RESEARCH

A Prospective Trial of a Clinical Pharmacy Intervention in a Primary Care Practice in a Capitated Payment System

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ABSTRACT

BACKGROUND: There is evidence that pharmacist interventions improve clinical outcomes. The few studies that address economic outcomes (a) often report estimated instead of actual medical costs, (b) report only medication costs, or (c) have been conducted in settings that are not typical of community-based primary care.

OBJECTIVES: To (a) determine whether a clinical pharmacist's recommendations to physicians regarding optimizing medication therapy are related to medical costs in capitated patients in an internal medicine practice, and (b) compare what primary care physicians (PCPs) in a comparison group actually did proactively to optimize medication therapy versus what a clinical pharmacist would have recommended to them.

METHODS: This was a prospective, controlled study comparing 2 internal medicine practices. Study enrollment was performed using a screening process carried out every 1-2 weeks on a rolling basis for 1 year from July 2001 through June 2002. Eligibility criteria for prospective enrollment were (a) 1 or more risk factors: at least 1 chronic disease or an event (e.g., emergency room visit, adverse drug reaction, medication nonadherence) or aged 50 years or older, (b) a scheduled visit to see a PCP within 2 weeks from the screening date or a diagnosis of diabetes without a PCP visit during the first 6 months of the study, (c) need for optimization of medication therapy as determined by a clinical pharmacist on the screening date, and (d) 12 months of continuous insurance eligibility before enrollment in the study. For inclusion in the final study analyses, patients were also required to have continuous insurance eligibility through 12 months from study enrollment. One clinical pharmacist made recommendations to optimize medication therapy in the intervention group. For the comparison group, the same pharmacist proposed recommendations that remained concealed from the physicians. The primary outcome measure was per patient per year (PPPY) medical cost, based on plan liability (gross allowable costs minus patient costs), excluding prescription drug cost. Additional outcome measures included numbers of outpatient visits, hospital admissions, emergency room (ER) visits per 1,000 patients, and hospital days; and percent of recommendations that were accepted by the PCPs. Changes in outcome measures from the pre-intervention to post-intervention period were compared across study groups in a difference-in-difference analysis, using the Student's *t*-test for normally distributed data and the Mann-Whitney *U*-test (nonparametric) for skewed data.

RESULTS: There were 127 and 216 adult patients in the intervention and comparison groups, respectively. The primary outcome, change in mean PPPY medical (excluding pharmacy) cost, did not differ significantly between the groups ($P=0.711$). The between-group difference in the change in ER visits per 1,000 patients approached statistical significance ($P=0.054$). Intervention group patients were more likely than comparison group patients to have the following issues addressed: medication nonadherence (85.7% vs. 40.0%, respectively; $P=0.032$), untreated indication (72.6% vs. 11.5%, $P<0.001$), suboptimal medication choice (60.0% vs. 5.9%, $P<0.001$) and cost-ineffective drug therapies (72.1% vs. 6.5%, $P<0.001$). Of the estimated number of actionable opportunities identified for the comparison group (but concealed from the physicians), 23.5% were adopted by comparison group physicians without any assistance from a clinical pharmacist.

CONCLUSION: Compared with patients of PCPs who received no input from a clinical pharmacist, patients of PCPs who received clinical pharmacist recommendations were more likely to have several medication-related issues addressed, including medication nonadherence, untreated indications, suboptimal medication choices, and cost-ineffective drug therapies. However, total medical (excluding pharmacy) costs for the intervention and comparison groups were not significantly different.

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What is already known about this subject

- Pharmacists can optimize medication therapy, resulting in improved patient outcomes, such as decreased exacerbations in patients with congestive heart failure and improved blood sugar management in patients with diabetes.
- Pharmacists are effective at recognizing potential and actual drug-related problems, such as drug-induced conditions and clinically relevant drug interactions.
- Pharmacist interventions can limit health care costs in specific groups of patients such as Medicaid and some health maintenance organizations.

What this study adds

- Patients in the intervention group were more than twice as likely to have medication nonadherence issues addressed (85.7% vs. 40.0%, $P=0.032$), 6 times as likely to have a medication prescribed that was indicated but not prescribed previously (72.6% vs. 11.5%, $P<0.001$), 10 times as likely to be prescribed an optimal medication for their condition (60.0% vs. 5.9%, $P<0.001$) and 11 times as likely to have their PCP prescribe more cost-effective therapies (72.1% vs. 6.5%, $P<0.001$).
- Of the estimated number of actionable opportunities identified by the clinical pharmacist for the comparison group but concealed from physicians, 23.5% were adopted by physicians without any intervention, whereas 76.5% were not adopted.
- The intervention and comparison groups did not significantly differ with respect to the study's primary outcome, change in per patient per year (PPPY) medical cost excluding costs for prescription medications ($P=0.711$). From the pre-intervention to post-intervention period, mean PPPY medical costs declined by 15.1% in the intervention group and increased by 39.7% in the comparison group; however, median 12-month costs increased in both study groups, from $1,045 to $1,411 in the intervention group and from $1,130 to $1,638 in the comparison group.

Studies have shown that pharmacist consultation programs can improve clinical outcomes by optimizing medication use in ambulatory patients.[1-5] Among patients in a heart failure clinic, a program of pharmacist evaluation (medication evaluation and recommendations, patient education and follow-up telemonitoring) resulted in a significant decrease in heart failure events and all-cause mortality. Study authors attributed this result to closer follow-up and optimizing doses of angiotensin-converting enzyme (ACE) inhibitors.[1] In 2 randomized trials of patients with hypertension, those who were treated collaboratively by physicians and pharmacists achieved better control of blood pressure than did those who were managed by the physician alone.[2,3] The physician-pharmacist team in 1 study increased medication optimization by titrating doses more effectively, switching to less expensive or more appropriate formulations of medications, and increasing appropriate laboratory monitoring.[2] Even when patients' medications were not changed, blood pressures were still improved. The authors speculated that improved medication adherence and beneficial education about hypertension contributed to these outcomes.[2] Collaboration between physicians and pharmacists has resulted in a higher rate of patients meeting their lipid-level goals than previously achieved without collaboration in the same practice.[4] The Asheville Project demonstrated that close collaboration between community pharmacists and patients with diabetes mellitus was associated with improved blood sugar management.[5]

The National Committee for Quality Assurance's key program for quality measurement is the Healthcare Effectiveness Data and Information Set (HEDIS). Since 2007, HEDIS has included measures of health care efficiency in the cost of care, referred to as "relative resource use" for chronic conditions. For example, asthma and cardiovascular conditions are measured both for quality, such as appropriate medication use and medication adherence, and for the cost of care.[6,7] Some studies of clinical pharmacist activities have concentrated on lowering medication costs,[8,9] but few have attempted to look at the impact on medical health care costs and utilization. Lowering medication costs has been accomplished by simplifying medication regimens, recommending less expensive alternatives, and providing pharmacotherapy consultation directly to patients.[8-10] In an effort to decrease medical health care costs and utilization, some studies have demonstrated that pharmacists effectively identify potential and actual drug-related problems, potentially resulting in cost avoidance.[8,10]

Previous studies that assessed clinical or medical cost outcomes were either conducted in U.S. Department of Veterans Affairs (VA) systems, in a setting where the patient was seen at a separate pharmacist visit, in a pharmacist-run clinic, or in populations that were dissimilar to general primary care internal medicine practices.[10-14] Although these studies describe effective models, they do not extrapolate well to the typical primary care, internal medicine practice where medical patients are most often seen by physicians and in which pharmacists typically have no access to pertinent medical information (e.g., medical history, progress notes, laboratory and other test results, and consult notes) necessary to make clinical recommendations to prescribers. Embedding a clinical pharmacist within the primary care practice can remove those barriers.

In the 2 years before the present study, 2 clinical pharmacists working for the Greater Rochester Independent Practice Association (GRIPA) had gained experience with a number of primary care physicians (PCPs) on how to improve medication use and prevent the known hazards associated with medication misuse in their patients. GRIPA is a unique partnership of more than 600 physicians and 2 hospitals in 2 counties in western New York. The pharmacists were located within the physician practice with little disruption to the normal office workflow. At that time, the pharmacists did not meet with the patients, but provided written recommendations to each patient's physician. The clinical pharmacist had opportunities to affect a patient's medication adherence, to ensure that the most appropriate medications were both prescribed and monitored appropriately, and to help prevent therapeutic duplication and adverse drug reactions. In addition, pharmacists served as a dynamic drug information resource for the physician. For patients whose care was affected by the clinical pharmacist's recommendations, a trend toward lowered medical health care costs and utilization was observed.[15,16] However, no comparison group of patients without the services of a clinical pharmacist was available at that time.

The primary purpose of the present study was to determine whether the recommendations of a clinical pharmacist embedded in a primary care practice, which had not previously received services from GRIPA's clinical pharmacists, would decrease the medical costs of capitated patients. The secondary purpose of the study was to compare actions taken by physicians in a comparison group, which received no pharmacist input, with actions taken by physicians who were provided recommendations by a clinical pharmacist.

Methods

Study Setting

This was a prospective, controlled study conducted in 2 primary care practices located in the suburbs of Rochester, New York. One practice served as the intervention group, and the other served as the comparison group. Physicians at both practices were members of GRIPA and had never received services from GRIPA's clinical pharmacists. ViaHealth, GRIPA's parent company, owns 2 hospitals and one-half of GRIPA; the physicians own the other half. GRIPA operates under financial risk contracts with insurance companies. A portion of the patients in these primary care practices were members of an insurance company with which GRIPA had a risk contract. The patients were enrolled in either the insurance company's commercial insurance plan or its Medicare insurance product. The risk contract provided GRIPA with an incentive to proactively optimize medical care to

decrease its financial risk. The medical cost data, termed "plan liability" in this study, were actual (not estimated) plan sponsor costs (gross allowable costs minus patient costs). The patients for whom GRIPA and their physicians are at risk are "capitated" patients. Although the plan was capitated, the physicians had incentive to submit all claims to receive payment for services provided. The risk contract provided opportunity for physicians to get paid more than the standard fees reimbursed through the claims submission and payment process.

The intervention group practice had 957 capitated patients, and the comparison group practice had 1,272 capitated patients, with 12.3% and 31.6% enrolled in the Medicare insurance product, respectively. The remaining capitated patients in each group were enrolled in the commercial insurance product. Both practices consisted of internal medicine physicians, with 2 physicians in the intervention group and 4 physicians in the comparison group. The intervention group was privately owned, whereas the comparison group was owned by ViaHealth. Both practices used paper-based medical records and appointment scheduling systems. The 2 physicians in the intervention group had practiced for 18 and 6 years, respectively, whereas the 4 physicians in the comparison group had been in practice for 20 years on average (range 17-25 years).

One clinical pharmacist worked within both practices and brought a laptop computer to record her activity in a secure database. At the intervention group practice, the pharmacist did not have Internet access. The comparison group practice was equipped with computers with limited Internet access, which the pharmacist could use if needed. The clinical pharmacist recorded medication recommendations that were either provided to physicians (intervention group) or concealed (comparison group).

Written informed consent was obtained from the physicians at both practices. The ViaHealth Clinical Investigations Committee (institutional review board) approved this study.

Patient Selection

Patients enrolled in this study were continuously enrolled in 1 of the 2 contracted insurance products (commercial or Medicare) for the entire 12 months before their study enrollment date to ensure that there were complete baseline claims data. The patient selection period, during which patients were entered into the study in a rolling screening and enrollment process conducted by the clinical pharmacist every 1-2 weeks, began on July 1, 2001, and ended on June 30, 2002. Patient membership status was provided to the pharmacist at study initiation, and insurance claims were used to determine each patient's risk factors, which were used as part of the entry criteria in the study (Table 1). To be eligible for enrollment into the study, patients had to be scheduled for an appointment with a PCP within 1-2 weeks of the screening date or have a diagnosis of diabetes mellitus documented in their claims but no PCP visit during the first 6 months of the study. The second criterion served to identify patients with diabetes mellitus that did not have optimal follow-up care. Patients identified on the appointment schedule had to meet at least 1 of the following 2 criteria: (a) 1 or more of the risk factors listed in Table 1, identified through *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), Diagnosis Related Group (DRG), or Current Procedural Terminology (CPT) codes found in each patient's insurance claims for the 12 months before April 2001, or (b) absence of any of the above risk factors, but aged 50 years or older. Finally, a need for medication optimization was required for study entry; patients meeting the other study criteria were enrolled only if the clinical pharmacist recorded recommendations to optimize medication therapy, whether reported to the PCP (intervention group) or concealed (comparison group).

TABLE 1 Risk Criteria for Study Entry: Hospital and Medical Claim Codes

	ICD-9-CM	DRG	CPT
Diabetes	250.XX	294, 295	
Congestive heart failure	428.XX	115, 124, 125, 127	
Coronary artery disease	410, 410.9 411.XX, 412-414.XX, (Except 414.1 414.10, 414.11 or 414.19)	106, 107, 109, 112, 116, 121, 122, 123, 132, 140	33510-33545
Asthma	493.XX	096, 097	
Chronic obstructive pulmonary disease	491-492.XX 493.2 496.XX	088	
Hypertension	401-405.XX	134	
Hypercholesterolemia	272.XX		
Migraine	346.XX		
Atrial fibrillation	427.31, 427.32	138, 139	
Adverse drug reaction	995, 995.1, 995.2		
Noncompliance with medical treatment	V15.81		
Any emergency room visit			99281-99285
Tobacco abuse disorder	305.1, 989.84		

CPT = Current Procedural Terminology; DRG = Diagnosis Related Group; ICD-9-CM = International Classification of Disease, Ninth Revision, Clinical Modification.

Each patient's study enrollment date was the first date on which the pharmacist made a recommendation for that patient. Post-enrollment follow-up lasted 12 months for each patient. Thus, to be included in the final study analyses, the patient had to maintain continuous insurance eligibility and remain in the care of the same PCP for the 12 months after the study enrollment date. Insurance eligibility was determined by a monthly membership roster sent to GRIPA from the insurance company. The membership status and risk factor evaluation of the patients in the physician practices were updated in January 2002.

Description of the Intervention

In both practices, the same clinical pharmacist reviewed each patient's medical record and assessed whether the patient's medication therapy could be optimized. For the intervention group, the clinical pharmacist provided the PCP with written recommendations (consult note) regarding drug-related problems similar to those described by Strand et al.[17] All consult notes were completed before the patient's appointment with the PCP. The consult notes were not meant to be a permanent part of the medical record and were labeled accordingly, which likely limited physicians' potential concerns about medical malpractice or liability related to these notes. The consult notes were written on colorful paper and placed conspicuously in the paper medical record.

For the comparison group, the clinical pharmacist documented in the database the recommendations for each patient, which remained concealed from the PCP; physicians in the comparison group practice were asked to "act as though the clinical pharmacist present in the office is invisible." The estimated number of actionable opportunities for the comparison group was (a) calculated by multiplying the recommendation acceptance rate for the intervention group (the percentage of clinical pharmacist recommendations that were actually adopted by intervention physicians) times the number of concealed recommendations for the comparison group, and then (b) compared with the actual number of changes made by comparison group physicians without clinical pharmacist assistance. The pharmacist also documented in the privacy-secured database all known chronic diseases and other demographic information for both study groups, including height and weight, if these data were available in the medical record.

Medical record reviews were conducted for all patients who were enrolled in the study. The medical record included medical history, physical exam, consult notes, laboratory data, and other test results. For 72.9% and 39.3% of the capitated patients in the intervention and comparison group, respectively, the pharmacist had access to claims data reflecting the patient's prescription refill (pharmacy) claims from the patient's insurance company. Pharmacy claims data were available only for the capitated patients that had a prescription benefit through the insurance company with which GRIPA had a risk contract. For instance, there were no pharmacy data on patients who had medical insurance but filled all their prescriptions through the VA. None of the physicians had direct access to the pharmacy claims data. The pharmacist interpreted the pharmacy claims data and distilled that information into her consult notes as needed to optimize medication therapy. However, because pharmacy data were not available for all study patients, costs for prescription drugs could not be assessed except in the aggregate.

In addition to providing proactive recommendations to the intervention group physicians, the clinical pharmacist was available to help with any medication-related problems or drug information issues at the physicians' or staff's request. The clinical pharmacist also offered physician education, patient counseling, adherence monitoring and education as deemed appropriate. Patient counseling was done only on an as-needed basis, was not directed at any particular condition, and generally dealt with medication nonadherence. Otherwise, most of the medication adherence issues were simply brought to the attention of the PCPs for them to address during the patient's visit.

The clinical pharmacist was not available to the comparison group physicians for consultation during the study period. However, an a priori decision was made that, if a significant finding were discovered during a medical record review in the comparison group that required immediate attention to prevent patient harm, the clinical pharmacist would consult the physician and the patient would be discontinued from the study.

The clinical pharmacist recorded physician responses to each recommendation at 6 months and 12 months after the recommendation was made, in both the intervention and comparison groups. Recommendations made by the pharmacist that were no longer applicable by the time of the patient's appointment were excluded from the analysis. The clinical pharmacist recorded a physician response as "accepted" if there was evidence documented within the medical record indicating that the recommendation was followed (e.g., a change in a prescription, a laboratory test ordered).

Once patients met all criteria for inclusion, the study was conducted with an intent-to-treat analysis. Whether or not the physician adopted the pharmacist's recommendation, that patient was included in the final analysis.

Outcome Measures

Medical costs and utilization were obtained from medical claims data contained in the GRIPA data warehouse. These data originated from each enrolled patient's insurance company. Cost (plan liability) was calculated as a per patient per year (PPPY) amount for the primary outcome and tabulated for all claims for hospitalizations, emergency room (ER) visits, radiology and laboratory tests, PCP visits, and specialty visits. Although included in medical costs, inpatient costs also were tallied separately. The utilization data included number of hospitalizations, ER visits, PCP visits and specialty visits, and hospital length of stay in days. Hospitalizations were identified by any claim with a valid diagnosis related group or a revenue code between 100 and 219 (room and board) as long as the facility type was not a skilled nursing facility or nursing home. Medical costs and utilization were determined for 12 months before and after each patient's enrollment date.

Prescription cost data were available only in aggregate as a one-time report provided by the insurance company. Investigators did not have access to complete prescription medication claims data because GRIPA was not at financial risk for medication

expenses. Thus, no patient-level analyses of prescription data were performed.

Episode Treatment Groups (ETGs) for each group were not available at the start of the study but were calculated based on historic information before study analysis was completed. ETGs identify and quantify an episode of care that spans inpatient, outpatient, and all ancillary services, including pharmaceuticals, and takes into consideration patient age and comorbidities.[18] ETGs were believed to be important to include in the study analyses to determine the degree of similarity of the 2 groups throughout the study because ETGs are a clinically useful tool to measure health care demand.[18]

Statistics

Before the study, interest had been expressed in looking at the response variables by different age groups as well as over the entire population, because published studies about clinical pharmacist interventions have typically been in patients with chronic disease and often in older age groups.[1,10-12,15] Two subgroups—age 65 or younger versus older than age 65—were compared. Other subgroups were created for 3 age categories—20-50 years, 51-65 years, and older than age 65—and the data for these 3 subgroup populations were analyzed separately.

Categorical data (e.g., rates, percentages) were analyzed using the likelihood ratio chi-square test for differences in proportions, comparing the intervention group and comparison group. The variables analyzed included sex, age category, weight category, and presence or absence of comorbidities and risk factors including congestive heart failure (CHF), diabetes mellitus, coronary artery disease (CAD), asthma, chronic obstructive pulmonary disease, and current cigarette smoking.

Continuous data were examined, using histograms and scatter plots, to determine distribution characteristics and relationships with other variables. Normally distributed data were analyzed using Student's *t*-tests for 2-group differences. Non-normally distributed data were analyzed using the Mann-Whitney *U*-test, which is a nonparametric test for 2-group comparisons. Baseline variables analyzed with these methods included age, ETGs, and body mass index (BMI). Study outcome measures were assessed using a difference-in-difference analysis by subtracting pre-intervention values from post-intervention values and comparing the change amounts by study group.

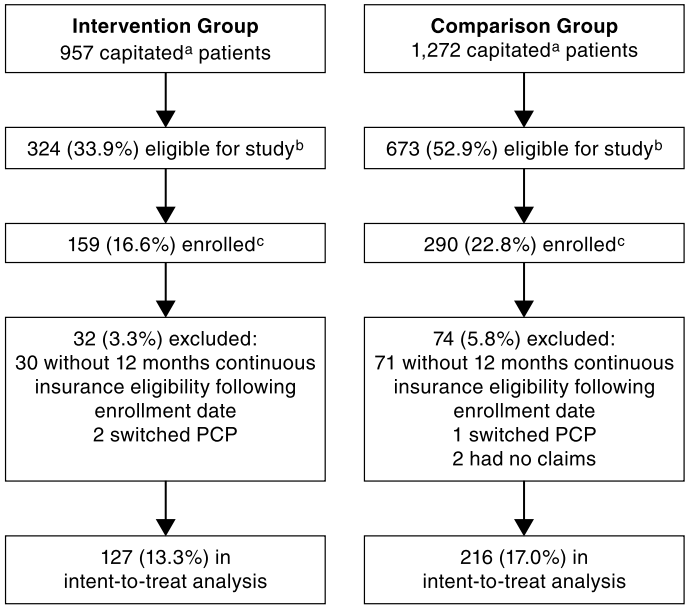
Statistical significance was determined using an alpha level of 0.05. Statistical analysis was performed using the Minitab version 13.32 (Minitab Inc., State College, PA) and SPSS versions 13.0 and 14.0 (SPSS Inc., Chicago, IL) statistical packages.

Results

Study Enrollment

Counts of eligible patients who were enrolled between July 2001 and June 2002, patients excluded, and patients included in the final data set are shown in Figure 1. More than 80% of the enrolled patients met more than 1 risk factor determined from insurance claims (data not shown). Two percent of the enrolled patients were identified because they had a diagnosis of diabetes with no scheduled appointment during the first 6 months of the study. The only patient in the comparison group with a significant finding that required the clinical pharmacist to make an urgent recommendation to the comparison group physician was excluded for not having 12 months of continuous insurance eligibility after study enrollment. Thus, no patients in the comparison group were discontinued from the study solely because of clinical pharmacist interaction with the comparison group physicians. Of patients who met all the criteria for enrollment in the prospective phase of the study (i.e., of those who were assigned to either the intervention group [n=159] or the comparison group [n=290]), exclusions for failure to maintain continuous insurance eligibility were made for 30 (18.9%) of intervention group and 71 (24.5%) of comparison group subjects.

FIGURE 1 Patient Enrollment



[a] *Capitated: Enrolled in an insurance plan with which the Greater Rochester Independent Practice Association had a risk contract.*
[b] *Eligible for study: Met at least 1 risk criteria in Table 1 or aged 50 years or older; and 12 months of continuous insurance eligibility before screening by clinical pharmacist for possible study enrollment.*
[c] *Enrolled in study: Patient had a scheduled appointment with PCP within 1-2 weeks of screening the appointment schedule or had diagnosis of diabetes and did not have a visit with PCP during first 6 months of study; and had at least 1 pharmacist recommendation that was either provided to PCP before appointment (intervention group) or concealed (comparison group).*
PCP=primary care physician.

TABLE 2 Demographic and Clinical Characteristics of Patients at Study Enrollment

Characteristics	Intervention Group (n=127)	Comparison Group (n=216)	*P* Value/Statistical Test[a]
Age in years, mean [SD]	59.6 [11.6]	68.2 [12.7]	<0.001 M-W
Age, number (%)			<0.001 chi-square
20-50 years	25 (19.7%)	22 (10.2%)	
51-65 years	58 (45.7%)	48 (22.2%)	
>65 years	44 (34.7%)	146 (67.6%)	
Sex, male (%)	35.4%	42.1%	0.229 chi-square
Select chronic conditions (%)			
CHF	4.7%	4.2%	0.807 chi-square
Diabetes mellitus	23.6%	19.0%	0.306 chi-square
CAD	14.2%	22.2%	0.068 chi-square
Asthma	11.0%	8.8%	0.484 chi-square
COPD	13.4%	10.7%	0.446 chi-square
Current smoker	13.4%	9.7%	0.297 chi-square
Prospective risk (ETG)			
Aged 20-50 years	0.99	1.21	0.197 *t*-test
Aged 51-65 years	1.76	1.78	0.454 *t*-test
>65 years	2.81	2.89	0.596 *t*-test
Weight category,[b] number (%)	**(n=118)**	**(n=210)**	
Normal weight	16 (13.6%)	59 (28.1%)	0.003 chi-square
Overweight	24 (20.3%)	49 (23.3%)	0.532 chi-square
Obese	63 (53.4%)	92 (43.8%)	0.095 chi-square
Morbidly obese	15 (12.7%)	10 (4.8%)	0.009 chi-square
BMI (kg/m^2), mean [SD][c]	32.06 [7.51]	28.45 [5.67]	<0.001 *t*-test

[a] *P values were determined from independent 2-sample t-tests for continuous variables and likelihood ratio chi-square tests for categorical variables; the Mann-Whitney U-test for 2 independent sample groups was used when the continuous variables were not normally distributed.*

[b] *Normal weight = BMI ≤25 kg/m^2, overweight = BMI 25.1-27.99 kg/m^2, obese = BMI 28-39.9 kg/m^2, morbidly obese = BMI >40 kg/m^2.*

[c] *4.7% and 2.3% of patients in the intervention and comparison groups, respectively, did not have calculated BMI measures because their height data were unavailable.*

BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; chi-square = likelihood ratio chi-square test; COPD = chronic obstructive pulmonary disease; ETG = Episode Treatment Group; kg/m^2 = ratio of weight in kilograms to height in meters squared; M-W = Mann-Whitney U-test; t-test = Student's t-test for independent groups.

Demographics

Patient demographics at study enrollment are shown in Table 2. The mean [SD] age of patients in the intervention group (59.6 [11.6]) was younger than in the comparison group (68.2 [12.7]; $P<0.001$). There was a nonsignificant ($P=0.068$) trend toward lower rates of CAD in the intervention group (14.2% and 22.2% for intervention and comparison groups, respectively). The prospective risks (ETGs) for each age group were similar. The intervention group had a higher proportion of morbidly obese patients than did the comparison group (12.7% vs. 4.8%, respectively; $P=0.009$).

In conducting analyses for the 3 age groups shown in Table 2, the greatest attention was given to the largest group of patients (older than 65 years of age), though the data are not shown. Among patients older than 65 years of age, the mean age was younger in the intervention group (72.3) than in the comparison group (75.6), and the comparison group had a higher proportion of patients older than 80 years of age. Also, among patients older than 65 years of age, the BMI, selected disease conditions, and ETGs were similar between the intervention and comparison groups. Because of the small number of patients in the other 2 age groups, results for these age groups are not presented in this report. However, these results are available from the primary author by request.

Primary and Secondary Outcomes

All Patients: Mean (SD) PPPY medical costs (excluding costs for prescription medications) declined by 15.1% ($755) in the intervention group, from $4,995 ($15,774) pre-intervention to $4,240 ($11,391) post-intervention, and increased by 39.7% ($1,435) in the comparison group, from $3,616 ($8,256) to $5,051 ($14,862; Table 3). Median 12-month costs increased in both study groups, from $1,045 to $1,411 in the intervention group and from $1,130 to $1,638 in the comparison group. The

TABLE 3 Cost Outcomes in the 12 Months Before and After Study Enrollment Date

Cost Outcomes	Intervention Group (n=127)		Comparison Group (n=216)		*P* Value[a]
Total medical cost[b]	**Median**	**Mean [SD]**	**Median**	**Mean [SD]**	
PPPY before	$1,045	$4,995 [$15,774]	$1,130	$3,616 [$8,256]	0.993[a]
PPPY after	$1,411	$4,240 [$11,391]	$1,638	$5,051 [$14,862]	0.213[a]
PPPY difference	$238	–$755 [$15,617]	$257	$1,435 [$15,710]	0.711[a]
Percent change		–15.1%		39.7%	
Inpatient cost					
PPPY before	$0	$2,090 [$12,983]	$0	$1,213 [$6,144]	0.751[a]
PPPY after	$0	$1,415 [$7,665]	$0	$1,434 [$6,904]	0.324[a]
PPPY difference	$0	–$675 [$156,965]	$0	$221 [$9,065]	0.452[a]
Percent change		–32.3%		18.2%	

[a] *M-W = Mann-Whitney U-test; the Mann-Whitney U-test for independent 2-sample groups was used when the continuous variables were not normally distributed.*

[b] *Total medical cost excluding outpatient pharmacy costs. Cost outliers were not removed from this analysis and ranged from a decrease of $1.8 million for 1 patient in the intervention group to an increase of $1.7 million for another patient in the comparison group and were attributable to hospitalizations for cancer treatments, congestive heart failure, and major surgeries, including 1 liver transplant.*

Cost = plan sponsor costs (gross allowable minus patient costs); PPPY = per patient per year.

intervention and comparison groups did not differ with respect to the study's primary outcome, change in PPPY medical cost ($P=0.711$).

Secondary outcomes are displayed in Table 4. Both before and after the intervention, intervention group patients had a lower average number of PCP visits than did comparison group patients. However, the between-group difference in the mean change in PCP visits from pre-intervention to post-intervention was not statistically significant ($P=0.914$). From the pre-intervention to the post-intervention periods, hospital admissions per 1,000 patients increased from 206.0 to 221.0 (7.3%) in the intervention group and from 121.0 to 204.0 (68.6%) in the comparison group, although the between-group difference in the amount of change from pre-intervention to post-intervention did not reach statistical significance ($P=0.329$). ER visits per 1,000 patients declined by 44.1% in the intervention group (from 127.0 to 71.0) and increased by 57.6% in the comparison group (from 144.0 to 227.0); the between-group difference in the change amounts approached statistical significance ($P=0.054$).

Prescription cost was compared at an aggregate level, with no statistical analyses available. The intervention group's prescription claims cost (insurance plan liability) increased by 17.4% (from $105,000 to $123,227), whereas the comparison group's prescription claims cost decreased by 10.1% (from $90,135 to $81,042).

Patients Older Than 65 Years of Age: For patients older than 65 years of age, study groups did not significantly differ with respect to the study's primary outcome, change from pre-intervention to post-intervention in medical costs (data not shown). However, the intervention group's average PPPY cost increased 29.7%, whereas the comparison group's cost increased 65.8% from before to after the intervention. ER visits decreased by 1.6% in the intervention group and increased by 60.4% in the comparison group.

Clinical Pharmacist Interventions: The clinical pharmacist made 271 recommendations to the intervention group with an average of 2.1 recommendations per patient versus 286 concealed recommendations for patients in the comparison group with an average of 1.3 per patient. In the intervention group, 189 (69.7%) of the recommendations were accepted, whereas 47 (16.4%) of the concealed recommendations were acted on by comparison group physicians. Thus, assuming that about 70% of the concealed (comparison group) recommendations were actionable (i.e., would have been acted upon by the comparison group physicians if the recommendations had been made and not concealed), comparison group physicians identified 47 of 200, or about 23.5%, of actionable opportunities on their own without the services of a clinical pharmacist.

Figure 2 shows broad categories of recommendations accepted in the intervention group resulting in more optimal care for those patients. Table 5 provides specific examples of recommendations within these broad categories. Intervention group patients were more than twice as likely as comparison group patients to have medication nonadherence issues addressed (85.7% vs. 40.0%, $P=0.032$), and 6 times as likely to have a medication prescribed that was indicated but not prescribed previously (72.6% vs. 11.5%, $P<0.001$). Among patients at risk for cardiovascular events, intervention group patients were more than 8 times as likely as comparison group patients to be started on daily aspirin (90.9% vs. 11.1%, $P<0.001$; data not shown in figure) and more than 7 times as likely to receive pneumonia vaccination as recommended by the Centers for Disease Control and Prevention (76.9% vs. 10.0%, $P<0.001$; data not shown in figure). Intervention group patients

TABLE 4 *Utilization Outcomes in the 12 Months Before and After Study Enrollment Date*

Utilization Outcomes	Intervention Group		Comparison Group		*P* Value[a]	Statistical Test
	(n=127)		(n=216)			
PCP visits	**Mean**	**SD**	**Mean**	**SD**		
PPPY before	4.5	4.2	5.7	6.3	0.027	M-W
PPPY after	5.3	4.2	6.3	4.3	0.029	M-W
Difference	0.9	3.2	0.6	5.4	0.914	M-W
Percent change	17.8%		10.5%			
SCP visits						
PPPY before	9.6	12.2	9.8	11.1	0.347	M-W
PPPY after	9.3	12.5	10.5	11.9	0.133	M-W
Difference	–0.3	9.5	0.7	12.5	0.774	M-W
Percent change	–3.1%		7.1%			
Hospital admissions per 1,000 patients[b]						
Before	206.0	1042.0	121.0	4140.0	0.753	M-W
After	221.0	1374.0	204.0	719.0	0.267	M-W
Difference	15.0	604.0	83.0	716.9	0.329	M-W
Percent change	7.3%		68.6%			
Emergency room visits per 1,000 patients						
Before	127.0	471.0	144.0	445.0	0.473	M-W
After	71.0	313.0	227.0	545.0	0.001	M-W
Difference	–56.0	524.1	83.0	596.5	0.054	M-W
Percent change	–44.1%		57.6%			
Hospital days[b]						
PPPY before	5.37	3.13	8.84	11.37	0.132	*t*-test
PPPY after	4.36	2.18	5.07	5.21	0.496	*t*-test
Difference	1.01	2.70	3.77	8.85	0.133	*t*-test
Percent change	–18.8%		–42.6%			

[a] *P values were determined from independent 2-sample t-tests for continuous variables; the Mann-Whitney U-test for independent 2-sample groups was used when the continuous variables were not normally distributed.*

[b] *Hospitalizations were identified by any claim with a valid diagnosis related group or a revenue code between 100 and 219 as long as the facility type was not a skilled nursing facility or nursing home.*

M-W = Mann-Whitney U-test; PCP = primary care physician; SCP = specialty care physician; t-test = Student's t-test for independent groups.

were 10 times as likely to be prescribed an optimal medication for their condition (60.0% vs. 5.9%, $P<0.001$) and more than 11 times as likely to be prescribed more cost effective therapies (72.1% vs. 6.5%, $P<0.001$).

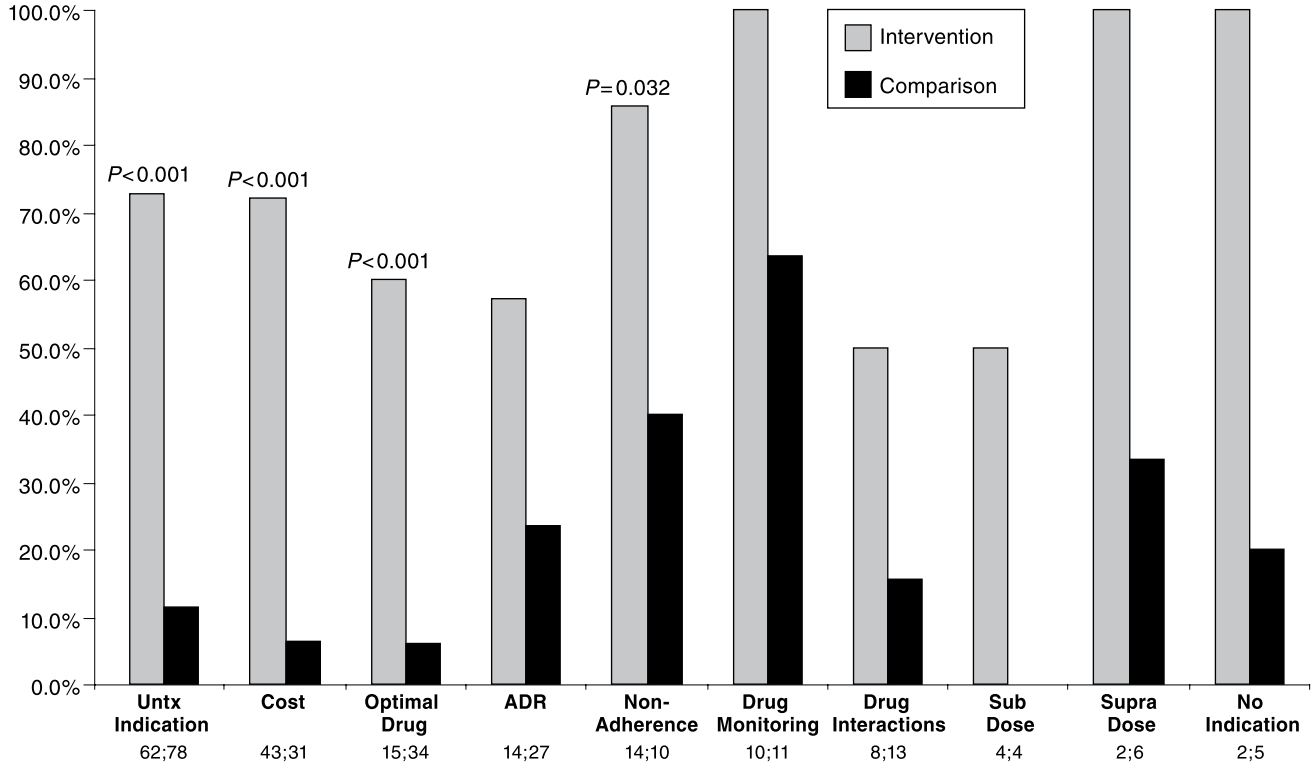
Discussion

This study demonstrated that embedding a clinical pharmacist to work within a primary care physician's office benefits patient care and that physicians readily adopt opportunities to optimize medication therapy when they are provided with clinical pharmacist recommendations. Although the difference in medical costs between the intervention group and the comparison group was not statistically significant, a nonsignificant trend suggests that the intervention may have had a positive effect on medical costs and warrants further investigation with a larger sample size. The trend in patients older than 65 years of age revealed that the average PPPY cost increased by 29.7% for the intervention group, compared with 65.8% for the comparison group, but again this difference was not statistically significant.

To our knowledge, the current study is the first to demonstrate in detail the types and frequency of opportunities to improve medication therapy by physicians who were not provided with clinical pharmacist interventions. This study showed that physicians appear to act on only about one-quarter of these opportunities when they are without the assistance of a clinical pharmacist.

The Impact of Managed Pharmaceutical Care Resource Utilization and Outcomes in Veterans Affairs Medical Centers (IMPROVE) study of an older high-risk population described similar increases in PPPY health care costs for both the intervention group (20.7%) and the comparison group (29.7%).[11] The PPPY cost in the IMPROVE study was calculated differently, in that it included the cost of the pharmacist cognitive services and medications and relied on estimated medical costs for the primary outcomes. Many other studies presenting medical health care cost outcomes have also been based on estimated costs,[8,12,14,20-22] whereas fewer studies used actual costs.[5,13,23,24]

FIGURE 2 Percentage of Optimal Care Opportunities Accomplished[a]



[a]*Numbers below the recommendation category represent the total number of recommendations for the intervention group and comparison group respectively. P values were determined from likelihood ratio chi-square test.*

ADR=adverse drug reaction; Sub=subtherapeutic; Supra=supratherapeutic; Untx=untreated.

We were unable to assess differences in drug cost between the intervention group and comparison group in the present study because study enrollment criteria did not require that patients had prescription drug coverage during any part of the study. The insurer did not grant access to individual prescription medication financial data because GRIPA was not at risk for medication costs. However, aggregated pharmacy claims cost data suggested an increased cost in the intervention group. This cost finding is similar to those of other similar studies in which the pharmacists had access to the patients' medical records and did not limit pharmacist services to one disease state. These studies showed a trend of slightly higher annual cost of prescription medication (5.7%-8.6%) in the intervention groups.[24-26] In the present study, despite the clinical pharmacist's ability to lower the cost of some medications, one of the most common recommendations was to start a new medication when it was indicated but previously overlooked by the physician. This pattern potentially increased medication cost. The intervention group was 6 times as likely as the comparison group to have a new medication started. Some medications initiated during the study were calcium and vitamin D supplements for the prevention or treatment of osteoporosis, or daily aspirin for patients with diabetes mellitus, which would not be expected to change the overall prescription medication costs. However, other medications were initiated to treat hyperlipidemia, provide ACE inhibitors for patients diagnosed with diabetes mellitus or CHF, or assure that CAD patients had fresh sublingual nitroglycerin.

Unique to this study was that outcomes for "usual care" with regard to medication management were documented and compared with outcomes for the intervention in a primary care practice. This design provided greater understanding of what might have potentially been accomplished for the patients receiving usual care, had they received the services of a clinical pharmacist. Figure 2 shows that many potential opportunities appeared to exist for physicians to optimize medication therapy. Hanlon et al. also recorded concealed recommendations for a randomized

TABLE 5 Specific Examples of Optimal Care Opportunities

Description of Optimum Care Intervention Type	Examples of Recommendations:
Untreated indication: Recommendation to start a medication for a medical condition that is currently untreated but considered a standard of care	• Statins for patients with coronary artery disease and low-density lipoprotein cholesterol above goal • Angiotensin-converting enzyme inhibitor for patient with diabetes and microalbuminuria
Cost: Recommendation for an equally effective but less expensive medication	• Use one-half tablet of a higher strength tablet of the same medication to achieve the dose (e.g., 80 mg of atorvastatin, one-half tablet daily, instead of 40 mg of atorvastatin daily). • Change prescription to 1 tablet of a higher strength instead of multiple tablets of lower strength to achieve the dose (e.g., 40 mg of atorvastatin twice daily to 80 mg of atorvastatin once daily).
Optimal drug: Recommendation to replace a current medication with a more appropriate medication based on patient characteristics, comorbidities, and pharmacokinetic or other characteristics of the medication	• Glipizide is preferred over glyburide in patient aged 71 years with chronic kidney disease. • Switch from a long-acting benzodiazepine (flurazepam) to a shorter-acting benzodiazepine such as oxazepam in elderly patient with insomnia.
Adverse drug reactions: Identification of a potential or actual adverse drug reaction	• For patient with prostate cancer on leuprolide acetate, consider calcium and vitamin D administration and bone density test because there is bone loss associated with administration of leuprolide. • Avoid pioglitazone or rosiglitazone in patient with stage 3 congestive heart failure.
Nonadherence: Evidence that the patient is not taking the medication as prescribed	• Address nonadherence with patients with osteoporosis who have stopped filling their prescription for alendronate. • Address nonadherence with a patient prescribed a statin whose cholesterol has increased dramatically yet not been addressed at previous appointments.
Drug monitoring: Identification of inappropriate medication monitoring and recommending appropriate medication monitoring	• Order a serum potassium determination for patient started on hydrochlorothiazide more than 1 year ago. • Order thyroid-stimulating hormone determination for patient with change in levothyroxine dose more than 3 months ago who does not have current blood work done.
Drug interactions: Identification of clinically relevant drug interactions or warning of potential drug interactions	• Assure that patient treated for hypothyroidism and starting on calcium supplement does not take calcium and levothyroxine together. • Limit acetaminophen dosing to less than 2 gm per day in patient on chronic carbamazepine, which can induce acetaminophen conversion to toxic metabolite.
Subtherapeutic dose: Recommendation for alternative dosing for someone on a subtherapeutic dose	• Increase angiotensin-converting enzyme inhibitor dose to goal dose per congestive heart failure standards. • Increase calcium and vitamin D supplement to achieve recommended total daily intake.
Supradose: Recommendation for alternative dosing for identification of a patient prescribed a dose that is inappropriately high or should ideally be titrated downward	• Starting dose of niacin extended-release tablets at 1,000 mg is unlikely to be tolerated by patient; suggest 500 mg at bedtime. • Patient taking conjugated estrogens, 0.9 mg daily—attempt titrating estrogen dose to minimum effective dose for postmenopausal symptoms.
No indication: Recommendation to discontinue a medication that appears to lack an indication	• Discontinue proton pump inhibitor in a patient recently discharged from hospital with new prescription for a proton pump inhibitor without a gastrointestinal condition. • Discontinue 1 mg folic acid daily supplement in a patient who discontinued oral methotrexate more than 1 year ago.

control group and found that, similar to the present study's results, 55.1% of intervention group and 19.8% of control group physicians enacted the clinical pharmacist's recommended changes.[27]

In the present study, between-group differences in the rates of optimized medication therapy may have contributed to the trend in lower hospital admissions and ER visits for patients provided with clinical pharmacist services. For example, medication nonadherence, leading to poor disease control, also can lead to increased hospitalizations and can be an important driver of overall medical costs.[28] Although findings of some studies call into question the relationship between improved medication adherence and clinical outcomes or health care costs,[26,29] other studies have found a beneficial effect of adherence on clinical outcomes.[20,30] Recognizing drug interactions and adverse drug reactions are part of the expertise of a clinical pharmacist and may have contributed to minimizing ER visits in the intervention group as evidenced in other settings.[20-22,25] For example, the comparison group in the present study included a woman older than 80 years of age who was prescribed a low-dose tertiary

amine tricyclic antidepressant for suspected urge incontinence. Within weeks of starting this central nervous system active medication with anticholinergic activity, she suffered falls, resulting in hospitalization for fracture.

Unlike much of the published literature about health care systems such as the VA, this study took place in a typical primary care practice that did not have a common electronic medical record platform. This study also involved a privately owned medical practice that was not associated with either a pharmacy or medical school, unlike many of the studies conducted in ambulatory care pharmacist practice environments within the United States.[1,2,9,21,31-33] The clinical pharmacist's approach used in the present study could potentially take place in any community, in any doctor's office, with little disruption to workflow. Space is a precious commodity in primary care practices; using this particular model would allow clinical pharmacists to work in any type of space and flex their schedule according to the needs of the medical practice.

In contrast to other studies, patients who may have needed the most help with medication therapy were not excluded.[1,3,30,33] The IMPROVE study excluded patients who had a psychiatric illness requiring mental health services, poor understanding of written and spoken English, visual impairment and residence far from the physician office, or no working telephone.[19] The only ability required for patients in the current study was ability to physically make it to a physician office visit; there were no other limits.

Limitations

First, the medical practices were selected, not randomized. Recruiting physicians to participate in the comparison group was a challenging task, as the comparison group physicians did not benefit from participating. The physicians in the present study's comparison group were likely willing to participate because they had an understanding of the valuable role of a clinical pharmacist; they had past experience working with clinical pharmacists who managed anticoagulation and provided monthly education sessions on medications within a health maintenance organization. Neither physicians in the same practice nor patients were randomized, which may have biased the results. However, it did prevent the contamination that could have occurred if a single physician had worked with both intervention and comparison patients. This contamination, although not ideal for a research study, is typically something that clinical pharmacists strive for within a medical practice. Ideally, after a clinical pharmacist makes a recommendation 2 or 3 times, the physician tends to apply this knowledge appropriately to the remainder of similar patients in his or her practice.

Second, there are major concerns about whether the patient cohorts were comparable, particularly because of the difference in age. The intervention group and comparison groups differed at baseline; of patients with 12 months of pre-intervention eligibility, 25.9% of intervention and 45.3% of comparison patients were aged 66 years or older. The percentages of study patients excluded from the final analysis for not having 12 months of continuous insurance eligibility following the date of study enrollment were similar in the intervention group (30 of 159 patients or 18.9%) and the comparison group (71 of 290 patients or 24.5%). However, just 15.6% of the excluded patients in the intervention group were aged 65 years or younger, compared with 66.2% in the comparison group. This pattern appeared to be a result of an insurance change to a self-insured product made by 1 large employer in Rochester during this study, thus removing its participants from the capitated population. The employer change excluded so many younger patients in the comparison group that the difference in mean age between the 2 groups became even larger.

Third, we made an a priori decision to exclude all patients that did not have 12 months of continuous insurance eligibility after study enrollment; thus it is unknown how the clinical pharmacist interventions affected those patients that subsequently either died or disenrolled from the insurance plan. Fourth, the medical cost data contained some outlier cases that were not removed from our study sample because of our a priori decision to retain all eligible cases for final analysis. There were no patients with trauma or motor vehicle accidents, but a very small number of patients in both the intervention and comparison groups had extreme changes in 12-month medical costs; these changes ranged from a decrease of $1.8 million for 1 patient in the intervention group to an increase of $1.7 million for another patient in the comparison group. These charges were attributable to hospitalizations for cancer treatments, congestive heart failure, and major surgeries including 1 liver transplant.

Fifth, the general application of the study findings could be affected by several factors. The 69.7% acceptance rate of recommendations by physicians was higher than in many published outpatient studies.[23,24,26,34] This outcome may have been attributable to the use of only 1 person, the clinical pharmacist who performed the intervention, to determine the acceptance rate in each of the 2 study groups. However, the relationships built between the clinical pharmacist and physicians in the intervention group over the 12 months probably played a role in the success of the intervention as demonstrated in other studies in which authors surmised that interpersonal relationships between the pharmacist and physicians contributed to improved outcomes.[2,36] Although the present study did not measure whether acceptance of recommendations resulted in resolution of the identified problems, the acceptances did reflect positive care decisions moving in the direction of resolution. The IMPROVE study authors stated that 69% of their recommendations were resolved, but when they removed the interventions performed directly by the pharmacist (without needing physician approval), their resolution rate declined to 57%.[19]

Sixth, the study may have underestimated the benefits of the clinical pharmacist because one of the comparison group physicians also was a member of a pharmacy and therapeutics committee for another large insurer in Rochester, New York, and was acutely aware of medication related problems and money-saving opportunities. The average number of recommendations per patient in the intervention group versus the comparison group (2.1 vs. 1.3, respectively) might also have contributed to study findings. Lastly, the inclusion criteria for this study were rather broad. As a result of our findings, we have narrowed the criteria for consultation, limiting our target population to the most high-risk patients with multiple comorbidities.

Conclusion

A clinical pharmacist can promote optimal medication therapy in outpatients by working with primary care physicians within their office practices. Although the medical (excluding pharmacy) costs of the intervention and comparison groups did not differ significantly, a nonsignificant trend suggests that the intervention may have had a positive effect on medical costs and warrants further investigation with a larger sample size.

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