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Drug-Related Problems and Quality of Life in Arthritis and Low Back Pain Sufferers

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ABSTRACT

Objective: The objective of this study was to determine the relationship between drug-related problems (DRPs) and health-related quality-of-life (HRQoL) in ambulatory, community-dwelling patients with musculoskeletal disorders.

Methods: A 12-month, prospective, observational study was conducted in 12 independent community pharmacies in eastern Iowa. Ambulatory patients with self-reported diagnoses of osteoarthritis, rheumatoid arthritis, or low back pain were invited to participate. During quarterly visits to the pharmacy, patients used touch-screen computers to fill out the Short Form-36 (SF-36) general health survey. Using the results of these point-of-service health status assessments, community pharmacists interviewed patients to assess for DRPs. To examine the influences of different DRP characteristics on HRQoL and controlling for potential confounders, both univariate and multivariate analyses were performed using the change in physical component summary (PCS) score and mental component summary (MCS) score of the SF-36 from baseline to 12 months as the dependent variables. In each regression, the independent variables were those significant variables from the univariate analyses, as well as the types of DRPs and their outcomes.

Results: A total of 461 patients were enrolled in the study. Through 12 months, 926 cumulative DRPs were identified. Overall regression models were significant for the PCS and MCS scores, respectively. Two types of DRPs showed significant negative associations with change in PCS: wrong drug and needs additional drug therapy. One type of DRP showed significant negative association with change in MCS: needs additional drug therapy. Resolution or improvement in DRPs showed a significant positive correlation with change in MCS but not PCS.

Conclusions: Two DRPs, needs additional drug therapy and wrong drug, are associated with reduced self-reported physical health in arthritis and low back pain, while the DRP needs additional drug therapy is also associated with reduced self-reported mental health. Resolution of DRPs is associated with improvement in mental health in this cohort.

Keywords: drug-related problems, quality of life, arthritis, pharmacists.

Introduction

Economic and clinical outcomes of medical care are traditionally considered in tandem when examining the health of individual patients or populations. These two types of outcomes, however, fall short in evaluating the entire spectrum of health. A third health outcome is the patient-reported, humanistic outcomes of medical care. One popular example of such an outcome, health-related quality of life (HRQoL), describes the patient's perspective of their disease and treatment, their perceived need for health care, and preferences for treatment and outcomes [1,2]. The relationship among the clinical, economic, and humanistic outcomes of medical therapy is an important consideration when seeking to optimize pharmacotherapy regimens. For example, an antihypertensive drug may reduce blood pressure but cause harmful side effects that decrease overall well-being. The medication may be so costly that the patient must decide whether to pay for the medication or some other essential item, such as groceries.

A recent Institute of Medicine report highlighted the importance of medical errors in the health-care system [3]. Many of these errors are drug-related.

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These drug-related problems (DRPs) are increasingly recognized to have significant morbidity and mortality and contribute to rising health care expenditures [4–8]. Drug-related problems generally fall into categories of 1) overuse of medications (polypharmacy), which increases the likelihood of adverse events or drug interactions; 2) underuse of medications, where diseases are not treated with adequate doses of medication or conditions requiring treatment are not currently treated [9,10]; or 3) inappropriate prescribing, which refers to medications with low margins of safety that should always be avoided [11]. It is important that patients requiring multiple medications for their illnesses be systematically monitored for potential and existing DRPs that could impact their perceptions of their quality of life. Although adverse outcomes of medical care, including DRPs, are well studied in the hospital setting [6,12,13], there is a lack of information about the impact of DRPs and its relationship to patient-reported outcomes in ambulatory settings.

In a prospective, observational study of ambulatory community-dwelling arthritis sufferers, we highlighted the use of community pharmacies as a unique and efficient site to systematically collect patient-reported outcomes of medical care [14,15]. These point-of-care health status assessments were found to contribute to the pharmacists' ability to identify DRPs. The relationship of these DRPs to HRQoL has not been investigated. Arthritis illnesses account for significant health burden and reduced quality of life in the United States, resulting in annual expenditures of nearly $65 billion [16,17]. It is probable that these patients are at risk for medication-related morbidity because they often require therapy with multiple drugs that have significant toxicities. However, no studies have directly examined the link between DRPs and HRQoL in this population. Because an important goal of initiating drug therapy for treatment of chronic illnesses such as arthritis is to improve humanistic outcomes, it is of paramount concern to understand the potential negative impact of DRPs on HRQoL. The objective of this analysis was to investigate the relationship between DRPs and HRQoL in a cohort of arthritis and low back pain sufferers.

Methods

This was a 12-month prospective study beginning in February 1999 with a 6-week enrollment period. Twelve community pharmacies, which are constituents of the Outcomes Pharmaceutical Health Care Certified Pharmaceutical Care Network, participated in this study. The community pharmacies were located in eastern Iowa towns ranging from 3,500 to 110,000 persons.

Eligible patients were invited to participate if they met the following inclusion criteria: 1) new or established patients of the pharmacy; 2) documented of having received a minimum of a 3-month supply in the past 12 months of any nonsteroidal anti-inflammatory drug (NSAID), narcotic, or nonnarcotic analgesic (e.g., codeine, acetaminoiphen, tramadol) for the management of musculoskeletal disorders, specifically osteoarthritis, rheumatoid arthritis, or low back pain; 3) age of 18 years or older; 4) noninstitutionalized and willing to fulfilll the visit requirements; 5) able to read, write, and understand English; and 6) willing to provide informed consent to participate in this study. A central institutional review board approved the study, and all patients provided informed consent to participate.

At baseline and at each quarterly follow-up visit to the pharmacy for 1 year, patients completed the Short Form-36 (SF-36) general health survey [18] and answered questions about health-care resources used in the past 3 months, functional limitations associated with arthritis and low back pain, and side effects of their prescribed medications.

The Touch Outcomes Collector (Assist Technologies, Scottsdale, AZ) was utilized to administer the SF-36 survey and document patient-specific visit information. The touch-screen computer has the capability of administering and recording survey questionnaires in a longitudinal fashion and providing real-time data processing at the completion of the survey. Each pharmacy had a terminal and printer installed in a semiprivate location within the pharmacy. Touch-screen technology was chosen for ease of data collection, real-time accessibility, cost-effectiveness, and patient acceptability [19,20]. In addition to advantages of eliminating the need for paper surveys or mailed questionnaires, touch-screen technology was employed because some patients with arthritis and other musculoskeletal disorders would be expected to have difficulty using pen or pencil to complete surveys. Both patients and pharmacists provided data at each visit. A standard list of comorbid illnesses and demographics were asked at baseline. At each visit, the pharmacists documented prescription and over-the-counter medications taken by the patient into the touch-screen computer. The information entered each time into the patient file in the touch-screen computer was carried forward through each visit.

After the patient completed the questionnaire, two reports were immediately printed by the com-

puter and were used by the pharmacist as a focus for identifying DRPs. One report highlighted responses that were identified a priori by study investigators as clinically important indicators of functional status and health resource utilization. The other report included a graph of the patient's SF-36 health survey scores compared to age and sex adjusted population norms and all their previous visit scores.

The pharmacist reviewed the reports with the patient to determine if there were any health or medication issues that should be addressed. As part of the drug therapy assessment, the pharmacist used the same touch-screen system to document prescription and nonprescription medication use, any DRPs identified, and disease state to which each DRP was related, as well as any interventions or actions to resolve the DRPs, into a file linked to the patient survey. Drug-related problems were categorized into one of seven categories adapted from Strand et al. [9]. These categories are needs additional drug therapy, adverse drug reaction, dose too low, dose too high, inappropriate compliance, wrong drug, and unnecessary drug therapy.

After identifying DRPs, pharmacists initiated processes to resolve the identified DRPs at their discretion. Although pharmacists could make recommendations regarding prescription drug regimens to the patient's primary care physician, the physician performed all adjustments to the therapy. At the next follow-up visit, the outcome of each DRP was reported as resolved, improved, stable/unchanged, or worsened and recorded into the computer.

The measures of HRQoL used in the analyses were the physical component summary (PCS) and the mental component summary (MCS) of the SF-36. These component scores aggregate the eight scales of the SF-36 into a measure of physical health status and a measure of mental health status [21,22]. This approach limits the chance for finding aberrant statistical significance that might occur with multiple tests required for examination of each domain of the SF-36 as a dependent variable. Also, the use of the component summaries can simplify interpretation of findings. Because PCS and MCS scores result from aggregation and weighting of individual SF-36 domains, these summary scores should reflect a comprehensive view of the patient's quality of life.

To examine the association between HRQoL and DRPs, a change score was individually calculated for the PCS and the MCS by subtracting the baseline score from the 12-month score. Two multivariate regressions were performed, one in which the dependent variable was change in PCS and another in which the dependent variable was change in MCS. Univariate correlations, using Spearman's rho, were performed first between these difference scores and a set of baseline patient characteristics. Those baseline patient characteristics significant at $P < .05$ in the univariate analyses were then selected along with the cumulative 12-month frequencies of the seven categories of DRPs and the four DRP outcomes for inclusion in the final multivariate models. Information on type of DRP and outcome in the univariate analyzes was not included, because the relationship between these variables and change in PCS or MCS is the focal point of interest for the multivariate analyses. Because previous research has not shown one type of DRP or outcome to be more or less associated with changes in the HRQoL than another, we believed it was important to retain the DRP variables in the final model.

The baseline patient characteristics were grouped into the following main categories: demographics, comorbid illnesses, site/type of musculoskeletal disease, potential arthritis medication-related adverse effects, and health utilization. Many of these control variables have been previously associated with HRQoL for arthritis and other chronic conditions, and our analytic approach recognized this [17,21–26]. The specific composition of the baseline patient characteristics included demographics, which included marital status, education, age, sex, and presence of health insurance. Comorbid illnesses were grouped into one of three comorbidity indexes—cardiovascular, non-cardiovascular, and gastrointestinal. The cardiovasular comorbidity index had the sum of the following conditions reported by the patient: hypertension, angina, congestive heart failure, previous myocardial infection, and stroke. The non-cardiovascular index had the sum of the following conditions reported by the patient: diabetes, asthma/chronic obstructive pulmonary disease, Crohn's disease, any cancer, sciatica, osteoporosis, sleep problems, and depression. The gastrointestinal-related comorbidity index had the sum of the following conditions reported by the patient: history of ulcers, gastrointestinal bleeding, abdominal pain, or other. Additional characteristics obtained at the baseline were site/type of musculoskeletal disease including osteoarthritis of hip/knee and hand/wrist, rheumatoid arthritis, and lumbago. Potential arthritis-medication-related adverse effects had the sum of the following symptoms reported by the patient: pain in upper stomach, burping/belching, heartburn, bloating, sour taste, nausea, and bad breath. Finally, health utilization was obtained, which included the number of medications taken at 12

months, and the sum of the following tasks patients reported needing assistance with: arising, dressing and/or grooming, eating, walking, hygiene, gripping and/or opening things, reaching, and doing errands and/or chores.

To assess for site-specific confounding, one-way analysis of variance was performed using change in PCS and change in MCS as the dependent variables with site as the independent variables.

Results

A total of 461 patients initially were enrolled in the study. A total of 388 patients provided baseline and 12-month data. Descriptive information on the study population is shown in Table 1. The mean age of study participants was 59.2 years. Osteoarthritis and low back pain were the most common self-reported musculoskeletal disorders, followed by rheumatoid arthritis. Hypertension was the most common comorbidity reported (45%), followed by sciatica (34%). Nearly one-quarter of patients (25%) reported having stomach-related problems, sleep problems (25%), or depression (23%). No significant differences were observed for changes in PCS or MCS between sites involved in the study.

Information on the DRPs identified by community pharmacists is shown in Table 2. Of the cumulative 926 DRPs reported during the 12 months, the most common identified included needs additional drug therapy (32.8%), adverse drug reaction (17.3%), inappropriate compliance (15.9%), dose too low (15.1%), and wrong drug (9.5%). Data on DRP outcomes were available for 758 (82.0%) of the 926 cumulative DRPs identified. By 12 months, 536 (70.7%) of the DRPs for which an outcome was reported were resolved or improved, while 209 (27.6%) remained unchanged or stable. Only 13 (1.7%) of DRPs were reported as worsened.

In the univariate analyses, education was significantly positively associated with change in MCS ($P = .038$), while rheumatoid arthritis ($P = .008$) and number of medications ($P = .022$) were significantly negatively associated with change in PCS.

As shown in Tables 3 and 4, the overall regression models were significant for the PCS and MCS

Table 1 Demographics of study participants

Variable	Frequency (%)*
Age (years)	
Mean ± SD	59.2 ± 13.5
Range	19–94
Marital status	
Married	251 (64.7)
Other	136 (35.3)
Education level	
<4-year college degree	304 (78.6)
≥4-year college degree	83 (21.4)
Sex	
Men	116 (29.9)
Women	272 (70.1)
Health insurance	
Yes	369 (95.1)
No	18 (4.9)
Site of disease†	
OA, hip/knee	223 (57.5)
OA, hand/wrist	179 (46.1)
Rheumatoid arthritis	74 (19.1)
Low back pain	208 (53.6)
Smoking status	
Yes	49 (12.7)
No	338 (87.3)
Number of prescription medications	
0	5 (1.3)
1	76 (19.6)
2	119 (30.7)
3	85 (21.9)
4	56 (14.4)
5	28 (7.2)
≥6	19 (4.9)
Standardized PCS‡	
Baseline mean (SD)	34.41 (10.11)
Range	12.76–57.34
12-month mean (SD)	37.32 (10.89)
Range	11.88–60.25
Standardized MCS‡	
Baseline mean (SD)	48.78 (10.63)
Range	11.55–72.22
12-month mean (SD)	52.11 (10.49)
Range	17.26–74.20

*Frequency may not total 388 because of missing data.
†Conditions are not mutually exclusive.
‡Higher scores represent better health status.
Abbreviation: OA, osteoarthritis.

Table 2 Cumulative (12-month) drug-related problems identified during the study ($N_{patients} = 388$)

Description	Frequency (%)
Drug-related problem	
Needs additional drug therapy	304 (32.8)
Adverse drug reaction	160 (17.3)
Inappropriate compliance	147 (15.9)
Dose too low	140 (15.1)
Wrong drug	88 (9.5)
Unnecessary drug therapy	50 (5.4)
Dose too high	37 (4.0)
Diseases affected	
Osteoarthritis	316 (33.8)
Rheumatoid arthritis	93 (9.9)
Low back pain	80 (8.6)
Osteoporosis	69 (7.4)
Stomach-related problems	65 (7.0)
Cardiovascular problems	53 (5.7)
Anxiety/depression	46 (4.9)
Other	213 (22.8)
Outcome*	
Resolved/improved	536 (70.7)
Unchanged/stable	209 (27.6)
Worsened	13 (1.7)

Note: For Frequency, $N_{patients}$ is the total number of patients presenting for the 12-month visit and Total N_{DRPs} is the total number of drug-related problems identified during the study.
Total $N_{DRPs} = 926$.
*Information on outcome was available for 758 of the 926 total DRPs identified.

Table 3 Multivariate analysis of change in SF-36 PCS

Type of variable	Beta	*P* value
Drug-related problem		
Needs additional drug therapy	–0.146	.038*
Adverse drug reaction	–0.015	.800
Inappropriate compliance	–0.029	.654
Dose too low	–0.064	.302
Wrong drug	–0.141	.015*
Unnecessary drug therapy	–0.001	.990
Dose too high	–0.066	.228
Drug-related problem outcome		
Resolved	0.124	.071
Improved	0.034	.647
Unchanged	0.067	.325
Worsened	–0.055	.301
Site/type of musculoskeletal disease		
Rheumatoid arthritis	–0.139	< .01†
Health utilization		
Number of medications	–0.100	.047*

Note: $F = 2.107$, $P = 0.013$, and $R^2 = 0.069$ apply to entire model.
*Significance level .05.
†Significance level .01.

Table 4 Multivariate analysis of change in SF-36 MCS

Type of variable	Beta	*P* value
Drug-related problem		
Needs additional drug therapy	–0.183	.01†
Adverse drug reaction	–0.032	.575
Inappropriate compliance	–0.121	.066
Dose too low	–0.049	.435
Wrong drug	–0.108	.063
Unnecessary drug therapy	0.052	.345
Dose too high	–0.067	.220
Drug-related problem outcome		
Resolved	0.154	.05*
Improved	0.223	< .01†
Unchanged	0.100	.146
Worsened	0.020	.712
Demographics		
Education	0.114	.026*

Note: $F = 2.006$, $P = 0.023$, and $R^2 = 0.061$ apply to entire model.
*Significance level .05.
†Significance level .01.

change scores, respectively. The R^2 for the PCS change model was .069 ($F = 2.107$; $P < .05$). Significant associations were found for four variables. Two types of DRPs showed significant negative associations with change in PCS: wrong drug and needs additional drug therapy. No DRP outcome variable showed a significant correlation with change in the PCS score. Two baseline characteristic variables, self-reported rheumatoid arthritis and number of medications, were significantly negatively associated with change in PCS score.

The R^2 for the regression of the change in mental component score was 0.061 ($F = 2.006$; $P < .05$). Significant associations were identified for four variables. One type of DRP, needs additional drug therapy, was negatively associated with change in MCS score. In addition, the frequencies of both drug-related problem resolution and drug-related problem improvement was positively related to the change in mental component score. Education level was positively associated with change in MCS.

Discussion

Our results demonstrate that certain DRPs are associated with reduced HRQoL in community-dwelling, ambulatory arthritis, and low back pain sufferers. Two types of DRPs—"wrong drug" and "needs additional drug therapy"—were associated with reduced physical health summary scores, while one DRP—"needs additional drug therapy"—was associated with reduced mental health summary scores from the SF-36 health survey.

Drug-related problems can result in reduced quality of life for several reasons. For example, wrong drug could encompass a myriad of problems such as drug interactions, condition being refractory to the drug, contraindications present, or drug not effective for the condition [9]. The sequelae of such DRPs can result in continued symptoms of the disease or a new set of symptoms, which could contribute to reduced quality of life. It is not uncommon for a patient with osteoarthritis to use a number of different drugs (e.g., NSAIDs) to find one that is effective and also tolerable.

The DRP needs additional drug therapy reflects either the presence of an underlying condition that is not recognized or treated or that the patient could be receiving treatment but remain symptomatic. In the case of arthritis sufferers, this could be a patient taking the maximum dose of an anti-inflammatory agent but still experiencing pain, or it could be the case where one of their comorbid illnesses of significant health burden is suboptimally treated. Another recent study using community pharmacists to monitor drug therapy similarly found the need for additional therapy to be the most common DRP [28].

As expected, some of the baseline characteristic variables showed significant correlations with changes in the physical component summary and mental component summary scores. The presence of rheumatoid arthritis was negatively associated with change in the PCS. The progressive and destructive nature of rheumatoid arthritis is likely to be manifest as physical functioning and pain, which are two primary domains within the PCS. It has been previously shown that arthritis sufferers have lower HRQoL compared to their healthy counterparts [17]. The change in PCS was also sig-

nificantly negatively associated with the number of medications a patient was receiving. A greater number of medications may indicate poorer overall health, as well as associated lower physical health. In addition, because polypharmacy is often present in patients with chronic disease, the adverse effects of multiple medications could have themselves contributed to a lower PCS.

The level of education was positively associated with the change in MCS score. Perhaps attaining a higher level of education allows people to enter occupations that are associated with better mental health. Or, higher education could be related to better access to medical care, although most patients in the study reported having health insurance.

Positively addressing DRPs can be an important step to improving HRQoL. Resolution and improvement of DRPs was associated with significantly improved MCS scores, but the association did not reach statistical significance for PCS scores. It is possible that the act of following the population of patients over time helped them to feel better emotionally because greater attention was being given to their condition, but ultimately did not result in significant improvements in physical health for other reasons related to lack of drug efficacy or exhausting available resources and treatment options.

Many of the DRPs identified in the study could be resolved or improved when health care practitioners systematically monitored patient-reported outcomes. This study is an example of one innovative method to monitor drug therapy in an attempt to minimize the negative effects of DRPs. However, it was limited in that the process was entirely driven by the community pharmacist. Another possible approach is to utilize a structured multidisciplinary team that combines the expertise and availability of a number of health care practitioners. For example, pharmacists could be used as a point person in monitoring for DRPs and then communicating their findings to physicians. Physicians could oversee any adjustments in drug therapy or other changes intended to resolve a DRP. Previous studies have found that such a team approach can reduce the number of DRPs faced by patients [29,30].

Pharmacists practicing in community settings performed the drug therapy monitoring in our program. These individuals are well positioned to screen for potential and existing DRPs [31]. Increased utilization of pharmacists in nondispensing roles has been called for nationally as one strategy to improve medication use outcomes in addressing the recent Institute of Medicine report on medical errors [32]. Because they are the most accessible health care professional for many patients [33], pharmacists occupy a unique place in the health-care system that enables them to screen for drug interactions and adverse reactions, monitor therapeutic efficacy, and identify potential or existing DRPs.

There are several limitations to our study that must be noted. First, it was an observational study without a control group. We were not able to identify patient level factors associated with DRPs in DRP sufferers versus nonsufferers. Second, we did not examine change in HRQoL as a function of the total number or specific type of DRP resolved. Certain DRPs may result in more significant health burden than others; interventions directed at the more significant DRP could result in proportionately greater changes in health status. Third, although we note an association between decreased PCS and DRPs, our data are insufficient to explain whether this decrease is caused by DRPs or whether DRPs serve as a proxy for underlying medical or functional conditions associated with decreased physical HRQoL. Fourth, although the SF-36 is widely used to monitor HRQoL of populations, its utility at the patient level to help direct health care interventions has been questioned [34–37]. Other studies utilizing pharmacist management of drug therapy, which measured HRQoL using the SF-36 survey, have found a similar lack of effect, again possibly owing to the instrument not being sensitive enough to measure these changes [38–42]. The use of disease-specific health instruments (e.g., Arthritis Impact Measurement Scale) or the development of an health instrument specific for DRPs might be more useful in measuring the impact of DRPs on HRQoL.

Despite limitations to our study, it is apparent that DRPs contribute to reduced HRQoL in arthritis and low back pain sufferers. Given the multifaceted nature of drug therapy for chronic diseases, future research should examine where the most appropriate place is within the health care system to systematically and efficiently monitor drug therapy to identify and prevent DRPs from occurring. Future research also should examine whether changes in health care at the system level or at the site level are needed to most efficiently resolve DRPs when they develop. It appears that resolving DRPs is one step in helping improve HRQoL. This improved HRQoL may have important implications on future health resource utilization in this cohort of patients. Clinicians should actively screen

for potential and existing DRPs in patients with musculoskeletal disorders and resolve them accordingly.

Conclusions

Two DRPs, wrong drug and needs additional drug therapy, are significantly negatively associated with self-reported physical health in community-dwelling arthritis and low back pain sufferers, and the DRP needs additional therapy is also significantly associated with reduced self-reported mental health. Improvement and resolution of DRPs in this cohort is associated with significant improvements in mental health.

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References

1 Carr AJ, Higginson IJ. Measuring quality of life: are quality of life measures patient centered? BMJ 2001;322:1357–60.
2 Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Engl J Med 1996;334:835–44.
3 Kohn LT, Corrigan JM, Donaldson MS, editors. Too Err Is Human: Building a Safer Health System. Washington (DC): National Academy Press; 1999.
4 Manasse HR Jr. Medication use in an imperfect world: drug misadventuring as an issue of public policy. Part 1. Am J Hosp Pharm 1989;46:929–44.
5 Manasse HR Jr. Medication use in an imperfect world: drug misadventuring as an issue of public policy. Part 2. Am J Hosp Pharm 1989; 46:1141–52.
6 Johnson JA, Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Arch Intern Med 1995;155:1949–56.
7 Johnson JA, Bootman JL. Drug-related morbidity and mortality and the economic impact of pharmaceutical care. Am J Health Syst Pharm 1997;54:554–8.
8 Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. J Am Pharm Assoc 2001;41:192–9.
9 Strand LM, Morley PC, Cipolle RJ, et al. Drug-related problems: their structure and function. Ann Pharmacother 1990;11:1093–7.
10 Hanlon JT, Schmader KE, Ruby CM, Weinberger M. Suboptimal prescribing in older inpatients and outpatients. J Am Geriatr Soc 2001;49:200–9.
11 Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. Arch Intern Med 1997;157:1531–6.
12 Bates DW, Cullen D, Laird N, et al. Incidence of adverse drug events and potential adverse drug events: implications for prevention. JAMA 1995; 274:29–34.
13 Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. JAMA 1997;227:307–11.
14 Ernst ME, Doucette WR, Dedhiya SE, et al. Use of point-of-service health status assessments by community pharmacists to identify and resolve drug therapy problems in patients with musculoskeletal disorders. Pharmacotherapy 2001;21:988–97.
15 Osterhaus JT, Dedhiya SD, Ernst ME, et al. Health outcomes assessment in community pharmacy practices: a feasibility project. Arthritis Care Res 2002;47:124–31.
16 CDC. Impact of arthritis and other rheumatic conditions on the health-care system—United States, 1997. MMWR 1999;48:349–53.
17 Hill CL, Parsons J, Taylor A, Leach G. Health related quality of life in a population sample with arthritis. J Rheumatol 1999;26:2029–35.
18 Ware JE, Snow KK, Kosinski M, Grandek B. SF-36 Health Survey Manual and Interpretation Guide. Boston: New England Medical Center, The Health Institute; 1993.
19 Buxton J, White M, Osoba D. Patients' experiences using a computerized program with a touch-sensitive video monitor for the assessment of health-related quality of life. Qual Life Res 1998;7:513–9.
20 Lofland JH, Schaffer M, Goldfarb N. Evaluating health-related quality of life: cost comparison of computerized touch-screen technology and traditional paper systems. Pharmacotherapy 2000; 20:1390–5.
21 McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-item short-form health survey (SF-36). II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. Med Care 1993;31:247–63.
22 Ware JE Jr, Kosinski M, Bayliss MS, et al. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary results from the medical outcomes study. Med Care 1995;33:AS264–79.
23 Cox E, Kozma CM, Reeder CE. Multivariate analysis of health status scores. Pharmacoeconomics 1994;6:49–56.
24 Nichol MB, Harada ASM. Measuring the effects of medication on health-related quality of life in patients with rheumatoid arthritis. Pharmacoeconomics 1999;16(5 Pt 1):433–48.
25 Xuan J, Kirchdoerfer LJ, Boyer JG, Norwood GJ. Effects of comorbidity on health-related quality-

of-life scores: an analysis of clinical trial data. Clin Ther 1999;21:383–403.
26 Wolfe F, Kong SX, Watson DJ. Gastrointestinal symptoms and health-related quality of life in patients with arthritis. J Rheumatol 2000; 27:1373–8.
27 Briggs A, Scott E, Steele K. Impact of osteoarthritis and analgesic treatment on quality of life of an elderly population. Ann Pharmacother 1999; 33:1154–9.
28 Kassam R, Farris KB, Burback L, et al. Pharmaceutical care research and education project: pharmacists' interventions. J Am Pharm Assoc 2001; 41:401–10.
29 Krska J, Cromarty JA, Arris F, et al. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age Ageing 2001;30:205–11.
30 Hanlon JT, Weinberger M, Samsa GP, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. Am J Med 1996;100:428–37.
31 Rupp MT, DeYoung M, Schondelmeyer SW. Prescribing problems and pharmacist interventions in community practice. Med Care 1992;30:926–40.
32 Bootman JL. To err is human [editorial]. Arch Intern Med 2000;160:3189.
33 Knapp KK, Paavola FG, Maine LL, et al. Availability of primary care providers and pharmacists in the United States. J Am Pharm Assoc 1999; 39:127–35.
34 McHorney CA, Tarlov AR. The use of health status measures for individual patient level applications: problems and prospects. Qual Life Res 1994;3:43–4.
35 McHorney CA, Tarlov AR. Individual-patient monitoring in clinical practice: are available health status surveys adequate? Qual Life Res 1995; 4:293–307.
36 McHorney CA. Health status assessment methods for adults: past accomplishments and future challenges. Annu Rev Pub Health 1999;20: 309–35.
37 Patrick DL, Chiang Y. Measurement of health outcomes in treatment effectiveness evaluations: conceptual and methodological challenges. Med Care 2000;38 Suppl II:S14–25.
38 Pickard AS, Johnson JA, Farris KB. The impact of pharmacist interventions on health-related quality of life. Ann Pharmacother 1999;33:1167–72.
39 Carter BL, Barnette DJ, Chrischilles E, et al. Evaluation of hypertensive patients after care provided by community pharmacists in a rural setting. Pharmacotherapy 1997;17:1274–85.
40 Carter BL, Malone DC, Billups SJ, et al. Interpreting the findings of the IMPROVE study. Am J Health-Syst Pharm 2001;58:1330–7.
41 Erickson SR, Slaughter R, Halapy H. Pharmacists' ability to influence outcomes of hypertension therapy. Pharmacotherapy 1997;17:140–7.
42 Vol CI, Farris KB, Kassam R, et al. Pharmaceutical care research and education project: patient outcomes. J Am Pharm Assoc 2001;41:411–20.