymmetric dosing, there are instructions that indicate oxycodone HCl controlled-release tablets should be taken every 12 hours. Despite the different measures of utiliza-
tion used in this study versus the prescription pattern study reported by Malkin et al., which was based on a claims database analysis using California Medicaid (Medi-Cal) data, the findings are consistent; that is, oxycodone HCl controlled-release is prescribed, on average, and taken, on average, more frequently than every 12 hours, thereby supporting the validity of the our conclusions. Our study results also suggest that a pharmacoeconomic evaluation based solely on the PI dosing recommendations may lead to an inaccurate assessment of the true costs of these agents.

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Abstracts From Professional Poster Presentations at AMCP’s 2003 Educational Conference

The following poster presentations have been prepared for the Academy of Managed Care Pharmacy’s 2003 Educational Conference, October 15-18, 2003, in Montreal, Quebec, Canada.

For more information about the studies described below, please contact the corresponding authors, indicated by an asterisk (*), whose addresses are listed in full. The names of individuals who are scheduled to present at the meeting are underlined. Abstracts were edited by Marissa Schlaifer and Mark Brueckl.

**ANGIOTENSIN-CONVERTING ENZYME INHIBITORS AND ANGIOTENSIN RECEPTOR BLOCKERS: UTILIZATION AND ADHERENCE RATES IN MEMBERS WITH DIABETES OF A MEDICAID MANAGED CARE PLAN**

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**INTRODUCTION:** Evidence suggests that populations with comorbid diabetes and cardiovascular (CV) disease or nephropathy benefit from therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB). This study evaluates the utilization and adherence rates of ACE inhibitor/ARB therapy in members of a Medicaid managed care plan.

**METHODS:** A computerized claims query identified 1,698 members aged 18 to 65 years who were continuously enrolled between July 2001 to June 2002 and had at least one medical claim for diabetes. The average age for this population was 48 years and 70% of the members were female. Members were subdivided into 4 groups: Group 1–diabetes and renal disease; Group 2–diabetes and hypertension; Group 3–diabetes, renal disease and hypertension; Group 4–diabetes without hypertension or renal comorbidities.

**RESULTS:** Utilization of ACE inhibitor/ARB therapy occurred in 47%, 71%, 85%, and 19%, respectively. The presence of hypertension was a significant predictor of receiving an ACE inhibitor/ARB in members with and without renal disease (P<0.0001). Adherence measures for ACE inhibitors, ARBs, and combination products illustrated a medication possession ratio of 86.4%, persistence of 97% at 3 months to 71% at 12 months, and a median gap of 8.47 days.

**CONCLUSION:** This study revealed that the utilization of ACE inhibitors/ARBs in Groups 1 and 4 was low compared to groups that contained members with comorbid hypertension. Additionally, members were late obtaining refills and not persisting with therapy. Future interventions in this health plan will focus on increasing appropriate utilization of ACE inhibitors/ARBs and improving adherence to therapy.

**LEARNING OBJECTIVES:**
1. Discuss the evidence for therapy with an ACE inhibitor and/or an ARB in members with diabetes plus a cardiovascular or renal comorbidity.
2. Describe the prevalence of ACE inhibitors/ARBs in a Medicaid managed care population.
3. Discuss differences in adherence measures for this cohort.

**ANTIBIOTIC RESISTANCE: A COLLABORATIVE APPROACH TO DECREASE ANTIBIOTIC UTILIZATION AND REDUCE ANTIBIOTIC RESISTANCE**

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**INTRODUCTION:** Antibiotic resistance is a growing problem and may result from the overuse of antibiotics. In fact, the Centers for Disease Control and Prevention (CDC) estimates that 50% of all antibiotic prescriptions are inappropriate. The collaboration’s objective is to reduce antibiotic utilization, thereby decreasing antibiotic resistance, through community partnerships in antibiotic resistance education campaigns.

**METHODS:** IHC Health Plans (HPI) partnered with other managed care organizations (MCOs), public agencies, professional organizations, and pharmaceutical manufacturers to reduce the inappropriate use of antibiotics through public and professional education. Our public education efforts included a major media campaign, participation in kids’ fairs, training sessions for day-care providers, and distributing brochures and posters. Our professional education program included continuing medical education sessions, attendance at physician meetings, and direct mailings. We also distributed more than 20,000 cough and cold kits for physicians to give to patients seeking medical treatment for nonbacterial infections. To measure the impact of our program, pharmacy claims were analyzed (10/01/00 to 03/31/01 versus 10/01/00 to 03/31/02).

**RESULTS:** Utah statewide data reflect an absolute change of -8.74% and a relative change of -11.66% in total antibiotic utilization. HPI data showed similar reductions in utilization and decreased costs, including an 8.38% decrease in prescriptions per 1,000 members, a 19.8% decrease in per-member-per-month costs, and a 4.81% reduction in total antibiotic cost without a corresponding decrease in respiratory encounters.

**CONCLUSIONS:** Educating the public and health care professionals about the rising threat of antibiotic resistance can decrease antibiotic utilization. This partnership proves that...
MCOs can effectively work within an alliance to effect change in public health that improves care and reduces cost.

**LEARNING OBJECTIVES:**
1. Learn effective means of educating the public about antibiotic resistance.
2. Learn how to work with prescribers to educate their patients about a public health concern such as antibiotic resistance.
3. Understand how building and working within an alliance can produce positive results for a managed care organization.
4. Learn how to reduce costs and utilization while positively impacting physician perception of the health plan.

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**Clinical Appropriateness and Financial Outcomes of Prior-Authorization Requirements for OxyContin in a Medicaid Program**

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**INTRODUCTION:** To examine the clinical and economic outcomes associated with a prior-authorization (PA) requirement for OxyContin.

**METHODS:** Per-member-per-month (PMPM) claims and expenditures for OxyContin and substitution C-2 narcotic medications that did not require PA approval were compared for 1 year preimplementation and 1 year postimplementation of the PA requirement using autoregression analysis. Diagnoses and health services use of patients who were prescribed OxyContin but did not attempt PA approval after a pharmacy edit were compared to those who did obtain PA approval.

**RESULTS:** Approximately 20% of patients who received a prescription for OxyContin post-PA implementation did not attempt to obtain PA approval. Greater than 99% of patients who attempted to obtain PA approval for OxyContin were approved. Postimplementation, PMPM claims and expenditures for OxyContin decreased significantly (P < .001) without an increase in PMPM trend. The PMPM trend in claims for other C-2 narcotics slowed (P < .01) without any additional risk factor apart from being aged >65 years. Risk factors associated with receiving preventive GI therapy among those patients at risk for NSAID-related GI complications was more prevalent than the overutilization of gastroprotection in those with no GI risk factors. Patients with a history of diabetes or hypertension were less likely to receive a GI preventive therapy.

**CONCLUSIONS:** In our study, the underutilization of GI preventive therapy in patients at risk for GI complications was more prevalent than the overutilization of gastroprotection in those with no additional risk factor apart from being aged >65 years old. Risk factors associated with receiving preventive therapy did coincide with published literature.

**LEARNING OBJECTIVES:**
1. Reflect on the appropriateness of use of anti-inflammatory drugs in one patient population in Nova Scotia, Canada.
2. Recognize the gastrointestinal (GI) risk factors associated with the use of a GI preventive therapy in one patient population in Nova Scotia, Canada.
3. Understand how the appropriateness of use of anti-inflammatory drugs varies according to the number of risk factors for GI complications.
4. Consider how the results observed in this study population can effectively work within an alliance to effect change in public health that improves care and reduces cost.
may relate to other patient populations and health policy formation.

**COMPARISON OF HEALTH CARE COSTS AFTER TREATMENT WITH INHALED CORTICOSTEROIDS AND LEUKOTRIENE RECEPTOR ANTAGONISTS FOR ASTHMA**

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**PURPOSE:** To compare in a managed care population asthma-related health care costs after initiation of treatment with inhaled corticosteroids (ICSs) and leukotriene receptor antagonists (LTRAs).

**METHODS:** Patients selected from managed care organizations (PHARMetrics Integrated Outcomes Database) with an asthma diagnosis (493.xx) and new prescription for ICS/LTRA within 1 year were included. Prescription date was the index date used for analysis. Log-transformed asthma-related treatment charges were compared for the year after the index date using ordinary least-squares regression; asthma-related charges from the previous year and propensity score were covariates. Propensity score was calculated based on patient demographics and previous health care utilization to balance groups based on baseline differences.

**RESULTS:** ICS (n=28,061; mean age ±SD, 34.7 ± 19.7 years) and LTRA (n=8,470; mean age ± SD, 30.8 ± 0.3 years) groups had similar baseline health care utilization. Log-transformed mean postindex asthma-related charges were significantly lower in the ICS group ($679 versus $1017; beta = -0.523, P<.001) overall and in propensity subclasses (P<.001). Results were similar for patients ≤18 years (beta = -0.612, P<.001) and >18 years (beta = -0.469, P<.001). Of patients started on LTRAs, 2,923 (35%) were using ICSs within 1 year, whereas 3,897 (14%) started on ICSs added LTRAs the following year.

**CONCLUSION:** Managed care patients newly treated with ICSs have lower mean health care costs than those treated with LTRAs in the year after initiation of treatment.

**LEARNING OBJECTIVES:**
1. Assess the real-world effectiveness of ICS therapy.
2. Compare the economic benefits of the major classes of therapy for asthma.
3. Understand the benefits of using propensity scores to compare similar managed care patients.

**A COMPARISON OF THE COST IMPACT OF COVERAGE VERSUS NONCOVERAGE OF OVER-THE-COUNTER NONSEDATING ANTIHISTAMINES IN TWO MEDICAID PLANS**

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**INTRODUCTION:** The purpose of this study is to evaluate the impact of coverage of over-the-counter (OTC) loratadine on cost and possible cost shifting to nasal corticosteroids in Medicaid plans.

**METHODS:** Pharmacy claims data from Medicaid plans with and without coverage of OTC loratadine were compared. Cost per prescription and cost per user per month for the first half year of 2002 and 2003 were analyzed for nonsedating antihistamines (including OTC products), and nasal corticosteroids (including nasal antihistamines).

**RESULTS:** In the Medicaid plan that covers OTC loratadine, the cost per prescription for all nonsedating antihistamines decreased from $62.12 for the first half of 2002 to $55.95 for the first half of 2003 (9.9% reduction), and the cost per user per month decreased from $22.31 to $19.49 for the same time frame (12.6% reduction). The cost per prescription of nasal corticosteroids increased from $53.74 for the first half of 2002 to $55.95 for the first half of 2003 (4.0% increase), and the cost per user per month increased from $16.73 to $17.48 for the same time frame (4.5% increase). In the Medicaid plan that does not cover OTC nonsedating antihistamines, the cost per prescription of nonsedating antihistamine decreased from $61.36 for the first half of 2002 to $56.75 for the first half of 2003 (7.5% reduction), and the cost per user per month decreased from $19.38 to $18.25 for the same time frame (5.8% reduction). The cost per prescription of nasal corticosteroids increased from $57.67 for the first half of 2002 to $60.00 for the first half of 2003 (4.0% increase), and the cost per user per month increased from $16.10 to $16.80 for the same time frame (4.4% increase).

**CONCLUSION:** Data examined in this study revealed that the cost per prescription and the cost per user for nonsedating antihistamines have decreased more substantially in the plan that covers OTC nonsedating antihistamines (9.9% versus 7.5% reduction for the cost per prescription, and 12.6% versus 5.8% reduction for the cost per user per month). The changes for the cost per prescription and the cost per user per month of nasal corticosteroids were similar in both plans (4.0% versus 4.0% increases for cost per prescription, and 4.5% versus 4.4% increases for the cost per user per month).

**LEARNING OBJECTIVES:**
1. Recognize the cost impact of OTC loratadine inclusion on Medicaid formularies.
2. Evaluate the cost shifting to nasal steroids when nonsedating antihistamine are not covered.
**COST AVOIDANCE OF HYPOGLYCEMIC EVENTS BY AN INSULIN THERAPY ENHANCEMENT PROGRAM IN A MEDICARE POPULATION**

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**INTRODUCTION:** Based on the MedMarx 2001 Data Report*, insulin remains the leading product involved in harmful medication errors. It has been associated most often with improper dosing/quantity and omission errors. Safety issues with insulin delivery can be attributed to a system error with prescription writing or administration error with patient technique or product selection. The objective of this program was to determine the incidence rate of hypoglycemic events in patients using insulin in the elderly population and conversion rate of these patients to an insulin doser device for ease of administration.

**METHODS:** A retrospective analysis was made using ICD-9 CM codes for hypoglycemic admissions based on a 250.xx code and therapeutic misadventures ICD-9 CM code 962.3 from January 2002 to March 2003. Patients were matched to insulin usage through pharmacy claims data. Prescribing physicians were contacted and educated on the benefits of using a doser device to avoid incidence of a second admission. Reevaluation of pharmacy claims data confirmed whether a switch was made in patients identified and whose physician had switched to a doser device.

**RESULTS:** Approximately 1,000 patients were identified as having an admission due to a hypoglycemic event during the period of time evaluated. Conversions were made only if the prescribing physician consented to the change. A significant number of patients were switched to the doser device. Reevaluation of admissions based on same ICD codes confirmed whether a switch was made in patients identified and whose physician had switched to a doser device.

**CONCLUSIONS:** Results of this program provide further evidence that removing patient variability in administering insulin can result in reduced medication errors and hypoglycemic events to a health plan. A physician intervention program can achieve a significant cost avoidance.

**LEARNING OBJECTIVES:**
1. Increase awareness that insulin is one of the leading products in harmful medication errors.
2. Determine the incidence of hypoglycemic events in patients receiving insulin in an elderly population.
3. Evaluate the impact of switching patients to an insulin doser device and cost avoidance of hypoglycemic events in patients converted.

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**COST-EFFECTIVENESS AND BUDGET IMPACT OF ZOMITRIPTAN NASAL SPRAY**

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**OBJECTIVE:** To estimate the cost-effectiveness and budget impact of zolmitriptan nasal spray 5 mg (ZNS) from the perspective of a U.S. managed care organization (MCO).

**METHODS:** We constructed an Excel model to compare ZNS to sumatriptan nasal spray 20 mg (SNS) and 50 mg and 100 mg tablets. Model inputs include drug and nondrug health care costs and 2-hour response and 24-hour recurrence rates. Costs are from publicly available sources. Effectiveness estimates are from placebo-controlled trials and published meta-analyses. Model outputs include total drug and health care costs and incremental cost-effectiveness ratios (ICERs). Sensitivity analyses are performed on all inputs. Budget impact assumes a prevalence of treated migraineurs in an MCO of 10%. We assume that 10% of them will use ZNS, half switching from SNS and half from oral sumatriptan.

**RESULTS:** In the base case, ZNS results in lower costs than SNS and higher costs than oral sumatriptan, but with better effectiveness than all 3 alternatives. Compared with oral sumatriptan (50 mg), ZNS achieves ICERs of $46/additional 2-hour response and $27/additional total headache response (i.e., response without recurrence). Compared with oral sumatriptan (100 mg), ZNS achieves ICERs of $18/additional 2-hour response and $17/additional total headache response. Budget impact is likely to be negligible (decrease of 1 cent per member per month), derived from cost savings due to SNS-to-ZNS switches balanced by potential cost increases due to oral sumatriptan-to-ZNS switches.

**CONCLUSIONS:** ZNS offers a cost-effective alternative to sumatriptan nasal spray or tablets, with nominal budget impact to a U.S. MCO.

**LEARNING OBJECTIVES:**
1. Learn how costs and outcomes associated with migraine treatments may be considered using incremental cost-effectiveness and budget impact analyses.
2. Evaluate a new option for migraineurs from an MCO formulary budget and population health standpoint.
3. Resolve questions regarding the sensitivity of modeled analyses to changes in base-case assumptions due to clinical and economic uncertainty.
COST IMPACT OF ADJUNCTIVE ATYPICAL ANTIPSYCHOTIC USE IN BIPOLAR DISORDER

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INTRODUCTION: To compare the economic impact of selected atypical antipsychotic agents as adjunctive therapy for bipolar disorder on total mental health-related expenditures.

METHODS: Texas Medicaid patients with bipolar disorder who were undergoing continuous mood stabilizer therapy and given risperidone (n = 159), olanzapine (n = 217), or quetiapine (n = 48) between January 1998 and September 1999 were retrospectively analyzed in an intent-to-treat pharmacy and mental health service database for a period of 1 year before and 1 year after initiation of atypical antipsychotic therapy. Postinitiation comparisons were made between study groups after controlling for any differences in demographics, preinitiation expenditures, and utilization patterns.

RESULTS: Patients taking risperidone had significantly lower (P<0.01) mental health-related pharmacy costs (mean [SD], $2,492 [$1,584]) than those receiving olanzapine ($3,315 [$2,055]) and numerically but not significantly lower costs than those given quetiapine ($2,947 [$1,679]). Total postinitiation mental health payer costs were not significantly different between risperidone ($5,429 [$5,985]), olanzapine ($6,448 [$6,143]), and quetiapine ($6,620 [$5,277]) groups.

CONCLUSION: When compared with olanzapine, risperidone as adjunctive therapy to mood stabilizers had a more positive economic impact on mental health-related pharmacy costs despite the lack of differences in total mental health-related expenditures.

LEARNING OBJECTIVE:
Evaluate the relative Texas Medicaid costs associated with risperidone and olanzapine in the treatment of bipolar disorder.

COST IMPLICATIONS OF HEPATITIS C PHARMACOTHERAPY IN A HEALTH CARE PLAN

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INTRODUCTION: To characterize hepatitis C (HCV) pharmacotherapy utilization and associated cost among members of a Midwest health care plan.

METHODS: A retrospective database analysis of pharmacy and medical claims for 1.6 million lives, from 1/1/99 to 5/31/02, was performed. Members with ICD-9 codes for HCV infection (70.41, 70.44, 70.51, and 70.54) and complete benefit coverage were included for analyses. NDC codes identified treatment patterns for HCV. Comorbidity was assessed by Schneeweiss clustering methodology.

RESULTS: Of the plan members diagnosed with HCV, 2,108 met study criteria (median age of 46 years, 61% male). Only 467 (22.2%) individuals received treatment. Alcohol and drug abuse were the most common comorbidity (24.4%). Peg-Interon + Ribavirin (RBV) combination therapy accounted for 70% of index prescriptions since the fourth quarter of year 2001. Mean medication possession ratios ranged from 0.85 to 0.99. At week 12, there was no significant difference in patient dropout between Peg-Interon + RBV and Rebetron. At week 24, 43.3% of Peg-Interon+RBV and 33.3% of Rebetron patients discontinued therapy. Mean monthly cost of drug therapy was $1,154 for Peg-Interon+RBV and $697 for Rebetron. For members utilizing HCV-related antidepressants and growth factors (treating anemia and neutropenia), mean additional costs were $614 and $5,966, respectively.

COST IMPLICATIONS OF HEPATITIS C PHARMACOTHERAPY IN A HEALTH CARE PLAN

**CONCLUSIONS:** Plans incur substantial expense due to HCV. Patient drop-out from therapy before presumed viral eradication may increase future HCV-related medical costs. Therefore, patient persistence with therapy as well as the cost of adjuvant medications needs to be considered when developing a policy for HCV prescription drug coverage.

LEARNING OBJECTIVES:
1. Discuss the impact of new hepatitis C therapy on health care costs.
2. List the comorbid conditions associated with hepatitis C patients.
3. Describe the medication use patterns observed in patients.

COX-2 INHIBITORS: THE RIGHT DRUG FOR THE RIGHT PATIENT

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INTRODUCTION: Blue Care Network (BCN) has developed a comprehensive program to ensure all nonsteroidal anti-inflammatory drugs (NSAIDs) are used both safely and appropriately.

METHODS: BCN restricts access to the COX-2 inhibitors through formulary placement, prior authorization, and step-therapy criteria. BCN also requires once-daily dosing of these agents. Although these restrictions decrease the overall cost of this drug class, they may also lead physicians to use traditional NSAIDs inappropriately. This could result in increased risk of gastrointestinal bleed for certain patients. To decrease risk exposure and ensure appropriate treatment for its members, BCN developed an NSAID safety report to identify the members who are at potential increased risk of gastrointestinal (GI) bleed yet are receiving a traditional NSAID on a chronic basis. Members who meet criteria are identified and reported to the primary care physician. An explanatory letter provides information regarding the use of GI protective treatment. Specific claim information is available if a change in prescription was required. These notices have resulted in changed prescriptions that help ensure medication safety for our members.
RESULTS: The average cost of an NSAID prescription at BCN in 2002 was $29 compared with $85 reported at a comparable plan with no prior-authorization requirements. The COX-2 agents represented 17.6% of all NSAIDs dispensed at BCN compared with 51% at the compared plan. Based on the difference in use of the COX-2 inhibitors between the 2 plans, BCN calculated a savings of $4.8 million in 2002.

CONCLUSIONS: BCN’s comprehensive process of prior authorization, coupled with its NSAID safety report to identify members at risk of GI bleed, helps to ensure appropriate use of these agents.

LEARNING OBJECTIVES:
1. Identify mechanisms to control costs associated with NSAID use.
2. Review reports that provide safety information to the physician to decrease the risk of gastrointestinal bleed in selected patients.
3. Identify potential cost savings associated with a targeted formulary management program.

DEVELOPING AND IMPLEMENTING AN INTERACTIVE DISEASE THERAPY MANAGEMENT PROGRAM

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INTRODUCTION: As a Pharmacy and medical management company and now a specialty pharmacy, Prescription Solutions is in a unique position not only to impact several aspects of patient care but also to measure that impact. Our interactive Disease Therapy Management program will improve quality of care for enrolled participants through education and communication and will establish an efficient mechanism of reporting data.

METHODS: The Prescription Solutions interactive Disease Therapy Management Program was developed using National Community Pharmacists Association protocol, the American Academy of Family Physicians recommendations, and current clinical information. Clinical pharmacists developed both member- and provider-based educational materials as well as clinical and functional assessment tools. The assessment tools will be used as a basis for patient-specific care plans that will be sent to members and their corresponding physicians. A program-specific database has been designed to serve as a confidential record of the enrolled member’s medical information obtained from pharmacist or nurse interviews with the enrolled participants. Enrolled members will be contacted at least monthly, but possibly more frequently as needed. All interactions between Prescription Solutions clinical staff and the member or physician will be documented in the database.

CONCLUSIONS: By using our pharmacy claims data, the information collected from our enrolled members during consultations, and the results of member-based surveys, we will be able to analyze the impact of an interactive Disease Therapy Management program on quality of life, medication compliance, and overall medical costs.

LEARNING OBJECTIVES:
1. Understand the rationale behind developing an interactive Disease Therapy Management program.
2. Describe the steps involved in implementing an interactive Disease Therapy Management program.
3. Assess the impact of an interactive Disease Therapy Management program on quality of life, medication compliance, and medical costs.

DEVELOPMENT AND IMPLEMENTATION OF AN INTERNAL PRIOR-AUTHORIZATION PROCESS FOR A MIDWEST HEALTH PLAN

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INTRODUCTION: Develop internal medication prior-authorization (PA) process to better enforce the formulary and PA criteria, improve reporting, and enhance local control.

METHODS: Staff were already establishing PA criteria. Software, in compliance with NCQA criteria, was developed to eliminate manual data gathering and streamline other steps of the PA process, including generation of member/provider notification and creation of a database of electronic records with required data elements. Staffing requirements were determined based on the current volume of PAs and enrollment.

RESULTS: Formulary compliance increased from 91.2% to 95.2% over the first year. Requests increased from 590/month in 2001 to 658/month in 2002. Relative differences in approval rates were seen (8% to 10%). The combination of the database and an existing query tool provides access to reports previously not available, which are used for formulary and policy decisions, including number of requests by products, prescriber, etc. Additional reports include tracking individual pharmacist decisions and decision reversal rates. The internal process provided flexibility to meet changes in NCQA and ERISA requirements. An internal PA process also avoids third-party NCQA delegation. Member/provider notifications automatically generated can be modified quickly with tailored messages for individual requests. Problems in the claims processing system are more easily identified by monitoring PAs received. For 0.102 PA requests per member per year, daily staffing requirements are 1.0 FTE technician and 0.5 FTE pharmacist.

CONCLUSIONS: Formulary compliance and PA criteria enforcement improved. The number and utility of the reports increased. Local control enhances provider panel relationships.

LEARNING OBJECTIVES: Audience participants will be able to:
1. Describe the process of developing an internal prior-authorization process.
2. Identify key elements necessary to have an internal prior-authorization process.
3. Outline the advantages and disadvantages of an internal prior-authorization process.

■ DEVELOPMENT OF A TOOL TO ASSIST PLANS WITH COMMUNICATING THE PHARMACY BENEFIT

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OBJECTIVES: To develop and obtain feedback on the usefulness of the Pharmacy Benefit Communication Grid developed by the Academy of Managed Care Pharmacy.

METHODS: The Pharmacy Benefit Communication Grid is comprised of 3 sections. The first defines strategies and methods of communication to stakeholders in health care delivery. The second describes the types of messages (i.e., formulary, step therapy, network pharmacies, etc.) managed health care organizations (MCOs) use to communicate. The third section suggests mechanisms for setting goals and obtaining feedback from customers to help MCOs improve their performance. The investigators surveyed 7 MCOs to determine content and face validity of the Grid.

RESULTS: Using a modified version of the Grid, the investigators assessed how and to whom responding MCOs currently communicate the pharmacy benefit and discerned the Grid’s potential usefulness and value. Six of the 7 MCOs surveyed stated they would use the Grid with or without modifications. The majority of the respondents believe that they do a good job communicating to their members and internal customers but not as well when communicating to providers and external customers.

CONCLUSION: Health plans and pharmacy benefit managers can apply the Grid to identify deficiencies and improve their communications with various stakeholders in the medication use process.

■ ECONOMIC COMPARISON OF ERYTHROPOIESIS-STIMULATING THERAPIES (EST) IN TREATING CHEMOTHERAPY-RELATED ANEMIA (CRA) IN PATIENTS WITH LUNG CANCER


INTRODUCTION: To compare expected erythropoiesis-stimulating therapy (EST) cost and cost per hematopoietic response (HR) in patients with lung cancer from a payer perspective.

METHODS: An 18-week economic model, reflecting clinical practice guidelines (NCCN 2003), was constructed using data from published clinical and community-based trials of EST in chemotherapy-related anemia (CRA). HR was defined as achieving 2 g/dL rise in hemoglobin (Hb) or Hb ≥12 g/dL in absence of transfusion. The initial fixed regimen of epoetin alfa (EPO) was 40,000 U once weekly (QW), with titration permitted after week 4 to 60,000 U QW if Hb <1 g/dL. The initial weight-based regimen of darbepoetin alfa (DARB) was 2.25 mcg/kg/QW, with titration permitted after week 6 to 4.5 mcg/kg/QW if Hb <1 g/dL (70 kg weight assumed). Costs were calculated using average wholesale price (2003 Red Book) and percent of patients responding to dosing regimens.

RESULTS: The expected cost for DARB was 71% higher than EPO ($19,900 vs. $11,667, respectively). Reasons for this cost differential are 2-fold: (1) 53% higher initial therapy cost of DARB than EPO (increase $252/week) and (2) fewer cases responding to the DARB initial regimen (39%) versus EPO (45%). The cost per HR was higher for DARB than EPO ($39,019 versus $18,833, respectively). One-way sensitivity analyses indicated DARB requires either an unachievable HR of 106% or a 52% reduction in acquisition cost to demonstrate comparable cost-effectiveness to EPO.

CONCLUSIONS: In this model, EPO is more effective and less costly than (dominates) DARB in treating CRA in patients with lung cancer.

LEARNING OBJECTIVES:
1. Understand the cost of EST for CRA in patients with lung cancer from a managed care perspective.
2. Investigate the cost and outcomes of treating CRA in patients with lung cancer.
3. Recognize the cost differential between competing ESTs.

■ THE ECONOMIC IMPACT OF DIVALPROEX SODIUM VERSUS ATYPICAL ANTI PSYCHOTICS IN COMMERCIALLY INSURED AND MANAGED MEDICAID POPULATIONS

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OBJECTIVE: To quantify differences in the annual costs of psychiatric-related care for patients with psychoses who were newly treated with divalproex sodium or an atypical antipsychotic.

METHODS: Data were obtained between January 1997 and March 2002 based on integrated pharmacy and medical claims from 58 managed care organizations. Patients with a diagnosis of bipolar disorder or schizophrenia were classified into 4 groups based on the first prescription observed after a 6-month washout period: divalproex sodium, risperidone, olanzapine, or other. Claims were then examined for the 12-month period following initiation of the index medication. Analyses were conducted on all patients as well as a subgroup enrolled in managed Medicaid products. Average annual per-
Abstracts From Professional Poster Presentations at AMCP’s 2003 Educational Conference

**RESULTS:** A total of 19,751 patients were identified (n = 1,557 for managed Medicaid). The average age of patients in the sample was 37 years; 60% of patients were female. Patients in the Medicaid subset were substantially younger (mean of 30 years). Average annual costs of psychiatric-related care were 28% to 41% lower among those receiving divalproex sodium ($3,263) relative to atypical antipsychotics ($4,527–$5,519); differences were manifested primarily in lower medication and hospitalization costs. Differences were similar but more marked in the managed Medicaid subgroup ($4,406 versus $6,872–$7,759). All differences were statistically (P<0.01) significant after controlling for differences in demographic and clinical characteristics between groups.

**CONCLUSIONS:** Use of divalproex sodium may be cost saving relative to atypical antipsychotics among commercially insured persons with psychotic disorders.

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**EFFECT OF CLINICAL INTERVENTION ON PATIENTS WITH HEPATITIS C**  
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**INTRODUCTION/OBJECTIVE:** This prospective study was performed to identify noncompliant hepatitis C patients and evaluate the benefit of pharmacist intervention on participants’ compliance.

**METHODS:** Patients aged 18 to 65 years, within a managed care organization, were selected for evaluation and assigned to a control or intervention group. Implementation included the development of educational tools, establishment of the monitoring role of pharmacist, and education of physicians. The patients in the control group received no intervention while the intervention group received educational materials and follow-up calls.

**RESULTS:** The data reveal 69% of patients in the intervention group were compliant versus 36% of patients in the control group.

**CONCLUSION:** Based on preliminary results, written and verbal education has a beneficial effect on patients’ compliance level. Results may be attributed to close, frequent follow-up.

**LEARNING OBJECTIVES:**
1. Understand the differences in use patterns for hepatitis C patients undergoing treatment.
2. Compare the cost-effectiveness of improving compliance.
3. Describe 1 method of increasing medication compliance.

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**EFFECT OF PREVENTIVE HEADACHE THERAPY WITH BOTULINUM TOXIN TYPE A ON EMERGENCY ROOM UTILIZATION**  
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**INTRODUCTION:** Emergency room (ER) visits contribute substantially to the cost of treating headache disorders. Preventive treatment with botulinum toxin type A (BoNT/A) has been shown to be effective for treating headache disorders.

**OBJECTIVE:** The purpose of this study was to compare ER utilization rates before and after preventive headache treatment with BoNT/A.

**METHODS:** ER visits during the 6-month periods before and after BoNT/A treatment for disabling headache disorders were determined by a retrospective chart review of patients in the Kaiser Permanente Health care System.

**RESULTS:** ER utilization data were available for 76 BoNT/A patients. Most of the patients (79%) had episodic headaches (29% migraine; 16% tension type headache; 34% mixed headache) and 21% had chronic daily headache. An analysis of pre-BoNT/A patients showed that 66% had no ER visits, 24% made 1 visit, and 10% had more than 1 ER visit. In contrast, for post-BoNT/A patients, 84%, 13%, and 3% had 0, 1, and more than 1 ER visit, respectively. There was a decrease in the number of ER visits for 23 (30%) patients and an increased ER utilization in 8 (10%) patients. This shift in ER utilization after BoNT/A treatment was statistically significant (Chi-square = 7.258, df = 1, P = 0.007).

**CONCLUSIONS:** These results indicate that BoNT/A treatment for disabling headaches significantly reduced ER utilization in a subset of patients. Further research is needed to identify the headache population at high risk for ER utilization that has the most potential for benefit with BoNT/A treatment relative to the reduction of the overall burden of headache.

**LEARNING OBJECTIVES:**
1. Assess the potential of BoNT/A treatment of disabling headache disorders.
2. Investigate the impact of BoNT/A preventive treatment headache on ER utilization rates.
3. Determine the initial characteristics of patients that might show reductions in ER utilization as a result of BoNT/A treatment.
EVALUATION OF A CLINICAL INTERVENTION CENTER ON ANTIDEPRESSANT MEDICATION ADHERENCE IN MANAGED CARE

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OBJECTIVE: To evaluate a clinical intervention center (CIC) program implemented to improve adherence to antidepressant medications.

METHODS: Antidepressant new starts (no antidepressant claim during the previous 4 months) ≥18 years were enrolled in the program, and their claims were monitored for nonadherence (defined as >10 days late in fills). Prescribing physicians were notified of patient nonadherence by the CIC via phone and fax. A 6-month follow-up retrospective pharmacy claims analysis was conducted to compare medication utilization of the intervened population to a control population, which consisted of nonadherent antidepressant new starts not enrolled in the program. Endpoints measured include number of claims, quantity dispensed, gap days between fills, and adherence to therapy squares and logistic regression models were used to estimate differences and identify characteristics affecting health care expenses within each group.

RESULTS: Mental and other health care expenses for family members living with patients with serious mental illnesses increased compared with controls as follows: bipolar disorder, $8.85/PPPM (213%, P<0.0001) and $10.65/PPPM (7.4%, P<0.0001); schizophrenia, $4.03/PPPM (81%, P<0.0001) and $5.96/PPPM (4.2%, P<0.005); major depression, $8.24/PPPM (219%, P<0.0001) and $9.46 (6.5%, P<0.0001). Within all 3 groups, men were less likely to use mental health care services (P<0.002), and the likelihood of mental health care use increased with longer illness duration (P<0.005). Other health care expenses were higher for parents and spouses of patients (P<0.0001–P<0.01) and with longer illness duration (P<0.0001–P<0.0005); men had lower expenses (P<0.0001–P<0.05).

CONCLUSION: Living with a person with serious mental illness significantly increases health care expenses of family members, especially for mental health care. Family members of patients with bipolar and major depressive disorders have higher health care expenses than those of patients with schizophrenia among commercially insured persons.

LEARNING OBJECTIVES:
1. Learn the effect mental and other health care expenses have on family members of patients with serious mental illnesses.
2. Learn the characteristics associated with higher mental and other health care expenses among family members of patients with serious mental illnesses.
3. Learn which mental disorders are associated with higher mental and other health care expenses.

EFFECTS OF ELECTRONIC PRESCRIBING ON FORMULARY COMPLIANCE IN THE AMBULATORY SETTING: A RETROSPECTIVE CLAIMS DATA ANALYSIS

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INTRODUCTION: Handheld devices used for electronic prescribing (e-Prescribing) provide formulary information at the point of care. The purpose of the study was to assess the effects of e-Prescribing on physicians’ formulary compliance and generic utilization by examining pharmacy claims from a large national managed care organization.

METHODS: One year of paid pharmacy claims were analyzed to assess the impact of e-Prescribing on formulary compliance and generic utilization. A sample of 126 providers using e-Prescribing was randomly selected (e-Prescriber group). A matched sample of 126 traditional prescribers was selected, matched to the e-Prescriber group by ZIP code and specialty (traditional prescriber group).

All paid pharmacy claims were examined for each prescriber group. For the e-Prescriber group, this included all prescriptions dispensed, not just those prescribed using an e-Prescribing device. Generic utilization was also assessed in each group. Subanalyses examined specific drug classes for formulary compliance and generic utilization.

RESULTS: e-Prescribers and traditional prescribers showed high levels of formulary compliance, 83.63% and 82.16%, respectively (P<0.05). This was equivalent to the overall prescriber population from which samples were selected, 82.04%.

CONCLUSIONS: An examination of paid pharmacy claims from a large, national managed care organization showed no differences between e-Prescribers and traditional prescribers in terms of formulary compliance or generic utilization. Future studies should examine keystroke data at the point of care to observe more detail about drug selection methods.

EFFECTS ON MENTAL AND OTHER HEALTH CARE COSTS OF FAMILY MEMBERS OF PATIENTS WITH BIPOLAR, SCHIZOPHRENIC, AND MAJOR DEPRESSIVE DISORDER

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OBJECTIVE: To measure effects on mental and other health care expenses of family members of patients with bipolar disorder, schizophrenia, and major depression.

METHODS: Using data from a 2-million member health plan, the authors estimated and compared expenses for mental and other health care services per person per month (PPPM) of family members of patients with bipolar disorder, schizophrenia, and major depressive disorder with those of controls. Ordinary least squares and logistic regression models were used to estimate differences and identify characteristics affecting health care expenses within each group.

RESULTS: Mental and other health care expenses for family members living with patients with serious mental illnesses increased compared with controls as follows: bipolar disorder, $8.85/PPPM (213%, P<0.0001) and $10.65/PPPM (7.4%, P<0.0001); schizophrenia, $4.03/PPPM (81%, P<0.0001) and $5.96/PPPM (4.2%, P<0.005); major depression, $8.24/PPPM (219%, P<0.0001) and $9.46 (6.5%, P<0.0001). Within all 3 groups, men were less likely to use mental health care services (P<0.002), and the likelihood of mental health care use increased with illness duration (P<0.005). Other health care expenses were higher for parents and spouses of patients (P<0.0001–P<0.01) and with longer illness duration (P<0.0001–P<0.0005); men had lower expenses (P<0.0001–P<0.05).

CONCLUSION: Living with a person with serious mental illness significantly increases health care expenses of family members, especially for mental health care. Family members of patients with bipolar and major depressive disorders have higher health care expenses than those of patients with schizophrenia among commercially insured persons.

LEARNING OBJECTIVES:
1. Learn the effect mental and other health care expenses have on family members of patients with serious mental illnesses.
2. Learn the characteristics associated with higher mental and other health care expenses among family members of patients with serious mental illnesses.
3. Learn which mental disorders are associated with higher mental and other health care expenses.
(measured by medication possession ratio [MPR]). A multivariate analysis was performed to control for differences in pharmacy benefit and a t test was used to evaluate endpoints between the 2 groups.

**RESULTS:** The intervention (N = 564) and control (N = 7,409) groups were similar in age and gender; however, average copay per patient per claim was higher in the control ($17.25 versus $9.18). Average number of claims and quantity consumed per patient were higher in the intervention group (4.7 versus 4.4 claims, \( P = 0.02 \); 217 versus 185 quantity consumed, \( P < 0.001 \)). The intervention group demonstrated decreased number of gap days between medication fills by 8 days (\( P = 0.0018 \)). Average MPR, adjusted for copay, resulted in 6.3% points higher for the intervention group (\( P < 0.001 \)).

**CONCLUSION:** Physician notification of patients late in filling antidepressant medications can significantly improve patient adherence with drug therapy.

**LEARNING OBJECTIVES:**
1. Understand the goals and components of a depression medication adherence program implemented in a managed care organization.
2. Learn the methodology used to evaluate antidepressant medication adherence using pharmacy claims data.
3. Evaluate antidepressant medication utilization patterns.

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**EVALUATION OF AN OXYCONTIN EDUCATIONAL AND PRIOR-AUTHORIZATION PROGRAM IN A MEDICAID FEE-FOR-SERVICE (FFS) PROGRAM**

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**PURPOSE:** To evaluate the impact of an educational and prior-authorization program on the appropriate prescribing of OxyContin and potential substitute narcotic analgesics and health care utilization in a Medicaid FFS population.

**METHODS:** The educational intervention targeted OxyContin prescribers and focused on ways to prevent diversion of controlled substances. The prior-authorization program required a medical necessity review for any OxyContin prescription(s) exceeding 3 tablets a day or more than 2 concurrent strengths. A preapproach-postapproach using descriptive time series and bivariate analyses of administrative claims were used to assess utilization of OxyContin and other narcotic analgesics as well as emergency department and physician outpatient visits for chronic pain and cancer.

**RESULTS:** At 6 months postintervention, the prescribing of multiple OxyContin tablets and the days of multiple strengths use was reduced by 84% and 22%, respectively. Among Medicaid FFS enrollees, OxyContin use decreased 3.7%; however, the trend appears to be increasing. Other narcotic analgesic use increased 9.9% with fentanyl patch users increasing by 27%. There were no significant changes in the number of users or
days of multiple concurrent long-acting narcotic use and outpatient or emergency department visit use for chronic pain and cancer. **CONCLUSIONS:** The intervention was effective in improving OxyContin prescribing without adversely affecting health care utilization. In addition, it appears that physicians are switching to a less-abusive dosage form (i.e., fentanyl patches) and are appropriately prescribing a single long-acting analgesic to control pain. Continued monitoring is necessary to determine if these trends are maintained.

**LEARNING OBJECTIVES:**
1. Understand the impact of an OxyContin educational and prior-authorization program on the use of OxyContin and other potential substitute narcotic analgesics.
2. Understand the impact of a drug-focused educational and prior-authorization program on health care utilization.
3. Describe methods to characterize drug and health care use using administrative claims.

**EVALUATION OF UTILIZATION PATTERNS AND CLINICAL OUTCOMES OF A NOVEL ERYTHROPOIETIC AGENT, DARBEPOETIN ALFA (DARBEPOETIN), FOR CHEMOTHERAPY-INDUCED ANEMIA IN A PRIVATE PAYER POPULATION: A MULTICENTER RETROSPECTIVE CHART REVIEW STUDY**

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**OBJECTIVE:** To compare initial dosing patterns and outcomes of darbepoetin (~3-fold longer half-life than Epoetin alfa [epoetin]) with current dosing and outcomes of epoetin in chemotherapy-induced anemia (CIA) patients with private insurance.

**METHODS:** Drug utilization and laboratory data were abstracted from medical charts of anemic patients undergoing chemotherapy. Sixteen community or hospital oncology clinics provided consecutive records of patients initiated on epoetin or darbepoetin therapy from April 1 to July 31, 2002, or August 1 to October 4, 2002, respectively. Twelve weeks of chart data from private-payer patients (health maintenance and preferred provider organizations) were analyzed using descriptive statistics; missing hemoglobin values and values within 28 days of a transfusion were imputed using the last-value-carried-forward approach.

**RESULTS:** Overall, 1,391 (752 darbepoetin, 639 epoetin) records were abstracted. The private-payer population comprised 35% (254/735) of darbepoetin and 37% (206/558) of epoetin records. Most of these patients received an initial dose of 200 mcg darbepoetin every 2 weeks (Q2W) (72%, n = 184) or 40,000 U epoetin once weekly (QW) (77%, n = 159). In this subset, dose was escalated for 13.6% of darbepoetin and 16.4% of epoetin patients at weeks 8.3 and 9.7, respectively. The mean imputed change from baseline in hemoglobin after 12 weeks of treatment was 1.0 g/dL for darbepoetin and 1.1 g/dL for epoetin. Similar findings were observed in the other payer groups. **CONCLUSION:** The use of darbepoetin 200 mcg Q2W for CIA in the private payer population has been adopted as standard clinical practice and achieves similar clinical outcomes compared with epoetin 40,000 U QW.

**HEALTH CARE SERVICE AND PHARMACY COSTS ASSOCIATED WITH LOW-BACK PAIN PATIENTS NEWLY STARTED ON EITHER TRANSDERMAL FENTANYL OR CONTROLLED-RELEASE OXYCODONE**

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**INTRODUCTION:** To explore whether differences in health care service and pharmacy costs in low-back or spinal-pain patients newly started on either transdermal fentanyl (TDF) or controlled-release oxycodone (CRO) tablets exist.

**METHODS:** Using medical and pharmacy claims data from MedStat’s MarketScan database (1997-2000), low-back or spinal-pain patients ≥18 years newly started on TDF or CRO were identified. Newly started was defined as no long-acting opioid within the 6 months prior to the index date. Index date was designated as the date of each subjects’ first long-acting opioid prescription. Patients’ health care utilization and pharmacy costs were followed for a total of 6 months after opioid initia
tion. Ordinary least square regression models were used after controlling for severity markers. Severity markers included comorbid pain conditions, previous health care utilization and cost, non–pain-related comorbidities, patient demographic characteristics (age, gender), and health plan type. T tests were used to compare total and pharmacy costs between the TDF and CRO arms.

**RESULTS:** Analyses occurred on 1,454 TDF and 7,505 CRO patients. Patient characteristics were similar with regard to age, gender, pain-related comorbidities, and all other comorbid pain conditions. Total health care costs across the entire cohort were $5,594 for TDF compared with $5,059 for CRO (P<0.01). Pharmacy costs across the entire cohort were $2,239 for TDF compared with $1,574 for CRO (P<0.01).

**CONCLUSION:** When controlling for patient characteristics and severity markers, total health care and pharmacy costs were lower in the CRO patients newly started on CRO compared to patients newly started on TDF for low-back and spinal pain.

**LEARNING OBJECTIVES:**
1. Understand whether differences in health care service and pharmacy costs in low-back pain patients newly started on either transdermal fentanyl or controlled-release oxycodone tablets exist.
2. Understand why cost differences exist.
3. Ability to use this information to investigate and evaluate if
this same difference exists at their institution.

**IMPACT OF A PHARMACIST-LED ACADEMIC DETAILING PROGRAM TO INCREASE ANGIOTENSIN-CONVERTING ENZYME INHIBITORS (ACEI) UTILIZATION AMONG DIABETIC PATIENTS**

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**INTRODUCTION:** The benefits of angiotensin-converting enzyme inhibitor (ACEI) therapies in diabetic patients have been well documented. Unfortunately, many diabetic patients are not receiving optimal drug therapy with respect to ACEIs. Academic detailers, pharmacists who educate physicians on various clinical and patient related topics, are in a unique position to promote appropriate ACEI therapy for diabetic patients. The purpose of this study is to evaluate the impact of a clinical pharmacist’s intervention on therapy optimization in diabetic patients in a Medicaid population.

**METHODS:** Drug history data from 1,633 recipients (426 prescribers) receiving antidiabetic therapy without concurrent ACEI therapy were reviewed. A control group of 1,397 patients (359 prescribers) was also identified. The corresponding treating physicians were assigned to an academic detailing pharmacist based on geographic location. The pharmacists attempted to visit each physician’s office to discuss optimal therapy and to distribute chart stuffers, i.e., reminder notes, to be placed in the patient’s chart. The effect of pharmacist interventions on utilization was determined by comparing preintervention data (3 months) with postintervention data (3 months).

**RESULTS:** Pharmacist interventions increased the total utilization of ACEIs in a diabetic population by 2% (41 patients) as compared to control. The total increase in utilization of ACEIs by prescriber was 21.6% (92 prescribers) in the active group versus 17.0% (61 prescribers) in the control group. The total number of prescriptions for ACEIs was increased from the preintervention level of 0 to the postintervention level of 232 for the intervention group. For the control group, the total number of prescriptions for ACEIs was increased from the preintervention level of 0 to the postintervention level of 149. Interestingly, the amount paid per prescriber per month was slightly lower in the intervention group in the postperiod ($20.49) than in the control group ($20.71). This may be due to increased emphasis on generic ACEIs.

**CONCLUSION:** Our findings suggest that pharmacists’ interventions modestly improved appropriate therapy in diabetic patients. Because chart stuffers can be filed and not considered until the patient presents for a follow-up, results of the intervention may not fully be realized until 1 year postintervention.

**LEARNING OBJECTIVES:**
1. Recognize the importance of pharmacists performing drug profile reviews and therapeutic interventions diabetic therapy.
2. Establish the importance of reviewing patient therapy from a clinical and cost perspective.
3. Learn about the impact of improved antidiabetic therapy on utilization and cost.

**IMPACT OF A SLEEP-MANAGEMENT TARGETED-DISEASE INTERVENTION PROGRAM**

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**INTRODUCTION:** The purpose of the Sleep Management Targeted Disease Intervention (TDI) program was to promote the appropriate treatment of insomnia, reduce inappropriate long-term sedative-hypnotic therapy, and improve quality of care within a large managed care organization (MCO).

**METHODS:** The prescribers of sedative-hypnotics and their patients on inappropriate long-term sedative-hypnotic therapy were identified using pharmacy claims data. Long-term sedative-hypnotic therapy was defined as patients receiving sedative-hypnotics greater than 30 days over a 6-month period. Once these members were identified, physician-specific reports listing patients who were on long-term sedative-hypnotics were generated and mailed to the physicians. The physician also received educational materials along with the physician-specific report.

**RESULTS:** A $0.027 per-member-per-month savings was achieved within a large MCO population. Of the patients targeted for the program, 38% had fewer than 30 days or no sedative-hypnotic supply in the 6-month postintervention period. Sedative-hypnotic utilization decreased by 31% with an annual pharmacy cost savings for sedative-hypnotics of more than $964,000.

**CONCLUSIONS:** The Sleep Management TDI program was an effective method to promote the appropriate treatment of insomnia by reducing inappropriate utilization of long-term sedative-hypnotics. Implementation of the Sleep Management TDI program resulted in significant pharmacy cost savings within a large MCO population.

**LEARNING OBJECTIVES:**
1. Describe the steps involved in implementing a Sleep Management TDI program to promote the appropriate treatment of insomnia.
2. Evaluate the potential benefits of a Sleep Management TDI program to members, providers, and MCOs.
3. Discuss the impact of a Sleep Management TDI program on utilization and pharmacy costs of sedative-hypnotics.
**IMPACT OF ELECTRONIC PRESCRIBING TECHNOLOGIES ON GENERIC COMPLIANCE**

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**Purpose:** Electronic prescribing technology was implemented in 2,400 physician offices. We hypothesized that by providing physicians with generic drug status and alternatives at the point of prescribing, generic utilization would increase.

**Methods:** Generic rates were compared pretechnology and posttechnology installation. Analyses were conducted to determine the percentage of time a physician changed his or her originally prescribed medication when presented with a clinically relevant generic alternative postselection of the original drug. Statistical testing (t tests) was used to determine presignificance versus postsignificance.

**Results:** Presentation of generic status and alternatives at the point of prescribing led to a 14.3% increase in generic substitution (i.e., the percentage of time a generic medication was prescribed when a generic alternative was available; P<.01) and a 7.6% increase in generic dispensing (i.e., the percentage of time a generic medication was ever dispensed, P<.01) between January and December 2002. Ninety-four percent of this increase was driven by passive presentation of generic status at the point of prescribing. The remaining 6% improvement was driven by alternative messaging after the physician selected a branded product. The increase in generic prescribing was immediate upon implementation and sustained over time.

**Conclusions:** Managed care organizations and benefits managers should consider the promotion of electronic prescribing technologies as a cost-effective alternative to potentially expensive and intrusive physician generic education programs. Additional benefits of electronic prescribing include potential reduction in medication errors and reductions in the amount of rework and member inconvenience associated with the prescription process.

**Learning Objectives:**
1. Learn the potential value of electronic prescribing technologies in promoting the use of generic medications.
2. Understand the potential return on investment of electronic prescribing technologies versus traditional forms of communication (fax, phone, mail).
3. Recognize some of the potential barriers to electronic prescribing acceptance in the physician community.

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**IMPACT OF OVER-THE-COUNTER LORATADINE MARKET ENTRY IN MANAGED CARE HEALTH PLANS**

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**Introduction:** To evaluate the impact of over-the-counter (OTC) loratadine on utilization trends of prescription nonseating antihistamines (NSA), intranasal corticosteroids (INS), and leukotriene blockers (LEK).

**Methods:** Pharmacy claim databases from 10 managed care health plans (with different pharmacy benefit designs and plan membership range from 120,000 to more than 2 million) were utilized. Monthly utilization; drug cost per member per month; percent utilizing members and market share of prescription NSA, INS and LEK for each health plan were measured from September 2001 to September 2003. Rates of switch from loratadine to other prescription products were also measured. Results of health plans that have programs of various intensities in place to promote OTC switch were compared. Data through September 2003 will be presented at the meeting. Results through March 2003 were reported in the abstract.

**Results:** Within 3 months post-OTC loratadine market entry, the percentage of members utilizing prescription NSA and the total ingredient cost spent on prescription NSA were reduced by approximately 20% in all health plans (comparing 1Q03 data to that of 1Q02). Rates of switch from loratadine to other prescription products were low, with a majority of the patients switched to desloratadine. Pharmacy cost savings were higher in health plans that have high baseline loratadine market share and point-of-service edits in place to prevent switch to other prescription NSA.

**Conclusions:** Availability of OTC loratadine resulted in rapid reduction in the number of prescription NSA utilizers, and the economic impact varied dependent on the health plan’s baseline utilization patterns and programs in place to encourage OTC switch.

**Learning Objectives:**
1. Learn about the methodology used to evaluate the impact of OTC product market entry on trend in utilization and costs.
2. Understand the impact of different pharmacy benefit designs and interventions on utilization behavior of prescription medications for seasonal allergy.
3. Discuss the economic impact of OTC loratadine from a managed care perspective.
**INCIDENCE OF PREVENTABLE DRUG-RELATED MORBIDITY IN OLDER ADULTS IN NOVA SCOTIA, CANADA**

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**INTRODUCTION:** Our purpose was to determine the incidence of preventable drug-related morbidities (PDRM) in older adults in one area of Nova Scotia, Canada.

**METHODS:** Our study population consisted of seniors in the Western part of the Halifax Regional Municipality, using 1998 and 1999 data. The database contained claims information pertaining to all inpatient admissions, emergency department visits, physician office visits, ambulatory prescription medication use, and clinical laboratory results. The incidence of PDRM was determined by identifying individuals in the database who matched 1 of 52 clinical indicators of PDRM that were developed in a previous stage of the study, through computerized searches in the database.

**RESULTS:** In the 1998 data, 1,990 individuals who matched at least 1 of the 52 PDRM indicators were found in 21,890 older adults, for an overall incidence rate of 90.9 per 1,000. In the 1999 data, 1,678 individuals who matched at least one of the 52 indicators were found in 22,197 older adults, for an overall incidence rate of 75.6 per 1,000. The indicators were subdivided by gender and age and were organized into 7 disease/condition groupings for further analysis.

**CONCLUSIONS:** This study has helped to quantify the magnitude of the problem of PDRM in older adults in this region of Nova Scotia. In the future, these indicators could be used as screening tools to identify areas for improvement in care or seniors at risk for adverse drug-related events.

**LEARNING OBJECTIVES:**
1. Provide pharmacists with an understanding of the magnitude of the problem of preventable adverse consequences of medication use.
2. Determine the most commonly occurring types of preventable drug-related morbidities in older adults.
3. Discuss the potential uses of quality indicators of PDRM in a population database.
4. Enable pharmacists to improve the medication use system by discussing strategies that foster a safer and more effective medication use system.

**MEDICATION CHECK-UP PROGRAM PROMOTES PATIENT MEDICATION SAFETY**

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**INTRODUCTION:** Implementation of a medication check-up program promotes medication safety by encouraging patients to let their physicians know about all the medications they are taking.

**METHODS:** Members 55 years and older taking multiple maintenance prescription medications over a 3-month period were identified through prescription claims data (n = 6951). Members were mailed program kit materials in October 2002. Kit materials included a medication check-up program brochure, a personal medication card, and a bag to gather all their prescription and over-the-counter medications in and bring to their next physician visit for review. Members were instructed to have their physician fill out a questionnaire to record any changes/clarifications made for their medications as a result of their medication check-up. The impact on prescription claims history was also analyzed.

**RESULTS:** Based on completed questionnaire forms received from November 2002 through June 2003, at least 923 patients (13.3%) used the bag and brought their medications to their physician for review. After reviewing the contents, physicians instructed 317 patients (34%) to make changes in their medications. Of these 317 patients, 209 (66%) received dosage changes, 193 (61%) were advised to discontinue one or more of their existing medications, and 177 (56%) were advised to begin taking at least one new medication. Physicians also indicated that side effects or drug interactions were potentially avoided in 341 patients (37%) and medication directions/patient questions were clarified for 466 patients (50%). Based on available prescription claims data, patients with >10 maintenance medications had an overall decrease in the median number of maintenance medications after program implementation. No measurable reductions occurred in patients with fewer than 10 maintenance medications.

**CONCLUSIONS:** A medication check-up program promotes additional opportunity for screening of potential medication-related problems and supports the physician and patient in making informed health care decisions about medications. Claims data show measurable impact on members taking 10 or more medications.

**LEARNING OBJECTIVES:**
1. Learn how to implement a medication check-up program.
2. Understand how a medication check-up program supports patient medication safety initiatives.
3. Discuss the clinical impact of a medication check-up program on medication prescribing, utilization, and potential avoidance of unnecessary medication-related problems.
MEDICATION COMPLIANCE AND HOSPITALIZATION IN SCHIZOPHRENIA

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OBJECTIVE: To investigate the relationship between medication compliance and hospitalization in schizophrenia.

METHODS: A 12-month retrospective evaluation of California Medicaid schizophrenic patients with ≥2 dispensings for an antipsychotic during the enrollment period and ≥2 prescription within 6 months of the enrollment period (i.e., index date). Several alternative compliance measures were investigated, including medication possession ratio, consistence, persistence, and maximum gap in therapy. Logistic regression was used to analyze the odds of being hospitalized at least once during the study period. Compliance, age, ethnicity, sex, and Medicare eligibility were evaluated as independent measures.

RESULTS: 4,325 subjects were eligible (mean [SD] age = 44.2 ± 12.3 years; 58.5% were male; 56.5% were white). Approximately 49% were Medicare-eligible at some time, and 15.1% were hospitalized at least once during the study period. A 10% improvement in compliance, consistence, and persistence was associated with 13%, 16%, and 10% lower odds of hospitalization (P<0.0001 for all), respectively. Patients with a 1–10, 11–30, and >30 day maximum gap in their medication had 1.98, 2.82, and 3.96 higher odds of hospitalization (P = 0.0042, P<0.0001, P<0.0001), respectively, than subjects with no gap. Medicare eligibility was associated with increased odds of hospitalization compared with patients who were not Medicare eligible (P<0.0001). Sex was not a significant predictor of hospitalization in our analysis.

CONCLUSION: Decreased compliance is associated with an increased risk of hospitalization in schizophrenic patients.

LEARNING OBJECTIVE:
Understand the significant association between poor medication compliance and increased risk of hospitalization.

MEDICATION SAFETY: FOCUSED PHARMACY CLAIMS REPORTS HELP PREVENT ADVERSE DRUG EVENTS

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INTRODUCTION: Blue Care Network (BCN) Pharmacy Services has developed a multifaceted reporting program to help improve medication safety for its members. BCN’s medication safety reports focus on areas frequently cited as contributing to adverse drug events. Reports are generated quarterly by the Pharmacy Services Department using prescription claims data.

METHODS: By reviewing member-specific prescription claims information, the physician can consider possible adjustments to the member’s treatment to avoid adverse events. BCN’s quarterly Multi-Drug Review provides drug-drug and drug-disease interaction information, information regarding duplicative treatment, and suggestions to simplify the member’s drug treatment. BCN’s Drugs in the Elderly report identifies members over 65 years who are receiving a medication that should generally be avoided in the elderly population. A Controlled Substance Review report identifies members who have received 9 or more controlled substances over a 3-month period from 3 or more physicians using 3 or more pharmacies.

RESULTS: A recently launched Maximum Dose report identifies members with a claim for a psychotherapeutic medication that reflects a higher than recommended dose of the drug. This report is provided to the prescriber instead of the member’s primary care physician so that any necessary dosage change can be easily processed. BCN’s new NSAID Safety report identifies members who are at risk of gastrointestinal bleed and who are receiving chronic doses of a traditional nonsteroidal anti-inflammatory agent.

CONCLUSION: These reports all require the physician to provide feedback to BCN. Responses indicate that these reports have been a valuable tool to the prescriber or primary care physician and have been used to decrease the risk of adverse drug events for BCN members.

LEARNING OBJECTIVES:
1. Identify reporting opportunities to decrease the risk of adverse events.
2. Review distribution methods and issues relating to confidentiality.
3. Describe follow-up methods to ensure medication safety reports are being reviewed by the prescriber or primary care physician.

MEMANTINE ENHANCES AUTONOMY IN ALZHEIMER’S DISEASE PATIENTS

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OBJECTIVE: Alzheimer’s disease (AD) is characterized by a progressive deterioration of mental and physical functions reducing patient autonomy, which is associated with a decrease in quality of life and predicates institutionalization and additional cost of care. This study sought to assess the impact of memantine on autonomy by using the Activities of Daily Living (ADL) scales.

METHODS: Autonomy was assessed from the results of a 6-month double-blind, randomized trial. Clustering methods (K-means) using basic and instrumental ADL scales (ADCS-ADL) were used to categorize patients into autonomous and dependent groups. The validity of this classification was tested
by comparing sociodemographic, clinical, and economic characteristics. In order to estimate the impact of memantine on autonomy, a logistic model controlling confounding factors (age, sex, duration of illness, severity and autonomy at baseline) was applied.

**RESULTS:** Dependent patients (n = 106) had longer disease duration (P<0.05); poorer MMSE, NPI, and SIB scores (P<0.001); and higher total societal cost (P<0.001) than autonomous patients (n = 146). For patients who were autonomous before randomization to either memantine or placebo, fewer memantine patients became dependent compared to placebo patients (OR = 1.95, P<0.05).

**CONCLUSION:** Memantine enhances autonomy in moderate to severe AD patients, which could explain the lower societal costs for memantine-treated patients.

**LEARNING OBJECTIVES:**
1. Appreciate the impact of autonomy on various outcomes in Alzheimer's disease.
2. Understand the methodology involved in assessing autonomy in Alzheimer's patients.
3. Assess the impact of memantine treatment on autonomy in Alzheimer's patients.

### MIGRAINE DISEASE MANAGEMENT PROGRAM: DOCUMENTING OUTCOMES RELATED TO EDUCATIONAL INTERVENTIONS FOR PATIENTS IN A MANAGED CARE SETTING

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**PURPOSE:** This migraine-management program was undertaken to determine the impact of member and physician interventions on enhancing patient care among migraineurs in a managed care setting.

**METHODS:** Health plan members with an ICD-9 diagnostic code for migraine (346.XX) were invited to enroll in a disease management program by completing a Migraine Therapy Assessment Questionnaire (MTAQ). Members electing to enroll in the program subsequently received informational mailings along with a follow-up MTAQ survey to assess care improvement. The members' treating physicians were provided with educational materials and migraine-management tools.

**RESULTS:** A comparison of the 789 patients who completed both baseline and follow-up questionnaires revealed that 7 of 9 questions demonstrated statistically significant improvement in migraine management. Members reported a decrease in emergency or urgent care visits (16.5% to 12.2%, P = 0.002), a decrease in missed work or school due to migraine (61.8% to 50.9%, P = 0.000), and an improvement in satisfaction with migraine treatment (61.2% to 69.1%, P = 0.000). Members also reported improved symptom relief 2 hours postmigraine medication administration (67.2% to 71.1%, P = 0.021), improved ability to return to previous activity within 2 hours (55.7% to 61.7%, P = 0.001), a decrease in the number of migraine attacks per month (62.3% to 58.7%, P = 0.027), and enhanced understanding regarding migraine triggers (51.5% to 59.3, P = 0.000).

**CONCLUSION:** The use of appropriate educational resources and tools through a migraine disease management program impacted outcomes related to patient perception of quality of life and satisfaction with their migraine treatment plan.

†MTAQ is a trademark of Merck and Co., Inc.

**LEARNING OBJECTIVES:**
1. Understand the impact of patient educational interventions on enhancing patient care.
2. Recognize enhancements in quality of life of migraine sufferers through the active use of disease management principles and tools.
3. Recognize the impact of a migraine management program on health care resource utilization in a managed care setting.

### OUTCOMES OF AN MCO PROGRAM TO SWITCH LOW-RISK PATIENTS ON CONCOMITANT THERAPY WITH A COX-2 SPECIFIC INHIBITOR FROM A PROTON PUMP INHIBITOR TO AN H2 ANTAGONIST

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**PURPOSE:** To evaluate the feasibility and financial impact of switching a histamine-2 receptor antagonist (H2RA) for a proton pump inhibitor (PPI) in patients with no clinical reason for concurrently taking a PPI and a cyclooxygenase (COX)-2 specific inhibitor.

**METHODS:** Physicians, pharmacists, and patients were sent letters explaining the benefits of changing antulcer treatment in patients who do not have a history of gastrointestinal disease from a concurrent COX-2 specific inhibitor and PPI regimen to a COX-2 specific inhibitor and H2RA regimen. Waiver of copayment for H2RAs created a patient incentive. Four physicians and 2 pharmacist roundtable events were held to provide forums for discussion of the intervention program. Patients who had a clinical reason for being on a COX-2 specific inhibitor and a PPI were not encouraged to switch from the combination. Costs in this latter group of patients were expected to be offset in the long term by the health care system through lower GI event rates and lower GI-related medical resource utilization. The primary outcome measures were the PPI switch rate and a cost comparison of the 6-month preintervention and 6-month postintervention antulcer and nonsteroidal anti-inflammatory drug (NSAID) cost (PPI, H2RA, COX-2 specific inhibitor, and NSAIDs) for the intervention region and a similar control region.

**RESULTS:** A total of 20 patients on a COX-2 specific inhibitor and a PPI changed the PPI to an H2RA due to this program...
(15.4% of a potential 130 switches). Of the 20 patients, 8 (one third) were switched by the managed care organization’s (MCO’s) call center, and 12 (two thirds) were switched by the patient’s physician subsequent to receiving clinical data from the MCO. The mean per-patient cost for antulcer and NSAID medications rose 2.12% ($5.10) in the intervention region compared with 9.21% ($21.88) in the control region in the 6 months following the intervention. The larger increase in per-patient drug cost in the control region was statistically significant compared with the intervention region ($13.74, P = 0.008). This difference in cost yields an estimated savings of $119,758. The savings do not include the cost of the interventions and only reflect one fifth of the MCO’s total population and, therefore, savings. The rise in the number of prescriptions for antulcer and NSAID medications was not statistically significant for either region in the 6 months after the intervention began.

CONCLUSION: Switching from a PPI to a H2RA in low-risk patients concurrently taking a PPI and a COX-2 specific inhibitor is not an easy task for an MCO. Actual drug therapy switches are difficult to accomplish due to physician and patient resistance. However, the overall cost savings to an MCO may be substantial.

KEYWORDS: Concomitant use, COX-2 inhibitor, Proton pump inhibitor, Managed care organization

LEARNING OBJECTIVES:
1. Evaluate the feasibility of switching an H2RA for a PPI in MCO patients with no clinical reason for concurrently taking a PPI and a COX-2 specific inhibitor.
2. Evaluate the financial impact to an MCO of switching an H2RA for a PPI in patients with no clinical reason for concurrently taking a PPI and a COX-2 specific inhibitor.
3. Evaluate how a MCO may positively influence physician prescribing habits through educational interventions.
4. Understand some potential limitations of MCO drug-switch programs.

PARTNERSHIP WITH PROVIDER GROUP INCREASES SUCCESS OF PHARMACY INITIATIVES

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INTRODUCTION: Blue Care Network (BCN) Pharmacy Services credits its relationships with key physician groups throughout Michigan for its success in holding the line on pharmaceutical costs while maintaining quality of care and service for its members.

METHODS: A midsized contracted group of 57 primary care physicians and 65 specialists in central Michigan was targeted by BCN to decrease its excessive utilization and its high medical and prescription costs. In April 2001, BCN hired a clinical pharmacist to work directly with physician groups in this region. An improved understanding of the pharmacy benefit, increased collaboration on pharmacy initiatives, increased generic use, and a lower than expected rise in pharmacy cost has resulted from this relationship.

RESULTS: BCN provides key reports to its physicians to improve formulary compliance and generic utilization. Detailed claims information is also provided to reflect prescribing opportunities within specific therapeutic classifications. On an ongoing basis, the clinical pharmacist meets with physicians and group representatives to provide educational materials and identify areas of prescribing opportunity. Targeted therapies include proton pump inhibitors, nonsteroidal anti-inflammatory drugs, and antidepressants. Physicians are encouraged to use their personal digital assistants to download BCN’s formulary information. A company-wide generic drug campaign included polished advertisements for generic Prozac and generic Glucophage to further support the use of generic medications. In addition to physician education, BCN provides member information pamphlets and brochure racks to contracted physicians.

CONCLUSION: This important relationship between the contracted physician group and BCN has helped to slow the rising cost of pharmaceuticals. While BCNs overall per member per month pharmacy cost rose by 14.28% from 2001 to 2002, members assigned to this mid-Michigan group of physicians experienced only a 7.8% increase. In addition, ongoing communication with this group has increased participation by the physicians in newly implemented initiatives by Pharmacy Services.

LEARNING OBJECTIVES:
1. Recognize the importance of developing and maintaining relationships with contracted physician groups.
2. Describe at least 3 programs that will contribute to decreased pharmacy cost.
3. Review marketing materials for generic drugs.

PHYSICIAN AND PATIENT DOSE OPTIMIZATION COMMUNICATIONS REDUCE DRUG SPEND

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OBJECTIVE: To measure the drug-spend savings opportunity and patient satisfaction impact of migrating patients to a higher-strength tablet for select pharmaceuticals while maintaining the same daily dose. By lowering the number of tablets taken daily without a change in dosage, we hypothesized improved patient convenience and a reduction in drug spend would result.

METHODS: Four high-cost therapeutic categories with opportunities for tablet reduction were identified: Proton pump inhibitors, selective serotonin reuptake inhibitors, lipid-lowering agents (statins), and nonsteroidal anti-inflammatory drugs. Patients with opportunities for dose optimization (dosing of 1.5 to 3 pills per day) and their physicians were contacted about reducing the number of tablets taken daily. Physician accept-
ance rates and the impact on drug spend was measured for a 6-month follow-up period. Patients accepting the switch were interviewed to assess patient perceptions of the dose optimization experience.

RESULTS: For the identified categories, physicians were contacted about a dose optimization opportunity for 1,996 prescriptions (0.9% of total prescription volume for those categories). Fifty-two percent of communications resulted in a successful change to an optimized dose. The conversions resulted in a 60% decrease in drug spend for prescriptions with an optimized dose during the follow-up period (p < 0.01). Of all patients contacted about their experience, 97% indicated they were receptive to the change in dosage.

CONCLUSIONS: Dose optimization presents an opportunity to decrease drug spend through a program with low impact to patients. With rising drug costs, leveraging dose optimization offers a method for decreasing drug spend and optimizing stakeholder relationships.

LEARNING OBJECTIVES:
1. Learn how, with minimal impact to the patient or physician, a dose optimization program can decrease drug spend.
2. Learn how dose optimization benefits patients.

**PREDICTORS OF DISCONTINUATION OF TOLTERODINE AND OXYBUTYNIN FOR TREATMENT OF OVERACTIVE BLADDER**
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OBJECTIVE: To identify predictors of discontinuation of overactive bladder (OAB) therapy (i.e., long-acting tolterodine and oxybutynin or short-acting oxybutynin).

METHODS: Using pharmacy claims data from a health plan with more than 2 million members, patients with at least 1 OAB therapy claim between April and December 2001 were identified. Patients were included if they were continuously enrolled for 9 months following the first OAB prescription and did not have an OAB claim in the previous 6 months. A logistic regression analysis was performed to identify predictors of drug discontinuation. Variables included age, gender, drug dispensing channel, income, education, and concurrent pharmacotherapy (i.e., antibiotic for urinary tract infection [UTI]). National census data were used to extract socioeconomic information based on members’ residential areas.

RESULTS: A total of 2,807 OAB therapy utilisers were identified (mean age 60 years, 74% female). Approximately 50% of patients discontinued therapy in the first 3 months, and 69% of patients discontinued therapy over the 9-month study period. Predictors of discontinuation included use of short-acting oxybutynin, receiving medication from retail versus mail order pharmacies, younger age, female, higher education level, and concurrent use of antibiotics for UTI. Patients on long-acting products and patients filling prescriptions at mail order were associated with lower risk of discontinuation with a relative risk reduction of more than 50% for these variables.

CONCLUSIONS: Age, socioeconomic status, drug selection, drug dispensing channel, and concurrent antibiotic use were significant predictors for OAB therapy utilization behavior. Development of OAB quality improvement programs should take this into consideration.

LEARNING OBJECTIVES:
1. Recognize pharmacy utilization patterns, including drug discontinuation rates, of various medications for the treatment of overactive bladder.
2. Understand the patient characteristics, including demographics, socioeconomic status, and comorbidities, of
patients receiving drug treatments for overactive bladder.
3. Learn about the factors that are associated with OAB therapy discontinuation.

**PREVALENCE AND ECONOMIC BURDEN OF RHINITIS IN MANAGED CARE PATIENTS TREATED FOR ASTHMA**


INTRODUCTION: The objective of this study was to assess the prevalence of rhinitis in managed care patients with newly diagnosed asthma and its impact on asthma therapy and cost.

METHODS: Patients were selected from several managed care organizations (Source: PHARMetrics Integrated Outcomes Database); those who received a new prescription for an inhaled corticosteroid, leukotriene receptor antagonist, or long-acting β-agonist from 1998 to 2000 were included in the analysis. Resource utilization related to asthma and rhinitis were compared in patients with and without comorbid rhinitis in the year after new asthma treatment.

RESULTS: Of 42,581 patients with newly treated asthma, 16,648 (39.1%) also had a rhinitis diagnosis. Patients with both asthma and rhinitis were significantly younger (age 32.2 versus 36.4 years, *P* < .001) and were more likely to have received a diagnosis of acute sinusitis (39% versus 22%, *P* < .001) and upper respiratory tract infection (37% versus 30%, *P* < .001) during the study period compared with patients with asthma only. Patients with both asthma and rhinitis were also significantly more likely to receive a leukotriene receptor antagonist as initial therapy (23.1% versus 17.8%, *P* < .001) and incurred significantly higher asthma-related treatment charges ($823/patient versus $734/patient, *P* < .001) during the 12 months after initiating asthma therapy.

CONCLUSIONS: Allergic rhinitis is commonly observed in managed care patients treated for asthma and appears to impart a substantial impact on asthma treatment and cost.

LEARNING OBJECTIVES:
1. Recognize the prevalence and economic burden that allergic rhinitis has on newly diagnosed asthmatics.
2. Review variations in treatment patterns due to comorbid disease.
3. Identify newly diagnosed asthmatics who should be considered for allergic rhinitis.

**REDUCING FRAUD AND ABUSE THROUGH RETROSPECTIVE CLAIMS ANALYSIS**

Wheeler CJ*, Buttitta P, Modi B, Wogen, S. Medco Health Solutions, Inc., 100 Parsons Pond Dr., Franklin Lakes, NJ 07417

OBJECTIVE: Fraudulent or abusive use of the pharmacy benefit is wasteful and potentially harmful to the patient. We theorized that through careful analysis of high utilization patterns and communication to patients’ physicians and pharmacists, we could identify abusive patients and limit their behavior.

METHODS: Through retrospective claims analysis, we identified 8,974 patients as potential “high utilizers.” Subsequent targeted physician and pharmacy communications used to validate suspected fraudulent behavior led to the identification of 51 patients abusing their pharmacy benefit. After restricting this cohort to a single pharmacy, per patient plan costs were measured 90 days prerestriction and postrestriction date. Changes in plan cost and prescription volumes were analyzed for significance using a signed rank test.

RESULTS: On average during 2002, high-utilization patients visited 7 pharmacies, filled 85 prescriptions, and accumulated $4,830 in plan cost, which is significantly more than the average for prescriptions (13, *P* < .01) and plan cost ($669, *P* < .01). Narcotics and analgesics accounted for 50.3% of their plan cost. For the restricted cohort (n = 51), the baseline 90-day plan cost was $1,437 per patient. Postintervention, we observed a 33% reduction in plan cost ($480; *P* < .01).

CONCLUSIONS: Patterns of excessive utilization can be indicative of abuse of the pharmacy benefit. Retrospective claims analysis and collaboration with physicians and pharmacists to restrict high utilization patients to a single pharmacy are successful strategies in reducing abuse and lowering plan cost.

LEARNING OBJECTIVES:
1. Learn how high utilization patients can be targeted to reduce plan cost.
2. Learn how restricting high-utilization patients might impact plan cost.

**SURVEY OF PARTICIPANT OPINIONS AND PERCEPTIONS ABOUT A PROVINCIAL PHARMACY TRIAL PRESCRIPTION PROGRAM**

Lopatka H * Alberta Drug Utilization Program, University of Alberta, 305 Campus Tower, Edmonton, Alberta, T6G 1K8, Canada

INTRODUCTION: The purpose of the research was to examine participating seniors’ opinions and perceptions about a community pharmacy provincial trial prescription program. The survey was part of a broader impact evaluation.

METHODS: The objectives of the study were to collect opinions and perceptions about the social marketing, trial process, side effects, effects on waste and cost, pharmacist intervention, general awareness about medications, and overall program. A telephone survey consisting of 34 questions was administered to 241 randomly selected seniors who participated in the program. The survey was administered through the University of Alberta population research laboratory. Descriptive analysis of the responses was performed.

RESULTS: Pharmacists were identified as the most frequent source of hearing about the program (90%). Generally respondents were supportive (80%–90%) of individual aspects of the
design of the program with the exception of the inconvenience of having to return to the pharmacy for the balance portion of the prescription (which only 5% supported). Approximately 60% felt the program improved their awareness and knowledge of their medications, 90% felt costs related to drug waste were reduced, and more than 90% would like to participate again.

**CONCLUSIONS:** Participants perceived the program to be valuable and appeared satisfied with all but one aspect of the program. The results provided evidence to support a decision on continuing the program.

**LEARNING OBJECTIVES:**
1. Learn about a community pharmacy trial prescription program.
2. Evaluate the research methodology used for a provincial community pharmacy program.
3. Reflect upon the views of patients about a provincial community pharmacy program.

### TOTAL HEALTH BENEFITS AND PRODUCTIVITY COST IMPACT OF MUSCULOSKELETAL CONDITIONS IN AN EMPLOYER GROUP

Queyrouze B, Pham HT*, McKeithen TM, Ross R, McCoy M, Yalda A. Pfizer/Phar­macia, 11265 Abbey Glen Ln., Austin, TX 78753

**OBJECTIVE AND PERSPECTIVE:** To determine the economic impact of musculoskeletal conditions in an employer group with regard to medical, pharmacy, worker’s compensation (WC), short-term disability (STD), and presenteeism costs.

**METHODS:** Medical, pharmacy, WC, and STD databases for 2001 were examined for employees of the Federal Reserve Bank (FRB) to determine the economic impact of musculoskeletal conditions. An online employee survey using a modified Work Limitation Questionnaire (WLQ) provided data to assess productivity loss due to presenteeism. Productivity loss was quantified according to the WLQ Index score, which is an empirically validated algorithm for the relationship between self-report and objectively measured work productivity.

**RESULTS:** Medical and pharmacy survey data were available for 232 (65.5%) and 250 (70.6%) employees, respectively. Based on the WC and STD analysis, there were 272 absent days due to musculoskeletal conditions, and $30,245 in disability was paid to employees. There were 11 WC musculoskeletal claims, which cost the employer $98,421. Medical and pharmacy musculoskeletal claims totaled $19,813 and $14,019, respectively. Musculoskeletal conditions also negatively impacted on the job performance, resulting in a 9.1% reduction in productivity. When annualized, the health benefit, disability, and lower productivity cost impact per FRB employee due to musculoskeletal conditions were WC: $278, medical: $85, pharmacy: $60, lost time paid: $84, STD: $1.50, and presenteeism: $2,063.

**CONCLUSION:** The impact of musculoskeletal conditions can be costly, especially their impact on lost productivity. Employer-based interventions focusing on managing musculoskeletal conditions should be evaluated and implemented to manage potential short- and long-term economic impact.

**LEARNING OBJECTIVES:**
1. Recognize the economic impact of musculoskeletal conditions with regard to total health benefits and lost productivity to an employer.
2. Understand how presenteeism (lost productivity) was measured and quantified.
3. Identify and discuss potential employer-based interventions to manage musculoskeletal conditions and potential economic impact.

### TREATMENT OF ALLERGIC RHINITIS IN MANAGED CARE PATIENTS WITH COMORBID ASTHMA: INHALED NASAL CORTICOSTEROIDS VERSUS ORAL ANTIHISTAMINES

Leibman C*, Roberts C, McLaughlin T, O’Dowd L. AstraZeneca LP, DCC2-2W, 1800 Concord Pike, Wilmington, DE 19803

**PURPOSE:** To compare health care utilization and asthma exacerbations of managed care patients with allergic rhinitis and asthma who received initial rhinitis therapy with inhaled nasal corticosteroids (INS) versus oral antihistamines (OAH).

**METHODS:** Patients selected from managed care organizations (PHARMetrics Integrated Outcomes Database) with an asthma diagnosis (ICD-9 493.xx), new prescription for INS or OAH, and either an allergic rhinitis ICD-9-CM code (477.xx), new prescription for INS or OAH, postindex prescription charges were $396 for INS and $471 for OAH (PHARMetrics Integrated Outcomes Database). The final cohort was comprised of patients who received initial rhinitis therapy with inhaled nasal corticosteroids (INS) versus oral antihistamines (OAH) for 1 year pretherapy and posttherapy were compared (repeated-measures ANOVA). Risk of asthma exacerbation (ED visit/hospitalization) was calculated using logistic regression; cohort and preindex exacerbations were covariates.

**RESULTS:** Patients (N = 4,850) were similar regarding age (P = .104), sex (P = .852), region (P = .194), and preindex asthma exacerbations (P = .584). Pretherapy mean rhinitis-related charges were $111 for the INS group and $104 for OAH. Postindex prescription charges were $396 for INS and $471 for OAH (P = .0001). Asthma exacerbations occurred in 259 (5.3%) INS and 241 (5.1%) OAH patients pretherapy and 211 (4.4%) INS and 248 (5.1%) OAH patients posttherapy (OR, 0.831; 95% CI, 0.687-1.006).

**CONCLUSIONS:** Managed care patients with rhinitis and asthma treated initially with INS have fewer asthma exacerbations and statistically significantly lower rhinitis-related costs than those treated with OAH.

**LEARNING OBJECTIVES:**
1. Describe the economic impact of allergic rhinitis interventions in managed care patients with comorbid asthma.
2. Understand the protective effect of treatments commonly used for upper airways disease on asthma exacerbations
3. Compare the value of classes of medications in the treatment of allergic rhinitis patients with comorbid asthma

**UNDERSTANDING MOTIVATORS OF BRAND-DRUG UTILIZATION WHEN GENERICS ARE AVAILABLE**

Choe, N*, Burke ME, Wogen, SE. Medco Health Solutions, Inc., 100 Parsons Pond Dr., Franklin Lakes, NJ 07417

**OBJECTIVE:** To understand the key drivers for branded product utilization when a generic product is available. This information can be used to develop appropriate strategies to encourage generic substitution among patients taking multisource medications.

**METHODS:** A quantitative survey was sent to 1,500 patients. Patients receiving the survey filled a multisource medication between May 1, 2002, and October 31, 2002, and were identified as recurrent multisource brand users.

**RESULTS:** Twenty-four percent (n = 362) of patients contacted responded to the survey. Of those, 83.7% were aware that a generic medication was available for the branded product they were taking. Fewer than 18% of respondents specifically requested a brand-name medication from either their physician or pharmacy and 59.1% discussed generics with their physician. Primary reasons that would motivate patients to try a generic included: physician assurance that the generic was as safe and effective as the brand product (89.02% would take generic) and pharmacist assurance that the generic was safe and effective (59.84% would take the generic).

**CONCLUSIONS:** Patients rely strongly on the advice of their physician, and to a lesser degree their pharmacist, when making decisions about generic versus brand medications. Physician-awareness campaigns on the safety and effectiveness of generic medications, as well as identifying ways to encourage physicians to more often talk to patients about generic alternatives, may be an effective strategy for increasing generic substitution rates.

**LEARNING OBJECTIVES:**
1. Understand key barriers that prevent patients from taking generic medications when generics are available.
2. Identify strategies to remove barriers preventing patients from taking generic medications when generics are available.
Managed Care Pharmacy Residency and Fellowship Programs

The following is a partial list of available managed care pharmacy residency and fellowship programs compiled as of August 2003. The residencies listed were submitted by AMCP members in response to AMCP’s call for residency program listings. This is not a comprehensive list of all available programs. AMCP provides this listing solely as a service to its readers. This list does not imply AMCP’s endorsement of any particular program nor does AMCP guarantee the availability of any of the programs listed. AMCP has made reasonable efforts to verify the accuracy of the information provided; however, we cannot assume responsibility for any errors that may appear. If you are aware of additional residency and fellowship programs not listed here, please contact AMCP at (800) TAP-AMCP.

### ADVANCE PCS

**Managed Care**

- **Accredited:** AMCP/ASHP
- **Length of Program:** 12 months
- **Number of Positions:** 4 (2 in Maryland, 1 in Texas, 1 in Arizona)
- **Affiliation:** University of Maryland, Texas Tech University, University of Arizona

- **Application Deadline:** 1/1/04
- **Starting Date:** 7/1/04
- **Estimated Stipend:** $33,300
- **Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD or equivalent experience

**Fringe Benefits:** 3 weeks paid personal leave, paid sick leave, full medical and dental, tuition assistance toward specified degree programs

**Special Features:** Off-site rotations, university affiliation, ambulatory care clinic, disease management, industry experience

**Contact Information:**

Babette Edgar, PharmD, BCPS, MBA  
VP, Business Development

Center for Health Improvement

AdvancePCS  
11350 McCormick Rd.

Executive Plaza II, Suite 1000

Hunt Valley, MD 21031

(410) 785-2182  
(410) 785-2140

babette.edgar@advancespcs.com

### AMERICAN SERVICE GROUP

**Managed Care**

- **Accredited:** Yes
- **Length of Program:** 1-year or 2-year option
- **Number of Positions:** 1
- **Affiliation:** Various universities

- **Application Deadline:** 2/28/04
- **Starting Date:** 7/1/04
- **Estimated Stipend:** $35,000
- **Onsite Interview:** Yes

**Educational/Special Requirements:** None

**Fringe Benefits:** 2 weeks vacation, health insurance, free parking, professional meetings, other management, pharmaceutical industry

**Special Features:** Off-site rotations, university affiliation, ambulatory care clinic, disease management, industry experience

**Contact Information:**

Peter Mikhail  
Vice President Clinical Services

America Service Group/Secure Pharmacy Plus  
416 Mary Lindsay Polk Dr., Suite 515

Franklin, TN 37067

(615) 771-1457  
(615) 771-4557

peter.mikhail@securepp.com

### AMERICAN HEALTH CARE

**Clinical Therapeutics**

- **Accredited:** ASHP
- **Length of Program:** 12 months
- **Number of Positions:** 2
- **Affiliation:** None

- **Application Deadline:** 2/15/04
- **Starting Date:** 7/1/04
- **Estimated Stipend:** $33,000
- **Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD

**Fringe Benefits:** Medical, dental, vision, holidays and vacation

**Special Features:** Clinical therapeutics/managed care

**Contact Information:**

Grover Lee, PharmD  
American Health Care  
3001 Douglas Blvd., #320

Roseville, CA 95611

(916) 773-7227

grover@americanhealthcare.com
AON CONSULTING
Pharmacy Benefits Consulting
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 2/15/04
Starting Date: 7/1/04
Estimated Stipend: $36,000
Onsite Interview: Yes
Education/Special Requirements: PharmD
Fringe Benefits: 2 weeks paid vacation, paid holidays, medical/dental insurance, travel budget, professional meetings
Special Features: Aon Consulting is the fifth largest employee benefits consulting firm nationwide. This unique program provides residents with the opportunity to help employers and health plans better manage and control the prescription drug benefit for their employees or members. Residents will be exposed to all aspects of pharmacy benefit management consulting: plan design modeling, formulary analysis, clinical programming, disease management, audits, regulatory, trends and forecasting through proprietary actuarially-based models. Residents will interact with benefit administrators, major PBMs, PPOs, HMOs, and disease management firms nationally.
Contact Information:
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Assistant Vice President
Aon Consulting
200 E. Randolph St., Suite 900
Chicago, IL 60601
(312) 381-4955
(312) 381-0239
connie_f_perry@aoncons.com

BLUE CARE NETWORK/IBA
Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: Ferris State University/Michigan State University-Kalamazoo
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $32,000
Onsite Interview: Yes
Education/Special Requirements: PharmD
Fringe Benefits: Health/dental, insurance, 2 weeks vacation, paid holidays
Special Features: Travel and registration reimbursement for 1 national conference, Great Lakes Residency Conference, and Pharmacy Residents conference; no weekend or evening shifts

BLUE CROSS BLUE SHIELD OF ALABAMA
Managed Care
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04 (negotiable)
Estimated Stipend: $32,000
Onsite Interview: Yes
Education/Special Requirements: PharmD or equivalent experience
Fringe Benefits: Paid vacation, personal holiday leave, health/dental insurance, no on-call responsibilities
Special Features: This program provides the resident with the opportunity to experience a true integrated medical and pharmacy system. The areas of focus will include pharmaceutical care, drug information, formulary management, clinical program management, disease state management, and outcome studies. The resident also will complete a research project suitable for publication. This program will incorporate communication and time-management skills.
Contact Information:
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Birmingham, AL 35244
(205) 220-6526
(205) 220-2939
jwong@bcbsal.org

BLUE CROSS BLUE SHIELD OF KANSAS CITY
Managed Care/Outcomes Research/Pharmaceutical Industry
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: Abbott Laboratories Inc.
Application Deadline: 2/15/04
Starting Date: 7/1/04
Estimated Stipend: $30,000
Onsite Interview: Yes
Education/Special Requirements: None
Managed Care Pharmacy Residency and Fellowship Programs

Fringe Benefits: 2 weeks vacation, financial assistance to attend professional meetings, health insurance

Special Features: Upon the successful completion of the residency, the trainee should be qualified to work in a variety of settings such as managed care organizations, pharmacy benefit management companies, or pharmaceutical industry positions related to managed care. The program will follow the RLS model for AMCP/ASHP residency programs and incorporate the unique needs and interests of the resident into the program, but the resident will work on certain core competencies: evaluation of products for formulary review/contracting, utilization management, working with pharmacy and physician networks, marketing of employee benefit management to employers, disease state management, individual and population-based case management, guideline development and dissemination, QA/QI activities; and a pharmacoeconomics/outcomes research project. In addition, rotations with Abbott Laboratories can be arranged in relation to the interests of the resident. These could include health economics, sales training, and managed market account management.

Contact Information:
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Kansas City, MO 64131
(816) 395-3506
(816) 802-4404
owen.neff@bcbskc.com

BLUE SHIELD OF CALIFORNIA
Managed Care Pharmacy Systems
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 2/1/04
Starting Date: 7/1/04
Estimated Stipend: $55,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD degree from an accredited school of pharmacy, completion of a pharmacy practice residency or equivalent experience, 3 letters of recommendation, letter of intent, and on-site interview

Fringe Benefits: Health/dental/vision benefits; 20 days of paid time off, including professional leave (with travel allowances); and 9 holidays; no on-call responsibilities

Special Features: This residency instills the philosophy that health care outcomes need to be considered from all relevant perspectives (patient, provider, and payer). Residents participate in the development of drug policy, clinical guidelines, pharmacy benefits, and population-based disease management; pharmaceutical contracting support/analysis; and quality improvement. This program teaches residents to conceptualize, integrate, and transform accumulated experiences and knowledge into improved drug therapy for managed care patients.

Contact Information:
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stephen.harris@blueshieldca.com

CAREMARK, INC.
Managed Care Specialty-Analytics and Outcomes
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Illinois at Chicago; Midwestern University-Chicago College of Pharmacy
Application Deadline: 1/1/04
Starting Date: 7/1/04
Estimated Stipend: $38,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD with experiential or internship-based experience in the managed care/PBM industry

Fringe Benefits: Comprehensive medical, dental, and life insurance plan; 2 weeks paid vacation; holidays; employee stock purchase program; flexible spending program; travel budget

Special Features: Caremark is a leading pharmaceutical services company, providing comprehensive drug benefit services to approximately 24 million participants throughout the United States. Caremark’s clients include corporate health plans, managed care organizations, insurance companies, unions, government agencies, and other funded benefit plans. The Analytics and Outcomes Residency will provide the resident with a unique opportunity to work on initiatives that foster proactive management of pharmaceutical and overall health care costs. It offers the ability to work with large data sets and perform various pharmaceutical cost analyses such as plan design modeling, formulary analysis, and clinical outcomes. As part of a core sales and account management team, the resident will have the opportunity to interact directly with clients, consultants, and various other benefit providers. While the focus is on analytics, the resident will be exposed to various areas in pharmacy benefit management such as clinical program development and implementation, operations, sales, account management, clinical sales support, marketing and communications, trade relations, pharmaceutical services, and therapeutic services.

Contact Information:
Anita Allemand
Manager, Client Analytic Services

www.amcp.org Vol. 9, No. 5 September/October 2003 JMCP Journal of Managed Care Pharmacy 483
Managed Care Pharmacy Residency and Fellowship Programs

Caremark, Inc.
2211 Sanders Rd.
Northbrook, IL 60062
(847) 559-3923
(847) 559-5475
anita.allemand@caremark.com

CLINICAL PHARMACOLOGY SERVICES, INC.
Ambulatory Care/Clinical Research
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 2/1/04
Starting Date: 6/1/04
Estimated Stipend: $34,000
Onsite Interview: Yes
Educational/Special Requirements: None
Fringe Benefits: Sponsorship to professional meeting and Southwestern Residency Conference
Special Features: None
Contact Information:
Dr. Daniel Buffington
Director
Clinical Pharmacology Services
6825 E. Fowler Ave.
Tampa, FL 33617
(813) 983-1500
(813) 983-1501
danbuffington@cpshealth.com

COVENTRY HEALTH CARE/PHARMACIA
Pharmacy Benefits Management
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $30,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: 2 weeks vacation
Special Features: Attend professional managed care meeting
Contact Information:
Shawn Burke
Director of Pharmaceutical Services
Coventry Health Care, Inc.
8320 Ward Pkwy.
Kansas City, MO 64114
(866) 460-4410
(866) 795-3995
sburke@cvty.com

VA MEDICAL CENTER—CINCINNATI DEPARTMENT
OF VETERANS AFFAIRS
Pharmacy Practice—Primary Care Emphasis
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 3
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $33,000, $2,245 FICA, $3,124 other benefits
Onsite Interview: Yes
Educational/Special Requirements: PharmD or equivalent experience
Fringe Benefits: Vacation, paid holidays, sick days, and administrative time off for selected meetings
Special Features: None
Contact Information:
Jo-Ann Caudill
Residency Program Director
Cincinnati VA Medical Center
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Cincinnati, OH 45220
(513) 861-3100, ext. 4034
(513) 475-6322
jo-ann_caudill@med.va.gov

ECKERD HEALTH SERVICES
Pharmacy Benefits Management
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Pittsburgh School of Pharmacy
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $31,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: Comprehensive benefits package, no weekends/holidays, attend professional managed care meetings
Special Features: The University of Pittsburgh School of Pharmacy and Eckerd Health Services (EHS), one of the nation's largest pharmacy chain-based prescription management firms, offers an opportunity to practice in a dynamic PBM environment and gain a clinical and administrative perspective in managed pharmacy benefit plans for a wide variety of clients. Multifaceted experience will include DUR criteria development, clinical intervention activities, P&T activities, clinical systems development, and new business development/ client services/ marketing support.
Contact Information:
Sina Carlson
Manager, Clinical Communication and Education
**Prescription Benefit Management**

**Accredited:** ASHP (Managed Care Pharmacy Systems)

**Length of Program:** 12 months

**Number of Positions:** 1

**Affiliation:** None

**Application Deadline:** 1/31/04

**Starting Date:** 7/1/04 (negotiable)

**Estimated Stipend:** $36,500

**Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD with completion of a postgraduate year; pharmacy practice residency or equivalent experience highly desirable

**Fringe Benefits:** 1 week paid time off plus holidays; medical, dental, long-term disability and life insurance; expenses for 1 regional and 1 national convention

**Special Features:** This program provides the resident with rotational and longitudinal experiences in the delivery of PBM clinical services to members, clients, and physicians, including drug information/evaluation, formulary management, utilization management, and clinical programs. The year also consists of elective experiences allowing the resident to pursue specific areas of interest in PBM pharmacy; completion of a research project suitable for presentation at a national conference or publication in a peer-reviewed journal, and professional development in the areas of communication skills, project management, and time management.

**Contact Information:**
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Express Scripts-BLO280
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Bloomington, MN 55439-0842
(952) 837-7840
(952) 893-4773
frearr@express-scripts.com

**GROUP HEALTH/ST. LOUIS COLLEGE OF PHARMACY**

**Managed Care Pharmacy Practice**

**Accredited:** No

**Length of Program:** 12 months

**Number of Positions:** 1

**Affiliation:** St. Louis College of Pharmacy

**Application Deadline:** 1/31/04

**Starting Date:** 7/1/04

**Estimated Stipend:** $28,000

**Onsite Interview:** Yes

**Educational/Special Requirements:** PharmD; prior pharmacy practice residency preferred

**Fringe Benefits:** Health insurance, professional leave, 10 days vacation and holidays, travel/registration for professional activities, e-mail/Internet access, slide making and computer support, medical library services

**Special Features:** None

**Contact Information:**
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St. Louis College of Pharmacy
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St. Louis, MO 63110
(314) 367-8700
(314) 367-2784
mmaddux@stlcop.edu
HARVARD VANGUARD MEDICAL ASSOCIATES

Managed Care Pharmacy
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: Massachusetts College of Pharmacy and Health Sciences
Application Deadline: 1/7/04
Starting Date: 7/1/04
Estimated Stipend: $30,000
Onsite Interview: Yes
Educational/Special Requirements: BS in Pharmacy or PharmD
Fringe Benefits: Comprehensive medical plan, 2 weeks paid vacation, professional travel allowance
Special Features: None
Contact Information:
William McCloskey
Massachusetts College of Pharmacy & Health Sciences
179 Longwood Ave.
Boston, MA 02115
(617) 732-2167
(617) 732-2244
wmccloskey@mcp.edu

HEALTH PARTNERS

Managed Care Pharmacy
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: Competitive
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: Health insurance, vacation and holidays
Special Features: Travel/registration for 1 national meeting
Contact Information:
Barbara Zarowitz, PharmD
VP, Pharmacy Care Management
Henry Ford Health System
30100 Telegraph Rd., Suite 200
Bingham Farms, MI 48025
(248) 723-0264
(248) 642-6094
bzarowi1@hfhs.org

HORIZON/MERCY

Managed Care Pharmacy
Accredited: Horizon Healthcare of New Jersey/Mercy Health System of Southeastern Pennsylvania
Length of Program: 12 months
Number of Positions: 1
Affiliation: Horizon Healthcare of New Jersey/Mercy Health System of Southeastern Pennsylvania
Application Deadline: 2/1/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD or equivalent experience; eligible for New Jersey state licensure
Fringe Benefits: Paid vacation, full medical/dental/retirement benefits
Special Features: Medicaid managed care HMO, unique focus on government programs, pharmacy case management, formulary and disease state management, development of clinical policies, outcomes research, assist with PharmD student oversight, ambulatory care experience, professional development courses, attendance to at least 1 national conference

Contact Information:
Sam Currie, RPh
Manager, Clinical Pharmacy
Horizon/Mercy
210 Silvia St.
West Trenton, NJ 08628
(609) 538-0700
(609) 538-1698
scurrie@horizon-mercy.com

HUMANA, INC.

Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/1/04
Starting Date: 7/1/04
Estimated Stipend: $32,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD preferred
Fringe Benefits: Health, dental, 401K, 3 weeks vacation, relocation allowance
Special Features: None

Contact Information:
Donna Howell-Smith, RPh, MBA
Director, Clinical Pharmacy Programs
Humana, Inc.
500 W. Main St.
Louisville, KY 40202
(502) 580-3550
(502) 508-3399
dhowellsmith@humana.com

JANSSEN

Drug Information
Accredited: No
Length of Program: 12 months
Number of Positions: 3
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: n/a
Onsite Interview: Yes
Educational/Special Requirements: None
Fringe Benefits: None
Special Features: None

Contact Information:
Cheryl Pavia, PharmD
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(609) 730-3138
cpavia@janus.jnj.com

KAISER FOUNDATION HEALTH PLAN OF THE MID-ATLANTIC STATES, INC.

Managed Care Pharmacy
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 1/9/04
Starting Date: 7/1/04
Estimated Stipend: $34,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD preferred; pharmacy licensure eligibility in DC, MD, or VA
Fringe Benefits: Medical benefits; selected holidays; sick, vacation, and education leave
Special Features: In addition to helping develop new and innovative programs, the resident will participate on the Pharmacy & Therapeutics Committee, teach patient education classes, provide pharmacy staff continuing education, assist in educating pharmacy students, and complete residency projects and presentations.

Contact Information:
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Director, Managed Care Pharmacy Practice Residency Program
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Silver Spring, MD 20904
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(301) 572-3399
katrin.fulginiti@kp.org

KAISER PERMANENTE

Managed Care
Accredited: No
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 1/1/04
Starting Date: 7/1/04
Estimated Stipend: 36,400
Onsite Interview: yes
Educational/Special Requirements: BS/PharmD. This is a specialty residency in managed care with emphasis on pharmacy practice management.
Fringe Benefits: Medical benefits, 10 days sick/vacation leave, 5 holidays, $500 for national meeting, plus expenses paid for Western States Residency meeting

Special Features: emphasis in administration/practice management

Contact Information:
Susan Downard, RPh
Area Pharmacy Manager
Kaiser Permanente
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Aurora, CO 80011
(303) 326-6764
(303) 739-3574
Susan.L.Downard@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—WEST LOS ANGELES

Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: Graduate of accredited college of pharmacy and licensed or eligible for California licensure. Good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, optical insurance; holidays; vacation/sick leave

Special Features: Hospital and ambulatory care experiences in the nation’s largest integrated care organization, preventative and disease-state management in an integrated managed care setting. Flexible program molded to the resident’s interests.

Contact Information:
Michael Cinnamond
Inpatient Pharmacy Director; Residency Program Director
Kaiser Permanente Medical Care Program at West Los Angeles
6041 Cadillac Ave., Suite 237
Los Angeles, CA 90034
(323) 857-2044
(323) 857-2870
michael.d.cinnamond@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—CALIFORNIA

Pharmacy Practice and Drug Information Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 26
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes

Educational/Special Requirements: Graduate of accredited college of pharmacy and licensed or eligible for California licensure. Good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, optical insurance; holidays; vacation/sick leave

Special Features: Hospital and ambulatory care experiences in the nation’s largest health maintenance organization, preventative and
Managed Care Pharmacy Residency and Fellowship Programs

disease state management in an integrated managed care setting.

Contact Information:
Elaine Watanabe, PharmD
Pharmacy Services Manager—Recruitment
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(714) 796-4826
Elaine.G.Watanabe@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—LOS ANGELES MEDICAL CENTER

Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 1/6/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes

Educational/Special Requirements: Graduate of accredited college of pharmacy and licensed or eligible for California licensure; good communication skills required. Resident will develop a project with targeted care outcomes and present at Annual Western States Conference.

Fringe Benefits: Medical, dental, optical insurance; holidays, vacation/sick leave

Special Features: The Kaiser Permanente Los Angeles Medical Center is the tertiary care center for Kaiser Permanente in Southern California and provides comprehensive inpatient, outpatient, and ambulatory care services to Kaiser Permanente members. This residency program provides development and training for recently graduated pharmacists, with an emphasis on pharmaceutical care and leadership to a diverse community. This program will allow residents to become familiar with pharmacy practice in an integrated health care program.

Contact Information:
Steve Litsey
Pharmacy Leader—Metro Service Area
Kaiser Permanente Pharmacy Operations Services
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(323) 783-7609
toni.a.rodriguez@kp.org

KAISER PERMANENTE MEDICAL CARE PROGRAM—TRI CENTRAL

Pharmacy Practice
Accredited: ASHP
Length of Program: 1 year
Number of Positions: 2
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes

Educational/Special Requirements: Recent graduate of an accredited school of pharmacy and eligible for California licensure, college transcript(s), 3 letters of recommendation, curriculum vitae

Fringe Benefits: 2 weeks paid vacation; 6 paid holidays; sick leave; health benefits, including dental/optical (also dependents); uniforms; office space; and reimbursement for off-site experiences

Special Features: The resident will become familiar with the various aspects of pharmacy practice in a large health maintenance organization. The residency includes experiences in acute and ambulatory care practice, drug information/drug-use policy development, and practice management. Experiences in drug information, asthma management, anticoagulation, hyperlipidemia, home health, and pharmacoconomics are important segments of this residency. Time is allowed for the resident to pursue an area of particular interest. Residents participate on the P&T Committee, teach patient-education classes, and serve as a preceptor for pharmacy students and pharmacy interns during the residency year.

Contact Information:
Robert Endo
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(626) 851-5813
robert.n.endo@kp.org

KAISER PERMANENTE OF CALIFORNIA

Medical Care/Drug Information
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 4/15/04
Starting Date: 7/1/04
Estimated Stipend: $41,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD, pharmacy practice residency program or equivalent experience, excellent communication skills, eligible for California licensure, 3 letters of recommendation

Fringe Benefits: Medical, dental, optical insurance; 10 days time
Managed Care Pharmacy Residency and Fellowship Programs

off; attendance at 1 pharmacy conference

Special Features: None

Contact Information:
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mirta.millares@kp.org

Kaiser Permanente of Colorado

Primary Care/Managed Care

Accredited: No
Length of Program: 12 months
Number of Positions: 3
Affiliation: None
Application Deadline: 1/1/04
Starting Date: 7/1/04
Estimated Stipend: $36,400
Onsite Interview: Yes

Educational/Special Requirements: PharmD and pharmacy practice residency or equivalent experience

Fringe Benefits: Health benefits, travel support to 1 national meeting and residency conference

Special Features: Experience in preeminent clinical pharmacy group; primary care services, anticoagulation, cardiac risk; disease state management (asthma, diabetes); specialty services (cardiology, drug information, long-term care, infectious diseases, mental health, and nephrology)

Contact Information:
Rachana Patel, PharmD, BCPS, CDE
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Kaiser Permanente of Georgia

Managed Care Pharmacy Practice

Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: None
Application Deadline: 1/10/04
Starting Date: 7/1/04
Estimated Stipend: $30,000
Onsite Interview: Yes

Educational/Special Requirements: PharmD degree, eligible for New Jersey licensure; managed care rotation or experience preferred

Fringe Benefits: Complete medical coverage, paid holidays, and vacation

Special Features: Professional development trainings, paid membership to AMCP and ASHP; travel and registration to educational meetings

Contact Information:
Darlene Mednick
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Novartis Pharmaceuticals Corporation

Health Economics & Outcomes Research Fellowship

Accredited: No
Length of Program: 2 years
Number of Positions: 2
Affiliation: Duke University; Scott & White Health Plan/University of Texas
Application Deadline: 12/31/2003
Starting Date: 7/1/04
Estimated Stipend: $35,000-$40,000
Onsite Interview: Yes
Educational/Special Requirements: Advanced degree in health services research, public health, health policy, pharmacy, economics, medicine, or other related areas, with some experience in outcomes research
Fringe Benefits: Medical insurance, vacation
Special Features: The Fellows will gain familiarity with outcomes research principles/application and experience in designing research studies that examine economic, clinical, and humanistic outcomes. The first year is spent at an academic/managed care institution and the second year with Novartis's Health Economics & Outcomes Research Department.
Contact Information:
Feride Frech, RPh, MPH
Associate Director, Health Economics & Outcomes Research
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080
(862) 778-5094
(973) 781-3018
feride.frech@pharma.novartis.com

OPTIMA HEALTH PLAN/SENTARA HEALTHCARE

Managed Care
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 2/15/04
Starting Date: 7/1/04
Estimated Stipend: $32,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD from an accredited school of pharmacy or equivalent experience, on-site interview, and eligible for Virginia licensure
Fringe Benefits: 2 weeks of paid vacation, uninterrupted stipend during minor illness, health insurance plan; travel assistance for continuing education events and other professional activities
Special Features: Resident will have exposure to an integrated health care system and system-wide pharmacy services, including a Drug Information Center. The resident will have the opportunity to precept students from Virginia Commonwealth University and Hampton University Schools of Pharmacy and work with medical residents from the Eastern Virginia Medical School.
Contact Information:
Elizabeth Brusig, PharmD, BCPS
Clinical Pharmacist
Optima Health Plan
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(757) 552-7519
(757) 552-7516
elbrusig@sentara.com

PHARMACEUTICAL CARE NETWORK

Managed Care Pharmacy Practice
Accredited: ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: $37,500
Onsite Interview: Yes
Educational/Special Requirements: Graduate of accredited college of pharmacy and licensed or eligible for California licensure
Fringe Benefits: Paid vacation and sick leave, health/dental/vision benefits, and educational support to attend professional meetings
Special Features: This residency will provide training in formulary management, provider drug therapy education, drug benefit design, outcomes analysis, and prior authorization. The resident will participate in drug utilization review and P&T committee presentations and interface with pharmacists from a variety of professional fields. The resident will learn to use PCN's MedIntelligence software to identify drug therapy problems and make appropriate interventions. This program includes rotations in direct patient care, drug information, and an opportunity to rotate through the California Pharmacists Association.
Contact Information:
Amy Shin, PharmD
9343 Tech Center Dr., Suite 200
Sacramento, CA 95826-2563
(916) 361-4450
(916) 414-4650
resident@pharmcarenet.com

PHARMACY MANAGEMENT CONSULTANTS/OKLAHOMA UNIVERSITY

Managed Care Pharmacy
Accredited: ASHP—Managed Care Pharmacy Systems
Length of Program: 12 months
Number of Positions: 1
Affiliation: Oklahoma University College of Pharmacy
Application Deadline: 2/1/04
Starting Date: 7/1/04
Estimated Stipend: $30,000
Onsite Interview: Yes
Educational/Special Requirements: Pharmacy degree
Fringe Benefits: 10 days vacation, health and dental coverage, faculty appointment at the level of clinical instructor, sponsorship to at least 1 professional meeting
Special Features: Evaluate health plan formularies, develop clinical guidelines, evaluate retrospective and prospective DUR criteria, develop educational intervention programs, serve as preceptor for pharmacy students
**Managed Care Pharmacy Residency and Fellowship Programs**

**PRESCRIPTION SOLUTIONS**

**Managed Care**
- Accredited: ASHP
- Length of Program: 12 months
- Number of Positions: 1
- Affiliation: None
- Application Deadline: 1/10/04
- Starting Date: 7/7/04
- Estimated Stipend: $37,500
- Onsite Interview: Yes
- Educational/Special Requirements: PharmD, licensed to practice in California
- Fringe Benefits: 2 weeks paid vacation, paid holidays, sick days, travel reimbursement
- Special Features: Drug therapy management, developing clinical guidelines for appropriate drug use, formulary management, legal and regulatory affairs, professional meetings and seminars, (required to attend the ASHP Midyear Clinical Meeting, CSHP Seminar, AMCP Educational Conference, and Western State Conference)

**Contact Information:**
Glenn Yokoyama, PharmD
Director, Residency Program
C/O Prescription Solutions
3515 Harbor Blvd.
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(714) 825-3742
glenn.yokoyama@rxsol.com

**RUTGERS UNIVERSITY/ HORIZON BLUE CROSS BLUE SHIELD OF NEW JERSEY**

**Managed Care Organization**
- Accredited: No
- Length of Program: 12 months
- Number of Positions: 2
- Affiliation: Rutgers University, the State University of New Jersey
- Application Deadline: 1/15/04
- Starting Date: 7/1/04
- Estimated Stipend: $30,000
- Onsite Interview: Yes
- Educational/Special Requirements: PharmD; eligible for New Jersey state license
- Fringe Benefits: Full medical coverage, dental and retirement benefits
- Special Features: No weekend or staffing requirements; teaching and preceptoring, if desired; graduate courses offered at Rutgers University; industry and PBM perspectives of managed care

**Contact Information:**
Saira A. Jan, MS, PharmD
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Associate Director, Pharmacy Management at Horizon BCBSNJ
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**UNITED HEALTH CARE**

**Managed Care Pharmacy**
- Accredited: No
- Length of Program: 12 months
- Number of Positions: 1
- Affiliation: St. Louis College of Pharmacy
- Application Deadline: 1/31/04
- Starting Date: 7/1/04
- Estimated Stipend: $28,000
- Onsite Interview: Yes
- Educational/Special Requirements: PharmD, prior pharmacy practice residency preferred
- Fringe Benefits: Health insurance, professional leave, 10 days vacation and holidays, travel/registration for professional activities, e-mail/Internet access, slide making and computer support, medical library services
- Special Features: None

**Contact Information:**
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mmaddux@stlcop.edu

**UNIVERSITY OF ILLINOIS AT CHICAGO AND WALGREENS HEALTH INITIATIVES**

**Fellowship—Outcomes Research**
- Accredited: No
- Length of Program: 2 years
- Number of Positions: 1 (University of Illinois and Walgreens Health Initiatives)
- Application Deadline: 3/1/04
- Starting Date: 7/1/04
Managed Care Pharmacy Residency and Fellowship Programs

Estimated Stipend: $36,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD or MD (or equivalent) and completion of a pharmacy practice or managed care residency
Fringe Benefits:
Special Features: This is a 2-year fellowship jointly offered by Walgreens Co. and Walgreens Health Initiatives (a pharmacy benefit management company) and the Center for Pharmacoeconomic Research at the University of Illinois at Chicago. The aim of the program is to train clinical pharmacists to conduct research in drug therapy outcomes and pharmacoeconomics in the managed care setting. Knowledge and experience will be gained in the use of research tools to evaluate economic, humanistic, and clinical outcomes of drug therapy and clinical programs. Presentation and publication of research findings in peer-reviewed venues is expected. The fellowship is designed to facilitate career opportunities in managed care, health provider organizations, consulting, academia, or the pharmaceutical industry.

Contact Information:
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Center for Pharmacoeconomic Research
833 S. Wood St. (MC 886)
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II UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY/CARE FIRST BLUECROSS BLUESHIELD

Managed Care Pharmacy
Accredited: Yes
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Maryland
Application Deadline: 1/10/04
Starting Date: 7/1/04
Estimated Stipend: $31,500
Onsite Interview: Yes
Educational/Special Requirements: Graduate degree in pharmacy
Fringe Benefits: Health insurance, parking, support for national meeting attendance and poster presentation
Special Features: Appointment as a clinical instructor at the University of Maryland School of Pharmacy, Ambulatory Care Clinics at HMO; office with computer/references at managed care organization

Contact Information:
Catherine Cooke, PharmD
Adjunct Professor
University of Maryland School of Pharmacy
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catherine.cooke@pfizer.com

II UNIVERSITY OF OKLAHOMA COLLEGE OF PHARMACY

Pharmacy Benefit Design & Utilization Management
Accredited: No
Length of Program: 12 months
Number of Positions: 1
Affiliation: University of Oklahoma College of Pharmacy
Application Deadline: 1/31/04
Starting Date: 7/1/04
Estimated Stipend: $25,000
Onsite Interview: Yes
Educational/Special Requirements: Pharmacy degree from an ACPE-accredited school of pharmacy
Fringe Benefits: Health and dental insurance, 2 weeks paid time off
Special Features: Faculty appointment

Contact Information:
Elgene Jacobs, PhD
Associate Professor
University of Oklahoma College of Pharmacy
1110 N. Stonewall
Oklahoma City, OK 73117
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(405) 271-1647
elgene-jacobs@ouhsc.edu

II WALGREENS HEALTH INITIATIVES

PBM
Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 2
Affiliation: University of Illinois; Midwestern University-Chicago College of Pharmacy
Application Deadline: 1/9/04
Starting Date: 7/1/04
Estimated Stipend: $35,000
Onsite Interview: Yes
Educational/Special Requirements: PharmD
Fringe Benefits: Medical plan, 2-week vacation, holidays, travel expense budget
Special Features: This managed care pharmacy residency program is designed to allow the residents to work within the various departments of a Pharmacy Benefits Management firm including, but not limited to, care management, drug use policy, PBM operations, clinical sales, and specialty pharmacy. The residents will gain practical experience and develop skills related to disease management, health outcomes, medication management strategies, formulary management, drug utilization review, drug information, and other clinical services. Additionally, residents will have the opportunity to gain exposure to the pharmaceutical industry, be
Managed Care Pharmacy Residency and Fellowship Programs

involved in professional organizations, and precept pharmacy students.

Contact Information:
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Residency Program Coordinator
Walgreens Health Initiatives
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### WELL POINT PHARMACY MANAGEMENT

**Managed Care Pharmacy**

Accredited: AMCP/ASHP
Length of Program: 12 months
Number of Positions: 1
Affiliation: None
Application Deadline: 1/15/04
Starting Date: 7/1/04
Estimated Stipend: TBD
Onsite Interview: Yes

Educational/Special Requirements: PharmD or equivalent experience

Fringe Benefits: Information available upon request

Special Features: Off-site rotations, health plan, and PBM experience. This rotation is designed to provide the resident with an overall managed care experience. The resident will rotate through several departments within the PBM, including clinical affairs, account management, trade relations and contracting, product development, and clinical analysis. The experience will also include experiential sites at a major California-based health plan.

Contact Information:
William Waugh, PharmD
Director, Clinical Affairs
WellPoint Pharmacy Management
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West Hills, CA 91304
(818) 313-5077
(818) 313-5110
william.waugh@wellpoint.com
TENSION HEADACHE or MIGRAINE?

“New Tools & Therapy to Help Your Patients Find Relief”

Join us for a live one-hour Webcast presented by thought leaders in the treatment of migraine. A live question and answer session will follow the presentation.

Faculty

Merle Diamond, M.D.
Associate Director
Diamond Headache Clinic
Chicago, IL

Richard Lipton, M.D.
Department of Neurology
Department of Epidemiology
and Population Health
Albert Einstein College
of Medicine
Bronx, NY

Richard Wenzel, Pharm.D.
Clinical Pharmacist
Diamond Headache Clinic
Inpatient Unit
St. Joseph Hospital
Chicago, IL

Accreditation

Pharmacy
Professional Education Services Group is accredited by the American Council on Pharmaceutical Education as a provider of continuing pharmaceutical education. ACPE Universal Program Number 006-006-03-116-L01. This program provides 1.0 contact hour (0.1 CEU) of continuing education credit. Following completion of a program evaluation form, continuing education statements of credit will be mailed to participants within 4 weeks. Initial release date: November 12, 2003. Program expiration date: November 17, 2004.

Nursing
This activity for 1.2 contact hours is provided by Professional Education Services Group, which is accredited as a provider of continuing education in Nursing by the American Nurse Credentialing Center's Commission on Accreditation. Activity number: 829-031-560-41. Expiration date: November 17, 2004.

Nurse Practitioner
This program has been granted 1.2 contact hours of continuing education by the American Academy of Nurse Practitioners. Approval is valid through November 12, 2001.

November 12, 2003 at 8pm ET
www.professionaledservices.com

Learning Objectives

1. Summarize the prevalence of migraine and the societal impact in terms of disability, work loss, and health care expenditures

2. Explain the current understanding of migraine's pathophysiology

3. Describe validated tools to improve screening and diagnosis of migraine

4. Discuss opportunities for health care professionals in the overall management of headache disorders

5. Outline the role of various treatment options for migraine including the triptan agents and other agents

Target Audience

This continuing medical education activity is intended for pharmacists, nurses and nurse practitioners with an interest in new tools and therapies to differentiate and treat migraine headaches.

Sponsored and managed by

This activity is supported through an unrestricted educational grant from Pfizer, Inc.

To pre-register for this program, please visit www.professionaledservices.com and select "live programs" then follow the prompts.

Save this reminder!
11/12/03 at 8pm ET
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