Predicting Costs Of Care In Chronic Kidney Disease: The Role Of Comorbid Conditions

D Smith, G Nichols, C Gullion, E Johnson, D Keith

Citation

D Smith, G Nichols, C Gullion, E Johnson, D Keith. *Predicting Costs Of Care In Chronic Kidney Disease: The Role Of Comorbid Conditions*. The Internet Journal of Nephrology. 2006 Volume 4 Number 1.

Abstract

We examined the relationship between cost of care, CKD and comorbidities (proteinuria, coronary artery disease, congestive heart failure (CHF), diabetes mellitus, hypertension, anemia, and hyperlipidemia. Cases were adults with two estimated GFR <90ml/min/1.72m^2 as follows; 60-89 (GFR 2); 30-59 (GFR 3); and 15-29 (GFR 4). Controls were matched on age and gender. Subjects were followed for up to 66 months and costs were annualized and weighted by months of observation. Linear regression was used to predict costs as a function of disease category, controlling for comorbidities. We found that total costs over the follow-up period for those with CKD were almost $5,000 higher than controls for GFR 4, and almost $2,600 higher in GFR 2 and 3. Anemia and congestive heart failure independently raised total costs by almost $5,700, but the effect of anemia is greatest at earlier stages of CKD.

Work on this paper was done at the Center for Health Research Kaiser Permanente, Northwest, Portland Oregon.

The source of support was received from Amgen

INTRODUCTION

Approximately 20 million Americans are thought to have chronic kidney disease (CKD).([1]) The age, gender, and race adjusted incidence of end stage renal disease (ESRD) has increased from 293 per million to 334 per million population over the period from 1996 to 2001, a 14% increase,([2]) suggesting that CKD is growing public health concern. Furthermore, patients with CKD at any stage are much more likely to die than to progress to transplantation or dialysis, and are also more likely to die than their age and gender matched controls.([3])

The economic consequences of CKD have not been well enumerated. One previous study suggested that patients with CKD have cumulative expenditures over a 5.5 year period that are more than double their age and gender matched controls.([4]) While kidney disease costs have been analyzed in relation to diabetes ([5],[6]) and for the time period immediately prior to dialysis,([7]) little work has focused on the contribution of comorbidities in the setting of CKD. The economic implications of renal dysfunction extend beyond health care resource use. There are, for example, profound implications for quality of life and productivity losses. Data on direct health care resource use and indirect implications are necessary in order to perform economic evaluations of both new and currently used interventions in the treatment of renal disease.

The cost of care for patients with certain comorbidities (eg cardiovascular disease and diabetes) is disproportionately greater when patients also have CKD,([4]) suggesting an interaction between CKD and certain comorbidities. Further research into the complex relationship of CKD and attendant comorbid conditions may help to guide disease management to help achieve better outcomes. This study was undertaken to shed further light on the relationship between total cost of medical care and comorbid conditions for those with CKD.

METHODS

Kaiser Permanente Northwest (KPNW) is a not-for-profit group-model HMO that provides comprehensive health care to approximately 450,000 individuals in the Northwest area of the United States. KPNW has linked electronic databases that include patient level information on hospitalizations, outpatient visits, laboratory results and pharmacy utilization that were used in this research. This study was approved by the Research Subjects Protection Office of KPNW.

To establish a cohort with chronic disease, cases included all members of KPNW with a GFR greater than 15 ml/min/1.73m$^{2>}$ and less than 90 ml/min/1.73m$^{2>}$ in 1996

(the index GFR), followed by a second GFR below 90 ml/min/1.73m$^{2>}$ at the next serum creatinine measurement that occurred at least 90 days later. The Modification Diet in Renal Disease Study (MDRD) formula([8]) was used to estimate GFR. We did not have access to data on patient's race (a variable included in the MDRD formula), so our method underestimates GFR by 21% for blacks. However, the impact of the bias is likely to be small given that blacks make up less than 5% of KPNW's population.

A total of 27,998 members were identified as cases of CKD. We categorized these members into three levels of baseline kidney function: GFR 15-29 (n=777); GFR 30-59 (n=11,278); and GFR 60-89 (n=15,943) had GFR 60-89 at baseline. We then selected an age and gender matched comparison group (1 person per case) from enrollees who did not meet the criteria for inclusion as a case and were eligible for at least 90 days from the index GFR of their matched case. Subjects were followed for 1 year from the date of the index GFR, or until death, disenrollment from the health plan, or advancement to ESRD as defined by dialysis, transplant, or GFR less than 15 ml/min/1.73m$^{2>}$. Because identification of a patient with CKD required a serum creatinine measurement, cases were more potentially more likely to have had a resource utilization event (i.e., outpatient or inpatient visit) that led to the laboratory measurement, potentially creating an artificially high starting point for costs. In order to reduce this bias, we counted costs for the one-year period beginning 60 days after the index GFR.

COSTS OF CARE

The costing method used was developed and validated by economists at the Kaiser Permanente Center for Health Research.([9]) Standard costs for units of medical care (ie. office visits and direct hospital service components) are identified from aggregate departmental expenditures and administrative costs and other indirect and joint costs are allocated to units of direct costs. These standard unit costs are multiplied by utilization volume to obtain total costs. The pharmaceutical costs reported approximate retail costs in the local market. For care provided in non-KPNW facilities, we used as costs the amounts that KPNW actually paid to vendors for procedures, hospitalizations, and professional and related services. All costs were adjusted to reflect 2001 prices. KPNW's expenditures include essentially all the costs of acute inpatient care received by its members, nearly 100% of outpatient costs (fewer than 10% of members use an out-of-plan service in any given year), and nearly all pharmacy costs (fewer than 5% of prescriptions are filled outside the plan).

Categories of cost included prescriptions, outpatient visits, and inpatient stays. To isolate the cost impact of CKD, we identified 6 conditions that are known to be associated with kidney dysfunction.([10]) We identified four of these conditions using ICD-9-CM codes (see Appendix) that were present in the electronic medical record at baseline for coronary artery disease, congestive heart failure, diabetes mellitus, and hypertension.

Figure 1

Appendix

Comorbidity	ICD-9 CM Codes
Coronary Artery Disease	410.xx - 414.xx (excluding 414.10, 414.11, 414.19)
Congestive Heart Failure	428.0, 428.9, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 429.4A, 429.9B, 429.9A, 428.1
Hypertension	401.xx - 405.xx
Diabetes	250.xx

The other two comorbid conditions, anemia and proteinuria, were identified from the laboratory results database. Anemia was defined as a hemoglobin less than 12 G/dl. In order to minimize inclusion of anemia from non-renal causes, those with anemia were required to have a normal mean corpuscular volume (MCV). Proteinuria was defined as 1+ or greater protein on urinalysis within 6 months of the index GFR; people with a negative urinalysis or no urinalysis were considered to not have proteinuria. To minimize inclusion of individuals with elevated protein secondary to infection, we further required a leukocyte esterase of less than 10/ul on the same urinalysis.

STATISTICAL ANALYSIS

We conducted ordinary least squares (OLS) regression analysis using SAS PROC GLM (SAS version 6.12 and 8.2, Cary NC) to predict costs of care as a function of comorbidities, age and gender. Using OLS has been recommended in the face of skewed cost data,([11]) given a large dataset like the one used here.([12]) Costs were weighted by observation months and annualized. To assess effect modification, we examined two-way interactions with severity of CKD and comorbid conditions; the final model includes only significant ($p<0.05$) interactions. Previous analyses have shown that patients with NKF K/DOQI stage 2 CKD have costs very similar to stage 3, perhaps because proteinuria is required for stage 2 disease, but not for stage 3. To test this, we plotted GFR against cost for those with and without proteinuria.

RESULTS

As shown in Table 1, prevalence of all comorbidities was greatest in subjects with the poorest renal function (p<.001 for all comorbidities). Patients with poorer renal function were also more likely to be older and female (p<.001). Follow-up time over the one-year costing period (beginning 60 days post-index) was 11.2 months for those with baseline GFR 15-29, 11.8 months for those with GFR 30-59 and 60-89, and 11.0 months for comparison subjects. Average total cost (Table 2) increased with decreasing renal function (p<.001). This table also reveals that, as anticipated, the cost data were skewed to the right.

Figure 2

Table 1: Baseline Characteristics

	GFR Category			Comparison
	15 – 29	30 - 59	60 - 89	Group
N	777	11,278	15,943	27,998
Average Age (yrs)	73.6	71.6	61.3	65.4
% male	35.9	37.8	45.2	41.9
Average Follow-up time (months)	11.5	11.9	11.9	11.9
Percent with:				
Proteinuria	27.0%	10.1%	10.9%	1.4%
Anemia	34.1%	10.3%	6.2%	3.0%
Coronary Artery Disease	25.1%	17.7%	9.3%	6.2%
Congestive Heart Failure	21.6%	9.6%	2.7%	1.8%
Diabetes Mellitus	28.4%	17.5%	14.1%	5.3%
Hypertension	52.9%	46.7%	30.1%	16.8%
Hyperlipidemia	14.7%	14.1%	13.3%	7.4%
Peripheral Vascular Disease	8.9%	4.4%	1.6%	1.3%

Figure 3

Table 2: Total Costs

	GFR Category			Comparison
	15 - 29	30 - 59	60 - 89	Group
Mean	$12,834	$7,614	$6,394	$3,111
(std dev)	($58,711)	($46,729)	($43,411)	($25,969)
Percentiles:				
1st	$482	$220	$83	$0
25th	$3,295	$1,821	$1,386	$497
Median	$6,815	$3,509	$2,853	$1,350
75th	$17,096	$7,653	$6,282	$2,970
99th	$110,717	$69,689	$62,182	$40,982

Costs differ very little between GFR 55 and 89, but then begin to steadily increase. Regression results indicating the relationship of total cost, renal function and comorbid conditions are shown in Table 3.

Figure 4

Table 3: Models of Annualized Total Costs (weighted)

	Without Interactions		With Interactions	
	Parameter		Parameter	
	Estimate	p value	Estimate	p value
Comparison Group (Intercept)	$619	0.0102	$541	0.0251
GFR 15 - 29	$4,777	0.0001	$5,729	0.0001
GFR 30 - 59	$2,591	0.0001	$3,146	0.0001
GFR 60 - 89	$2,568	0.0001	$2,732	0.0001
Age	$30	0.0001	$29	0.069
Male Gender	($182)	0.0498	($169)	0.0001
Proteinuria	$3,906	0.0001	$3,939	0.0001
Anemia	$5,366	0.0001	$5,827	0.0001
Coronary Artery Disease	$2,346	0.0001	$2,310	0.0001
Congestive Heart Failure	$5,219	0.0001	$5,189	0.0001
Diabetes Mellitus	$1,533	0.0001	$1,491	0.0001
Hypertension	$45	0.6788	$943	0.0001
Hyperlipidemia	($191)	0.2101	($206)	0.1763
Peripheral Vascular Disease	$4,064	0.0001	$2,206	0.0002
Smoking	$380	0.0016	$385	0.0014
Anemia x GFR 60-89			$977	0.068
Anemia x GFR 30-59			($1,604)	0.0021
Anemia x GFR 15-29			($3,951)	0.0001
DM x GFR 60-89			($385)	0.3138
DM x GFR 30-59			$279	0.4829
DM x GFR 15-29			$3,271	0.0004
HTN x GFR 60-89			($1,114)	0.0001
HTN x GFR 30-59			($1,660)	0.0001
HTN x GFR 15-29			($2,487)	0.0019
PVD x GFR 60-89			$2,355	0.0081
PVD x GFR 30-59			$2,408	0.0017
PVD x GFR 15-29			$5,398	0.0004
R^2			0.083	0.086

Two regressions are shown, 1 without interactions (simple model) and one showing significant two-way interactions for CKD severity and several comorbidities. In addition to CKD, anemia and CHF contribute the most to overall cost of care, followed by proteinuria and coronary artery disease. The interaction terms reveal that the relative effects of anemia and hypertension decrease with worsening renal function, while the relative effects of diabetes and peripheral vascular disease increase with worsening renal function. Coefficient contrasts on the full model indicate that costs for each stage and controls are significantly different ($p < 0.05$; data not shown).

There is a clear increase in cost for those with proteinuria across all levels of GFR, but it is less pronounced in more severe renal disease.

DISCUSSION

Our results show that health care costs are greater for patients with CKD than for age and gender matched control subjects even after adjustment for comorbidities commonly associated with CKD, and that the cost difference increases with worsening disease. Further, we found that cost impact of certain comorbid conditions depends on the severity of kidney disease.

Specifically, we found that patients with early chronic kidney disease consume approximately $2,200 more per year in medical care than their age- and sex-matched control patients without recognized kidney disease. Control patients without comorbidities consumed approximately $550 per year, while early chronic kidney disease patients without comorbidities consumed approximately $2,750 per year. That $2,200 difference was smaller than the crude (unadjusted) difference ($3,000) before controlling for comorbid conditions, which reflects the higher prevalence of these conditions among patients with chronic kidney disease. The crude cost estimates also overstate the impact of progressing from mild (GFR, 60 to 89) to intermediate (GFR, 30 to 59) chronic kidney disease: After adjustment for comorbid conditions, the apparent $1,200 difference between these cohorts was reduced to about $400. While the cost for the most severe disease group (GFR, 15-29) remained higher than the less severe disease after adjustment ($2,600) it was not as great as the differential suggested by the crude estimate ($5,500).

Of the comorbid conditions that we evaluated, anemia, congestive heart failure, and proteinuria were the strongest independent predictors of total medical costs. All other factors being equal, the cost of managing a patient with anemia was $5,800 higher than a patient without recognized anemia – and was stronger than the independent predictive effect of having late stage chronic kidney disease ($5,700). The estimate for the independent effect of congestive heart failure on cost was almost as high at $5,200. Several conditions, anemia, diabetes, hypertension and peripheral vascular disease, also modified the total cost by stage of chronic kidney disease. For example, the cost difference between stages of chronic kidney disease increased markedly depending on whether patients also had recognized anemia: patients with early stage chronic kidney disease and

recognized anemia were about $2,200 more expensive than their matched controls, while patients with late stage disease and recognized anemia were about $1,000 more expensive than their age and gender matched controls. Peripheral vascular disease emerged as an expensive predictor, adding $7,600 to those with the most severe disease and $4,500 for those with milder disease.

The finding that, even after adjustment for important comorbid conditions, costs are substantially increased in those with renal disease, suggests that kidney disease independently adds significant burden to those with an already complicated clinical picture. This is consistent with previous research that demonstrated an independent association between renal function and costs in a cohort with diabetes.([5]) It is also possible that poor renal function may be a marker for more severe manifestation of the comorbidities included in our multivariate models.

Previous research indicated that patients with stage 2 CKD have costs that are very similar to those in stage 3 CKD([4]); the current study provides some further explanation. In our data, patients with GFR 55-59, the least severe of stage 3 CKD, comprised the single largest proportion of that group (n=3,884 verses 2,689 for the next largest 5ml/min/1.73m$^{2>}$ GFR increment). Because the costs we report represent weighted averages of all members of a given stage, stage 3 costs were most heavily influenced by patients with the least severe disease. While a "cut-point" of GFR 60 may make clinical sense, our data suggest that from a cost standpoint, a cut-point of GFR 55 may better discriminate stages 2 and 3. Current NKF/KDOQI staging guidelines require proteinuria to be present for defining stage 2 (GFR 60-89) but not stage 3 (GFR 30-59). Not only did we find a substantial impact of proteinuria across all levels of GFR, that impact appeared greatest in patients with better kidney function. Therefore, the requirement of proteinuria for stage 2 but not stage 3 disease generates higher costs for stage 2 patients, further explaining the surprisingly close stage 2 CKD and stage 3 CKD costs from previous work.

Our analysis shows that anemia, CHF, proteinuria, coronary artery disease and peripheral vascular disease have the greatest impact on cost of care in patients with CKD. Targeting these conditions for disease management programs may prove to be a useful method of relieving burden of disease in those with CKD. What we cannot tell from our work, however, is the extent to which managing these diseases already contributes to the cost of care.

For anemia treatment, the use of erythropoetin is easy to identify. We found that erythropoetin use was low and contributed less than $200 even in the most severe stages of kidney disease, suggesting that treatment of this condition may be adding little to our estimates. Whether or not erythropoetin treatment is cost effective in the CKD population is open to question. Some economic modeling in patients requiring hemodialysis has shown that maintaining a hemoglobin level of 11.0 – 12.0 g/Dl versus 9.5 – 10.5 g/Dl may be cost effective (the predicted cost per quality adjusted life year is $50,000 to $60,000).([13]) Further work is needed to understand the true benefits of anemia treatment in the CKD population, however. There remain questions regarding which CKD patients stand to benefit, what outcomes might be improved, and when is the most effective time to treat. Focused research to more fully enumerate the potential cost-effectiveness of these programs is essential to the wise use of disease management resources.

This work has some limitations that should be recognized. First, this work did not utilize a prospective random sample of patients, meaning that one cannot make inferences regarding prevalence of kidney disease or relative sizes of populations between levels of severity. Second, patients with both incident and prevalent disease were included in the study. Because of this, our population was heterogeneous with respect to the natural history of their disease. This means that while our findings give a reflection of a steady state to be found within the given population, they are less useful for estimating lifetime disease burden. Third, our control group may not have been completely free of CKD (they may have simply not have had a serum creatinine test done), just as comorbid disease ascertainment may not have been complete in all patients. We cannot predict the direction of the bias that this misclassification would cause, but to the extent that those misclassified as being disease free have a disease burden that is less severe (and therefore less costly) than patients who are appropriately classified, the bias is probably conservative. It should also be noted that cases may have more health care use than controls simply because of opportunities for contact with the system. This is probably not of great concern since more than 90% of controls had at least one outpatient visit.

A significant strength of our approach is that we have included patients whose routine laboratory work indicated renal disease, even if they lacked a physician's diagnosis. In fact, most patients we identified with CKD did not have such a diagnosis in their records. Those with GFR 15 to 29

(NKF/KDOQI stage 4 ([1]) were the most likely to carry the diagnosis (<50%), followed by those with GFR 30 to 59 (NKF/KDOQI stage 3 ([1]) (<10%), and fewer with GFR 60-89 (<2%). Systematic screening for elevated serum creatinine values in the entire HMO population would identify additional patients with chronic kidney disease who were excluded from our analyses, but the cost estimates reported here are the most comprehensive to date

This study reveals that CKD – which was mostly undocumented in patient's medical records – is a strong predictor of high cost even after controlling for related comorbid conditions. In the case of those with the most severe disease (GFR 15 to 29) the cost attributable to CKD alone (over $5,000) is greater than the annual per person cost of care reported by the Centers for Medicare and Medicaid ($4,245).([14]) Recent research has suggested that treatment with statins for individuals with moderate renal disease may slow disease progression.([15]) Given the potential clinical and economic importance of these findings, the next step is to collect these data prospectively to evaluate how much of the cost differences can be explained by misclassification (i.e., can we assume that no recorded diagnosis mean no disease?) and selection bias (i.e., are the patients who visit the clinic and receive diagnoses a random sample of everyone who was screened?).

CONCLUSION

Patients with CKD have a greater total cost of care than age and gender matched controls, even after controlling for CKD-related comorbidities. This suggests that the development of CKD may add extra burden to patients and the health care system. Combined with increasing incidence of kidney disease, these data strongly argue the need for better understanding of cost-effective treatment programs in CKD. This study provides essential data to aid in developing such sound economic strategies.

ACKNOWLEDGMENT

Funded by Amgen: the contract gave full rights of publication to the investigators. The funders did review the study but did not participate in the conceptual design, data analysis, or interpretational aspects.

CORRESPONDENCE TO

David H Smith, PhD
Investigator, Center for Health Research Kaiser Permanente, Northwest
3800 N Interstate Ave
Portland OR, 97211
Phone: (503) 335 6302
Fax: (503)335-6311
E-mail david.h.smith@kpchr.org

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Author Information

David H. Smith, Ph.D.
Center for Health Research Kaiser Permanente, Northwest

Gregory A. Nichols, Ph.D.
Center for Health Research Kaiser Permanente, Northwest

Christina M. Gullion, Ph.D.
Center for Health Research Kaiser Permanente, Northwest

Eric S. Johnson, Ph.D.
Center for Health Research Kaiser Permanente, Northwest

Douglas Keith, M.D.
Department of Nephrology, Royal Victoria Hospital, McGill University Medical School