

Potentially Inappropriate Medication Use in a Medicare Managed Care Population: Association with Higher Costs and Utilization

OBJECTIVE: To describe the prevalence of potentially inappropriate medication (PIM) use (defined by the Beers criteria) and association with resource utilization in a Medicare managed care population.

METHODS: Retrospective review of a health maintenance organization (HMO) administrative database claims data for a subset of Medicare managed care patients 65 years of age and older to compare persons on PIMs (cases) with persons not on PIMs (comparisons). Measures included costs, inpatient and outpatient utilization, number of prescriptions, patient demographics, diagnoses, prescriber information, clinical data including self-rated health, and the Charlson Comorbidity Index.

RESULTS: The prevalence of PIM use in this Medicare managed care population was 24.2% (541/2,336). Eighty-eight of the 146 individuals on two or

more inappropriate medications had 4–13 providers prescribing all their medications. Those on a PIM had significantly higher total, provider, and facility costs, and a higher mean number of inpatient, outpatient, and emergency room visits than comparisons after controlling for sex, Charlson comorbidity index, and total number of prescriptions.

CONCLUSIONS: Our study revealed a high prevalence of potentially inappropriate medication use among older adults in a managed care plan and an association with high resource utilization. In this study, we sought to gather evidence to guide the future development of an intervention and educational program to decrease the use of high-risk medications in older adults.

KEYWORDS: Pharmacy claims, cost, quality

J Managed Care Pharm 2001; 407–13

by Donna Marie Fick, Jennifer L. Waller,
John Ross Maclean, Richard Vanden Heuvel, J. Gary
Tadlock, Marc Gottlieb, and Charles B. Cangialose

Medication toxicity and drug-related problems can have profound health, safety, and economic consequences for older adults and have been implicated in up to 30% of hospital admissions in the elderly. In addition, adverse drug events (ADE) may be related to preventable problems in the elderly, such as depression, constipation, falls, immobility, confusion, and hip fractures.^{1, 2, 3} A 1997 study of ADE found 35% of ambulatory older adults on five or more medications experienced an ADE and 29% required health care services (physician, emergency room [ER], or hospitalization) for the ADE.² Some two-thirds of nursing facility residents have ADEs over a four-year period and one in seven of these ADEs may result in hospitalization.^{4, 5}

Nonsteroidal anti-inflammatory (NSAID) gastropathy is the most common ADE hospitalization of the elderly.^{4, 5} The average cost of such admissions is over \$14,000 and up to 90% may be preventable.^{6, 7} A 1996 study of 75,350 Medicaid enrollees found \$500 million of excess utilization in persons using NSAIDs.⁷ Cardiac and sedative hypnotics account for the second largest categories of drugs causing adverse events. A 1987 study found that drug-related problems led to more than 30,000 hip fractures annually at a cost of over \$1 billion.³

Recent studies estimate that the human and economic cost of medication-related problems vastly exceeds the Institute of Medicine (IOM) findings on deaths from medical errors, which were estimated to cost \$8 billion annually in the United States.⁸ Perry estimated that drug-related problems cause 106,000 deaths annually at a cost of \$85 billion, while others have estimated the cost of medication-related problems to be \$76.6 billion for ambulatory care, \$20 billion for hospitals, and \$4 billion for nursing home facilities.^{1, 9, 10, 11} If medication-related problems were ranked as a disease by cause of death, they would be the fifth-leading cause of death in the United States.¹² The prevention and recognition of drug-related problems in the elderly and other vulnerable populations is perhaps the principal challenge in patient safety in the next decade.

The IOM report has increased attention to solutions for unsafe medication practices in the care of older adults. There are many ways to define medication-related problems in the elderly, including the use of lists containing specific drugs to

Authors

DONNA MARIE FICK, Ph.D., R.N., C.S., is Assistant Professor, School of Medicine, Medical College of Georgia (MCG), and Research Health Scientist, Department of Veterans Affairs, Augusta, GA; JENNIFER L. WALLER, Ph.D., is Assistant Professor, Office of Biostatistics, MCG; JOHN ROSS MACLEAN, M.D., is Associate Professor, Director of Health Services Research, School of Medicine, MCG. RICHARD VANDEN HEUVEL is Systems Analyst, Department of Medical Management BlueCross and BlueShield of Georgia (BCBS); J. GARY TADLOCK is Director of Pharmacy, Corporate Medical Division, BCBS; and MARC GOTTLIEB is Assistant Vice President, Medical Management Information, Department of Medical Management, BCBS. CHARLES B. CANGIALOSE, Ph.D., is Health Economist, and Kerr L. White Institute for Health Services Research, Atlanta, GA.

AUTHOR CORRESPONDENCE: Donna Marie Fick, Ph.D., R.N., C.S., Medical College of Georgia, 1120 15th St., Room HB 2010, Augusta, GA 30912-3165; Tel: 706-721-4078; Fax: 706-721-0504; E-mail dfick@mail.mcg.edu.

ACKNOWLEDGEMENTS: The authors acknowledge the contributions of R.C. Robinson, Jr., and Billie Lamar in the preparation of this manuscript. Approval was received for this study by the appropriate institutional review board for the protection of human subjects. Individual informed consent was not required. This study was presented in part at the Gerontological Society of America's 52nd Annual Scientific Meeting, November 22, 1999, in San Francisco, California.

This study was supported by a grant through the Center for Health Care Improvement, a collaborative venture of Blue Cross and Blue Shield of Georgia and the Medical College of Georgia.

Copyright© 2001 Academy of Managed Care Pharmacy, Inc. All rights reserved.

avoid.¹³ The most widely used consensus criteria for medication use in older adults are the Beers criteria.^{14, 15} This list is based on expert consensus developed through an extensive literature review with a bibliography and questionnaire evaluated by nationally recognized experts in geriatric care, clinical pharmacology, and psychopharmacology using a modified Delphi technique. The panel was asked to rate the severity of any problems that might arise from the use of certain medications in older persons and come up with a specific list of medications to be avoided. The Beers criteria have been widely used to survey clinical medication use, analyze computerized administrative data sets, and evaluate intervention studies to decrease medication problems in older adults. In 1999 they were adopted by the Health Care Financing Administration (HCFA) for nursing home regulation.¹⁶ However, in the managed care arena, there are few published data on medication-related problems.

This study used population-based data to evaluate prescribing and resource utilization for older adults in a managed care setting and defined potentially inappropriate medications (PIM) using Beers criteria.¹⁷ The aim of this study was to describe the prevalence of potentially inappropriate medication (PIM) use, the resource utilization, and the outcomes associated with PIM use in a Medicare managed care ambulatory population.

Methods

This study used a retrospective review of a Southeastern health maintenance organization's (HMO's) administrative claims data for a subset of Medicare managed care patients 65 years of age and older by comparing persons on PIMs (cases) with persons not on PIMs (comparisons). Measures included costs, inpatient and outpatient utilization, number of prescriptions, patient demographics, diagnoses, prescriber information, clinical data including self-rated health, and the Charlson Comorbidity Index.

Main Outcome Measures

The Beers criteria were used to identify and measure PIM use.¹⁷ Our study included only those medications defined as inappropriate by the latest criteria for community-living older adults and that are recommended to be avoided in the elderly regardless of dosage or diagnoses. This list is described in more detail elsewhere.^{13, 17} Multiple prescriptions for the same medication were counted only once in all calculations.

Each administrative claim provided a unique identifier for the patient, the prescriber, the drug prescribed, and payments and charges. Costs, for the purposes of this study, reflected payments made directly to the provider by the HMO. Costs included facility, provider, and prescription components.

Health status was measured by a one-item measure of self-rated health from the SF-36 with five choices (excellent, very good, good, fair, poor). This measure has been found to correlate with overall health status.¹⁸ The health-status item was extracted from the Pra instrument that is administered by tele-

TABLE 1 Distribution of Each Inappropriate Medication in Order of Frequency (N=2,336)

Inappropriate Medication	n	Percent
Propoxyphene and combination products	224	9.6
Amitriptyline (Elavil, Limbitrol, or Triavil)	73	3.1
Cycloenzaprine (Flexeril)	49	2.1
Hydroxyzine (Bistaril, Atarax)	37	1.6
Diazepam	36	1.5
Promethazine (Phenergan)	33	1.4
Carisoprodol (SOMA)	31	1.3
Indomethacin	29	1.2
Ticlopidine	26	1.1
Hyosycamine	18	0.8
Doxepin	17	0.7
Chlorzoxazone (Paraflex)	15	0.6
Dicyclomine (Bentyl)	13	0.6
Dipyridamole (Persantine)	12	0.5
Oxybutinin (Ditropan)	11	0.5
Meperidine	9	0.4
Methocarbamol (Robaxin)	11	0.4
Methyldopa	9	0.4
Belladonna	8	0.3
Chlor-trimeton	6	0.3
Flurazepam (Dalmane)	6	0.3
Barbituates	5	0.2
Chlordiazepoxide (Librium)	5	0.2
Clidinium-chlordiazepoxide	5	0.2
Cyproheptadine	5	0.2
Disopyramide (Morpace)	5	0.2
Metaxalone (Skelaxin)	5	0.2
Reserpine hydrochlorothiazide	5	0.2
Trimethobenzamide (Tigan)	5	0.2
Diphenhydramine (Benadryl)	3	0.1
Ergot mesyloids (Cyclospasmol)	1	0.1
Meprobamate	1	0.1
Pentazocine (Talwin)	3	0.1
Propantheline	1	0.1
Reserpine	2	0.1
Chlorpropamide (Diabinese)	0	0.0
Phenylbutazone	0	0.0

TABLE 2 Chi-Square Tests Between Individuals Prescribed (Cases) and Not Prescribed (Comparisons) Potentially Inappropriate Medications (PIM)

Variable	Cases (n=541)		Comparisons (n=1,795)		X ² /p value	
	n	Percent	n	Percent		
Female	368	68.21	1,029	57.33	20.482	0.001
Age 85 years or older	26	4.81	93	5.18	0.121	0.728
Self-Rated Health^a					38.498	0.001
Excellent	61	12.92	329	21.05		
Very good	145	30.72	543	34.74		
Good	173	36.65	522	33.40		
Fair	78	16.53	148	9.47		
Poor	15	3.18	21	1.34		

^a301 records were missing self-rated health.

TABLE 3 T-tests Between Individuals Prescribed (Cases) and Not Prescribed (Comparisons) Potentially Inappropriate Medications (PIM)

Variable	Cases (n=541)		Comparisons (n=1,795)		p value
	Mean	SD	Mean	SD	
Age	73.07	6.10	72.49	6.13	0.0535
Number of inpatient visits	0.54	1.31	0.19	0.66	0.0001
Length of stay	3.86	2.71	4.35	4.14	0.1924
Number of ER visits	0.34	0.84	0.15	0.44	0.0001
Number of office visits	17.84	26.94	11.72	20.12	0.0001
Number of outpatient visits	1.79	2.28	0.98	1.45	0.0001
Number of unique prescriptions	10.15	4.85	5.57	4.09	0.0001
Number of unique inappropriate prescriptions	1.34	0.62	0.00	0.00	—
Charlson Comorbidity Index	1.02	1.49	0.65	1.21	0.0001
Paid Amount					
Total	4,472.43	8,011.43	2,065.38	4,537.46	0.0001
Facility	2,568.19	5,836.90	984.45	2,961.40	0.0001
Provider	1,530.89	2,728.40	821.61	1,898.74	0.0001
Prescription	373.35	248.20	259.32	264.45	0.0001

phone to all enrollees of the HMO after enrollment. The Pra instrument has been found to predict higher health utilization.¹⁹ The Pra instrument was conducted on all the subjects in our study less than one year from the date of our data abstraction. Comorbidity was measured using the Charlson index, adapted for use with administrative databases. Comorbid conditions were classified with an *International Classification of Diseases* (ICD-9) code, then assigned a weighted index that takes into account both the number and seriousness of different co-morbid diseases. Both the original Charlson Comorbidity Index and the ICD-9 code adapted index have established reliability and validity in multiple populations and have been

found to be associated with hospital length of stay, death, and hospital expenditures.²⁰

Sample

The HMO database identified 2,336 individuals age 65 and older continuously enrolled from June 1, 1997, through October 31, 1998. All claims filed for these individuals were extracted. Among the 2,336 individuals, cases were defined as those individuals who had filled a prescription for a PIM and the comparisons were defined as those individuals who had not filled any PIM prescription. Individuals whose first PIM was filled after April 30, 1998, were excluded from cost and utilization

TABLE 4 ANCOVA Results For Total, Provider, Facility, and Prescription Paid Cost Between Cases and Comparisons, N=2,197

Variable	Model R ²	Mean or Slope	MS	F-Value (dfn,dfd)	p-value
Total Cost	0.2742		4.549E+9	206.99 (4, 2196)	0.0001
Sex			3.122E+8	14.21 (1, 2196)	0.0002
Female		2,253.62			
Male		2,925.34			
Charlson Comorbidity Index		1,954.65	1.294E+10	588.96 (1, 2196)	0.0001
Total number of prescriptions		45.62	7.415E+8	33.74 (1, 2196)	0.0001
Case status			4.510E+8	20.52 (1, 2196)	0.0001
Cases		4,584.61			
Comparisons		2,065.38			
Provider cost	0.3056		7.466E+8	241.13 (4, 2196)	0.0001
Sex			5.485E+7	17.55 (1, 2196)	0.0001
Female		820.88			
Male		1153.03			
Charlson Comorbidity Index		842.09	2.402E+9	775.86 (1, 2196)	0.0001
Total number of prescriptions		12.15	5.255E+7	16.97 (1, 2196)	0.0001
Case Status			2.188E+7	7.07 (1, 2196)	0.0079
Cases		1,554.62			
Comparisons		821.61			
Facility cost	0.1866		1.443E+9	125.68 (4, 2196)	0.0001
Sex			9.826E+7	8.56 (1, 2196)	0.0035
Female		1,132.74			
Male		1,508.64			
Charlson Comorbidity Index		1,090.50	4.028E+9	350.92 (1, 2196)	0.0001
Total number of prescriptions		21.37	1.626E+8	14.17 (1, 2196)	0.0002
Case status			2.812E+8	24.50 (1, 2196)	0.0001
Cases		2,628.99			
Comparisons		984.45			
Prescription cost	0.4307		1.690E+7	414.62 (4, 2196)	0.0001
Sex			1.481E+5	3.63 (1, 2196)	0.0568
Female		299.99			
Male		263.67			
Charlson Comorbidity Index		22.06	1.648E+6	40.43 (1, 2196)	0.0001
Total number of prescriptions		12.11	5.226E+7	1282.03 (1, 2196)	0.0001
Case status			4.436E+4	1.09 (1, 2196)	0.2970
Cases		401.00			
Comparisons		259.32			

Note: Controlling for sex, Charlson Comorbidity Index, and total number of prescriptions among those with at least six months of data following an inappropriate medication prescription.

analyses (n=139), ensuring that individuals in the PIM group had at least six months after their first potentially inappropriate prescription in which to incur costs and utilization. The sample resulted in 541 individuals in the PIM group and 1,795 indi-

viduals in the comparison group.

Statistical Analysis

Statistical significance was assessed at an alpha level of 0.05 and

all statistical analyses were performed in SAS version 6.12. Basic chi-square and t-tests were performed on the total sample of 2,336 individuals to examine differences between those who had been prescribed a PIM and those who had not. Differences in demographics were determined. Where the cell sizes were too small to perform a valid chi-square test, a Fisher's exact test was performed. Likewise, the percentage of individuals on each PIM was determined.

A series of analysis of covariance (ANCOVA) models corresponding to the four types of paid costs (total, provider, facility, and prescription) and four types of utilization (inpatient stays, outpatient visits, office visits, and ER visits) were used to assess whether costs were different between those prescribed a PIM and the comparison group. Potential covariates included sex, total number of prescriptions, and the Charlson Comorbidity Index. Variables not statistically significant at the 0.05 alpha level were removed from the analysis of covariance model.

Results

Prevalence and Demographics

Table 1, page 408, shows the number of individuals who were prescribed each PIM. The prevalence of PIM use in this Medicare managed care population was 24.2% (541/2,336). Of the 146 individuals on two or more inappropriate medications, 88 had 4–13 providers prescribing all their medications (data not shown). Significant differences between those prescribed and those not prescribed a PIM were found for sex and self-rated health (see Table 2, page 409). Those on PIMs were more likely to be female and less likely to rate their health as “excellent” or “very good” than those not on PIMs.

Utilization and Costs

Table 3, page 409, shows the t-tests that indicated that those on PIMs had a higher mean number of inpatient visits, ER visits, office visits, outpatient visits, and total unique prescriptions; a higher mean Charlson Comorbidity Index; and higher mean total, facility, provider, and prescription paid costs. The ages of the individuals on PIMs were not significantly different from those not on PIMs. The total number of prescriptions prescribed for cases was 12,363 (1,763 of which were PIMs); 22,585 prescriptions were prescribed for the comparison group.

The ANCOVA results (Table 4, page 410, and Table 5, page 412) indicated statistically significant differences between cases and comparisons even after controlling for sex, Charlson Comorbidity Index, and total number of prescriptions; total, provider and facility costs; and inpatient, outpatient, and ER visits. Those on a PIM had significantly higher total, provider, and facility costs and a higher mean number of inpatient, outpatient, and ER visits than comparisons after controlling for sex, Charlson Comorbidity Index, and total number of prescriptions. Although

not statistically significant, those on PIMs also had higher prescription costs and office visits than those not on PIMs.

Discussion

Our study of Medicare managed care patients found a prevalence rate for PIMs similar to other studies in nonmanaged care populations. Of 6,171 elders who were sampled from the National Medical Expenditure Survey, physicians prescribed inappropriate medications for nearly a quarter of those living in the community.^{13, 21} Our study also found a significant association between the number of PIMs and the total number of medications prescribed.^{13, 22} Patients on inappropriate medications were prescribed twice as many medications as those not on PIMs (10 versus 5). This is the first study, however, to look at this problem in a population of Medicare managed care individuals and to find differences in resource utilization and costs for patients with and without these medications.

In our study, it appears that inappropriate medication use is associated with increased utilization and higher costs. Those on a PIM had significantly higher total, provider, and facility costs and a higher mean number of inpatient, outpatient, and ER visits than those not on an inappropriate medication. Without a clinical case note review and closer examination of related costs we cannot say for sure that the excess utilization in the case group reflects the effects of PIM use or is attributable to other patient characteristics, but the association remained even after controlling for comorbidity and other variables. Our study is supported by previous studies that have found that specific PIMs such as NSAIDs and the benzodiazepines have been associated with adverse outcomes and increased costs.⁷ However, another recent study on the relationship between inappropriate drug use, functional status decline, and mortality in 3,234 patients from the Duke cohort did not find an association with mortality and inappropriate drug use as measured by the Beers criteria after controlling for covariates.²³ Our study is the first to find an association between inappropriate medications as measured by the Beers criteria and resource utilization.

The application of Beers criteria and other tools for identifying PIM use may enable providers to plan interventions for decreasing both drug-related costs and overall costs, thus preventing ADE admissions in the elderly.^{22, 24} Though the results from this retrospective study should not be viewed as providing a definitive means to assess the appropriateness of care and drug prescribing, this analysis offers an important role in institutional quality improvement efforts. Interventions to reduce the number of PIMs prescribed must occur at both a national and local level. Strategies might include providing patient and provider education to increase the awareness of the clinical and quality implications of the use of these drugs, improving HMO and physician office monitoring systems, using consultant and geriatrics-trained pharmacists, and creating teaching environ-

TABLE 5 ANCOVA Results For Inpatient, Outpatient, Office, and ER Visits Between Cases and Comparisons, N=2,197

Variable	Model R ²	Mean	MS	F-Value (dfn,dfd)	p-value
Inpatient visits	0.1890		74.7031	127.70 (4, 2196)	0.0001
Sex			2.5927	4.43 (1, 2196)	0.0354
Female		0.24			
Male		0.29			
Charlson Comorbidity Index		0.24	195.6358	334.43 (1, 2196)	0.0001
Total number of prescriptions		0.01	15.3290	26.20 (1, 2196)	0.0001
Case status			14.0385	24.00 (1, 2196)	0.0001
Cases		0.58			
Comparisons		0.19			
Emergency room visits	0.0525		8.4861	30.32 (4, 2196)	0.0001
Sex			0.0058	0.02 (1, 2196)	0.8850
Female		0.19			
Male		0.18			
Charlson Comorbidity Index		0.06	13.2203	47.23 (1, 2196)	0.0001
Total number of prescriptions		0.01	2.7650	9.88 (1, 2196)	0.0017
Case status			6.6003	23.58 (1, 2196)	0.0001
Cases		0.36			
Comparisons		0.15			
Outpatient Visits	0.1243		190.8526	77.80 (4, 2196)	0.0001
Sex			41.2347	16.81 (1, 2196)	0.0001
Female		1.25			
Male		0.91			
Charlson Comorbidity Index		0.33	370.9412	151.22 (1, 2196)	0.0001
Total number of prescriptions		0.01	67.6214	27.57 (1, 2196)	0.0001
Case status			51.0252	20.80 (1, 2196)	0.0001
Cases		1.73			
Comparisons		0.98			
Office visits	0.2218		5.8032E+4	156.22 (4, 2196)	0.0001
Sex			4.252E+3	11.45 (1, 2196)	0.0007
Female		11.87			
Male		14.42			
Charlson Comorbidity Index		7.08	1.696E+5	456.59 (1, 2196)	0.0001
Total number of prescriptions		0.20	1.367E+4	36.81 (1, 2196)	0.0001
Case status			0.635E+3	1.71 (1, 2196)	0.1911
Cases		18.18			
Comparisons		11.72			

Note: Controlling for sex, Charlson Comorbidity Index, and total number of prescriptions among those with at least six months of data following an inappropriate medication prescription.

ments that focus on high quality, collaborative geriatric care.

■ Limitations and Qualifications

This study was limited to using administrative data in a man-

aged care population that may or may not be generalizable to other populations. We acknowledge the well-known limitations of administrative data²⁵, including concern over the validity of the measures and the accuracy of the data in particular in mak-

ing an association with physician costs, charges, and the amount paid by the HMO. Controlling for burden of disease by adding the Charlson Comorbidity Index addresses some of the aforementioned concerns, and having at least six months of claims data following the first PIM prescription further strengthens the results. Still, claims data do not provide sufficiently detailed clinical information on the patients receiving the medications to allow for sophisticated comparisons of clinical complexity. Administrative data are subject to changes in benefits and data collection methods. The cost data, while reflecting what the HMO paid, included HMO benefits and copayments that may vary by member benefits and variations in cost for the same procedure or medication. In addition, medication costs were capped at \$500 per member per year. Lastly, the Beers criteria, like any other criteria or guideline, need to be updated on a regular basis to reflect the rapid adoption and turnover of drugs on the market and the changing nature of our knowledge of aging and disease.

Future Steps

The findings have implications for patient education, policy formulation, and research. This study is one step in a collaborative program of health care improvement between industry and academic partners. We sought to gather evidence to guide the further development of an intervention and educational program to decrease the use of potentially high-risk medications in older adults.

In a follow-up study we are analyzing individual PIMs and their association with drug-related problems via chart review and a standard measure for ADE to further investigate the reasons for increased utilization. These results should be seen as an opportunity to improve the quality of ambulatory care for older adults. Future studies should compare the fee-for-service group with the managed care population, describe the problem of PIM use in the inpatient population of older adults, and test interventions for decreasing the use of PIMs in the elderly.

References

1. Bootman JL, Harrison DL, Cox E. The health care cost of drug-related morbidity and mortality in nursing facilities. *Arch Internal Medicine* 1997; 157: 2089-96.
2. Hanlon JT, Schmader KE, Kornkowski MJ et al. Adverse drug events in high risk older outpatients. *J Geriatrics Soc* 1997; 45: 945-48.
3. Ray WA, Griffin MR, Downey W. Benzodiazepines of long and short elimination half-life and the risk of hip fracture. *JAMA* 1989; 262: 3303-07.
4. Cooper JW. Adverse drug reaction-related hospitalizations of nursing facility patients: A four-year study. *Southern Medical J* 1999; 92: 485-90.
5. Cooper JW. Probable adverse drug reactions in a rural geriatric nursing home population: A four-year study. *J American Geriatrics Soc* 1996; 44: 194-97.
6. Cooper JW. Reducing falls among patients in nursing homes [letter; comment]. *JAMA* 1997; 278: 1742, discussion 1743.
7. Smalley WE, Griffin MR, Fought RL, and Ray WA. Excess costs from gastrointestinal disease associated with nonsteroidal anti-inflammatory drugs. *J General Internal Medicine* 1996; 11: 461-69.
8. Institute of Medicare. To err is human. Building a safer health system. Kohn LT, Corrigan JM, Donaldson MS, eds. Washington: National Academy Press, 1999; 1-14.
9. Bates DW, Spell N, Cullen DJ et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. *JAMA* 1997; 277: 307-11.
10. Johnson JA, Bootman JL. Drug-related morbidity and mortality: A cost-of-illness model. *Arch Internal Med* 1995; 155: 1949-56.
11. Perry DP. When medicine hurts instead of helps. *Consultant Pharmacist* 1999; 14: 1326-30.
12. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *JAMA* 1998; 279: 1200-05.
13. Stuck AE, Beers MH, Steiner A et al. Inappropriate medication use in community-residing older persons. *Arch Internal Med* 1994; 54: 2195-200.
14. Lindley CM, Tully MP, Paramosothy V, Tallis RC. Inappropriate medication is a major cause of adverse drug reactions in elderly patients *Age & Aging* 1992; 21: 294-300.
15. Montamat SC, Cusak BL, Vestal RE. Management of drug therapy in the elderly. *New Engl J Med* 1989; 321: 303-09.
16. Beers MH. Aging as a risk factor for medication-related problems. *Consultant Pharmacist* 1999; 14: 1337-40.
17. Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. *Arch Internal Med* 1997; 157: 1531-36.
18. Ware JJ, Kosinski M, Keller SD. A 12-Item Short Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical Care* 34 1996; 34: 220-33.
19. Pacala JT, Boulton C, Reed RL, Aliberti E. Predictive validity of the Pra instrument among older recipients of managed care. *J Amer Geriatrics Soc* 1997; 45: 614-17.
20. Charlson ME, Pompei P, Ales KL, MacKenzie R. A new method of classifying prognostic co-morbidity in longitudinal studies: Development and validation. *J Chronic Diseases* 1987; 373-83.
21. Wilcox SM, Himmelstein DU, Woolhandler S. Inappropriate drug prescribing for the community-dwelling elderly. *JAMA* 1994; 272: 292-96.
22. Nolan L, O'Malley K. Prescribing for the elderly. Part I: Sensitivity of the elderly to adverse drug reactions. *J Amer Geriatrics Soc* 36 1988; 36: 142-49.
23. Hanlon JT, Fillenbaum G, Kuchibhatla M et al. Inappropriate drug use, functional status decline, and mortality among community dwelling elderly. *Gerontologist* 2000; 40: 37.
24. Williams B, Betley C. Inappropriate use of nonpsychotropic medications in nursing homes. *J Amer Geriatrics Soc* 1995; 43: 513-19.
25. Wholey DR, Padman R, Hamer R, Schwartz S. The diffusion of information technology among health maintenance organizations. *Health Care Management Rev* 25 2000; 25: 24-33.