Disease Management in Chronic Kidney Disease

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Chronic kidney disease (CKD) is a growing health problem of epidemic proportions both in the United States and worldwide. The care of CKD patients, before and after starting dialysis, remains highly fragmented resulting in suboptimal clinical outcomes and high costs, creating a high burden of disease on patients and the health care system. Disease management (DM) is an approach to coordinating care for this complex population of patients that has the promise of improving outcomes and constraining costs. For CKD patients not yet on dialysis, the major goals of a DM program are (1) early identification of CKD patients and therapy to slow the progression of CKD, (2) identification and management of the complications of CKD per se, (3) identification and management of the complications of comorbid conditions, and (4) smooth transition to renal replacement therapy. For those CKD patients on dialysis, focused attention on avoidable hospitalizations is a key to a successful DM program. Multidisciplinary collaboration among physicians (nephrologist, primary care physician, cardiologist, endocrinologist, vascular surgeons, and transplant physicians) and participating caregivers (nurse, pharmacist, social worker, and dietician) is critical as well. There are several potential barriers to the successful implementation of a CKD/end-stage renal disease DM program, including lack of awareness of the disease state among patients and health care providers, late identification and referrals to a nephrologist, complex fragmented care delivered by multiple providers in many different sites of care, and reimbursement that does not align incentives for all involved. Recent experience suggests that these barriers can be overcome, with DM becoming a promising approach for improving outcomes for this vulnerable population.

Index Words: Chronic kidney disease; End-stage renal disease; Disease management; Disease management organization; Medicare

Chronic kidney disease (CKD) is a public health problem approaching epidemic proportions in the United States, with more than 19 million patients identified as having some form of kidney dysfunction.[1] There are a number of major initiatives underway for early screening, identification, and treatment of CKD patients by the National Kidney Foundation, the National Institutes of Health (via the National Kidney Disease Educational Program), and the Centers for Disease Control and Prevention. Early diagnosis of CKD can lead to interventions that may slow the progression of disease, permit identification and treatment of complications of CKD and associated comorbid conditions, and smooth the transition to end-stage renal disease (ESRD). In addition, the currently fragmented care delivered to patients on dialysis can be substantially reorganized by applying the principles of care coordination. These organized approaches to treating CKD and ESRD patients are examples of advanced care management (also referred to as disease management), which is being used to improve clinical outcomes while constraining the costs of care for patients with a wide variety of chronic diseases.[2,3]

The National Kidney Foundation defines CKD as any impairment of kidney function as evidenced by decreased glomerular filtration rate (GFR) or other evidence of kidney damage, the latter including proteinuria, hematuria, abnormal kidney biopsy, or abnormal kidney imaging study[4] (Table 1). CKD can be classified into 1 of 5 stages with CKD stage 5 including patients with GFR <15 mL/min as well as patients with ESRD on dialysis (Table 2). Even though patients with CKD will not require dialysis until they reach stage 5, the complications from CKD itself

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Dr. Nissenson is supported in part by the Richard Rosenthal Dialysis Fund.

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1548-5595/08/1501-0006$34.00/0
doi:10.1053/j.ackd.2007.10.011

Table 1. Definition of Chronic Kidney Disease Criteria

1. Kidney damage for ≥3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by *either*:
   - Pathological abnormalities; or
   - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR <60 mL/min/1.73 m^2 for ≥3 months, with or without kidney damage

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Abbreviation: GFR, glomerular filtration rate.

(anemia, metabolic bone disease, acidosis, and malnutrition) and associated comorbid conditions (cardiovascular disease, diabetes, and hypertension) can be seen at much earlier stages and worsen as the disease progresses. In fact, patients with stage 3 and stage 4 CKD are much more likely to die, generally from cardiovascular disease, than to progress to ESRD.[5] Late diagnosis of CKD, late or lack of referral to the nephrologist, and failure to apply established care guidelines all lead to poor outcomes in CKD patients[6-8] (Fig 1). Similarly, failure to diagnose and treat complications of ESRD, manage comorbid conditions, and provide preventative care such as immunizations leads to poor outcomes, including avoidable hospitalizations. Such suboptimal care for CKD and ESRD patients is the target of disease-management (DM) programs for these vulnerable individuals.

In addition to poor clinical outcomes, the cost of caring for CKD and ESRD patients is quite high. In 2004, $25 billion dollars were spent in taking care of ESRD patients with $17 billion from Medicare. Only a third of total costs relates to the dialysis treatment itself and associated injectable medications, whereas a significant fraction of the remaining costs is related to preventable hospitalizations. The total cost to Medicare represented over 7% of the overall Medicare budget.[9] For CKD patients before starting dialysis, the majority of the costs are from hospitalizations, mostly incurred in the 6 months before the initiation of dialysis[10] (Fig 2). Recent data show that the costs during the month of initiation of dialysis are $25,000 to $35,000. According to CMS, the estimated annual cost for CKD patients is $28,000 and $65,000 to $85,000 for ESRD patients, both of which are considerably higher than the $5,000 for congestive heart failure and $10,000 for diabetes mellitus patients without CKD, respectively (Southwest securities estimates, the American Diabetes Association, Disease Management 2000 Directory, and various industry sources, personal communication, January 2007). The prevalence of CKD, including stage 5 continues to grow at a rate of about 5% per year,[9] and the burden on the existing health system is only going to get worse unless interventions are immediately implemented to improve clinical outcomes and constrain the costs of care.

Table 2. Stages and Prevalence of Chronic Kidney Disease (Age ≥20)

Stage	Description	GFR (mL/min/1.73 m^2)	Prevalence*	
			N (1000s)	%
1	Kidney damage with normal or ↑ GFR	≥90	5,900	3.3
2	Kidney damage with mild ↓ GFR	60–89	5,300	3.0
3	Moderate ↓ GFR	30–59	7,600	4.3
4	Severe ↓ GFR	15–29	400	0.2
5	Kidney failure	<15 (or dialysis)	300	0.1

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*Data for Stages 1–4 from NHANES III (1988–1994)[1]. Population of 177 million adults age ≥20 years. Data for Stage 5 from USRDS (1998)[2] include approximately 230,000 patients treated by dialysis, and assume 70,000 additional patients not on dialysis. GFR estimated from serum creatinine using Modification of Diet in Renal Disease Study equation based on age, gender, race and calibration for serum creatinine. For Stages 1 and 2, kidney damage estimated by spot albumin-to-creatinine ratio >17 mg/g in men or >25 mg/g in women on two measurements.
Abbreviation: GFR, glomerular filtration rate.

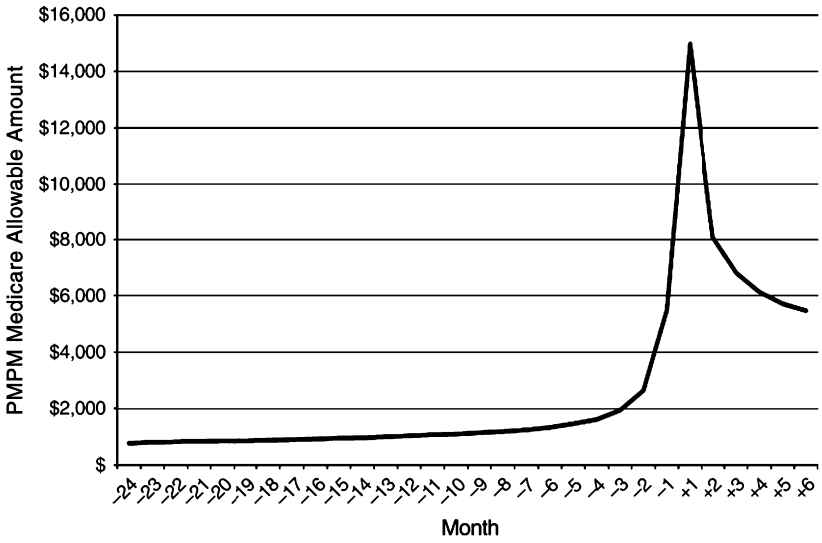

Figure 1. Kaplan-Meier plot of actuarial survival by timing of referral in propensity score matched population (n = 2,078). PMPM, per member per month.

Systemic barriers leading to suboptimal clinical outcomes and high costs in CKD patients include the following: (1) late diagnosis of CKD; (2) lack of awareness of the magnitude and significance of CKD by nonnephrologists; (3) fragmentation of care with multiple caregivers in myriad settings; (4) late referral to a nephrologist; (5) insufficient use of therapies

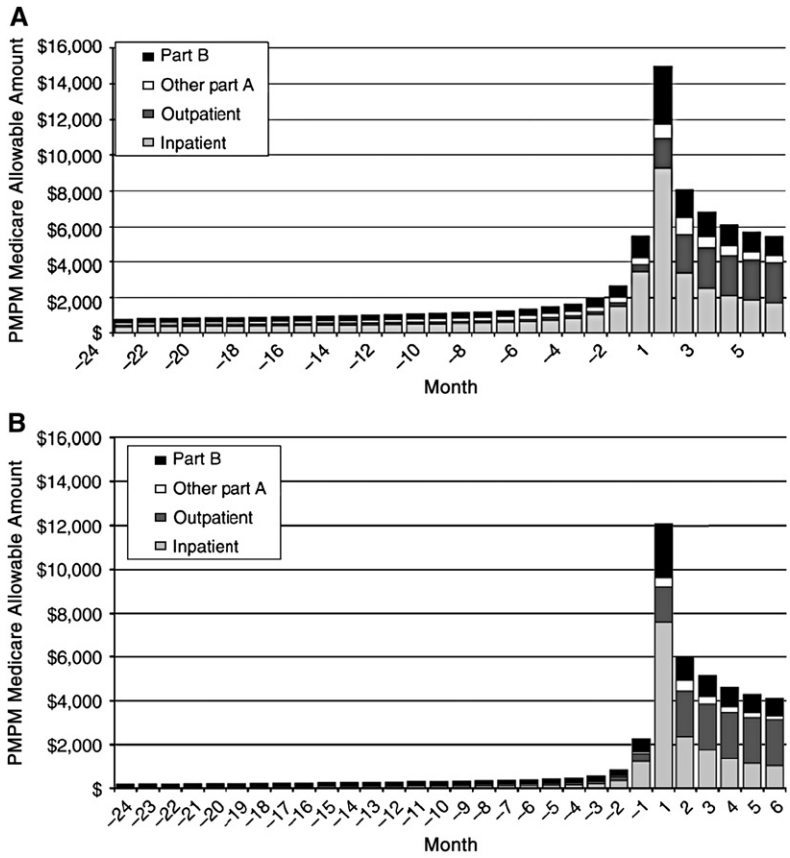

Figure 2. Overall distribution of per member per month (PMPM) Medicare-allowable cost (1995 through 1998) and variation in cost components among Medicare patients ≥67 years of age. (A) CKD. (B) CKD and neither diabetes nor cardiovascular disease. Month –1 denotes the month before initiation of dialysis, and month +1 denotes the month immediately after initiation of dialysis. Reprinted by permission from Macmillan Publishers Ltd.: Kidney International, St. Peter WL, Khan SS, Ebben J, et al: Chronic kidney disease: The distribution of health care dollars. Kidney Int 66:313–321, 2004. © 2004

to slow the progression of CKD; (6) insufficient treatment of complications of CKD or comorbid conditions; and (7) abrupt transition to renal replacement therapy, sometimes called the dialysis crash. For ESRD patients, fragmented care, inappropriate vascular access, lack of attention to management of comorbid conditions, and failure to provide preventative services are major drivers of poor clinical outcomes and high costs.[2,3] The use of disease-management approaches for patients with CKD and ESRD may hold the promise of assisting nephrologists in overcoming many of these barriers and, thus, improving key outcomes.

Windows of Opportunities

DM has been shown to have a positive impact on clinical outcomes including mortality and hospitalization in ESRD patients.[2,3] There is good reason to believe that similar improvements in care will be seen when DM is applied to earlier stages of CKD, focusing on the key opportunities described earlier including slowing the progression of CKD, identifying and treating the complications of CKD, managing comorbid conditions, and smoothing the transition to ESRD.

Trivedi and colleagues,[11] for example, used a complex mathematical model to predict the cost savings accrued by reducing the rate of decline of GFR in CKD patients, achievable by early identification, blood pressure and blood sugar control (the latter in diabetics), and the appropriate use of angiotensin converting enzyme inhibitor or angiotensin receptor blockers.[12] In addition, the Reduction in End Points in NIDDM (non–insulin-dependent diabetes mellitus) with the Angiotensin II Antagonist Losartan potassium (Cozaar®; Merck & Co., Inc., Whitehouse Station, NJ) trial showed that use of the angiotensin receptor blocker Losartan slowed the rate of progression of CKD to ESRD significantly with a significant associated economic impact.[13] Once the patient has advanced to CKD stage 3, there are numerous interventions that can be applied to treat associated complications of CKD and comorbid conditions. The use of erythropoietic-stimulating agents, phosphate binders, vitamin D, and sodium bicarbonate; the aggressive treatment of hypertension and blood sugar (in diabetics); the evaluation of cardiovascular disease and appropriate treatment; and early fistula placement are all approaches that are known to be beneficial but are often underused. Late referral to the nephrologist typically results in frequent hospitalizations as the need for dialysis approaches. Such late referral has been shown to increase the likelihood of the use of emergent dialysis at initiation, leading to high morbidity and mortality as well as excessive cost[10] (Fig 1). If DM can be applied at these earlier stages of CKD, the key elements of management are more likely to be introduced including early referral to the nephrologist, intensive patient education, selection of the most appropriate form of renal replacement therapy including preemptive transplantation and the various forms of home dialysis, timely placement of dialysis access, and treatment of complications of CKD and management of comorbid conditions.

The challenges for disease management in CKD and ESRD patients are 2-fold: (1) to show improved clinical outcomes over conventional care in a rigorous way using the appropriate analytic techniques and (2) to make a business case for the use of disease management in this setting. Are the disease management techniques needed to improve clinical outcomes more or less costly than the savings generated by the model?

DM: Background and Definitions

DM is a comprehensive, integrated approach to care delivery that is particularly suited for patients with complex chronic illnesses and emphasizes coordination of care across the spectrum of the particular disease or condition. The broad goals of DM are to improve clinical outcomes while constraining the costs of care. The focus is on both clinical and nonclinical interventions where and when they will have the maximum positive impact. The Disease Management Association of America describes DM as follows[14]:

1. A system of coordinated health care interventions and communications for populations with conditions in which patient self-care efforts are significant
2. Supports the physician or practitioner/patient relationship and plan of care

3. Emphasizes prevention of exacerbations and complications using evidence guidelines and patient empowerment strategies
4. Evaluates clinical, humanistic, and economic outcomes on an ongoing basis with the goal of improving overall health

Former Senator Bill Frist of Tennessee described DM in 1997 as "…a sophisticated approach to patient care that requires a knowledge of public health, disease history, health economics, and outcomes research to produce the most cost effective, continually improving, high quality care available" (personal communication, March 1997). He predicted a dramatic shift toward the use of DM for chronically ill Medicare patients in the future.

Objectives of CKD and ESRD DM Programs

Objectives are (1) early identification and management of CKD and its complications (CKD and ESRD), (2) slowing the progression of CKD (CKD only), (3) management of the comorbid conditions (CKD and ESRD), and (4) smoothing the transition to ESRD and renal replacement therapy (CKD only).

By focusing on these key areas, unnecessary hospitalizations will be avoided and the costs of care will be controlled. Successful DM for CKD and ESRD patients requires active leadership of the care team by the nephrologist. Working in collaboration with the members of the DM team, the nephrologist is central to the process. The role of the nephrologist includes at a minimum the following: (1) assisting in identification and selection of care managers, (2) leading the team for care plan development, (3) guiding the care manager regarding the implementation of the care plan, and (4) participating in quality care committee meetings and leads the continuous quality improvement process.

The Renal Physicians Association recognizes the many essential roles of the nephrologist when DM is used. The Renal Physicians Association recommends that nephrologists (1) learn about DM, risks and rewards; (2) examine their own practices in terms of processes, outcomes, costs, and data systems; (3) advocate for the inclusion of CKD patients in DM programs, not just ESRD patients; (4) assume the role of the principal care physician for CKD and ESRD patients; (5) support the broad scope of nephrology practice and be accountable for patient outcomes; and (6) insist on control of patient referral and avoid its delegation to primary care physicians.

Components of a Successful CKD/ESRD DM Program

To be successful, DM programs must include a number of key components, with the focus on a multidisciplinary team working in close collaboration with patients. Some elements of such a program include the following:

1. Patient identification: this can be performed by claims analysis using paid claims or laboratory data when available. Continuous procedural terminology and *International Classification of Disease, Ninth Revision* codes can be used for this purpose. For ESRD patients, this is not difficult because the Centers for Medicare and Medicaid Services (CMS) 2728 form (the form used to attest that ESRD is present required by Medicare) can be used as the indicator of the presence of ESRD. For CKD patients, however, identification via claims data can be more difficult, although the recent introduction of G-codes for billing purposes may make the identification process less difficult in the future.
2. Patient eligibility: this process step is needed to confirm that the patient indeed has ESRD or CKD and is eligible for the specific program, whether under Medicare or a commercial insurance plan.
3. Chief medical officer or medical director of the DM organization: this individual has medical/clinical experience and serves in a leadership and management role. He/she is responsible for ensuring that all medical management is coordinated, based on evidence, and reflects the most recent thinking about how to optimize outcomes.
4. Nephrologist: the active participation and leadership of the treating nephrologist is critical to the success of the DM program. To optimize outcomes, the nephrologist must serve in a principal care role, ensuring that all care is coordinated, renal-related

care is delivered, comorbid conditions are managed (either directly or through the appropriate use of consultants), and primary care/preventative care is delivered directly or through physician extenders or primary care physicians. In addition, the nephrologist works closely with the program to review outcomes data and assist in appropriately focusing local CQI initiatives.

5. Information technology (IT): IT is essential to the success of DM because of the complexity of caring for chronically ill patients. IT functions include providing educational materials to patients and providers, collecting and analyzing clinical outcomes and financial data, and the need to communicate in real time with the many members of the care team. DM will not succeed without a robust IT platform, which in addition to the previously mentioned elements, may serve as an electronic health record as well.
6. DM care nurse: a care nurse has a central role in the DM intervention. In CKD and ESRD DM programs, the nurse is generally field based but may also perform the needed tasks telephonically. Key functions include coordination of care, serving as a liaison between the patient, multiple physicians, and other elements of the health care delivery system. The care nurse helps in identifying suitable patients and assists in the integration of the care plan with proper follow-up. The care nurse also makes timely contact with the patient to make sure the patient is adhering to the plan of care and will attempt to resolve any hindrances if they exist. This will not only impact hospitalizations in the short-term but also impact the course of the disease and outcomes (morbidity and mortality). The care nurse will also promote communication among the physician and the support staff. In a CKD/ESRD DM program, it is crucial that the care nurse is well versed with nephrology and has advanced knowledge and training to handle the complex medical issues related to the kidney disease and comorbid conditions.
7. Other DM team members: depending on the specific DM model being used, physician extenders (nurse practitioners), pharmacists, dietitians, and others may be part of the multidisciplinary team. Each individual provides specific expertise in a particular content area but more importantly works as part of a comprehensive group to ensure efficient and effective care.

Evaluating DM Program Effectiveness

To ensure that the DM intervention is effective in improving health and economic outcomes, a robust evaluation of the program is required. The 2 primary categories of study designs relevant to DM evaluation are experimental (better known as the random controlled trial [RCT]), and quasi-experimental (which is generally referred to as an observational study design).[15-17]

The RCT is considered the gold standard research and program evaluation design. Randomization maximizes the internal validity of the study by allowing each individual within the population an equal opportunity to be selected for inclusion in the intervention and thus distributes variability equally among the groups being studied. The addition of an equivalent control group ensures that study outcomes are causally associated with the intervention and not a function of bias and/or competing extraneous confounding factors that may offer plausible alternative explanations for any change from the baseline measurement.[18,19] Although the RCT design is the most desirable, unless the study is being conducted in a tightly controlled environment, this model is not typically suited for many commercial endeavors.

Commercial DM programs do not randomly assign eligible individuals to treatment or control groups but instead invite those individuals to participate who meet particular clinical criteria. Given that these patients are specifically identified and enrolled because of their poorer health status (or higher risk), program outcomes are particularly susceptible to threats to validity such as selection bias and regression to the mean.[18,20] Fortunately, there are several quasi-experimental designs available to control for the effect of these biases. A well-designed DM program will provide the flexibility needed in choosing the appropriate evaluation techniques such as time series analysis,[21] regression discontinuity,[22] matched

pairs,[23] instrumental variables,[24] and survival analysis.[25]

There are several categories of outcomes that should be considered in measuring the effectiveness of a DM intervention, including (1) health-related behaviors, (2) clinical/physiologic indicators, (3) health status/quality of life, (4) health care utilization, and (5) medical costs.

Health-related behaviors have a tremendous direct and indirect impact on health status and disease progression and may include diet/nutrition, tobacco use, exercise, sleep, managing stress and anxiety, adherence to a treatment plan, and so on. Positive changes in these behaviors can be assumed to be directly associated with the intervention.

Clinical indicators are used to measure the program's impact on slowing or halting the progression of CKD and prevent or manage complications and comorbid conditions like cardiovascular disease, malnutrition, hypertension, anemia, and bone and mineral disease.

Health status and/or quality of life indices are typically gathered via patient self-report and can be measured through general health instruments (eg, Short-Form 36 or EuroQual-5 domain)[26,27,28] or a variety of disease-specific survey instruments.[29-32]

The only true mechanism by which commercial DM programs can realistically achieve cost savings is by reducing avoidable hospital admissions. This is because of the fact that the DM model does not typically include a hospital-based system for reducing length of stay and that successful interventions targeting chronic illness tend to increase physician office visits and medication usage.[33] Therefore, to conclude that that program intervention had a causal impact on overall medical costs, a significant reduction in disease-specific hospital admission rates must be realized as well. If DM program administrators wish to take credit for reduced utilization beyond the primary condition, they have to clearly show how the intervention impacted those measures and costs.

Experience With DM in CKD/ESRD Patients

There is more than 10 years of experience with DM in ESRD patients. This is both as part of demonstration projects funded by CMS and in the private sector. Kaiser Permanente of Southern California and Advanced Renal Options, a division of Blue Cross/Blue Shield, were the 2 participants in the demonstration projects with Kaiser Permanente achieving more favorable outcomes (mortality, cost of care, dialysis adequacy, fistula placement, and patient satisfaction) compared with the Advanced Renal Options project.[34] An explanation for this disparity in results was the difference in the way the programs were structured and the planning that went into them.[35]

In the private sector, there are currently 2 major commercial DM organizations that provide DM for CKD/ESRD patients: DaVita VillageHealth and Renaissance Health Care (El Segundo, CA). Clients include health plans and clinical practices that contract with these organizations to incorporate DM within their insurance plan or care model.

Potential Limitations of a DM program for CKD

Although DM has been successfully applied to disease states like diabetes mellitus, chronic obstructive pulmonary disease, asthma, and congestive heart failure, there are several potential barriers to successful implementation of a CKD/ESRD DM program. To start, CKD/ESRD is a much more complex disease than most other chronic illness that has multiple complications and comorbidities requiring concurrent management.

In addition, although the identification of ESRD patients is not difficult, identification of CKD patients is much more challenging and may be an obstacle to the success of a CKD DM program. CKD, like hypertension, is a silent disease with the majority of patients being asymptomatic until the disease is fairly advanced. In such cases, the only manner in which one can identify the disease state is by actively looking for it by laboratory tests including blood and urine studies. Currently, most CKD patients are identified via CPT codes assigned by providers. However, some physicians do not apply this code for billing purposes. Recently, CMS has proposed the use of a series of *International Classification of Disease, Ninth Revision* codes for

differentiating the stages of CKD. Unfortunately, many patients are missed because they have not seen a physician and/or have their blood/urine tested. Even when the blood is tested, a significant number of patients are missed because creatinine, instead of estimated GFR as measured by the Modification of Diet in Renal Disease (MDRD) equation, is being used to evaluate renal function. Creatinine has several limitations as the single test in assessing kidney dysfunction.[36] However, despite these limitations, Medicare claims data have been successfully used in accurately identifying CKD patients as shown in the 1,852-patient study in elderly Medicare patients hospitalized for myocardial infarction.[37]

The lack of commercial health insurers' recognition of CKD as a high-cost disease is also a significant barrier to the success of a CKD DM program. Major health plans are still focusing on the other major chronic health problems in the United States (diabetes mellitus, coronary artery disease, congestive heart failure, asthma, and chronic obstructive pulmonary disease), and it was not until recently that attention was paid to CKD as an equally important condition for DM intervention.

Another potential barrier to the success of a CKD DM program is the lack of support by nephrologists and other physicians. One possible reason is that physicians are conditioned to treating patients episodically, managing issues as they arise. Another reason may be that many physicians practice in a fee-for-service environment, and their income is often significantly dependent on inpatient hospital care. Optimizing patient care while maintaining a strong financial position might be a difficult but surmountable barrier. The introduction of pay for performance is 1 example of a recent approach to address this delicate and sensitive issue.

One final barrier is the cost of applying DM to CKD. A medical practice can implement its own DM program, but the costs of hiring the necessary staff including a case nurse, social worker, dietician, and a pharmacist might be prohibitive. It should be kept in mind, however, that ESRD patients already have access to a social worker and a dietician. The other option for a clinical practice is to outsource these services to a commercial DM organization. However, the return on investment must be sufficient to justify this approach. The vendor must be certain that the improvement in outcomes and lowering of the costs is possible within the budget provided by the practice. Currently, the care of CKD/ESRD patients is fragmented and suboptimal, and the DM approach is expected to achieve improvements in outcomes, including reduced medical care costs.

Conclusions

CKD is a growing epidemic and a huge burden on the health care system. The population of older, sicker patients with ESRD is growing as well. Both ESRD and CKD are associated with poor outcomes for multiple reasons including a lack of awareness by physicians and ineffective or late interventions. However, there are numerous opportunities to intervene, leading to the avoidance of unnecessary hospitalizations and constraint of cost. Targeted DM programs that address drug interactions, congestive heart failure and blood sugar control, vascular access, end-of-life care, and immunizations hold great promise in this regard and are currently being evaluated and implemented in DM programs for CKD and ESRD patients (A Hayek, personal communication, August 2007). Over the next few years, data should become available to be certain as to whether this approach to CKD/ESRD care can truly transform the lives of this vulnerable population. Additional challenges to optimizing outcomes include full engagement and participation of patients in their care and the high cost of necessary medications. Patient empowerment and involvement in care is one of the fundamental principles of DM and must be included in any successful DM program.

References

1. Coresh J, Astor BC, Greene T, et al: Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis 41:1-12, 2003
2. Nissenson AR, Collins AJ, Dickmeyer J, et al: Medical Advisory Board, RMS Disease Management, Inc. Evaluation of disease-state management of dialysis patients. Am J Kidney Dis 37:938-944, 2001 (erratum in Am J Kidney Dis 38:701, 2001)

3. Licht M, Crooks P, Donald L, et al: Progress in renal disease management: Optimal Renal Care. Nephrol News Issues 15:21-27, 2001
4. National Kidney Foundation: K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. Am J Kidney Dis 39: S1-S266, 2002 (suppl 1)
5. Sarnak MJ, Levey AS, Schoolwerth AC, et al: American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Kidney disease as a risk factor for development of cardiovascular disease: A statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Hypertension 42:1050-1065, 2003
6. Jungers P, Zingraff J, Page B, et al: Detrimental effects of late referral in patients with chronic renal failure: A case-control study. Kidney Int Suppl 41:S170-S173, 1993
7. Obrador GT, Pereira BJ: Early referral to the nephrologist and timely initiation of renal replacement therapy: A paradigm shift in the management of patients with chronic renal failure. Am J Kidney Dis 31:398-417, 1998
8. Winkelmayer WC, Owen WF Jr, Levin R, et al: A propensity analysis of late versus early nephrologist referral and mortality on dialysis. J Am Soc Nephrol 14:486-492, 2003
9. U.S. Renal Data System: USRDS 2004 annual data report: Atlas of end-stage renal disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, MD, USRDS, 2005
10. St Peter WL, Khan SS, Ebben JP, et al: Chronic kidney disease: The distribution of health care dollars. Kidney Int 66:313-321, 2004
11. Trivedi HS, Pang MM, Campbell A, et al: Slowing the progression of chronic renal failure: Economic benefits and patients' perspectives. Am J Kidney Dis 39: 721-729, 2002
12. Nissenson AR, Collins AJ, Hurley J, et al: Opportunities for improving the care of patients with chronic renal insufficiency: Current practice patterns. J Am Soc Nephrol 12:1713-1720, 2001
13. Remuzzi G, Ruggenenti P, Perna A, et al: RENAAL Study Group: Continuum of renoprotection with losartan at all stages of type 2 diabetic nephropathy: A post hoc analysis of the RENAAL trial results. J Am Soc Nephrol 15:3117-3125, 2004
14. Disease Management Association of America. Available at: http://www.dmaa.org/dm_definition.asp. Accessed November 27, 2007
15. Campbell DT, Stanley JC: Experimental and Quasi-experimental Designs for Research. Chicago, IL, Rand McNally College Publishing, 1966
16. Cook TD, Campbell DT: Quasi-experimentation: Design and Analysis Issues for Field Settings. Chicago, IL, Rand McNally College Publishing, 1979
17. Shadish SR, Cook TD, Campbell DT: Experimental and Quasi-experimental Designs for Generalized Causal Inference. Boston, MA, Houghton Mifflin, 2002
18. Linden A, Adams J, Roberts N: An assessment of the total population approach for evaluating disease management program effectiveness. Dis Manag 6: 93-102, 2003
19. Linden A, Roberts N: A users guide to the disease management literature: Recommendations for reporting and assessing program outcomes. Am J Manag Care 11:81-90, 2005
20. Linden A: Estimating the effect of regression to the mean in health management programs. Dis Manag Healt Outc 15:7-12, 2007
21. Linden A, Adams J, Roberts N: Evaluating disease management program effectiveness: An introduction to time series analysis. Dis Manag 6:243-255, 2003
22. Linden A, Adams J, Roberts N: Evaluating disease management program effectiveness: An introduction to the regression-discontinuity design. J Eval Clin Pract 12:124-131, 2006
23. Linden A, Adams J, Roberts N: Using propensity scores to construct comparable control groups for disease management program evaluation. Dis Manag Healt Outc 13:107-127, 2005
24. Linden A, Adams J: Evaluating disease management program effectiveness: an introduction to instrumental variables. J Eval Clin Pract 12:148-154, 2006
25. Linden A, Adams J, Roberts N: Evaluating disease management program effectiveness: An introduction to survival analysis. Dis Manage 7:180-190, 2004
26. Ware JE, Sherbourne CD: The MOS 36-item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. Med Care 30:473-483, 1992
27. Rabin R, de Charro F: EQ-5D: A measure of health status from the EuroQol Group. Ann Med 33: 337-343, 2001
28. Public Health Division: Report on the 1997 and 1998 NSW Health Surveys. Sydney, NSW Health Department, 2000. Available at: http://www.health.nsw.gov.au/public-health/hs98/euroqol_intro.htm. Accessed November 27, 2007
29. Spertus JA, Winder JA, Dewhurst TA, et al: Development and evaluation of the Seattle Angina Questionnaire: A new functional status measure for coronary artery disease. J Am Coll Cardiol 25: 333-341, 1995
30. Green CP, Porter CB, Bresnahan DR, et al: Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: A new health status measure for heart failure. J Am Coll Cardiol 35:1245-1255, 2000
31. Boyer JG, Earp JA: The development of an instrument for assessing the quality of life of people with diabetes. Diabetes-39. Med Care 35:440-453, 1997
32. Hays RD, Kallich JD, Mapes DL, et al: Development of the kidney disease quality of life (KDQOL) instrument. Qual Life Res 3:329-338, 1994

33. Linden A: What will it take for disease management to demonstrate a return on investment? New perspectives on an old theme. Am J Manage Care 12:217-222, 2006
34. Crooks P: The first ESRD managed care demonstration project: A Kaiser Permanente view. Nephrol News Issues 17:29-31, 34-5, 2003
35. Reynolds L, Geronemus R: A perspective on the Florida ESRD Demonstration Project. Nephrol News Issues 18:58, 60, 62, 2004
36. Levey AS, Bosch JP, Lewis JB, et al: A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med 130:461-470, 1999
37. Obrador GT, Ruthazer R, Arora P, et al: Prevalence of and factors associated with suboptimal care before initiation of dialysis in the United States. J Am Soc Nephrol 10:1793-1800, 1999