Patterns of Care for Patients with Chronic Kidney Disease in the United States: Dying for Improvement

WILLIAM F. OWEN JR.
Baxter Healthcare, Renal, Waukegan, Illinois; Duke Institute of Renal Outcomes Research and Health Policy, Duke University Medical Center, Durham, North Carolina.

Abstract. The burden of chronic kidney disease can be assessed by multiple criteria that underscore the need for improved detection, treatment, and outcome monitoring. Several process measures for the care of advanced CKD patients are examined herein. Twenty seven and 11% of patients with CKD in National Health and Nutrition Examination Surveys (NHANES) III had BP <140/90 and 130/85, respectively. In addition to inadequate prescription of antihypertensive drugs, another confounder is poor diagnostic recognition of CKD. Recent surveys of incident Medicare-eligible ESRD patients observed severe anemia in a preponderance of patients; mean and median hematocrit values were 27.7% ± 5.9 and 27.8%, respectively. Only 23 to 28% of these patients were prescribed epoetin alfa. Clinical practice guidelines recommend that <10% of maintenance hemodialysis patients should be chronically dialyzed using percutaneous catheters. A recent national survey of vascular access types among incident American hemodialysis patients found that 30%, 41%, and 29% were dialyzing through a catheter, prosthetic graft, and autologous fistula, respectively. Tunneled catheters are associated with a 39% annual increased risk of death. Based on pharmacokinetic assumptions about the minimum amount of solute clearance by hemodialysis needed for patient survival in ESRD, a GFR of 10.5 ml/min per 1.73 m^2 is needed. The mean GFR of incident ESRD patients in the United States was 9.5 ml/min per 1.73 m^2 in 2000. In addition to the wide international variability in modality treatment selection, geographic variability exists within the United States; <7 to >15% of the prevalent patients are treated by peritoneal dialysis across the country. Despite survival and quality-of-life benefits with transplantation, most eligible recipients in the United States have not been placed on a transplant waiting list 6 mo after beginning dialysis. Last, <40% of incident ESRD patients in the United States have received the recommended frequency of mammography, PAP examinations, or prostate-specific antigen (PSA) or HbA1c measurements. These deficiencies in care for patients with advanced CKD likely adversely influence the survival of US ESRD patients. Contemporary outcome information supports this contention. CKD patients referred to a nephrologist for the first time within 90 d of the start of dialysis have an approximately 40% to 60% increased risk of death during their first year of renal replacement therapy (RRT). Thirty-five percent of CKD patients are seen within 90 d of receiving RRT. In addition, if fewer than five nephrology visits occur, death risks are increased by 15%. These findings confirm the urgent need for improvement in healthcare delivery for CKD patient in the United States.

Burden of Chronic Kidney Disease in the United States

For the first time, the US Surgeon General's mandate for public health for America's citizenry, entitled *Healthy People 2010*, contains a chapter focused on CKD (1). The objectives of this new chapter are to articulate goals and provide strategies to reduce the incidence, morbidity, mortality, and health costs of CKD in the United States. The escalation of CKD to an urgent matter of public health concern is a consequence of the current and anticipated disease burden on the American population. The burden of CKD can be assessed by multiple criteria, all of which underscore the need for improved detection, treatment, and monitoring of clinical and fiscal outcomes.

From a patient-specific focus, a gauge of the success of an intervention like dialysis and kidney transplantation, which are repeated forms of life support, is patient mortality. Therefore, in the case of ESRD, the need for improvement is underscored by an annual adjusted mortality rate of 177 per 1000 patient-years in 2000 (2). This is a disappointing plateau in survival that cannot be accounted for by differences in patient case mix or reporting of mortality. Another method of viewing this mortality information is by viewing the remaining years of survival. For a 59 yr old with ESRD in the United States, the survival is worse than that of an equivalent patient with a diagnosis of prostrate or colon cancer (4.3 *versus* 13 and 8 yr, respectively) (3). An alternative perspective of the burden of CKD on the US population is in the growth of ESRD. In 1994, approximately 256,000 patients were treated for ESRD; by 2000, this number had increased to approximately 379,000 patients (4). Over this same interval, Medicare expenditures for ESRD patients increased from US$8.1 billion to $12.3 billion (4). Almost 6% of Medicare's budget was spent on the ESRD Program. Current predictions of incident patient growth and ESRD expenditures predict that by 2010, the number of prev-

Correspondence to Dr. William F. Owen, Jr., Chief Scientist, Baxter Healthcare, Renal, 1620 Waukegan Road, Waukegan, IL 60085-6730. Phone: 847-473-6307; Fax: 847-473-6903; E-mail: william_owen@baxter.com

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alent ESRD patients in the United States will increase to 661,000 (5).

A more robust quantitative approach to examine the societal burden of CKD in the United States is to examine less severe forms of kidney disease than ESRD. Based on serum creatinine concentration as a measure of kidney function, the National Health and Nutrition Examination Survey (NHANES) III, which evaluated a cross-sectional representative sample of 16,589 American adults between 1988 and 1994 calculated that more than 3,000,000 Americans may have a serum creatinine concentration of >1.7 mg/dl (6). Albeit lacking specificity for predicting progressive CKD, an increased sensitivity of measurement for renal dysfunction is offered by calculating the GFR. When a similar profile of renal dysfunction is developed based on the extrapolation of GFR using the Modification by Diet of Renal Disease (MDRD) transformation formula (7), 58% of the nondiabetic, adult US population have a GFR <80 ml/min per 1.73 m^2 (8). Therefore, it is not surprising that the prevention, detection, treatment, and complication reduction for CKD are of enhanced priority in the United States.

The patient with advanced CKD is especially apt for surveillance because (*1*) patients with advanced CKD are most likely to encounter health care professionals, (*2*) strong agreement exists among physicians about which processes of care to target, (*3*) process measures are readily available, and (*4*) these processes variably affect future clinical outcomes. To better characterize the state of care for CKD patients in the United States, it is convenient to view CKD as a continuous spectrum (9). From this perspective, many of the outcomes encountered in patients with ESRD are defined by disease states and processes of care that have been implemented (or not performed) during the phases of CKD before the need for renal replacement therapy (RRT). Using a stratification scheme developed by the National Kidney Foundation, Inc. (9), and adopted by the Renal Physicians Association (10), processes of care for patients with GFR of 30 to 15 ml/min per 1.73 m^2 (stage 4 CKD) are predictive of outcomes for patients with ESRD (GFR <15 ml/min per 1.73 m^2, stage 5 CKD). A growing body of contemporary literature supports this supposition. However, to date, no studies have demonstrated which of the many proposed processes of care that define adequate preparation of the CKD patients for RRT best predict survival with ESRD (10). Therefore, several process measures for the care of advanced CKD patients will be examined herein.

Processes of Care for the Advanced Chronic Kidney Disease Patient

Hypertension Control. Control of hypertension is viewed as a fundamental process of care for CKD and ESRD patients as this may attenuate the rate of progression of CKD to ESRD as well as reduce the risk of cardiovascular complications. Inadequate control of hypertension for the preponderance of hypertensive Americans has been repeatedly described (11). For example, the NHANES III survey demonstrated that 25%, 25%, and 15% of African Americans, Caucasians, and Mexican Americans, respectively, had BP controlled to the minimal acceptable range of <140/90. Similar levels of inadequate BP control were observed for patients with overt CKD (12). Twenty-seven percent and 11% of patients with CKD in NHANES III had BP <140/90 and 130/85, respectively. In cases where multiple antihypertensive medications are usually required to treat hypertension in the setting of end-organ damage, poor control is not surprising even among those patients treated for hypertension and kidney disease. These patients had a mean BP of 147/77 mmHg, and 48% were prescribed only a single antihypertensive medication. The small number of patients with adequate BP control should be viewed in the context of recommended values for BP control of ≤125/75 mmHg in CKD patients with proteinuria and ≤130/85 mmHg in patients without proteinuria (13). In addition to inadequate prescription of antihypertensive drugs, it appears that another confounder is the poor recognition of CKD. Despite the availability of widely disseminated clinical practice guidelines, recent audits of patient records show that implementation of these guidelines and even the simple recognition and/or communication of the presence of CKD is unsatisfactory (14,15). Among age-eligible Medicare beneficiaries, only 12.5% of hypertensive and 7.8% of diabetic patients with ≥1+ dipstick proteinuria received comments on this overt abnormality at hospital discharge. Similar patterns were observed among patients with serum creatinine levels ≥2 mg/dl. Despite the evidence indicating the substantial risks associated with impairment of renal function, the clinicians failed to recognize CKD among hypertensive patients, including those with diabetes (14). Furthermore, misconceptions about screening tools to evaluate renal function contributed to underrecognition of CKD.

Treatment of Anemia. Anemia management in CKD patients has been frequently scrutinized because it is an easily monitored care process. Moreover, by extrapolation from experiences in ESRD, treatment of anemia secondary to erythropoietin deficiency in CKD has been suggested to benefit CKD patients (16). Although there is far less direct evidence of benefit from anemia correction for CKD patients (10,17) than for patients on dialysis (18–20), there is no direct evidence of harm associated with anemia treatment for these patients. Therefore, it is surprising that several recent surveys of incident Medicare-eligible ESRD patients observed severe anemia in the majority of patients (2,21). Mean and median hematocrit values of 27.7% ± 5.9 and 27.8%, respectively, were reported. Although insurance coverage is available for the preponderance of CKD patients with anemia in the United States, only between 23% and 28% of these patients were prescribed epoetin alfa. There was minimal differentiation in this constrained prescription pattern for epoetin alfa by patient age, gender, or race. It is unclear why such limited adherence to clinical practice guidelines for anemia management in CKD exists, because there is a substantial improvement in anemia correction by 6 to 12 mo after RRT (2,22; Alan Collins, personal communication 2001). For prevalent hemodialysis patients in the United States, the mean Hct and EPO dose increased from 1994 to 1998 from 31.1% (± 5.2) to 34.1% (± 3.7) and 58.2 U/kg (± 41.8) to 68.2 U/kg (± 55.0), respectively, and >90% of the patients were prescribed epoetin alfa.

Vascular Access Placement for Hemodialysis. Like anemia management, widely distributed clinical practice guidelines for vascular access exist, offering advice for the timely placement and the preferred type of access for chronic use (23,24). The National Kidney Foundation Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines on Vascular Access recommends that <10% of maintenance hemodialysis patients should be chronically dialyzed using percutaneous catheters, operationally defined as continuous catheter use for >90 d. A recent national survey of vascular access types among incident American hemodialysis patients found that 30%, 41%, and 29% were dialyzed through a catheter, prosthetic graft, and autologous fistula, respectively (25). Moreover, for prevalent hemodialysis patients, catheters were used in 22% of cases. There are several justifiable reasons for protracted dialysis catheter use; these include the catheter as a bridge angioaccess device while the patient is awaiting living-related kidney donor transplantation or maturation of an autologous fistula, or as a salvage device for patients with no other potential form of access. However, these rationales are relatively uncommon.

A likely major contributor to the low autologous fistula rate is inadequate patient preparation. This is supported by the observation that only approximately 36% of incident ESRD patients in the United States recall being told to protect their upper arm veins in anticipation of the formation of an internal vascular access (26). Late referral to a nephrologist is also associated with increased catheter use in the United States and likely reflects inadequate time for usable vascular access creation and maturation. In an analysis of the referral pattern of period prevalent hemodialysis patients in the northeastern United States, approximately 35% were observed to have their first nephrologist referral within 90 d of initiating RRT (27). Late-referred patients had a 45% increased risk of receiving dialysis through a percutaneous catheter (28). Last, in addition to the increased risk of luminal thrombosis, infection, unreliable blood flows, central venous stenosis, shorter use life, and patient cosmetic concerns, tunneled catheters are associated with a 39% increased risk of death (29).

Timing the Initiation of RRT and Modality Selection. An intuitively critical component of the care of CKD patients is the timing of the initiation of RRT. Surprisingly, there is limited outcome data that support a preferred timing for the initiation of dialysis, whether this timing is based on symptoms, residual renal function, or GFR (10). However, based on pharmacokinetic assumptions about the minimum amount of solute clearance needed for patient survival in ESRD, a weekly Kt/V_r urea of 2.0 is equivalent to an unequilibrated Kt/V of 1.2 per hemodialysis session. This yields a renal urea clearance of 7 ml/min (normalized to V), renal creatinine clearance of 9 to 14 ml/min per 1.73 m^2, or a GFR of 10.5 ml/min per 1.73 m^2. Although the mean GFR of incident ESRD patients in the United States has increased from 7.2 to 9.5 ml/min per 1.73 m^2 from 1995 to 2000, most patients initiate dialysis at a level that may be associated with less than optimal outcomes (1,2).

A corollary issue is the choice of RRT. In addition to the wide international variability in modality treatment selection (5), geographic variability exists within the United States. For example, <7 to >15% of the prevalent patients are treated by peritoneal dialysis across regions of the United States (2). The reasons for such variability are complex, but seem greatly influenced by conscious and subconscious physician biases. When patients are queried about modality choices for dialysis, 18% and 26% prefer hemodialysis and peritoneal dialysis, respectively. In contrast, 53% and 16% of patients are selected by physicians for hemodialysis and peritoneal dialysis, respectively (26). When a conjoined decision is made, 31% and 48% of patients are selected for hemodialysis and peritoneal dialysis, respectively. Another contributing factor is the timing of referral to the nephrologists. Contradictory information exists about the relationship between late nephrology referral and peritoneal dialysis selection. A contemporary analysis with sustained longitudinal follow-up failed to demonstrate a relationship between the timing of nephrologist input and the initial modality selection (30). However, patients who were referred late and initially treated by peritoneal dialysis were 50% more likely to switch to hemodialysis over the subsequent 6 mo. This modality switch is associated with a substantial increment in the costs of care.

Kidney transplantation is the preferred treatment for ESRD because of the improved patient survival, even in comparison to patients who are on a kidney transplant waiting list (31). For example, in comparison to patients on a waiting list, the relative risk of death is reduced to 0.32 by year 1 after successful kidney transplantation. Despite substantial survival and health-related quality of life benefits, most eligible transplant recipients in the United States have not been placed on a transplant waiting list 6 mo after beginning dialysis (32). In 2000, only 22% of dialysis patients <70 yr old were placed on a kidney transplant waiting list in the United States (2). The risk of late referral is greatest for African Americans and Native Americans. In addition to the choice of treatment modalities, timing is an important consideration. For example, a retrospective cohort analysis suggests that CKD patients who are transplanted before the start of dialysis have improved transplant survival as compared with those transplanted after receiving dialysis (33). Obviously, patients referred late for transplant evaluations cannot undergo preemptive kidney transplantation.

Rehabilitation and Preventive Health Services. In view of the failure to address more critical components of care, it is not surprising that other important but less readily manageable components of CKD care, like patient rehabilitation, vocational, and preventive health services are all deficient in CKD patients in the United States. For example, most age- and health-eligible incident and prevalent patients with ESRD in the United States are unemployed. If vocational counseling and CKD education are offered to CKD patients with nonmanagerial jobs, the percent of patients that remain employed during ESRD doubles from 23% to 47% (34). Moreover, less than 40% of incident ESRD patients in the United States have received the recommended frequency of mammography, PAP examinations, and PSA or HbA1c measurements (35). Approximately one out of four diabetics with advanced CKD has had an eye exam, lipid profile, and HbA1c performed (2). Simi-

larly, only 43% and 10% of ESRD patients received influenza and pneumococcal vaccinations, respectively, in the United States in 2000 (2).

Effect on ESRD Patient Survival. It is imputed that these deficiencies in care for patients with advanced CKD adversely influence the survival of ESRD patients in the United States. Contemporary evidence supports this disturbing but intuitive contention (36,37). For example, CKD patients referred to a nephrologist for the first time within 90 d of the start of dialysis have an approximately 40% to 60% increased risk of death during their first year of RRT. If fewer than five nephrology visits occur, death risks are increased 15%. Thirty-five percent of CKD patients are seen within 3 mo of receiving RRT. Late referral is more common among blacks than whites and was adversely influenced by the type of physician caring for the patient (37,38). Thus, the need and opportunity to improve care for CKD patients clearly exists within the United States. Several legislative and regulatory initiatives are underway on a national level to eliminate fiscal and administrative barriers to appropriate CKD care. These initiatives are being supplemented by the development of clinical practice guidelines and performance measures to articulate best clinical practices and facilitate their monitoring.

"When there is a problem, he does not want to hear about it. When he hears, he does not listen. When he listens, he does not understand. When he understands, he does not follow-up. When he follows-up, it is always with half-measures."

The penultimate intent is to disprove this contention; the ultimate intent is to improve ESRD outcomes by focusing on CKD processes of care.

References

1. National Institute of Diabetes and Digestive and Kidney Diseases: *Healthy People 2010: Chronic Kidney Disease*, Bethesda MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2000
2. U.S. Renal Data System: *USRDS 2002 Annual Report: Atlas of End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2002
3. U.S Renal Data System: *USRDS 1993 Annual Report*, Bethesda, MD, 1993
4. U.S. Renal Data System: *USRDS 1999–2002 Annual Reports: Atlas Of End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1999–2002
5. US Renal Data System: *USRDS 1999 Annual Report: Atlas of End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 1999.
6. Jones CA, McQuillan GM, Kusek JW, Eberhardt MS, Herman WH, Coresh J, Salive M, Jones CP, Agodoa LY: Serum creatinine levels in the US Population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 32: 992–999, 1998
7. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D, for the Modification of Diet in the Renal Disease Study Group: A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Annal Int Med* 130: 461–470, 1999
8. Clase CM, Garg AX, Kiberd BA: Prevalence of low glomerular filtration rate in non-diabetic Americans: Third National Health And Nutrition Examination Survey (NHANES III). *J Am Soc Nephrol*, in-press
9. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. *Am J Kidney Dis* 39: S1–S242, 2002
10. Renal Physicians Association*: Appropriate Preparation of the Patient for Renal Replacement Therapy: Clinical Practice Guideline No. 3*, Rockville, MD, RPA 2002
11. National Center for Health Statistics: *Third National Health and Nutrition Examination Survey, 1988-1994: Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–94* [CD-ROM, rev. Sept. 1997], Hyattsville, MD, Centers for Disease Control and Prevention, 1996
12. Coresh J, Wei GL, McQuillan G, Brancati FL, Levey AS, Jones C, Klag MJ: Prevalence of high blood pressure and elevated serum creatinine level in the United States: Findings from the Third National Health and Nutrition Examination Survey (1988–1994). *Arch Intern Med* 161: 1207–1216, 2001
13. Bakris GL, Williams M, Dworkin L, Elliott WJ, Epstein M, Toto R, Tuttle K, Douglas J, Hsueh W, Sowers J, for the National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group: Preserving renal function in adults with hypertension and diabetes: A consensus approach. *Am J Kidney Dis* 36: 646–661, 2000
14. McClellan WM, Knight DF, Karp H, Brown WW: Early detection and treatment of renal disease in hospitalized diabetic and hypertensive patients: important differences between practice and published guidelines. *Am J Kidney Dis* 29: 368–375, 1997
15. Kissmeyer L, Kong C, Unwin RJ, Woolfson RG, Neild GH: Community nephrology: Audit of screening for renal insufficiency in a high risk population. *Nephrol Dial Transplant* 14: 2150–2155, 1999
16. NKF-DOQI: Clinical practice guidelines for the treatment of anemia of chronic renal failure: National Kidney Foundation-Dialysis Outcomes Quality Initiative. *Am J Kidney Dis* 30: S192–S240, 1997
17. Fink J, Blahut S, Reddy M, Light P: Use of erythropoietin before the initiation of dialysis and its impact on mortality. *Am J Kidney Dis* 37: 348–355, 2001
18. Collins AJ, Li S, St Peter W, Ebben J, Roberts T, Ma JZ Manning W: Death, hospitalization, and economic associations among incident hemodialysis patients with hematocrit values of 36 to 39%. *J Am Soc Nephrol* 12: 2465–2473, 2001
19. Collins AJ, Li S, Ebben J, Ma JZ, Manning W: Hematocrit levels and associated Medicare expenditures. *Am J Kidney Dis* 36: 282–293, 2000
20. Ma JZ, Ebben J, Xia H, Collins AJ: Hematocrit level and associated mortality in hemodialysis patients. *J Am Soc Nephrol* 10: 610–619, 1999
21. Owen WF, Szczech L, Johnson C, Frankenfield D: National perspective on iron as a clinical performance measure of maintenance hemodialysis patients. *Am J Kidney Dis* 34: S1–S9, 1999
22. Coladonato JA, Frankenfield DL, Reddan D, Klassen P, Szczech L, Johnson CA, Owen WF: Trends in anemia management among U.S. hemodialysis patients. *J Am Soc Nephrol* 13: 1288–1295, 2002

23. NKF-DOQI: Clinical practice guidelines for vascular access: National Kidney Foundation-Dialysis Outcomes Quality Initiative. *Am J Kidney Dis* 30: S150–191, 1997
24. NKF-K/DOQI: Clinical practice guidelines for vascular access: update 2000. *Am J Kidney Dis* 37: S137–S181, 2001
25. Reddan D, Klassen P, Frankenfield DL, Szczech L, Schwab S, Coladanato J, RoccoM, Owen WF: National profile of practices patterns for hemodialysis vascular access in the United States. *J Am Soc Nephrol*, in press
26. Woods JD, Turenne MN, Strawderman RL, Young EW, Hirth RA, Port FK, Held PJ: Vascular access survival among incident hemodialysis patients in the United States. *Am J Kidney Dis* 30: 50–57, 1997
27. Avorn J, Bohn RL, Levy E, Levin R, Owen WF, Winkelmayer WC, Glynn R: Nephrologist care and mortality in patients with chronic renal insufficiency. *Arch Int Med.* 162: 2002–2006, 2002
28. Avorn J, Winkelmayer W, Bohn RL, Levin R, Glynn RJ, Levy E, Owen WF: Delayed nephrologist referral and inadequate vascular access in patients with advanced chronic kidney failure. *J Clin Epidemiol* 55: 711–716, 2002
29. Klassen PS, Reddan DN, Schwab S, Szczech LA, Coladonato JA, Frankenfield DL, Owen WF: Association between vascular access types and hemodialysis patient mortality. *JAMA*, in review.
30. Winkelmayer WC, Glynn RJ, Levin R, Owen WF, Avorn J: Late referral and modality choice in end-stage renal disease. *Kidney Int* 60: 1547–1554, 2001
31. Wolfe RA, Ashby VB, Milford EL, Ojo AO, Ettenger RE, Agodoa LYC, Held PJ, Port FK: Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med* 341: 1725–1730, 1999
32. Epstein AM, Ayanian JZ, Keogh JH, Noonan SJ, Armistead N, Cleary PD, Weissman JS, David-Kasdan JA, Carlson D, Fuller J, Marsh D, Conti RM: Racial disparities in access to renal transplantation —clinically appropriate or due to underuse or overuse? *N Engl J Med* 343: 1537–1544, 2000
33. Mange KC, Joffe MM, Feldman HI: Effect of the use or nonuse of long-term dialysis on the subsequent survival of renal transplants from living donors. *N Engl J Med* 344: 726–731, 2001
34. Rasgon S, Schwankovsky L, James-Rogers A, Widrow L, Glick J, Butts E: An intervention for employment maintenance among blue-collar workers with end-stage renal disease. *Am J Kid Dis* 22: 403–412, 1993
35. Winkelmayer WC, Owen W, Glynn RJ, Levin R, Avorn J: Preventive health care measures before and after start of renal replacement therapy. *J Gen Int Med*, in-press
36. Avorn J, Bohn RL, Levy E, Levin R, Owen WF, Winkelmayer WC, Glynn R: Nephrologist care and mortality in patients with chronic renal insufficiency. *Arch Int Med* 162: 2002–2006, 2002
37. Kinchen KS, Sadler S, Fink N, Brokmeyer R, Klag MJ, Levey AS, Powe NR: The timing of specialist evaluation in chronic kidney disease and mortality. *Ann Int Med* 137: 479–486, 2002
38. Winkelmayer WC, Glynn RJ, Levin R, Owen WF, Avorn J: Determinants of delayed nephrologist referral in patients with chronic kidney disease. *Am J Kidney Dis* 38: 1178–1184, 2001