Effects of Multidisciplinary Case Management in Patients with Chronic Renal Insufficiency*

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PURPOSE: Though case management has been recommended to improve the outcomes of patients with costly or morbid conditions, it has seldom been studied in controlled trials. We performed a randomized, controlled clinical trial of an intensive, multidisciplinary case management program for patients with chronic renal insufficiency and followed patients for 5 years.

PATIENTS AND METHODS: We enrolled 437 primary-care patients (73% of those eligible) with chronic renal insufficiency (estimated creatinine clearance consistently <50 mL/min with the last serum creatinine level >1.4 mg/dL) who were attending an urban academic general internal medicine practice. The intensive case management, administered during the first 2 years after enrollment, consisted of mandatory repeated consultations in a nephrology case management clinic staffed by two nephrologists, a renal nurse, a renal dietitian, and a social worker. Control patients received usual care. Primary outcome measurements included serum creatinine level, estimated creatinine clearance, health services use, and mortality in the 5 years after enrollment. Secondary measures included use of renal sparing and potentially nephrotoxic drugs.

RESULTS: There were no differences in renal function, health services use, or mortality in the first, second, or third through fifth years after enrollment. There were significantly more outpatient visits among intervention patients, mainly because of the added visits to the nephrology case management clinic. There were also no significant differences in the use of renal sparing or selected potentially nephrotoxic drugs. The annual direct costs of the intervention were $89,355 ($484 per intervention patient).

CONCLUSION: This intensive, multidisciplinary case-management intervention had no effect on the outcomes of care among primary-care patients with established chronic renal insufficiency. Such expensive and intrusive interventions, despite representing state-of-the-art care, should be tested prospectively before being widely introduced into practice. **Am J Med. 1998;105:464–471.** ©1998 by Excerpta Medica, Inc.

Case management has come into vogue in recent years as a method for assuring high quality yet cost-effective health care. It seems logical to focus expertise and resources in a coordinated way on patients with selected costly or morbid conditions. Yet the few published studies of the effectiveness or cost-effectiveness of case-management interventions have had inconsistent results (1–10).

Chronic renal insufficiency is both morbid (11–13) and costly (14–16). The yearly US budget for treating end-stage renal disease approaches that of the National Institutes of Health (17). Once a decline in renal function has been noted, it usually proceeds along an inexorable downward course. Reducing intake of protein (18–21) and fat (22), and controlling blood pressure (21,23) and acid-base balance (24), have shown promise for halting decline in renal function. However, their effects in humans have been disappointing. Encouraging laboratory studies (25) and carefully controlled clinical trials (26–29) have suggested that angiotensin-converting-enzyme inhibitors are renal protective.

To maximize the chance of slowing the decline of renal function in patients with chronic renal insufficiency, we developed a comprehensive, multidisciplinary program for managing these patients. We then performed a randomized, controlled trial of this intervention among a sample of inner-city patients. The goals of the intervention were to stabilize renal function and control costs by maximizing the use of renal-protective drug and dietary therapy, minimizing exposure to nephrotoxic drugs (30,31), closely monitoring patients for declines in renal function and intervening quickly when they occurred, and overcoming logistic and financial barriers to obtaining appropriate care.

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METHODS

Study Site and Subjects

This study was approved by the Indiana University Institutional Review Board. Patients were recruited from the general medicine practice of the Regenstrief Health Center, a multispecialty outpatient facility affiliated with, and located adjacent to, Wishard Memorial Hospital, an urban public teaching hospital. The general medicine practice has been the site of many randomized trials of health services interventions in primary care (32–35). At the time of this study, it was divided into four identical practices, each of which met 8 half-days per week. More than 100 internal medicine residents and 40 faculty members practice in the general medicine practice in assigned half-day sessions. Since 1981, new physicians have been randomly assigned to available practice sessions (meaning those vacated by a departing housestaff or faculty member) while new patients have routinely been given the first available appointment to any physician. Repeated analyses have failed to demonstrate systematic differences between the sessions' physicians or patients (33–35). Therefore, random assignment by practice or session randomly assigns patients and their primary-care physicians.

To be eligible for this study, patients must have had all of the following: (1) primary care in the general medicine practice with at least one physician visit in the past year, (2) two serum creatinine levels at least 6 months apart with estimated creatinine clearances of $<$50 mL per minute at both times, calculated using the Cockroft and Gault equation corrected for body surface area (36), and (3) most recent serum creatinine concentration before enrollment $>$1.4 mg/dL. We chose these criteria to assure that the patients had chronic renal insufficiency. Patients were excluded if they were living in institutions (nursing homes or prisons) or could not communicate with the research assistants, either because of a sensory or neurologic deficit or because they could not speak and understand English.

Subject Enrollment

Once a week, we used the computerized Regenstrief Medical Record System (37) to identify eligible patients from among all patients with general medicine practice appointments. When eligible patients kept scheduled visits, they were approached in the waiting room by a research assistant who explained the study and invited the patient to participate. Those who agreed to participate signed an informed consent statement, after which the research assistant scheduled an in-home interview to occur within the following 2 weeks. During this interview, a trained interviewer took a full medical history that included an extensive review of the patient's medications and medication compliance, the latter using a validated instrument (38). They also administered the Sickness Impact Profile (39) to assess health status and quality of life, and the Patient Satisfaction Questionnaire (PSQ) (40). Results from these enrollment interviews have been published (13,41).

If an enrolled patient had serum creatinine and electrolyte levels recorded in his or her medical record in the 3 months before enrollment, these values were accepted as "enrollment" values. If no values were available, then blood was drawn in the general medicine practice by the research assistant and sent for a 12-test chemistry panel and serum electrolyte levels.

The Intervention

For this study, two of the four general medicine practice practices were randomly assigned to intervention status. Once enrolled, control patients were returned to the general medicine practice to receive primary care from their usual physicians. These physicians were free to refer patients to the regular renal clinic, located in the same multispecialty outpatient center.

After enrollment, intervention patients were scheduled to visit the nephrology case management clinic where they were evaluated by a faculty nephrologist (DWR) or a nephrology fellow (LEH), a renal nurse, a renal dietitian, and a social worker. The frequency of these nephrology case management clinic visits depended on the enrollment serum creatinine level: once every 6 months if it was $\leq$3 mg/dL, once every 4 months if it was $>$3 and $\leq$4 mg/dL, and once every 3 months if it was $>$4 mg/dL.

Intervention patients received a comprehensive program (Table 1). In the case management clinic, the nephrologists used the in-home interview data and printouts from the Regenstrief Medical Record System to determine whether the patients were taking potentially nephrotoxic drugs (eg, nonsteroidal anti-inflammatory drugs [30,42]) and potentially renal-sparing drugs (specifically converting-enzyme inhibitors or calcium channel blockers). The nephrologists focused heavily on medication compliance, reinforcing this behavior in patients while reconfiguring patients' often complex outpatient drug regimens to enhance compliance. The nephrologists also identified any aspects of preventive care (eg, visits to the ophthalmology clinic for patients with diabetes or aspirin use among patients with cardiac risk factors) for which the patients were eligible but had not received.

The renal nurse also stressed medication compliance in addition to helping patients overcome behavioral and logistic barriers to optimal care. She also taught self-help actions from which the patient might benefit. The renal dietitian took a detailed dietary history and prescribed a low protein, low potassium renal diet that was individualized to enhance compliance. Finally, the social worker took an in-depth social and financial history, paying particular attention to barriers to receiving care. Most importantly, she initiated enrollment of patients in those benefit programs for which they were eligible.

Table 1. The Nephrology Case Management Intervention

Intervention Component	Mechanism	References
Increase use of angiotensin-converting enzyme inhibitors	Review of drug list Letter to primary care provider; direct intervention by nephrologist	26–28
Improve blood pressure control	Medication review by nephrologist; compliance assessment and education by study nurse Letter to primary care provider; direct intervention by nephrologist	21,23
Decrease use of nephrotoxic drugs	Review of drug list; surveillance of patients admitted to the hospital or visiting the emergency room Letter to primary care provider	30,41
Decrease protein intake	Dietary counseling by renal dietitian	18–21
Decrease barriers to care	Social service interview Direct intervention by social worker; letter to primary-care provider	

After every nephrology case management clinic visit, the study nephrologists wrote a standardized letter to the patient's primary care physician that included a summary of all actions taken, suggestions for further care, and a summary of the clinic visit. A copy of the letter was also placed in the shared outpatient chart. If one of the study nephrologists judged that changes in intervention patients' care could not wait for the next scheduled primary care visit (eg, the blood pressure was very poorly controlled), he or she provided the needed care. All such drug changes were included in patients' outpatient drug list that is maintained by the Regenstrief pharmacy module (42) that prints a list of all active drugs before each general medicine practice visit. Prior studies and internal audits have shown that 95% of all general medicine practice patients receive all of their outpatient medications from the Regenstrief pharmacy.

The nurses in the nephrology case management clinic also received daily printouts from the Regenstrief Medical Record System that identified intervention patients who had visited the emergency department or been hospitalized. For patients visiting the emergency department, the study nurses reviewed patients' paper and electronic records and recorded the reasons for all visits and all nephrotoxic drugs that had been prescribed. These data were discussed with the study nephrologists who intervened directly with the patient if the immediate potential consequences were severe. Otherwise, they communicated their thoughts in a letter sent directly to the patient's primary care physician. A copy of each letter was placed in the patient's general medicine practice chart.

If an intervention patient was admitted to the hospital, a study nurse visited the patient and reviewed the inpatient chart. She noted the reasons for the hospitalization and whether the patient was being treated with potentially nephrotoxic drugs. A study nephrologist reviewed each report and, if necessary, contacted the inpatient physicians, offering advice on alternative drugs and appropriate dosing and monitoring of selected nephrotoxic drugs (eg, aminoglycosides).

Finally, a weekly program extracted from the Regenstrief Medical Record System all serum creatinine levels recorded from any care site for all intervention patients. If any value was increased by more than 0.2 mg/dL from either the enrollment value or the most recent value, the study nurse reviewed the paper and electronic medical records. She recorded all appropriate data and reported them to one of the study nephrologists who acted at his or her discretion.

Data Collection and Analysis

The intervention (or control) period lasted 2 years from each patient's enrollment date. The following data were extracted from the Regenstrief Medical Record System for these 2 years: laboratory test results, vital signs, drug therapy, clinical activity (outpatient and emergency department visits and hospitalizations), and diagnoses recorded at any clinical encounter. To assess any delayed or longer-term effects of the intervention, we also extracted data from the Regenstrief Medical Record System for postenrollment years 3 through 5. For drug therapy, a patient was considered to be taking a drug if it was ever prescribed in each of the three postenrollment periods (year 1, year 2, and years 3 through 5). To identify subjects who died, we used death certificate information supplied by the Indiana State Department of Health (which were also available through 1995), hospital death summaries, discharge status reports, and autopsy reports.

The unit of intervention and analysis was the patient. We compared categorical variables and continuous variables between intervention and control patients using chi-square and *t* tests. Before enrolling the first patient, we identified the following primary outcome variables: (1) renal functional decline (using the last serum creatinine level and calculated creatinine clearance [36] obtained in each postenrollment period), and (2) healthcare utilization (number of outpatient, emergency department, and inpatient visits in each postenrollment period). We performed all analyses by intention-to-treat. If no serum creatinine level were available in a year, we

assumed that it had not changed from the most recent value, which was carried forward.

We used Cox proportional hazards models (43) to assess the effect of the intervention on mortality while adjusting for age, sex, race, baseline serum creatinine level, and any baseline laboratory values, vital signs, and diagnoses whose distributions at enrollment were significantly different between intervention and control patients. For our three primary outcomes, we adjusted for multiple hypothesis testing by Bonferroni's method (44). This resulted in our accepting a two-tailed P value of <0.017 as significant. For the many secondary analyses, we corrected for multiple hypothesis testing by lowering the significance level from a P value of 0.05 to 0.005. Given the degree of renal dysfunction among control patients, we had 80% power to detect a difference of 0.7 mg/dL (26%) in serum creatinine, a difference of 6 mL/min (18%) in creatinine clearance, a difference of 0.6 days (46%) in hospitalizations, and a difference of 12% (35% relative reduction) in mortality between the two groups (all with a two-tailed alpha of 0.05).

We estimated the cost of the intervention by assuming that attending the weekly intervention clinic, writing letters to primary care physicians, and overseeing the renal nurse required 10% time of each of our study nephrologists. We also assumed that the program required a half-time renal nurse and 10% of a renal dietitian and a social worker. We calculated personnel costs by using the lowest salary in 1992 for an entry-level position in each category and adding each person's standard benefit package. We also assumed that the average patient would require 2.5 visits to the nephrology case management clinic each year and included only the facility charge for each visit. We did not include the costs of any laboratory tests performed or drugs prescribed by the case management clinic.

RESULTS

Enrollment began in June 1989 and continued for 2 years. During this time, 597 eligible patients kept general medicine practice appointments. Of these, 437 (73%) agreed to participate in the study and completed in-home interviews. Of the 160 patients not enrolled, 154 (96%) refused participation; for the remaining six (4%) the patient's physician deemed the study inappropriate for the patient. Of the 437 enrolled patients, 206 (47%) received primary care in the two general medicine practice practices randomly assigned to intervention status while 231 (53%) received care in the two control practices. Other than intervention patients having a significantly higher pulse rate and shorter stature, the two groups were quite similar (Table 2). There were no baseline differences in renal function, comorbid diagnoses, drug therapy, or laboratory test results. Renal insufficiency was in the mild-to-moderate range.

During follow-up years 1, 2, and 3 through 5, there were no differences between intervention and control patients in change in renal function, whether assessed using last serum creatinine level or calculated creatinine clearance (Table 3). Intervention patients had more outpatient visits in all postenrollment years, most of which were explained by their visits to the nephrology case management clinic. However, intervention patients also visited the ophthalmology clinic more often than control patients in the first 2 intervention years. There were no differences between intervention and control patients in emergency department visits, hospitalizations, or total inpatient days in years 1, 2, or 3 through 5.

Intervention patients had slightly less use of clonidine in the first year and potassium supplements in the second year, and slightly more use of calcium channel blockers in year 2 and years 3 through 5. Intervention patients were more often prescribed beta blockers during the second study year. In addition, there was a trend toward lower mean systolic blood pressure among intervention patients in years 3 to 5. However, none of these differences reached the predetermined level of significance (P <0.005) for these secondary outcome measures.

We repeated these analyses among the 28 intervention patients (14%) and 21 control patients (9%) who had enrollment serum creatinine levels of 3 mg/dL or greater and found no substantial differences in the results. Because patients receiving care in this practice received chronic dialysis at facilities the data of which were not readily accessible, we were unable to determine how many patients in each group required dialysis. However, there were no differences in either patients' maximum serum creatinine level or in the number of patients with levels >8 mg/dL.

By the end of 1995, 59 (29%) of the intervention patients and 77 (33%) of the control patients had died. Adjusting for age, sex, race, enrollment serum creatinine level, plus height and pulse at the enrollment visit, assignment to the intervention group offered no significant survival advantage (hazard ratio 0.90, 95% confidence interval 0.71–1.14, $P = 0.36$).

The estimated minimum yearly cost of the case-management program was $89,355 ($484 per intervention patient).

DISCUSSION

This intensive and expensive multidisciplinary case-management intervention had no important effects on renal dysfunction, health-care utilization, or mortality among a cohort of urban patients with established chronic renal insufficiency. Moreover, there were few demonstrable effects of the intervention on the management of intervention patients despite frequent and direct

Table 2. Characteristics of Study Patients at the Time of Enrollment*

Patient Characteristic	Intervention Patients (n = 206)	Control Patients (n = 231)	*P* Value
Age (years)	68 ± 11	69 ± 11	0.81
Female sex	68%	64%	0.32
African-American	81%	80%	0.79
Vital signs			
Weight (kg)	79 ± 19	78 ± 20	0.78
Pulse (beats/min)	80 ± 7	78 ± 9	<0.001
Systolic blood pressure (mm Hg)	143 ± 23	145 ± 26	0.31
Diastolic blood pressure (mm Hg)	83 ± 13	82 ± 12	0.67
Height (cm)	163 ± 10	165 ± 10	.003
Laboratory test results			
Serum creatinine level (mg/dL)	2.1 ± 0.8	2.1 ± 0.9	0.53
Creatinine clearance (mL/min)†	34 ± 10	34 ± 10	0.67
Serum albumin level (g/dL)	3.8 ± 0.4	3.8 ± 0.5	0.24
Blood glucose level (mg/dL)	130 ± 67	141 ± 81	0.12
Comorbid diagnoses			
Hypertension	98%	99%	0.21
Prior urinary tract infection	94%	96%	0.35
Diabetes mellitus	45%	42%	0.58
Ischemic heart disease	44%	51%	0.18
Heart failure	38%	42%	0.39
Osteoarthritis	38%	39%	0.97
Prior myocardial infarction	35%	39%	0.34
Prior stroke	19%	21%	0.55
Active drug therapy			
Angiotensin-converting-enzyme inhibitor	44%	48%	0.27
Calcium channel blocker	37%	37%	0.97
Thiazide diuretic	58%	52%	0.22
Loop diuretic	39%	38%	0.59
Potassium supplements	28%	25%	0.47
Oral hypoglycemic drug	15%	13%	0.54
Insulin	27%	26%	0.78
Cimetidine	30%	25%	0.25
Nonsteroidal anti-inflammatory drug	60%	63%	0.51
Sulfa-containing antibiotic	15%	21%	0.12
Clinical activity			
Previous general medicine practice visits	20 ± 11	20 ± 10	0.52
Previous emergency department visits	7 ± 8	7 ± 7	0.69
Previous hospitalizations	2.7 ± 2.7	3.1 ± 3.8	0.26
Previous renal clinic visits	0.4 ± 1.5	0.4 ± 1.5	0.87

* Continuous variables are presented as mean ± standard deviation.

† Calculated using the Cockroft and Gault equation corrected for body surface area (36) using the last serum creatinine available during the observation period.

communications between the study nephrologists and the patients' primary care physicians. However, a substantial proportion of patients at enrollment were already taking the drugs that were the focus of much of the nephrologists' recommendations: almost half of the control patients were taking angiotensin-converting-enzyme inhibitors. In addition, blood pressure control among control patients at enrollment was good. Still, more than a third of enrolled patients were not taking one of the target renal-sparing drugs, and more than half were taking a potentially nephrotoxic drug. Thus, there was room for improvement.

The lack of improvement, even in intermediate outcomes, may have been in part because the intervention relied on action by the patient's primary care provider. Though treatment recommendations were communicated directly in letters to providers that were also placed in the patient's outpatient chart, success still depended on the provider reviewing the letter at the time of a patient visit. Competing demands for time in the primary care

Table 3. Study Outcomes during Follow-up*

Patient Characteristic	Intervention Patients	Control Patients	*P* Value
First year after enrollment			
N of patients at beginning of period	206	230	
Weight (kg)	78 ± 19	78 ± 18	0.84
Systolic blood pressure (mm Hg)	144 ± 18	144 ± 20	0.86
Diastolic blood pressure (mm Hg)	82 ± 10	83 ± 10	0.71
Last serum creatinine level (mg/dL)	2.5 ± 2.1	2.3 ± 1.7	0.34
Creatinine clearance (mL/min)†	33 ± 14	34 ± 13	0.57
Angiotensin-converting-enzyme inhibitor	42%	45%	0.56
Calcium channel blocker	47%	45%	0.73
Cimetidine	21%	21%	0.93
Nonsteroidal anti-inflammatory drug	62%	58%	0.44
Sulfa-containing antibiotic	19%	19%	0.98
General medicine practice visits	4.8 ± 3.3	4.4 ± 3.1	0.22
Ophthalmology clinic visits	1.2 ± 3.1	0.6 ± 1.3	0.01
All outpatient clinic visits	12.7 ± 8.7	10.0 ± 8.3	0.001
Emergency department visits	1.4 ± 2.0	1.6 ± 2.7	0.40
Hospitalizations	0.6 ± 1.1	0.7 ± 1.2	0.63
Cumulative mortality at year 1	9 (4%)	19 (8%)	0.10
Second year after enrollment			
N of patients at beginning of period	197	212	
Weight (kg)	78 ± 19	78 ± 19	0.88
Systolic blood pressure (mm Hg)	143 ± 17	143 ± 18	0.68
Diastolic blood pressure (mm Hg)	80 ± 9	81 ± 9	0.75
Last serum creatinine level (mg/dL)	2.4 ± 1.7	2.2 ± 1.5	0.35
Creatinine clearance (mL/min)†	34 ± 14	34 ± 13	0.93
Calcium channel blocker	44%	35%	0.06
Cimetidine	17%	16%	0.69
Nonsteroidal anti-inflammatory drug	52%	50%	0.72
Sulfa-containing antibiotic	17%	19%	0.67
General medicine practice visits	3.9 ± 3.5	3.5 ± 2.9	0.10
Ophthalmology clinic visits	1.1 ± 2.6	0.5 ± 1.6	0.009
All outpatient clinic visits	10.6 ± 9.2	8.1 ± 6.8	<0.001
Emergency department visits	1.1 ± 2.1	1.3 ± 2.2	0.51
Hospitalizations	0.5 ± 1.0	0.5 ± 1.0	1.0
Cumulative mortality at year 2	21 (10%)	35 (15%)	0.12
Third through fifth years after enrollment			
N of patients at beginning of period	185	196	
Weight (kgs)	76 ± 20	75 ± 18	0.65
Systolic blood pressure (mm Hg)	142 ± 17	145 ± 17	0.22
Diastolic blood pressure (mm Hg)	79 ± 8	78 ± 9	0.32
Last serum creatinine level (mg/dL)	3.0 ± 2.6	2.7 ± 2.5	0.31
Creatinine clearance (mL/min)†	30 ± 16	34 ± 24	0.10
Angiotensin-converting-enzyme inhibitor	36%	33%	0.40
Calcium channel blocker	49%	35%	0.003
Cimetidine	17%	13%	0.24
Nonsteroidal anti-inflammatory drug	50%	44%	0.19
Sulfa-containing antibiotic	27%	23%	0.31
General medicine practice visits	8.0 ± 7.4	7.6 ± 8.0	0.31
Ophthalmology clinic visits	1.8 ± 3.8	1.2 ± 3.1	0.07
All outpatient clinic visits	26.0 ± 28	18 ± 19	<0.001
Emergency department visits	2.6 ± 3.5	2.8 ± 5.0	0.52
Hospitalizations	1.3 ± 1.8	1.3 ± 2.1	0.94
Cumulative mortality at year 5	59 (29%)	77 (33%)	0.29

* Continuous variables are presented as mean ± standard deviation.

† Calculated using the Cockroft and Gault equation corrected for body surface area (36) using the last serum creatinine level during the observation period.

practice, especially given a patient's other medical problems, may have decreased the likelihood of the provider noting and implementing the recommendations during primary care visits. This type of intervention might therefore be enhanced by a mechanism designed to bring recommendations to the attention of physicians at the time treatment decisions are made.

Another reason why this intensive case-management intervention failed may be that the targeted level of renal insufficiency was too mild to expect a measurable decline in 5 years. In addition, there could have been regression to the mean of renal function among intervention and control patients (45), reducing the number of patients who reached our preset endpoint. Patients most likely to exhibit a decline in renal function may have died due to comorbid conditions, leaving behind relatively healthy survivors for analysis. We chose to implement this program in an inner-city practice caring predominantly for African-American patients because of the large burden of hypertension, diabetes, and end-stage renal disease in those patients. These patients were high utilizers of health care. Yet our intensive outpatient intervention was ineffective in reducing their use of health services. In fact, intervention patients had significantly more outpatient visits, mostly due to their visits to the intervention clinic.

There are other relevant outcomes that we did not address, such as whether intervention patients were referred for intravascular access in a more timely manner, or whether there was improved management of anemia and secondary hyperparathyroidism. Nevertheless, we conclude that identifying patients with renal dysfunction and intervening with a multidisciplinary case-management team had no effects on renal function, mortality, or health-care utilization and cannot be recommended from the standpoint of the patient, the provider, or the payer. Our results add to the voices of caution suggesting that intensive case-management interventions may not have their expected results. Case-management programs should be tested with randomized trials where possible, or at least by well-designed time-series studies (46). Without such studies, increasingly scarce health-care resources may be spent on interventions that seem logical but have little or no effect on the targeted outcomes. When it comes to intensive, resource-consuming case-management interventions such as the one we studied here, a good dose of skepticism is healthy.

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