Outcomes and Care Associated with Residential Area Life Expectancy in Patients with ESRD

The general population of the United States faces significant geographic variation in health status due to complex factors that include regional differences in health indicators such as morbidity, mortality, and physical and mental disability. There is also regional variation in social determinants of health that include environmental and behavioral risk factors, access to healthcare and a healthy diet, education level, and socioeconomic status.

For example, the estimated life expectancy from birth in rural Virginia and Mississippi is approximately 65 years, compared with Gunnison, Colorado, and Fairfax, Virginia, where life expectancy is approximately 82 years. Results of empirical studies have suggested that the primary sources of this variation are factors such as individual behavior and environmental conditions.

In individuals with end-stage renal disease (ESRD), studies have assessed the association of area-level (ecologic) factors including median household income level, social deprivation, and income inequality on ESRD outcomes. Results of empirical studies have suggested that the primary sources of this variation are factors such as individual behavior and environmental conditions.

Medicare Paid $2.3 Billion in 2013 for Vascular-Access Related Services

Reliable access to the bloodstream is essential to successful treatment of end-stage renal disease (ESRD) with maintenance hemodialysis. Patients typically receive hemodialysis three times a week; the vascular access is the patient’s lifeline.

There are three types of hemodialysis vascular access: (1) arteriovenous fistula (AVF); (2) arteriovenous graft (AVG); and (3) central venous catheter (CVC). Numerous studies have found reduced morbidity and mortality in patients dialyzing

Risk of Mortality Higher in Patients with Kidney Disease and Pulmonary Hypertension

Patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) commonly experience pulmonary hypertension. Depending on the methods used to diagnose pulmonary hypertension and evaluate the stages of CKD, the prevalence ranges from 10% to 70%. One factor in the presence of pulmonary hypertension in patients with kidney disease is the pathophysiologic sequelae of CKD, including volume overload, congestive heart failure, endothelial dysfunction, and arteriovenous fistulas.

The typical definition of pulmonary hypertension is pulmonary artery mean pressure >25 mm Hg at rest, measured by right-sided cardiac catheterization. Because cardiac catheterization is invasive, pulmonary hypertension is often diagnosed using echocardiography to calculate estimated pulmonary artery systolic pressure (PASP). There are five categories of pulmonary hypertension defined by the World Health Organization based on cause: pulmonary arterial hypertension, pulmonary hypertension due to left-sided cardiac disease, pulmonary hypertension due to lung disease or hypoxia, chronic thromboembolic pulmonary hypertension, and pulmonary hypertension due to unclear multifactorial mechanisms.

Results of previous studies have suggested that there may be an association between pulmonary hypertension and increased risk for adverse outcomes in patients with CKD and ESRD. However, there are few data available on the magnitude of the
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Treatment of Diabetic Nephropathy: Are We Witnessing the Dawn of a New Era?

Diabetic nephropathy is the most common cause of end-stage renal disease. With the rates of type 2 diabetes reaching epidemic proportions worldwide, it is likely that diabetes as a cause of kidney failure will continue to increase. The current treatment of diabetic nephropathy focuses on tight control of blood sugar, control of blood pressure, and the use of renin-angiotensin blockade with either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB).

The emergence of sodium-glucose linked transporter type 2 (SGLT2) inhibitors, which are sodium-glucose cotransporter 2 inhibitors, has presented a unique opportunity to further slow kidney progression. Medicines in the SGLT2 inhibitor class include canagliflozin, dapagliflozin, and empagliflozin.

Zinman and colleagues in 2015 reported that empagliflozin was superior to placebo in reducing the risk of major cardiovascular events. In a follow-up secondary analysis of renal outcomes from this randomized trial, published in 2016, Wanner and colleagues reported that empagliflozin administration was also associated with significant renoprotection, including slowing the rate of decline in estimated glomerular filtration rate, progression of albuminuria, and initiation of renal replacement therapy. These results strongly suggested but didn’t prove that SGLT2 inhibitors might have an important role in slowing progression of diabetic nephropathy. Another randomized trial was needed to do this.

Therefore, the news that the CREDENCE (Canagliflozin and Renal Endpoints in Diabetes with Established Nephropathy Clinical Evaluation) trial—a double blind placebo controlled RCT evaluating the role of the SGLT2 inhibitor canagliflozin in renoprotection—was stopped early by the data monitoring committee due to positive efficacy results is striking.

CREDENCE assessed whether treatment with the SGLT2 inhibitor canagliflozin in patients with type 2 diabetes and stage 2 or 3 chronic kidney disease and macroalbuminuria provided kidney and vascular protection effect compared with placebo. The trial enrolled approximately 4400 patients. All patients were required to be treated with either an ACE inhibitor or an ARB 4 weeks prior to randomization. This news about CREDENCE comes following data presented recently at the American Diabetes Association from the CANVAS (Canagliflozin Cardiovascular Assessment Study) in which patients with type 2 diabetes at high risk for cardiovascular disease treated with canagliflozin demonstrated slowing in kidney progression compared with those treated with placebo.

What’s the bottom-line? The emerging data now strongly point to benefit in using SGLT2 inhibitors in the treatment of diabetic nephropathy. We are at the dawn of a new era where tight glucose control, blood pressure reduction, and renin angiotensin blockade will not be enough. The use of an SGLT2 inhibitor to both better manage blood sugar and reduce blood pressure will become an essential and key component to managing diabetic nephropathy and slowing progression of kidney disease.

REFERENCES
3. Evaluation of the Effects of Canagliflozin on Renal and Cardiovascular Outcomes in Participants With Diabetic Nephropathy [CREDENCE](https://clinicaltrials.gov/ct2/show/NCT02065791)
The earlier studies have not included evaluation of the costs related to AVF management in a representative hemodialysis population in the United States. Mae Thamer, PhD, and colleagues recently conducted a retrospective observational study utilizing national claims data to examine the costs to Medicare of vascular access creation, maintenance, and associated complications. Results of the study were reported in the American Journal of Kidney Diseases [2018;72(1):10-18].

Patients were stratified into cohorts based on timing of AVF creation relative to initiation of hemodialysis therapy. Costs were evaluated over 2.5 years of follow-up based on clinical outcomes. Study participants were elderly US Medicare beneficiaries who initiated hemodialysis therapy from 2010 to 2011. The study predictor was AVF primary and secondary patency and nonuse during the first year after AVF creation. The outcome of interest was annualized vascular access costs per patient per year.

The three study cohorts were (1) cohort 1 initiated hemodialysis therapy with a mature AVF (n=2704); (2) cohort 2 initiated hemodialysis therapy with a CVC and a maturing AVF (n=3530); and (3) cohort 3 initiated hemodialysis therapy with a CVC only and an AVF was created within 9 months of initiation of hemodialysis therapy (n=3901).

The AVF was placed approximately 5 months (median, 144 days) prior to dialysis therapy initiation in patients in cohort 1, who were less likely to be institutionalized, more likely to ambulate, had less cardiac and pulmonary disease, and had higher concentrations of albumin compared with the other two cohorts (P <.001 for all comparisons). There were also more women and a higher proportion of patients with ESRD in cohort 1 compared with cohorts 2 and 3 (P <.001). Compared with cohorts 1 and 2, those in cohort 3 were more likely to live in areas with the lowest median household income and were significantly less likely to have nephrology care prior to initiation of dialysis therapy (49% vs 8.0% for cohort 1 and 26.3% for cohort 2).

Of the patients in cohorts 2 and 3 who initiated hemodialysis therapy using a CVC with or without a maturing AVF, 46% of AVFs were not used for hemodialysis. Of AVFs that were used for hemodialysis, 40% to 63% required ≥1 interventional or surgical procedure before the first AVF use, and 70% to 80% required ≥1 interventional or surgical procedure within 1 year of creation. Patients in cohort 1 were more likely to maintain AVF patency in the first year (P <.001 for all comparisons). If the AVF was successfully used, subsequent abandonment of the AVF in the first year (secondary patency loss) was similar between groups (9.5% to 10.6%; pairwise comparisons P >.04).

In the first year after AVF creation, total mean annualized per patient per year vascular access costs were lowest for patients whose AVF maintained patency in year 1 compared with patients whose AVF experienced primary or secondary patency loss in year 1.

In 2013, fee-for-service Medicare paid $2.3 billion for services related to dialysis vascular access, accounting for approximately 12% of all payments related to ESRD. Of that amount, 50.1% was for inpatient care related to vascular access procedures or complications, 39.6% for invasive imaging and endovascular procedures, 8.6% for open surgical procedures performed on outpatients, 1.1% for anesthesia used in vascular access procedures, and 0.6% for noninvasive diagnostic imaging procedures.

Limitations cited by the authors included the inability to calculate vascular access costs for predialysis procedures and costs, lack of data on why such a large percentage of fistulas (nearly half) were never used, the lack of data for Medicare health maintenance organization patients or those with non-Medicare claims, lack of a comparison of costs between AVFs and AVGs, and only capturing costs from the perspective of the third-party payer.

In summary, the researchers said, “This study suggests that AVFs that experience dysfunction in the first year after creation, especially those that are never used for hemodialysis, result in substantially higher long-term costs. There remains an unmet clinical need for improving outcomes and reducing avoidable costs after AVF surgical creation.”

With an AVF. Compared with patients with an AVF, those with a CVC rates of cardiovascular events and all-cause and infection-related mortality are higher.

To achieve twin goals of improving health outcomes and lowering costs, the Centers for Medicare & Medicaid Services (CMS) promote the use of AVFs. In 2002, CMS created the Fistula First Initiative, with an initial goal of AVF use in 40% of prevalent hemodialysis patients; the goal was subsequently increased to 66%. Currently, the CMS Quality Incentive Program provides a financial incentive for providers to increase CVF use by imposing reimbursement penalties on dialysis units based in part on prevalence of AVFs.
The prevalence of pulmonary hypertension was 28% in the study population. Mean sample size was 247 (range, 36-2959), and mean follow-up ranged from 1 to 7 years. Three studies recruited patients with CKD stages 1 to 5, two were of kidney transplant recipients, and the remaining 11 included patients with ESRD undergoing dialysis. Of the 11 studies of dialysis populations, seven were limited to hemodialysis, two were limited to peritoneal dialysis, and two included both modalities.

In all 16 studies, pulmonary hypertension was diagnosed based on measurements using Doppler echocardiography. Ten studies used the diagnostic standard estimated PASP >35 mm Hg; four used alternative cutoff values (50, 37, 45, and 50 mm Hg), one adopted tricuspid regurgitant velocity >2.5 m/s as the diagnostic method, and another defined pulmonary hypertension as a tricuspid regurgitant velocity >2.5 m/s. Fourteen studies included data on all-cause mortality, representing 6472 participants. There were associations between pulmonary hypertension and increased risk for all-cause mortality among patients with CKD stages 1 to 5 (relative risk [RR], 1.44; 95% confidence interval [CI], 1.17-1.76; \( P < .001 \)), patients with ESRD receiving dialysis (RR, 2.33; 95% CI, 1.76-3.08; \( P < .001 \)), and recipients of kidney transplants (RR, 2.08; 95% CI, 1.35-3.20; \( P < .001 \)), with low heterogeneity (I\(^2\)=0%; 95% CI, 0%-71%).

TAKEAWAY POINTS
- Patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) commonly experience pulmonary hypertension, but there are few data available on the impact of pulmonary hypertension in those patient populations.
- Results of a recent systematic review and meta-analysis demonstrated an association between pulmonary hypertension and a substantially increased risk for all-cause mortality and cardiovascular events in patients with CKD and ESRD.
- Compared with patients with CKD stages 1 to 5, the risk was higher in patients with ESRD receiving dialysis.

Four studies representing 1959 participants reported the hazard ratio (HR) of cardiovascular mortality. In patients with CKD and ESRD, there was an association between pulmonary hypertension and increased risk for cardiovascular mortality (RR, 2.20; 95% CI, 1.23-3.93; \( P < .001 \)), with low heterogeneity (I\(^2\)=0%; 95% CI, 0%-85%). Seven studies involving 4601 participants assessed the higher risk for pulmonary hypertension on cardiovascular events. Results of meta-analysis revealed an increased risk for cardiovascular events in patients with CKD with pulmonary hypertension (RR, 1.67; 95% CI, 1.07-2.60; \( P < .02 \)), with moderate heterogeneity (I\(^2\)=65%; 95% CI, 22%-85%). There was also an association between higher risk for cardiovascular events in patients with ESRD receiving dialysis and pulmonary hypertension (RR, 2.33; 95% CI, 1.76-3.08; \( P < .001 \)), with low heterogeneity (I\(^2\)=0%; 95% CI, 0%-71%).

There were some limitations to the review cited by the authors, including the inability to control for confounding factors, the observational design of the study that precluded assessment of causality, the scarcity of data regarding the impact of pulmonary hypertension in patients with CKD stages 1 to 5, the possibility of outcome reporting bias, and the limited evidence for the two secondary outcomes (cardiovascular mortality and cardiovascular events).

The researchers said, “In conclusion, pulmonary hypertension is consistently associated with adverse outcomes, including all-cause mortality and cardiovascular events, in patients with advanced kidney disease. Risk stratification of CKD and ESRD could consider pulmonary hypertension as a significant predictor for long-term survival. Ultimately, randomized studies are needed to determine whether pulmonary hypertension treatments in patients with decreased kidney function can improve the excess mortality burden associated with the coexistence of these conditions.”
Researchers conducted a national retrospective cohort study to examine the association between residential area life expectancy and outcomes and processes of care for patients with end-stage renal disease living in the United States. Patients were categorized into quintiles based on life expectancy in residential counties: patients in quintile 1 (Q1) had lower life expectancies compared with patients in Q5.

There was an independent association between residential area life expectancy and mortality and processes of care measures for patients with ESRD.
INDICATION
Velphoro® (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

IMPORTANT SAFETY INFORMATION
• Velphoro must be administered with meals. Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, the tablets may be crushed.
• Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal (GI) surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.
• In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (6%).

VPhoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin. Take doxycycline at least 1 hour before Velphoro. Velphoro should not be prescribed with oral levothyroxine.

Please see Brief Summary on adjacent page or visit www.Velphoro.com for full Prescribing Information.

* A retrospective analysis of pharmacy data assessed the real-world effectiveness of Velphoro in 1,029 adult in-center hemodialysis patients who were switched to Velphoro during routine care. The study compared the proportion of patients with phosphorus levels ≤ 5.5 mg/dL and the mean prescribed phosphate binder pills/day at baseline (3 months prior to Velphoro; binders included sevelamer carbonate, calcium acetate, and lanthanum carbonate) and during Velphoro follow-up (6 months after switch to Velphoro, n=424). This was a noninterventional analysis and did not impact prescriptions or prescribing patterns.1

VELPHORO®
(sucroferric oxyhydroxide)
chewable tablets

INDICATIONS AND USAGE
Velphoro (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

DOSED AND ADMINISTRATION
Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, tablets may be crushed.

The recommended starting dose of Velphoro is 3 tablets (1,500 mg) per day, administered as 1 tablet (500 mg) 3 times daily with meals. Adjust by 1 tablet per day as needed until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. Titrate as often as weekly.

DOSED FORMS AND STRENGTHS
Velphoro (sucroferric oxyhydroxide) chewable tablet 500 mg.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal surgery, or with a history of hemosiderosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.

ADVERSE REACTIONS
In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (8%).

The following adverse reactions were identified during post approval use of Velphoro, and were reported voluntarily from a population of uncertain size.

Gastrointestinal Disorders: tooth discoloration
Skin and Subcutaneous Tissue Disorder: rash

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Medical Care North America at 1-800-323-5188 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin.

Take doxycycline at least 1 hour before Velphoro.

Velphoro should not be prescribed with oral levothyroxine.

USE IN SPECIFIC POPULATIONS
Pregnancy

Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 16 and 4 times, respectively, the human maximum recommended clinical dose on a body weight basis, and have not revealed evidence of impaired fertility or harm to the fetus due to Velphoro. However, Velphoro at a dose up to 16 times the maximum clinical dose was associated with an increase in post-implantation loss in pregnant rats. Animal reproduction studies are not always predictive of human response. There are no adequate and well-controlled studies in pregnant women.

Labor and Delivery

No Velphoro treatment-related effects on labor and delivery were seen in animal studies with doses up to 16 times the maximum recommended clinical dose on a body weight basis. The effects of Velphoro on labor and delivery in humans are not known.

Nursing Mothers

Since the absorption of iron from Velphoro is minimal, excretion of Velphoro in breast milk is unlikely.

Pediatric Use

The safety and efficacy of Velphoro have not been established in pediatric patients.

Geriatric Use

Of the total number of subjects in two active-controlled clinical studies of Velphoro (N=835), 29.7% (n=248) were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

OVERDOSAGE

There are no reports of overdosage with Velphoro in patients. Since the absorption of iron from Velphoro is low, the risk of systemic iron toxicity is low. Hypophosphatemia should be treated by standard clinical practice.

Velphoro has been studied in doses up to 3,000 mg per day.

HOW SUPPLIED/STORAGE AND HANDLING
Velphoro are chewable tablets supplied as brown, circular, bi-planar tablets, embossed with “PA 500” on 1 side. Each tablet of Velphoro contains 500 mg iron as sucroferric oxyhydroxide. Velphoro tablets are packaged as follows:

NDC 49230-645-51 Bottle of 90 chewable tablets

Storage

Store in the original package and keep the bottle tightly closed in order to protect from moisture.

Store at 25°C (77°F) with excursions permitted to 15 to 30°C (59 to 86°F).

PATIENT COUNSELING INFORMATION
Inform patients that Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, the tablets may be crushed (see Dosage and Administration).

Velphoro should be taken with meals.

Instruct patients on concomitant medications that should be dosed apart from Velphoro (see Drug Interactions).

Inform patients that Velphoro can cause discolored (black) stool.

Inform patients that Velphoro can cause tooth staining.

Inform patients to report any rash to their healthcare professional.

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Kidney Function Decline

Post Hoc Analysis of HALT-PKD Data Examines Patterns of Kidney Function Decline

According to Godela M. Brosnahan, MD, and colleagues, there are few data on a detailed examination of individual patterns of decline in estimated GFR (eGFR). Utilizing data from the HALT-PKD (Halt Progression of Polycystic Kidney Disease) trials, Dr. Brosnahan et al. conducted a longitudinal post hoc analysis to test the hypothesis that GFR decline in ADPKD is not always linear and that periods of stability can occur even in advanced cases. Results of the analysis were reported in the American Journal of Kidney Diseases [2018;71(5):666-676].

The current analysis included 494 HALT-PKD Study A participants and 435 HALT-PKD Study B participants. The Study A participants were younger and had preserved eGFR compared with Study B participants who were older and had reduced eGFR. Eligible participants had >3 years of follow-up and seven or more assessments of eGFR. Relevant measurements were longitudinal eGFR assessments using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation. Outcomes of interest were the probability of linear and nonlinear patterns of decline or of stable eGFR calculated for each participant form a Bayesian model of individual eGFR trajectories.

STUDY A
During mean follow-up of the 494 Study A participants, 62.5% (n=309) were classified as linear progressors, 21% (n=108) as nonlinear progressors, and 15.6% (n=77) as nonprogressors.

Some baseline characteristics, i.e., age, sex, baseline eGFR, and left ventricular mass index, were similar across the three groups. However, compared with both groups of progressors, the nonprogressors had significantly smaller total kidney volume (TKV) and height-adjusted TKV, higher renal blood flow, and lower urinary albumin excretion. The nonprogressor group also included a higher proportion of low-risk cases and a lower proportion of high-risk cases. Mean slopes for annual TKV increase for linear progressors, nonlinear progressors, and nonprogressors were 6.4% (95% confidence interval [CI], 6.0-6.8), 6.3% (95% CI, 5.6-7.0), and 4.8% (95% CI, 4.0-5.7), respectively (P=0.006 between groups).

During the trial, blood pressures were similar in the three groups; the number of medication steps required to achieve the blood pressure goal was slightly lower in the nonprogressor group. By definition, decline in eGFR was significantly greater in progressors compared with nonprogressors, who had no significant change in eGFR. Mean slopes for linear and nonlinear progressors were –3.5 (95% CI, –3.2 to –3.7) and –3.7 (95% CI, –3.3 to –4.0) mL/min/1.73 m² per year (P<.001 between groups). There was no association between age and rate of eGFR decline in linear progressors.

Sixty-two percent of nonprogressors had the PKD1 genotype and 84% had a family history of ADPKD. Patients in the progressor groups had slightly higher rates of acute kidney injury (AKI), but gross hematuria and hospitalizations were equally common in all three groups. With the exception of age, the three groups were similar in baseline characteristics; nonprogressors (14 men, 11 women) were older than progressors. There was no significant difference in muscle mass estimated by daily creatinine excretion; blood pressures and number of medication steps needed to achieve the blood pressure goal were also not different. Because none of the nonprogressors achieved an end point, they remained in the trial significantly longer, whereas >50% of progressors did reach an end point.

Nonprogressors had a nonsignificant decline in eGFR. Mean slopes for linear and nonlinear progressors were –3.9 (95% CI, –3.8 to –4.1) and –3.8 (95% CI, –3.3 to –4.2) mL/min/1.73 m² per year (P>.001 between groups). Among linear progressors, there was an association between younger age and faster progression; a 10-year decrease in baseline age resulted in a 0.86 mL/min/1.73 m² per year steeper eGFR slope (P<.001).

Two-thirds of the nonprogressor group had the PKD1 genotype. Of those, one-third had a truncating PKD1 mutation, but weak nontruncating mutations were more common. Seventy-six percent of nonprogressors had a family history of ADPKD.

In summary, the researchers said, “This is to our knowledge the first large analysis of the nonlinear progressor group experienced episodes of AKI; frequency of hospitalizations was similar in the three groups. There was no temporal relationship between those events and steeper eGFR slopes observed.

The relatively short observation time (5 to 8 years) and limited data on individual clinical events were cited by the authors as limitations to the study. Also cited was the absence of magnetic resonance imaging in Study B and the use of eGFR as opposed to measured GFR.

In summary, the researchers said, “This is to our knowledge the first large analysis of individual patterns of eGFR decline in ADPKD. Loss of kidney function is not always linear and rapid; prolonged stabilization of GFR can occur even in advanced disease. Future trials evaluating the effect of treatment on eGFR will need to recognize that eGFR slopes in ADPKD can have varying configurations and can change in 13% to 22% of patients without apparent cause.”

TAKEN POINTS
Results of earlier studies of autosomal dominant polycystic kidney disease (ADPKD) indicated that loss of kidney function commonly followed a steep and relentless course.

In a recent study, researchers tested the hypothesis that decline in glomerular filtration rate (GFR) is not always linear and rapid and that even in advanced disease periods of stability can occur.

Study results found that a substantial fraction of patients with ADPKD experience prolonged intervals of stable GFR; there was an association of lower body mass index with more stable kidney function in early disease.
Study Protocol: Outcomes in Dialysis Patients with Aortic Stenosis

Worldwide, the number of patients receiving maintenance dialysis is increasing. Diabetic nephropathy and hypertensive kidney disease account for many of these patients. In addition, chronic kidney disease (CKD) is an independent risk factor for cardiovascular disease, which leads to difficulty of aortic stenosis and traditional risk factors, including aging and comorbidity of diabetes; (3) there is an association between new onset and development of aortic stenosis and dialysis-specific factors, including hyperphosphatemia, hypercalcemia, and hyperparathyroidism; (4) patients with infection-related mortality rates, and new onset or development of aortic stenosis have poorer outcomes compared with patients without aortic stenosis at baseline; and (5) outcomes are poorer depending on stage of aortic stenosis.

Seventy-five centers in the Tokai region of Japan will enroll approximately 2400 patients with and without aortic stenosis during a 12-month enrollment period. Inclusion criteria are receiving outpatient maintenance dialysis for at least 12 months, age >20 years, echocardiography annually, and participation agreement. Outcomes of interest will be all-cause mortality rates, incidence of cardiovascular events, cardiovascular-related mortality rates, infection-related mortality rates, and new onset or development of aortic stenosis. Follow-up will continue until June 2023.

Outcomes of interest will be all-cause mortality rates, incidence of cardiovascular events, cardiovascular-related mortality rates, infection-related mortality rates, and new onset or development of aortic stenosis. Follow-up will continue until June 2023.

with dialysis therapy. While coronary heart disease is typical among patients with cardiovascular disease, patients on dialysis are increasingly being diagnosed with aortic stenosis.

Results of previous studies have indicated a relationship between aging, hypertension, diabetes, or lipid disorders with onset and progression of aortic stenosis. Due to factors that include hyperphosphatemia and anemia, patients on dialysis are more likely to develop aortic stenosis compared with the general population; however, there are few data available on morbidity rate and risk factors of aortic stenosis among dialysis patients. Data are also lacking on the association between aortic stenosis in dialysis patients and mortality or onset of cardiovascular events.

Daijo Inaguma, MD, PhD, and colleagues recently described study protocol for a multicenter, prospective cohort analysis in the Tokai region of Japan (Tokai Aortic Stenosis Cohort in Patients on Dialysis). The researchers are seeking to determine whether there is an association between morbidity of aortic stenosis in dialysis patients and mortality. The study protocol was reported online in BMC Nephrology [doi:10.1186/s12882-018-0877-6].

The study is designed to test the hypothesis that: (1) the prevalence of aortic stenosis is higher in patients on dialysis than in the general population; (2) there is an association between new onset and development of aortic stenosis and traditional risk factors, including aging and comorbidity of diabetes; (3) there is an association between new onset and development of aortic stenosis and dialysis-specific factors, including hyperphosphatemia, hypercalcemia, and hyperparathyroidism; (4) patients with infection-related mortality rates, and new onset or development of aortic stenosis have poorer outcomes compared with patients without aortic stenosis at baseline; and (5) outcomes are poorer depending on stage of aortic stenosis.

Seventy-five centers in the Tokai region of Japan will enroll approximately 2400 patients with and without aortic stenosis during a 12-month enrollment period. Inclusion criteria are receiving outpatient maintenance dialysis for at least 12 months, age >20 years, echocardiography annually, and participation agreement. Outcomes of interest will be all-cause mortality rates, incidence of cardiovascular events, cardiovascular-related mortality rates, infection-related mortality rates, and new onset or development of aortic stenosis. Follow-up will continue until June 2023.

Baseline is defined as the first echocardiography from July 2017 to June 2018. The researchers will review (1) age, sex, dialysis vintage, and original kidney disease, blood pressure, and resting heart rate; (2) comorbidities, including diabetes mellitus and malignancy; (3) medical history including hospitalization due to heart failure within 1 year, coronary heart disease, aortic disease, stroke, peripheral artery disease, malignancy, and history of parathyroidectomy; (4) medications, including renin-angiotensin blockers, calcium channel blockers, beta blockers, vitamin D receptor activators, calcimimetics, phosphate binders, and warfarin; (5) laboratory data including hemoglobin, platelet count, and serum albumin, alkaline phosphatase, uric acid, urea nitrogen, creatinine, adjusted calcium, phosphorus, magnesium, intact parathyroid hormone, ferritin, and C-reactive protein levels.

Aortic stenosis will be diagnosed using criteria based on the 2014 American Heart Association/American College of Cardiology Guideline (AHA/ACC) for the Management of Patients with Valvular Heart Disease: (1) mean pressure gradient (mPG) >20 mmHg or (2) aortic valve area (AVA) <1.0 cm² or (3) aortic maximum aortic jet velocity (Vmax) >2.0 m/s. Stages A to D of aortic stenosis will be evaluated according to the AHA/ACC Guideline.

Transathoracic echocardiography will be performed using commercially available ultrasound systems owned by each facility during enrollment and at 12, 24, 36, 48, and 60 months. Findings will be confirmed by a cardiologist. Doppler echocardiographic measurements will include the peak and trans-aortic mPG using the Bernoulli equation, and the AVA using the standard continuity equation or planimetry method in most facilities.

Survival prognosis and cardiovascular events will be assessed at the end of June 2019, 2020, 2012, 2022, and 2023. Development of aortic stenosis will be evaluated as new onset or annual change in aortic stenosis parameters (mPG, AVA, and aortic Vmax).

Patients will be classified based on the presence or absence of aortic stenosis, and on stage of aortic stenosis. Outcomes will be compared between the two groups.

Either the Thoracic Surgeons predicted risk of mortality score or the EuroScore is generally used in evaluations of risk in decision-making regarding selection of surgical treatment for patients with aortic stenosis with high risk, such as patients on dialysis. “However,” the current study’s researchers said, “the incidence of complications and morality associated with treatment have been higher in dialysis patients.”

Optimal treatment selection by stages of aortic stenosis in dialysis patients remains unknown. “Therefore, we expect that the results of our study will lead to a treatment strategy for dialysis patients with aortic stenosis.”

Trial registration: UMIN000026756
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**IMPORTANT SAFETY INFORMATION**

**Warnings and Precautions**
Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving parenteral iron products. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. Monitor patients for signs and symptoms of hypersensitivity during and after hemodialysis until clinically stable. Personnel and therapies should be immediately available for the treatment of serious hypersensitivity reactions. Hypersensitivity reactions have been reported in 1 (0.3%) of 292 patients receiving Triferic in two randomized clinical trials.

Iron status should be determined on pre-dialysis blood samples. Post dialysis serum iron parameters may overestimate serum iron and transferrin saturation.

**Adverse Reactions**
The most common adverse reactions (>3% and at least 1% greater than placebo) in controlled clinical studies include: headache, peripheral edema, asthenia, AV fistula thrombosis, urinary tract infection, AV fistula site hemorrhage, pyrexia, fatigue, procedural hypotension, muscle spasms, pain in extremity, back pain, and dyspnea.


For full Safety and Prescribing Information please visit www.triferic.com.
Time Trends in ESRD in France and Forecast to the Year 2030

Due to the increasing number of patients in France with end-stage renal disease (ESRD) requiring renal replacement therapy (RRT), the management of ESRD is a top public health priority. As of December 31, 2015, there were 82,295 patients receiving RRT: 54% of those were on dialysis and 46% were living with a functional renal transplant. Overall, the crude prevalence was 1232 per million inhabitants.

Two registries developed and managed by the French Biomedicine Agency include and follow patients with ESRD: the French Renal Epidemiology and Information Network (REIN), created in 2001 and specific to dialysis patients, and the CRISTAL registry, specific to transplant patients. REIN includes nephrologists, epidemiologists, patients, and public health representatives and is conducted both regionally and nationally.

The Provence-Alpes-Côte d’Azur (PACA) region integrated the REIN registry in 2004. The region has a high proportion of elderly people (19% age ≥65 years vs 17% for France). There are 81 dialysis centers, including two pediatric centers and two transplant units. Anne-Claire Durand, MSc, and colleagues recently conducted a longitudinal study to examine the time trend of RRT for ESRD in the PACA region between 2004 and 2015; the researchers also forecast the data to 2030. Study results were reported online in BMC Nephrology [doi.org/10.1186/s12882-018-0929-y].

A total of 10,055 new patients initiated RRT in the PACA region between January 1, 2004, and December 31, 2015. Of those, 97.7% (n=9822) initiated dialysis therapy and 2.3% (n=233) received a pre-emptive renal transplant. The number of new patients steadily increased by 3.4% since 2004 (rate ratio [RR], 1.034; 95% confidence interval [CI], 1.028-1.039).

Of the patients who initiated dialysis in the PACA region, the number of patients who resided outside of PACA ranged between 1.1% and 3.1%, depending on the year. Those patients lived in the two border regions (Rhône-Alpes and Languedoc-Roussillon). The proportion of pediatric patients <20 years of age ranged from 0.2% to 1.8%, depending on the year.

The number of patients with ESRD who initiated dialysis steadily increased since 2004 by an average of 3.1% per year. In 2004, 657 patients with ESRD began dialysis versus 975 in 2015 (RR, 1.031; 95% CI, 1.025-1.037; P<.001). There was a slight increase in the number of pre-emptive renal transplants during the study period (RR, 1.156; 95% CI, 1.111-1.203; P<.001).

Between 2004 and 2015, mean age at dialysis initiation increased by 1.6 years. Among patients >80 years of age, the increase was an average 6.9% (95% CI, 5.7%-8.0%; P<.001). The proportion of patients with comorbidities also increased by an average of 5.6% per year. The percentage of obese patients increased by nearly 10 points (RR, 1.23; 95% CI, 1.105-1.141; P<.001), percentage of patients with cancer by 5 points (RR, 1.085; 95% CI, 1.064-1.106; P<.001), and percentage of patients with diabetes mellitus by 3.8 points (RR, 1.056; 95% CI, 1.046-1.066; P<.001).

During the study period, the proportion of patients initiating therapy with peritoneal dialysis was low and has remained stable over the past 3 years, at ~8%. Of the patients who initiated therapy with hemodialysis, >88% began treatment in-center.

Since the start of the study period, there was an increase of 3.7% in the number of patients receiving RRT (RR, 1.037; 95% CI, 1.034-1.039; P<.001), from 4433 patients on December 31, 2004, to 6475 on December 31, 2015. During this period, ~1000 additional patients were counted in each of the two methods of RRT: 947 additional patients treated with dialysis (RR, 1.026; 95% CI, 1.024-1.059; P<.001) and 1095 additional patients living with a functional renal transplant (RR, 1.057; 95% CI, 1.053-1.061; P<.001).

The number of renal transplants performed in PACA since 2004 gradually increased by an average of 5.2% per year (RR, 1.052; 95% CI, 1.039-1.064; P<.001). The proportion of transplants from living donors also increased, from none in 2004 to 27 in 2015.

During the study period, the number of patients with ESRD treated by dialysis and living with a functional renal transplant increased linearly and continuously. According to the linear model, if those trends persist, by 2030 the PACA will have ~7871 patients on dialysis and ~3891 patients living with a functional renal transplant to be managed, representing ~3300 additional patients on dialysis than in 2015 and ~1435 additional patients living with a functional renal transplant. The PACA region will have ~600 additional patients initiating dialysis by 2030.

The researchers cited focusing on a single region in France with certain specificities such as older patients and a lower proportion of patients on peritoneal dialysis therapy compared with other regions as a limitation to the analysis. In conclusion, the researchers said, “The originality of this study is to focus on the number of ESRD patients and not only on incidence rates, which allows us to estimate the number of dialysis places expected in the future. This study highlighted the linear increase in the number of ESRD patients in 12 years, with no prospect of stabilization. These results enable the medical community and health authorities to anticipate the supply of care in qualitative or quantitative terms as well as to be a part of a public health approach aimed at integrating more preventive measures to combat obesity and diabetes in order to expect to stabilize the number of ESRD patients in the future.”
Results of recent analyses have shown that veterans receiving care from the Department of Veterans Affairs (VA) healthcare system are experiencing improvements in kidney health outcomes.

Susan T. Crowley, MD, and Katherine Murphy, MHSA, employees of the Veterans Health Administration, suggest that “scrutiny of the agency’s current care model may identify population health initiatives associated with improved outcomes that could potentially be adopted by other healthcare systems.” The authors offered their perspective on Delivering a “New Deal” of Kidney Health Opportunities to Improve Outcomes within the Veterans Health Administration online in the American Journal of Kidney Diseases [doi:10.1053/j.ajkd.2018.01.056]. Rates of risk factors for chronic kidney disease (CKD) in the veteran population exceed those in the general population; rates for diabetes mellitus, hypertension, and overweight/obesity in veterans are 24%, 46%, and 78%, respectively. Estimates of CKD among the VA population range from 4% to 36%, rates that are also higher than in the general population: the prevalence of stages 3 to 4 CKD in the VA population in 2011 was 11.1%, compared with 6.7% in the general population in the United States.

During the past ten years, total annual costs of care for the NDD-CKD population have increased steadily, to $18 billion in fiscal year 2016.

Beginning in the 1990s, the VA moved from an acute hospital care provider model to a prevention-focused primary care model. In 2010, the VA's primary care model was expanded to a comprehensive patient-aligned care team (PACT); kidney care is delivered through the PACT in a model focused on health promotion of longitudinal care. Collaborative primary-specialty care partnerships are supported by evidence-based policy; universal electronic medical records, performance measurement, teletechnology-enabled access, research, innovation, and veteran education.

Indications for nephrology consultation include estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m²; evidence for a rapid decline in eGFR (>5 mL/min/1.73 m²); when complications of CKD (i.e., anemia or abnormalities in calcium or phosphorus) arise; when nephrotic-range proteinuria exists; when the underlying cause of CKD or proteinuria is unclear; or when the patient's severity of disease exceeds the primary care physician's level of comfort. In fiscal year 2016, there were approximately 350,000 encounters with nephrology services other than dialysis.

Inpatient dialysis is available at 125 VA facilities and 74 VA facilities offer outpatient dialysis. Due to a limited capacity, the VA also relies on community providers for the delivery of maintenance dialysis to veterans. In 2013, the VA issued a national contract with 23 outpatient dialysis providers, using Medicare's payment model as a base.

Veterans eligible for home dialysis receive services at either VA dialysis programs or via contracts with community providers.

There are also seven regional VA kidney transplantation centers, offering transportation and indefinite immunosuppressive medications. VA enrollees are less likely to receive a kidney transplant than the general public, but are as likely as Medicare enrollees to be a kidney transplant recipient.

Out-of-pocket expenses for VA enrollees are limited. All virtual care is free, and copays for face-to-face care are nominal or waived. In addition, copays for monthly supplies of medications are capped or waivable.

In analyses of outcomes associated with CKD, trends are encouraging. The age-adjusted incidence rate of ESRD among veterans was 25% to 40% lower than that of nonveterans. The incidence rate of ESRD among veterans has seen a steady decline of 17% from 2009 through 2014.

While kidney care within the VA system meets or exceeds community care, there are opportunities for improvement. The VA has outlined strategies to achieve the agency's goals for improvements:

- Enhance veteran choice
- Ensure health system capacity
- Promote efficiency
- Build sustainability

In summary, the authors said, “As the nation confronts a fundamental revision of healthcare policy, it is imperative that the current paradigm of CKD health services is scrutinized for opportunities to increase healthcare value. Recent analyses of veteran kidney outcomes indicate a benefit of the VA care model for those with CKD. However, because room for improvement exists, the current paradigm is not yet enough for those with CKD. As a fully integrated healthcare system, the VA is uniquely poised to develop, test, and identify emerging tools and models of care to advance additional reforms in kidney health services. ‘Nearly a century ago, President Franklin D. Roosevelt urged the American people during the country’s worst economic crisis to embrace ‘bold, persistent experimenta tion’ to deliver a New Deal to the populace. Through bold and persistent experimentation in health service delivery, the VA can similarly help deliver a New Deal of kidney health opportunities to veterans and, by extension, to all citizens.”

Sixteen percent of VA enrollees, more than one million, are diagnosed with non-dialysis-dependent CKD (NDD-CKD). Compared with veterans without CKD, those with CKD are older (78% are >65 years of age), and 68% are nondiscretionary enrollees, having either a military service-connected disability or meet the low income criterion for VA care.

Estimates of aggregate expenditures for veterans with NDD-CKD demonstrate that while costs increase by CKD stage, the majority of expenditures are associated with the large population with stage 3 CKD. In 2010, the VA’s primary care model was expanded to a comprehensive patient-aligned care team (PACT); kidney care is delivered through the PACT in a model focused on health promotion of longitudinal care.
Polycystic kidney disease (PKD) is characterized by the progressive enlargement of numerous fluid filled cysts in the kidney. The 2 main types of PKD are ARPKD,* and the most commonly seen ADPKD.†

In your patients with ADPKD, COULD KIDNEY DAMAGE BE GOING UNNOTICED? eGFR‡ levels can remain steady over many years, but enlarging cysts continue to increase kidney volume, damaging renal tissue.2,3

Learn about the early signs of disease progression at UncoverPKD.com and screen your patients if you suspect they may be at risk.
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eGFR‡ levels can remain steady over many years, but enlarging cysts continue to increase kidney volume, damaging renal tissue.²,³

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*Autosomal recessive polycystic kidney disease.
†Autosomal dominant polycystic kidney disease.
‡Estimated glomerular filtration rate.

Histologic Findings in Patients Who Switched from Cyclosporine to Everolimus

Decisions regarding immunosuppression following kidney transplantation aim to ensure long-term graft survival. The survival of the graft is associated with a variety of factors that can lead to irreversible nephron loss and progressive dysfunction. Dysfunction commonly occurs relatively late, making graft function a poor marker for the severity of histologic changes such as early tubulointerstitial damage from ischemic-reperfusion injury, acute and subclinical rejection, calcineurin inhibitor (CNI)-related nephrotoxicity, and viral infections. Subclinical rejection is found in 30% to 50% of patients with stable grafts up to 1 year post-transplant, and in up to 15% of patients receiving tacrolimus; it is associated with subsequent tubulointerstitial damage.

One strategy to limit pathophysiologic damage to the graft is to minimize exposure to CNI therapy. Conversion from CNI therapy to the mammalian target of the rapamycin inhibitor everolimus within 6 months after kidney transplantation improves long-term graft function; however, this strategy can increase the risk of mild biopsy-proven acute cellular rejection (BPAR). Ute Eisenberger, MD, and colleagues recently conducted a post-hoc analysis of data from the ZEUS study to analyze histologic information gathered from indication and protocol biopsies up to 5 years after transplantation.

The ZEUS study randomized kidney transplant recipients at month 4.5 to switch to the everolimus or remain on cyclosporine (CsA)-based immunosuppression. Renal function in the cohort treated with everolimus was significantly improved at 5 years compared with the CsA cohort. BPAR occurred in 13.6% of patients in the everolimus cohort and 7.5% of patients in the control cohort (P=0.055). The difference in the BPAR rates was largely accounted for by grade 1 rejection. The post-hoc analysis included the presence of CNI-related toxicity, antibody-mediated rejection (AMR), and chronic/sclerosing allograft nephropathy. Results were reported online in BMC Nephrology [doi.org/10.1186/s12882-018-0950-1].

There were 300 patients in the intention-to-treat population (154 everolimus; 146 CsA). Of those, 269 (138 everolimus; 131 CsA) completed the 12-month core study; the 5-year visit was attended by 232 patients (123 everolimus; 109 CsA). With the exception of body mass index, which was higher in the everolimus group, other characteristics of recipients and donors were similar between the two treatment groups.

By year 5 post-transplant, 45.2% of patients in the everolimus group remained on everolimus in a CNI-free regimen. In the CsA group, 58.6% of patients were still receiving CsA and an additional 11 patients (7.6%) remained on CsA therapy but had switched to tacrolimus. Of patients with steroid therapy data available, 64.2% (n=79/125) of everolimus patients and 64.2% (n=70/109) of patients in the CsA group were receiving steroids at 5 years post-transplant.

At randomization, protocol biopsies were performed in 13.3% of patients (n=40; 22 everolimus; 18 CsA), and in 11.3% of patients (n=43; 17 everolimus; 17 CsA) at month 12. Prior to randomization, protocol biopsies were performed in 41.7% of patients (n=125) at a mean of 0.9 months post-transplant. Following randomization, a total of 178 investigator-initiated biopsies were performed (53 everolimus; 55 CsA). Of those, 67 were obtained by year 1 and 111 were obtained during years 2 to 5. In the everolimus group, the mean number of investigator-initiated biopsies between randomization and year five was 2.6, compared with 2.2 in the CsA group, at a mean of 20.2 and 19.5 months after transplantation, respectively.

**Characteristics of Patients on the Transplant Waitlist**

| Austin, Texas—The optimal treatment for patients with end-stage renal disease (ESRD) is renal transplantation. The qualification process for transplantation is complex and difficult to navigate for some patients. Deborah Evans, MA, LCSW, and colleagues conducted a data analysis to characterize patients listed as active on the transplant waiting list to improve understanding of the challenges involved in qualifying for a transplant. Results of the analysis were reported during a poster session at the National Kidney Foundation 2018 Spring Clinical Meetings in a poster titled “Characterization of End-Stage Renal Disease (ESRD) Patients on the Transplant Waitlist.”

Data from the electronic health records of a large dialysis organization were utilized in the analysis. Transplant waitlist status as of November 2017 was examined. The analysis compared patients listed as active with the overall patient population within categories of age, sex, ethnicity, dialysis vintage, modality, and geographic region.

The proportion of male patients listed as active was higher than that of female patients (10.6% vs 8.1%). There was variation in status listed as active by race/ethnicity: Hispanic, 11.9%; black, 9.9%; and white, 7.6%. Patients ≥40 years of age had the highest proportion of patients listed as active (18.5%) and those ≥80 years of age had the lowest proportion (0.2%). The proportion with status listed as active increased with dialysis vintage (1.7% for patients on dialysis ≥3 months vs 13.5% for those on dialysis ≥24–48 months).

When measured by dialysis modality, 8.1% of patients on in-center hemodialysis were listed as active, compared with 20.3% of those receiving home dialysis, and 20.1% of patients receiving peritoneal dialysis. When considered by state, the proportion of patients listed as active varied from 2.4% to 7.7%.

“Our analysis revealed considerable variation in the proportion of patients listed as active on the transplant waitlist based on a number of demographic and dialysis treatment criteria. It is likely that some of these differences reflect patient health status and engagement as well as factors specific to individual transplant programs. However, these findings may inform the design and targeting of education to ensure that all patients are able to make informed decisions about transplant as an alternative to their current modality,” the researchers said.


This study was funded by DaVita, Inc.
There were few cases of clinically undetected mild BPAR or other lesions in either treatment group revealed in results of protocol biopsies at randomization and at month 12; however, the group revealed in results of protocol biopsies at mild BPAR or other lesions in either treatment group, the incidence from randomization and two were grade 3. In the everolimus group, BPAR was detected in 11 patients grade 3 (one missing). In the CsA-treated group, BPAR was detected in 19 patients in the everolimus group and 18 of 20 in the CsA group graded mild (grade ≤2A).

In conclusion, the researchers said, “This analysis of histological findings in the ZEUS study to 5 years after kidney transplantation shows no increase in antibody-mediated rejection under everolimus-based therapy with a lower rate of CNI-related toxicity compared to a conventional CsA-based regimen, and confirms the preponderance of the mild BPAR seen in the main study after the early switch to CsA-free everolimus therapy.”

Of patients who underwent investigator-initiated biopsies between randomization and year 5, BPAR was detected in 19 patients in the everolimus group [19/154; 12.3%]; In the CsA–treated group, BPAR was detected in 11 patients [11/146].
The researchers reported results of the analysis during a poster session at the NKF 2018 Spring Clinical Meetings in a poster titled *Fenofibrate Use and Incidence and Progression of Chronic Kidney Disease in Patients with Type 2 Diabetes.*

Outcomes of interest were the association of fenofibrate use with change in estimated glomerular filtration rate (eGFR) and with time-to-development of microalbuminuria, macroalbuminuria, CKD, and renal failure. Serum creatinine was measured every 4 months; albuminuria was assessed yearly. To avoid early changes in eGFR related to fenofibrate exposure, 4-month eGFR was used as the initial eGFR measurement, and month 4 as the start of follow-up time. The analysis included data on 2636 participants in the fenofibrate arm and 2632 participants in the placebo arm. Median follow-up was 4 years. During the follow-up period, there was an association between use of fenofibrate and a lower rate of eGFR decline (–0.39 mL/min/1.73 m²/year in the fenofibrate group vs. –1.55 mL/min/1.73 m²/year in the placebo group; P < .01) and with lower incidence of microalbuminuria [hazard ratio (HR)] 0.75; 95% confidence interval [CI], 0.65-0.87], macroalbuminuria [HR, 0.73; 95% CI, 0.58-0.92] and CKD [HR, 0.79; 95% CI, 0.63-0.99]. There was no difference between the two groups in development of renal failure.

In conclusion, the researchers said, “Compared to placebo, fenofibrate use was associated with lower rates of incident CKD and progression of CKD in ACCORD. Fibrates may help reduce the incidence and severity of CKD in the diabetic population.”

Positive Efficacy Findings Bring Early Close to CREDENCE Trial

Positive efficacy findings have brought an early stop to the phase 3 CREDENCE trial. CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) was designed to test the efficacy and safety of INVOKANA® (canagliflozin) compared with placebo when used in addition to standard of care for patients with chronic kidney disease (CKD) and type 2 diabetes.

The decision to stop the trial was announced in a press release from the Janssen Pharmaceutical Companies of Johnson & Johnson. According to the release, the decision was based on a recommendation from the study’s Independent Data Monitoring Committee that met to review the data during a planned interim analysis. The data demonstrated that the trial had achieved prespecified criteria for the primary composite end point of end-stage renal disease (time to dialysis or kidney transplantation), doubling of serum creatinine, and renal or cardiovascular death, when used in addition to standard of care.

Co-chair of the CREDENCE Steering Committee, Vlado Perkovic, MBBS, PhD, FASN, FRACP, said, “Nearly half of all people with type 2 diabetes will develop chronic kidney disease, causing a high risk of kidney failure and cardiovascular disease, and impacting their quality and length of life, even with the current best available care. This huge unmet need is why it was so important for us to initiate the landmark CREDENCE renal outcomes trial over four years ago. We have accepted the advice of the Independent Data Monitoring Committee to stop the CREDENCE trial early due to demonstration of efficacy, and look forward to sharing the findings as soon as possible.”

CREDENCE is the first trial dedicated to renal outcomes in patients with CKD and type 2 diabetes against the background of standard of care. The trial enrolled approximately 4400 patients with type 2 diabetes and estimated glomerular filtration rate (eGFR) ≥39 to ≤90 mL/min/1.73 m², and advanced albuminuria.

James List, MD, PhD, global therapeutic area head, cardiovascular & metabolism at Janssen Research & Development, LLC, said, “Chronic Kidney Disease is a progressive condition that impacts a person’s overall health and well-being, and with millions of people worldwide with the disease, we know that there is a clear need for new treatment options. We are excited about the possibility of bringing forth INVOKANA (canagliflozin) as the first therapy to treat patients with chronic kidney disease and type 2 diabetes in more than 15 years. We look forward to presenting the full data from the CREDENCE trial at an upcoming medical meeting and with health authorities in the near future.”

The press release noted that at this time, INVOKANA is contraindicated for patients with severe renal impairment (eGFR <30 mL/min/1.73 m²), end-stage renal disease, or patients on dialysis. In addition, INVOKANA is not recommended when eGFR is persistently <45 mL/min/1.73 m².

cleared HD caps superior to Tego+Curos and standard hemodialysis caps in reducing blood stream infections (BSIs).1,2

Documented efficacy based on results from two major prospective, randomized clinical studies.1,2

>4,000 Hemodialysis patients

>500,000 Catheter days

80 Dialysis centers

~70% ↓ in BSIs

ClearGuard® HD Antimicrobial Barrier Cap is the only device that kills infection-causing bacteria inside a long-term hemodialysis catheter hub.

*chlorhexidine

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The ClearGuard HD Antimicrobial Barrier Cap has been shown to be effective at reducing microbial colonization in hemodialysis catheter hubs and to reduce the incidence of CLABSI in hemodialysis patients with catheters. See the Instructions for Use for full indications. Rx Only.

The association between sleep apnea and mortality is well established in the general population; there are few data on this association in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD). Hossam Abdalla, MD, and colleagues conducted a study designed to examine the association between severity of sleep apnea and mortality in patients with advanced CKD and ESRD. Results of the study were reported during a poster session at the NKF 2018 Spring Clinical Laboratory. The New York City facility is the first FMCNA lab of its kind and it is equipped with the interdisciplinary team, skill set, and state-of-the-art technologies needed to improve the delivery of life-sustaining dialysis therapy for end-stage renal disease patients,” the announcement added.

The laboratory will support and connect RRI’s computational biomedicine work with clinical research. Insights from bench tests in the laboratory will inform the mathematical modeling efforts, and models will then be validated in the laboratory prior to entering clinical studies. The team will collaborate to “simulate life-sustaining dialysis therapy, with the goal of developing therapeutic methods that can be built into dialysis machines and equipment used in clinics to make the delivery of dialysis safer and more effective,” the announcement added.

**Sleep Apnea Severity and Mortality in CKD and ESRD Patients**

**Nephrology Times**

**Renal Research Institute Expands NYC Renal Research Laboratory**

Fresenius Medical Care North America (FMCNA) has announced the expansion of its Renal Research Institute’s (RRI) New York City research laboratory. The expansion will enable RRI to “broaden its research capabilities in the renal space,” according to an announcement from FMCNA. The New York City facility is the “first FMCNA lab of its kind and it is equipped with the interdisciplinary team, skill set, and state-of-the-art technologies needed to improve the delivery of life-sustaining dialysis therapy for end-stage renal disease patient,” the announcement added.

The laboratory will support and connect RRI’s computational biomedicine work with clinical research. Insights from bench tests in the laboratory will inform the mathematical modeling efforts, and models will then be validated in the laboratory prior to entering clinical studies. The team will collaborate to “simulate life-sustaining dialysis therapy, with the goal of developing therapeutic methods that can be built into dialysis machines and equipment used in clinics to make the delivery of dialysis safer and more effective,” the announcement added.

**Article on Study Findings of ClearGuard HD Caps Receives Editor’s Award**

An article in the *American Journal of Kidney Diseases (AJKD)*, the official journal of the National Kidney Foundation, has received the AJKD Editor’s Choice award for outstanding publication in 2017. According to a press release from Pursuit Vascular, Inc., the article, “Dialysis Catheter-Related Bloodstream Infections: A Cluster-Randomized Trial of the ClearGuard HD Antimicrobial Barrier Cap,” Hymes et al., was “chosen for this award because of the significance of the findings to the nephrology field.” Pursuit Vascular is the manufacturer of the ClearGuard HD cap, an antimicrobial device for catheter-based dialysis patients. The study reported in the AJKD was conducted by Frenova™ Renal Research, a division of Fresenius Medical Care North America. Use of the ClearGuard HD cap was compared to standard caps in hemodialysis patients with central venous catheters (CVCs). The primary end point of interest was positive blood cultures as an indicator of bloodstream infections.

The ClearGuard HD cap is the only device cleared for sale in the United States that kills infection-causing bacteria inside a CVC hub. Results of the study demonstrated the superiority of ClearGuard HD caps to standard caps in patients with CVCs. Doug Killion, president and CEO of Pursuit Vascular, said, “This award recognized the crucial role that ClearGuard HD caps play in tackling the challenging and devastating complications of bloodstream infections in these patients. It’s an honor to receive such a distinction from the AJKD editorial team.”

**Microtip Partnership Assay Program for Renal Testing Launched**

Ortho Clinical Diagnostics, in collaboration with Diazyme Laboratories, Inc., is offering three new Microtip Partnership Assays. The Microtip Partnership Assay (MPA) program enables Ortho to validate and provide high value, esoteric testing. The three new assays are glycated serum protein, lipoprotein (a), and cystatin C. Cystatin C is a key marker for early diagnosis of chronic kidney disease and is a
complement to serum creatinine testing. The predictive accuracy for all-cause mortality and progression to end-stage renal disease can be improved by combining cystatin C and serum creatinine testing; the combination is a more sensitive marker in the "creatinine blind range" in kidney testing, according to a press release from Ortho Clinical Diagnostics.

Katherine M. Wang, MD, Named AKF Clinical Scientist in Nephrology

The American Kidney Fund (AKF) has named Katherine M. Wang, MD Clinical Scientist in Nephrology (CSN) fellow for 2018-2019. Dr. Wang is a second-year nephrology fellow at Stanford University. The CSN grant will fund her research in the effects of intensive treatment of hypertension in patients with chronic kidney disease and the factors associated with the inability to reach lower systolic blood pressure targets.

In a press release from the AKF, Dr. Wang said, "My research as an American Kidney Fund Clinical Scientist in Nephrology fellow will provide valuable insights into patient subgroups that may pose significant challenges in terms of achieving more intensive blood pressure targets. I am grateful to AKF and its commitment to fostering health care access, health literacy, and the prevention and early detection of kidney disease."

Incidence and Timing of ESRD from ADPKD Varies by Race

Austin, Texas—All races and ethnicities are affected by autosomal dominant polycystic kidney disease (ADPKD). However, despite an expectation that the prevalence of ADPKD would be similar among races, assessments in published literature regarding the incidence and age of end-stage renal disease (ESRD) secondary to ADPKD conflict among black and white patient populations with ADPKD.

Erin L. Murphy, MD, and colleagues conducted a retrospective study to examine incident patients with ESRD secondary to ADPKD for the period 2004 to 2013. Results of the study were reported during a poster session at the NKF 2018 Spring Clinical Meetings in a poster titled ESRD from ADPKD: US Incidence is Lower but Onset is Earlier in Non-Hispanic Blacks Compared to Non-Hispanic Whites.

Data from the United States Renal Data System (USRDS) were utilized for the study. Cases of ESRD secondary to ADPKD in the USRDS had the primary cause of ESRD identified as “polycystic kidneys, adult type (dominant)” on the End-Stage Renal Disease Medical Evidence Determination Report (form CMS-2728).

Covariates for the current analysis were race (non-Hispanic white or non-Hispanic black) and age at onset of ESRD. Ages were grouped until a count of >10 patients was reached. Age ranges varied from >40 years to ≤75 years. Population denominators used were yearly USRDS and US Census data.

Among patients who progressed to ESRD, non-Hispanic black patients were less likely than non-Hispanic white patients to develop ESRD secondary to ADPKD (odds ratio [OR] 0.38; 95% confidence interval [CI], 0.36-0.39). Following adjustment for US population differences, the risk of ESRD from ADPKD in non-Hispanic black patients remained lower (OR, 0.94; 95% CI, 0.91-0.96).

More young, non-Hispanic black patients (>40 years of age) had earlier ESRD secondary to ADPKD compared with non-Hispanic white patients (>40 years of age) [4.49 vs 7.68 years, difference, 3.19 years; 95% CI, 0.87-5.44, P = 0.017] for the combined years examined. Age of ESRD onset was lower among non-Hispanic black patients compared with non-Hispanic white patients [54.4 years vs 55.9 years, P = 0.001]. "ADPKD incidence in non-Hispanic blacks compared to non-Hispanic whites is similar, thought slightly lower. Blacks progress to ESRD at a younger age and thus may be at a higher risk for early progression to ESRD than previously recognized," the researchers said.

Source: Murphy EL, Dai F, Droher M, et al. ESRD from ADPKD: US incidence is lower but onset is earlier in non-Hispanic blacks compared to non-Hispanic whites. Abstract of a poster presented at the National Kidney Foundation 2018 Spring Clinical Meetings, April 10-14, 2018, Austin, Texas.
ACUTE KIDNEY INJURY
Study Underway to Examine Incidence of CKD after AKI in the ICU


Acute kidney injury (AKI) among patients in the intensive care unit (ICU) is associated with poor outcomes, including short- and long-term mortality, as well as increased risk of chronic kidney disease (CKD) in non-ICU patients. Guillaume Geri, MD, PhD, and colleagues recently described a prospective multicenter observational study designed to assess the incidence and determinants of CKD after AKI; the researchers are also seeking to develop a prediction score for CKD in ICU patients (NCT03282409).

The study will include 1200 patients who experienced AKI during a stay in the ICU and were discharged alive from the ICU. Patients will be monitored by a nephrologist at day 90 and every year for 3 years.

The primary outcome of interest is the occurrence of CKD, defined by a creatinine-based estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² or renal replacement therapy for ESRD in patients whose eGFR will be normalized (≥60 mL/min/1.73 m²) at day 90. Secondary outcomes include changes in albuminuria, slope of decline in eGFR and risk of ESRD in patients with preexisting CKD, cardiovascular and thromboembolic events, and health-related quality of life.

According to the researchers, “This is the first study prospectively investigating kidney function evolution in ICU patients who suffered from AKI. Albuminuria and eGFR monitoring will allow identification of ICU patients at risk of CKD who may benefit from close surveillance after recovery from AKI. Major patient and AKI-related determinants will be tested to develop a prediction score for CKD in this population.”

Minimal Change Disease and Complications from AKI

Kidney International. doi.org/10.1016/j.kint.2018.04.024

In 70% to 90% of nephrotic syndrome in children, the primary cause is minimal change disease; minimal change disease is also a cause of nephrotic syndrome in adults, including those >60 years of age. Because foot-process fusion impairs filtration of water and solutes, renal function is altered moderately in ~20% to 30% of patients. GFR is reduced by ~20% to 30% and returns to baseline with remission of proteinuria.

Patients with AKI may require dialysis for weeks or months to achieve remission of proteinuria and resolution of oliguria. One explanation of tubular cell ischemic necrosis may

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION: AURYXIA® (ferric citrate) is contraindicated in patients with iron overload syndromes

WARNINGS AND PRECAUTIONS:

• Iron Overload: Monitor ferritin and transferrin saturation (TSAT). Patients may require a reduction in dose or discontinuation of concomitant intravenous (IV) iron

• Risk of Overdosage in Children Due to Accidental Ingestion: Accidental ingestion and resulting overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Advise patients to keep AURYXIA out of the reach of children

PREGNANCY AND LACTATION: Overdosing of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes and fetal malformation. Rat studies have shown the transfer of iron into milk. There is possible infant exposure when AURYXIA is taken by a nursing woman

ADVERSE REACTIONS: In clinical trials, likely adverse reactions occurring in ≥5% of patients treated with AURYXIA were discolored feces, diarrhea, constipation, nausea, vomiting, cough, abdominal pain and hyperkalemia

To report suspected adverse reactions, contact Keryx Biopharmaceuticals at 1-844-445-3799

FOR MORE INFORMATION, VISIT AURYXIA.COM

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Previous studies have reported cases of AKI in approximately one-fifth to one-third of cases in adults without prior or concomitant renal disease. Male predominance is suggested by clinical attributes, as well as age >50 years, massive proteinuria, severe hyperalbuminemia, a background of hypertension, vascular lesions on kidney biopsy, and ischemic tubular necrosis.
be an effect of endothelin 1-induced vasoconstriction at the onset of proteinuria.

Some patients with AKI do not recover renal function. Among adults with minimal change disease, the primary factors associated with AKI are diuretic-induced hypovolemia and nephrotoxic agents. In the absence of intercurrent complications, AKI is uncommon in children. The primary risk factors are infection, nephrotoxic medication, and steroid resistance. “In all patients, the goal of supportive therapy is essentially to buy time until glucocorticoids obtain emission of proteinuria, which allows resolution of renal failure,” the researchers said.

"In all patients, the goal of supportive therapy is essentially to buy time until glucocorticoids obtain emission of proteinuria, which allows resolution of renal failure," the researchers said.

For the treatment of iron deficiency anemia in adult patients with chronic kidney disease (CKD) not on dialysis

**AURYXIA is the only oral iron tablet approved by the FDA for the treatment of iron deficiency anemia specifically in adult patients with CKD not on dialysis**

- Proven effective in patients who were previously intolerant of or had an inadequate therapeutic response to traditional oral iron supplements
  - Patients in the Phase III pivotal trial achieved results without the use of ESAs or IV iron
  - 52% of patients achieved the primary endpoint of a hemoglobin increase of ≥1.0 g/dL by Week 16
  - 18 percentage-point increase in mean TSAT at Week 16 from baseline
- Discontinuation rates due to adverse reactions were similar between AURYXIA and placebo (10% vs 9%)
- Convenient mealtime dosing
- Each tablet contains 210 mg of elemental iron

ESAs = erythropoiesis stimulating agents

Please see Brief Summary including patient counseling information on following page
Adverse reactions leading to discontinuation of AURYXIA (2.6%).

During the 16-week, placebo-control trial, 12 patients (10%) on AURYXIA and 116 patients treated with placebo in a 16-week, randomized, double-blind period and a study of 75 patients treated with AURYXIA and 73 treated with placebo in a 12-week randomized double-blind period. Dosage regimens in these trials ranged from 210 mg to 2,520 mg of ferric iron per day, equivalent to 1 to 12 tablets of AURYXIA.

Adverse reactions reported in at least 5% of patients treated with AURYXIA are listed in Table 1.

Table 1: Adverse Reactions Reported in Two Clinical Trials in at least 5% of patients receiving AURYXIA

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Reaction</th>
<th>AURYXIA % (N=119)</th>
<th>Placbebo % (N=188)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Adverse Reaction</td>
<td>75</td>
<td>62</td>
<td></td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>5</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>21</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>18</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>10</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

AURYXIA is contraindicated in patients with iron overload syndromes (e.g., hemochromatosis). Warnings and Precautions (2.7) iron absorption from AURYXIA may lead to excessive elevations in iron stores. In a 56-week safety and efficacy trial evaluating the control of serum phosphate levels in patients with chronic kidney disease on dialysis in which concomitant use of intravenous iron was permitted, 55% of patients treated with AURYXIA had a ferritin level >1500 ng/mL as compared with 13% (9%) of patients treated with active control. Assess iron parameters (e.g., serum ferritin and TSAT) prior to initiating AURYXIA and monitor iron parameters while on therapy. Patients receiving intravenous iron may require a reduction in dose or discontinuation of intravenous iron therapy. Risk of Overdose in Children Due to Accidental Ingestion: Accidental ingestion and resulting overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Advise patients of the risks to children and to keep AURYXIA out of the reach of children.

Adverse Reactions (4.1)

There are no empirical data on avoiding drug interactions between AURYXIA and other medications. The safety and efficacy of AURYXIA have not been established in pediatric patients. AURYXIA may cause discolored mouth and teeth. AURYXIA is contraindicated in patients with iron overload syndromes (e.g., hemochromatosis). There are no empirical data on avoiding drug interactions between AURYXIA and other medications. The safety and efficacy of AURYXIA have not been established in pediatric patients. AURYXIA may cause discolored mouth and teeth. AURYXIA is contraindicated in patients with iron overload syndromes (e.g., hemochromatosis).
outcomes in patients based on the dialysis provider at initiation of treatment. Elani Streja, MPH, and colleagues conducted a study to examine the association between dialysis provider and mortality and hospitalization in US veterans initiating dialysis. From 2007 to 2014, 68,727 US veterans initiated dialysis. The researchers examined the association of dialysis provider (VHA vs non-VHA) at treatment initiation with rates of mortality and hospitalization in the first 12 months following initiation. After accounting for demographics and comorbidities, the associations were examined across adjusted models.

The increase in weight assigned to residual kidney function due, in part, to uncertainty regarding how residual kidney function should be valued and incorporated into the dialysis prescription. More recently, guidelines have increased the weight given to residual kidney function, reducing the required treatment time in patients with residual function. The increase in weight assigned to residual renal function may be justified by knowledge that the native kidney performs functions not replicated by dialysis, including solute removal by secretion, according to researchers.

Sheldon C. Leong, MD, and colleagues conducted a study to determine whether plasma concentrations of secreted solutes are as well controlled in patients with residual function receiving hemodialysis twice weekly (n=9) as in anuric patients receiving hemodialysis three times per week (n=9).

The researchers measured the plasma concentration and residual clearance, dialytic clearance, and removal rates for urea and the secreted solutes hippurate, phenylacetylglutamine, indoxyl sulfate, and p-cresol sulfate in both groups.

Compared with patients in the three-times per week group with the same standard Kt/Vurea, patients in the twice-weekly group had lower hippurate and phenylacetylglutamine concentrations. Concentrations of indoxyl sulfate and p-cresol sulfate were similar in both groups. The observed pattern of solute concentrations was accounted for by residual secretory function, as revealed on mathematical modeling.

In conclusion, the researchers said, “Plasma concentrations of secreted solutes can be well controlled by twice weekly hemodialysis in patients with residual kidney function. This result supports further study of residual kidney function value and the inclusion of this function in dialysis adequacy measures.”

ELECTROLYTE DISORDERS

Risk Factors of Rapid Correction of Severe Hyponatremia
Clinical Journal of the American Society of Nephrology. 2018;13[7]:984-992

Serious complications, including osmotic demyelination, can result from rapid correction of severe hyponatremia. Jason C. George, MD, and colleagues conducted a study to examine the incidence and risk factors of rapid correction and osmotic demyelination. Rapid correction was defined as an increase in serum sodium of >8 mEq/L at 24 hours. Mannal chart review of all available brain magnetic resonance imaging (MRI) reports determined osmotic demyelination.

Mean age of the cohort was 66 years, 55% were women, and 67% had prior hyponatremia (last outpatient sodium <135 mEq/L). At 24 hours, median change in serum sodium was 6.8 mEq/L and 606 patients (41%) had rapid correction. There were associations between younger age, being a woman, schizophrenia, lower Charlson comorbidity index, lower serum sodium at presentation, and urine sodium <30 mEq/L and greater risk of rapid correction. Lower risk of rapid correction was associated with prior hyponatremia, outpatient use of aldosterone antagonist, and being treated at an academic center.

Brain MRI reports were available on 20% of the cohort (n=295). Nine patients showed radiologic evidence of osmotic demyelination; eight had incident osmotic demyelination (five of whom had beer potomania), five had hypokalemia, and seven had sodium increase >8 mEq/L over a 24-hour period prior to MRI. Five patients with osmotic demyelination had apparent neurologic recovery.

“Among patients presenting with severe hyponatremia, rapid correction occurred in 41%; nearly all patients with incident osmotic demyelination had a documented episode of rapid correction,” the researchers said.

END-STAGE RENAL DISEASE

Association of BMI and Outcomes in Patients with ESRD
Progress in Cardiovascular Diseases. doi.org/10.1016/j.pcad.2018.07.007

Complications associated with obesity include diabetes, hypertension, cardiovascular disease, and premature death, but in certain populations, a link between obesity and increasing body mass index (BMI) and improved survival has been seen in observational studies. This obesity paradox or reverse epidemiology has been seen in clinical settings that include end-stage renal disease (ESRD).

Explanations to debunk the obesity paradox have included residual confounding in some studies; however, recent discoveries have provided biologically plausible mechanisms in which higher BMI can be linked to longevity in certain patient populations. Neda Naderi, MD, and colleagues provided a review of recent clinical evidence detailing the association of BMI with outcomes in patients with chronic kidney disease, including those with ESRD.

According to the researchers, sophisticated epidemiologic methods that adjusted for confounding have found that the obesity paradox remains robust in ESRD. Further, some hypotheses posit that there may be an association between weight loss and cachexia and adverse outcomes that include cardiomyopathy, arrhythmias, and sudden death. These hypotheses suggest that the survival benefit seen in patients with obesity may be derived from the mechanisms that protect against inefficient energy utilization, cachexia, and protein-energy wasting.

“Given that in ESRD patients, treatment of traditional risk factors has failed to alter outcomes, detailed translational studies of the obesity paradox may help identify innovative pathways that can be targeted to improve survival,” the researchers said.
Stop Throwing Away Your Money, Part 2

In the last issue of Nephrology Times I addressed two common ways in which healthcare providers spend money needlessly. The first was employing management personnel with no financial training and the second was contracting with incompetent vendors. While incompetent managers and vendors may be giving an honest effort, there are, unfortunately, managers and vendors that are intentionally dishonest and manipulative. Getting rid of such people is vital to the success of your practice or facility.

DISHONEST OR UNETHICAL VENDORS

I am truly disgusted by those who intentionally lie and deceive in order to gain more power and control over a practice, its employees, and its finances. I cannot emphasize enough that if you have someone in a position of authority with whom you are romantically involved, it is absolutely essential to have a competent and neutral third party watch over your money and the management of your practice or facility. The same is true for a relative, including your spouse. Because my company is hired as a third party to provide billing services, we often find out what is really happening behind the doctor’s back. Following is a small example from my experiences with past clients.

In one instance, a manager of a large facility consistently failed to carry out simple and critical tasks such as signing payer contracts, depositing paper checks, filing reports on time, and seeing that medical records were kept up to date. The manager’s failures resulted in loss of revenue, penalties, confusion, and the loss of good employees. The facility was at great risk in the event of an audit or a survey.

However, when our staff tried to communicate some of the problems to the owner, the owner simply spoke with the manager, who lied and blamed others. The manager then became more hostile and less cooperative with us because we had politely dared to mention some of the problems we had noticed. What was the manager’s motive? The lack of financial controls left open the possibility that funds were being embezzled. The manager also had significant freedom in making purchases and no one was in place to oversee the manager’s spending and verify that funds were actually spent on what was claimed. To further cement control, the manager hired friends and placed them in key positions. These “friends” would back up the manager in the lies and deception, which caused the owner to think that others were causing the problems.

I am happy to report that the manager was finally replaced, but only after many years of deception that caused the facility and its owner, employees, and patients to suffer unnecessary consequences.

DISHONEST PRACTICE OR FACILITY MANAGERS

In general, vendors who participate actively in the renal industry cannot afford to be dishonest. Word normally spreads quickly throughout our relatively small industry about how someone was cheated or mistreated. However, vendors not associated with the renal industry may try to take advantage of providers—insurance vendors, computer and network sales and service personnel, phone countants, attorneys, bookkeepers, landlords, financial planners, consultants, and internet vendors, along with those that work in construction, remodeling, flooring, roofing, plumbing, heating and air conditioning, and on and on and on. Healthcare providers are prime targets for the dishonest because the widespread belief is that all providers are rich and are not careful with expenditures.

There are several things you can do before you contract with a vendor that can save you a lot of grief in the long run. The first is to obtain effective references. Recently, after I sent a list of three references to a prospective client, the prospect then asked me for references from three former clients and three current clients that were different from the three on the list I sent previously. In this way, my prospect was able to obtain a more complete picture of what our company is really like.

Another great source of references is a message board, which is normally run by associations with which you are affiliated. Write a quick post that names the type of service you are looking for and you will likely be amazed at the helpful feedback you receive from others.

If you are already contracted with a vendor you suspect may not be providing you adequate services or products at a fair price, contact others in the renal industry and ask how much they pay for similar services. Knowledge is your friend and you can make reasonable demands on your current vendors based on the feedback you receive from others.

Rick Collins is the director of business development for Sceptre Management Solutions, LLC, a company specializing in billing for outpatient ESRD facilities, nephrology practices, and vascular access. Your questions are welcome and he can be reached at rcollins@sceptremanagement.com or 801.775.8010.

Rick Collins

From the Field

Sceptre Management Solutions, LLC.

rcollins@sceptremanagement.com

801.775.8010

Stop Throwing Away Your Money, Part 2

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Analysis of Key Journal Studies • Focus on Transplantation • Abstract Roundup • From the Field

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Check out the online-exclusive content and round out your nephrology news experience.
The PRISMAFLEX System is one of the best tools we’ve used in our ICU. And with Baxter’s support, we can do so much for our patients now that we’ve implemented our Super User Program and CRRT Task Force.”

Juan Carlos Aycinena, MD

Dr. Aycinena dedicated himself to becoming a nephrologist because he wanted to be able to offer hope to the sickest patients. In the past 4 years that he has been using the PRISMAFLEX System, he feels like his team has been able to do so much more for those patients, especially since implementing a CRRT Task Force. Including Baxter on that Task Force was an important decision and just one example of how we are always striving to partner with our customers. Baxter is committed to supporting Dr. Aycinena and his team as they continue to optimize their CRRT program.

Watch Dr. Aycinena’s story at renalacute.com/stories

The PRISMAFLEX Control Unit is intended for:
Continuous Renal Replacement Therapy (CRRT) for patients weighing 20 kilograms or more with acute renal failure and/or fluid overload.
Therapeutic Plasma Exchange (TPE) therapy for patients weighing 20 kilograms or more with diseases where fluid removal of plasma components is indicated.
Rx Only. For safe and proper use of this device, refer to the Operator’s Manual.