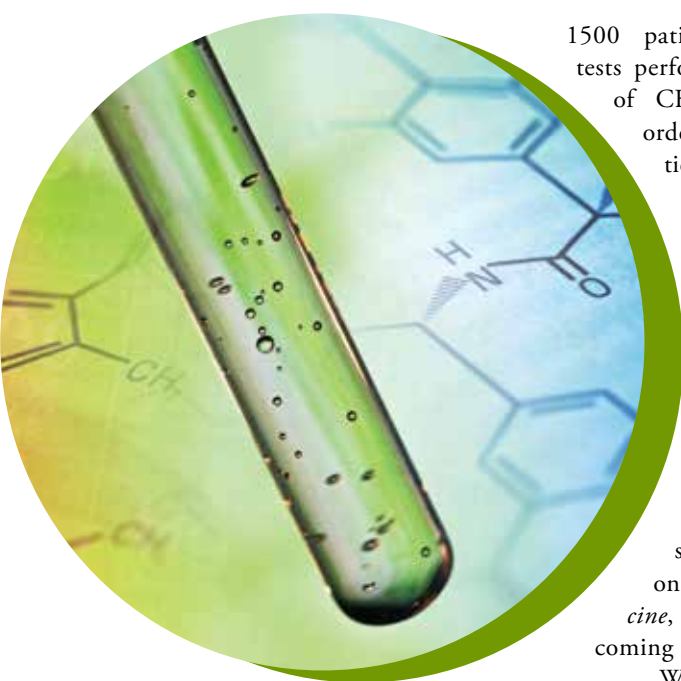


# Kidney News

April 2015 | Vol. 7, Number 4

## Testing for CKD: Which Tests Pull Their Weight?



**P**atients referred to nephrologists for evaluation of chronic kidney disease (CKD) undergo a lot of laboratory tests. But which tests contribute the most clinically relevant information? An analysis of nearly

1500 patients suggests that many tests performed for initial evaluation of CKD—including some tests ordered in a majority of patients—have little or no effect on patient diagnosis and management.

“We found that many tests are obtained frequently despite low rates of effect on diagnosis and management,” according to the report by Mallika L. Mendu, MD, MBA, of Harvard Medical School and colleagues. Their research letter was published online in *JAMA Internal Medicine*, and will appear in an upcoming print issue.

While emphasizing the need for further study, Mendu and colleagues conclude, “Reflexively ordering several tests for CKD evaluation and management may be unnecessary.” They are working on further analyses toward developing a more evidence-based, cost-conscious approach to CKD diagnosis.

“In this retrospective study of indi-

viduals undergoing an initial evaluation for CKD, the authors found that very few of the many tests ordered appeared to help the clinicians determine the cause of CKD or guide next steps in management,” said Amy W. Williams, MD, of the Division of Nephrology and Hypertension at Mayo Clinic College of Medicine, Rochester, Minn. “Although there are limitations to the study as the authors have well outlined, the finding highlights the need for a more targeted stepwise approach to the initial evaluation of CKD. The authors call for further investigation to determine pre-test probability of disease and identifying subgroups of patients who would benefit from more extensive evaluations.”

### Which CKD tests affect diagnosis and management?

The researchers analyzed 1487 patients diagnosed with CKD after referral to nephrology clinics affiliated with Brigham and Women’s Hospital and Massachusetts General Hospital from 2010 through 2012. “CKD is probably

*Continued on page 3*

## Inside

### Findings

Time-updated blood pressure is a stronger predictor of CKD progression than one-time measurement

### Policy

The Veterans Health Administration is the largest provider of kidney care in the nation, making it fertile ground for research; Rep. Tom Marino (R-PA) discusses bipartisan kidney care legislation

### Q and A: Health Disparities

*Kidney News* interviewed the acting director of the National Institute on Minority Health and Health Disparities. Learn more about the institute’s efforts to attract trainees and support a diverse workforce.

### New Award

The ASN Harold Amos Faculty Development Program award extends ASN’s commitment to diversity and inclusion

## High-Acid Diets May Increase Risk of Kidney Failure in Patients with Chronic Kidney Disease

By Tracy Hampton

**S**mall clinical trials have shown that reducing dietary acid load can slow the progression of chronic kidney disease (CKD), but long-term, population-based studies have been lacking. Now, in an analy-

sis of the 1988–1994 National Health and Nutrition Examination Survey (NHANES III), investigators revealed that patients with CKD who consumed high-acid diets were three times more likely to experience ESRD

than were patients who consumed low-acid diets. The findings suggest that efforts to improve diet quality at both the population and the individual patient levels could potentially improve CKD outcomes.

Researchers have noted that contemporary Western diets are becoming more acid based. Meat, fish, cheese, grain products, and rice are relatively strong net acidifying foods, whereas fruit (apples, peaches, and raisins), legumes, vegetables (spinach

*Continued on page 5*





TINY CRYSTALS.

BIG PROBLEM.

For many patients with gout, emerging science suggests that chronically elevated sUA and the resulting monosodium urate crystal deposition can be more serious and widespread in the body than we ever thought, leaving inflammation, bone erosion, and organ damage in its wake.<sup>1-5</sup>

Take a deeper look at [TheRealGout.com](http://TheRealGout.com)

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**References:**

1. Dalbeth N, Stamp L. Hyperuricaemia and gout: time for a new staging system? *Ann Rheum Dis*. 2014;73(9):1598-1600. 2. Paparo F, Zampogna G, Fabbro E, et al. Imaging of tophi with an extremity-dedicated MRI system. *Clin Exp Rheumatol*. 2011;29(3):519-526. 3. Schumacher HR Jr. The pathogenesis of gout. *Cleve Clin J Med*. 2008;75(suppl 5):S2-S4. 4. Taylor JW, Grainger R. Clinical features of gout. In: Terkeltaub R (ed). *Gout and Other Crystal Arthropathies*. 1st ed. Philadelphia, PA: Elsevier Saunders; 2012:105-120. 5. Terkeltaub R, Edwards NL. Disease definition and overview of pathogenesis of hyperuricemia and gouty inflammation. In: Terkeltaub R, Edwards NL (eds). *Gout: Diagnosis and Management of Gouty Arthritis and Hyperuricemia*. 3rd ed. Durant, OK: Professional Communications, Inc; 2013:19-47.

# Testing for CKD

Continued from page 1

the number one reason why patients are referred to nephrologists,” said Mendu. “Yet we don’t really have an understanding of why we are ordering the tests that we do, what tests we are ordering, and how useful they are.”

For each case, nephrology progress notes were reviewed to determine which tests “contributed to, confirmed, or established the underlying diagnosis of and/or any management decision related to CKD.” Although that process was unavoidably subjective, the researchers relied on documentation by providers, and included testing decisions that were specially stated in the nephrology progress notes that the results affected diagnosis and management decisions—including negative test results. An independent review of a random sample of records showed high interrater agreement.

With a median age of 70 and about one-fourth of minority race/ethnicity, the patients had high rates of typical CKD risk factors and comorbidities. Hypertension was present in 79 percent of patients, diabetes in 58 percent, and coronary heart disease in 26 percent. Most were on statins and beta blockers at the time of referral; more than 40 percent were taking an ACE inhibitor. At diagnosis, most patients had stage 3 CKD: stage 3a in 28.7 percent and 3b in 39.5 percent.

The patients underwent a total of 40 different tests—33 performed primarily for diagnosis and seven primarily for management. The most common tests were measurement of calcium, hemoglobin, phosphate, urine sediment, and parathyroid hormone; dipstick tests for blood and protein in urine; serum protein electrophoresis; and renal ultrasound.

## Highest-yield tests reflect main causes of CKD

The test with the highest diagnostic yield was hemoglobin A1c measurement, performed in 12.6 percent of patients. The results affected diagnosis in 15.4 percent of patients and management in 10.1 percent (Table 1). “That’s not that surprising given that the most common cause of CKD is diabetes, followed by hypertension,” said Mendu.

Similarly high yields were provided by the urine total protein to creatinine ratio, which affected diagnosis in 14.1 percent of patients and management in 13.7 percent; and urine microalbumin-to-creatinine ratio, which affected diagnosis and management in 13.0 and 13.3 percent of patients, respectively.

After that, the rates at which tests contributed to CKD diagnosis fell off sharply—including some commonly performed tests. Renal ultrasound was performed in about two-thirds of patients. Even though the results were abnormal in more than one-fourth of patients (26.8 percent), the findings

affected diagnosis in 5.9 percent of patients and management in just 3.3 percent.

Serum protein electrophoresis (SPEP) was also performed in more than two-thirds of patients, but affected diagnosis in just 1.4 percent of patients and management in 1.7 percent.

Cryoglobulins were measured in 5 percent of patients, and affected diagnosis and management in 5.4 percent of cases each. No other test performed in more than 5 percent of patients had a diagnostic yield of greater than 3.5 percent. Kidney biopsy affected diagnosis and management in every case—but was performed in only about 5 percent of patients.

Some tests did not affect diagnosis or management in any patient, including anti-neutrophil cytoplasmic antibodies, measured in about 14 percent of patients; and anti-glomerular basement membrane antibodies, assessed in about 4 percent.

Other tests were performed relatively often but contributed little information. For example, complement 3 and 4 were each tested in about one-fourth of patients, but had a diagnostic yield of about 1 percent. Hepatitis B and C testing were performed in about 17 percent of patients, but affected diagnosis in just one or two cases.

## Need for evidence-based approach to CKD testing

With a reported prevalence of about 13 percent and many possible causes, CKD carries high morbidity, high mortality, and high costs. The new study is a comprehensive assessment of the range and impact of tests used for CKD diagnosis.

Mendu previously reported similar conclusions in a study of patients with syncope—a common clinical problem with an even broader differential diagnosis (*JAMA* 2009; 169:1299–1305). “That study found kind of a similar thing, which is that we order lots of tests, and most of the time, those tests don’t really affect diagnosis and management,” she said.

So are patients with CKD undergoing too many tests? “I think it’s helpful for nephrologists to know that it’s probably not the best approach to just order a litany of tests when a patient comes to see you,” Mendu said. That’s an approach that’s a “probably low yield”—an important consideration in the current era of healthcare reform and accountability.

Timing is another important factor to consider, she said. “Ordering these tests is time-consuming, and so is following up the test results. And if it’s not really contributing to patient care, then we should probably be more thoughtful about how we order these tests.”

Of course, nephrologists have reasons for ordering some of the lower-yield tests, such as renal ultrasound and SPEP—they are looking for less common but critical diagnoses such as multiple myeloma and obstructive hydronephrosis. Mendu and colleagues have identified cases in

which those diagnoses were made, in an attempt to develop criteria and guidance for nephrologists and internists pursuing those diagnoses, which will be the topic of a manuscript currently in preparation. That paper will also seek to develop estimates of the costs of testing for CKD on the national level.

Ultimately, Mendu and colleagues write, “An evidence-based, targeted approach based on pretest probabilities of disease for diagnosis and management may be more efficient and reduce costs.” Such an effort would require further research, including studies in community-based patient samples and an emphasis on identifying patient subgroups who may benefit from more extensive evaluation.

“Many medical specialties and subspecialties, including nephrology, have

begun tackling the concerns of over-testing or inappropriate testing and healthcare systems have begun to embed decision support and hard stops into electronic health records and CPOE,” said Williams, who also serves as Medical Director of Hospital Operations for the Mayo Clinic Hospitals. “However, we need to better understand more effective and efficient approaches to the diagnosis and management of CKD. “We also need to share this knowledge with our primary care colleagues and non-nephrology subspecialists who may be the first to attempt CKD evaluation. Certainly our patients, as they see their co-pays increase, are depending on us to use resources wisely and in a patient-centered way and share our knowledge with their entire medical team.” ●

**Table 1**  
Effect of CKD tests on diagnosis and management

Most Common Tests for CKD	
Calcium	94.8%
Hemoglobin	84.0%
Phosphate	83.5%
Urine sediment	74.8%
Parathyroid hormone	74.1%
Urine protein	69.7%
Urine blood	69.9%
Serum protein electrophoresis	68.1%
Renal ultrasound	67.7%
Common Tests with High Diagnostic Yield	
Hemoglobin A1c	15.4%
Urine total protein:creatinine	14.1%
Urine microalbumin:creatinine	13.0%
Common Tests with High Effect on Management	
Parathyroid hormone	15.7%
Iron	15.2%
25-Hydroxyvitamin D	14.6%
Urine total protein:creatinine	13.7%
Urine microalbumin:creatinine	13.3%
Hemoglobin A1c	10.1%
Common Tests with Low Diagnostic Yield	
Renal ultrasound	5.9%
Serum protein electrophoresis	1.4%
Uric acid, hepatitis B and C, rheumatoid factor, many others	<1%



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## High-Acid Diets

Continued from page 1

and cauliflower), and potatoes are relatively strong net alkalinizing foods. The mechanisms by which acid-inducing diets affect kidney health are unknown, but tubular toxicity of elevated ammonium concentrations and activation of the renin-angiotensin system may be involved.

“Nutrition is emerging to the forefront as a major modifiable determinant of disease, with scientific evidence increasingly supporting the view that alterations in diet have important effects on health throughout life,” said Tanushree Banerjee, PhD, a researcher at the University of California–San Francisco and the lead author of the study published by the *Journal of the American Society of Nephrology*.

Banerjee and her colleagues analyzed information on 1486 adults who had CKD and were followed up for a median of 14.2

years. The investigators estimated the dietary acid load from 24-hour dietary recall data using previously validated equations.

In total, ESRD developed in 311 (20.9 percent) of the study participants. After adjustment for potential confounding factors, higher levels of dietary acid load were associated with increased risks of ESRD, with a 3-fold increased risk for the highest tertile and a 1.8-fold increased risk for the middle tertile compared with the lowest tertile. Even for a shorter follow-up of less than 6 years, the investigators noted a much greater risk of ESRD with high dietary acid load.

The risk of ESRD that was associated with dietary acid load increased as kidney function decreased. Also, high dietary acid load was strongly associated with ESRD risk among individuals with albuminuria of 30 mg/g or above compared with those with normal albuminuria below 30 mg/g. This suggests that higher dietary acid load may lead to kidney injury, which may portend progression to ESRD.

“Patients with CKD may want to pay more attention to diet consumption of acid-rich foods to reduce progression to kidney failure, in addition to employing recommended guidelines such as taking kidney-sparing medication and avoiding kidney toxins,” said Banerjee. “The high costs and suboptimal quality of life that dialysis treatments bring may be avoided by adopting a more healthy diet that is rich in fruits and vegetables.”

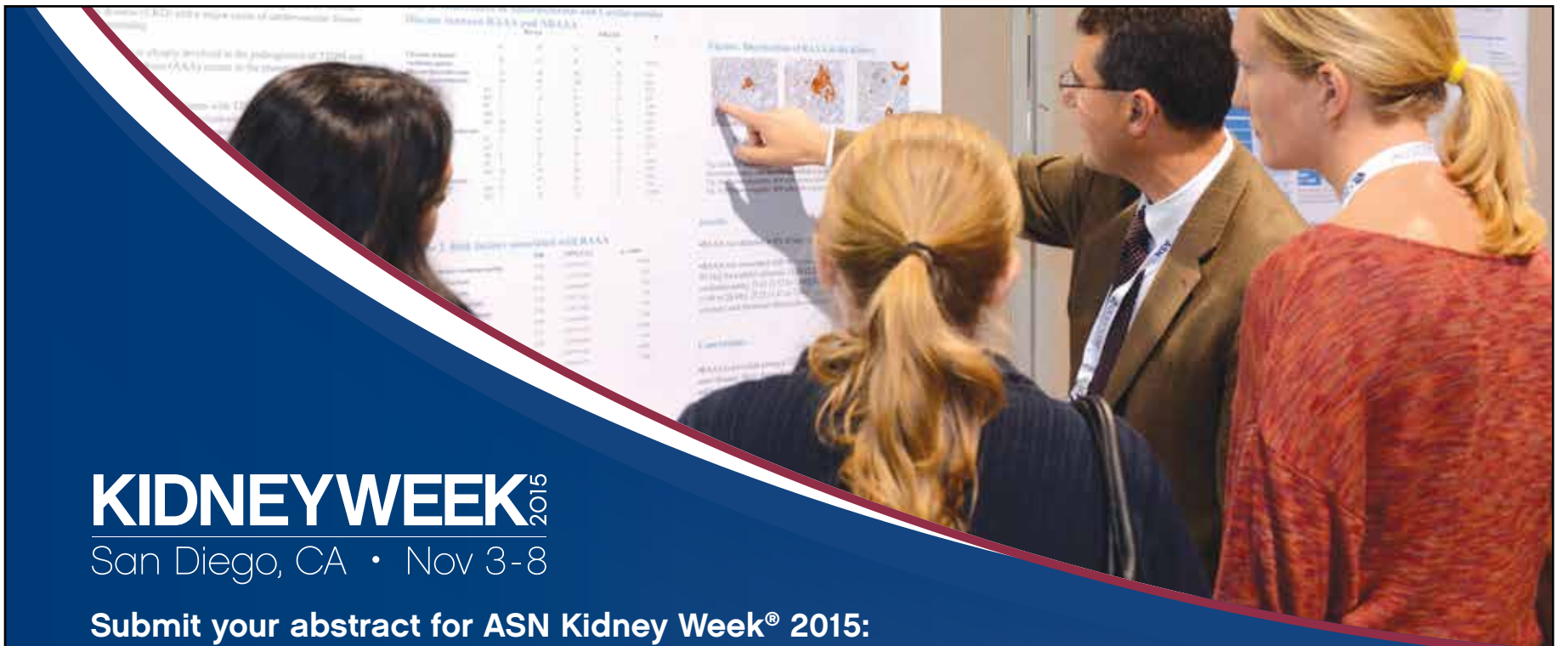
Muhammad Magdi Yaqoob, MD, PhD, FRCP, who was not involved with the study and is a professor and consultant in nephrology at the University of London & Barts Health National Health Service Trust, in the United Kingdom, noted that the research adds to the growing body of experimental and clinical evidence suggesting that acidosis can be a modifiable risk factor in the progression of CKD, but that studies with hard outcomes are needed to determine the safety and benefits of reducing dietary acid load in patients. “I strongly

recommend a definitive multicenter randomized controlled clinical trial of a low dietary acid load diet compared with a normal diet in patients with CKD stages 3b–5, with progression to renal failure as a primary endpoint,” he said. “Secondary endpoints should include quality of life, mineral and bone disorder, and protein energy wasting.”

Study coauthors include Deidra Crews, MD, Donald Wesson, MD, Anca Tilea, MS, Rajiv Saran, MD, Nilka Ríos Burrows, MPH, Desmond Williams, MD, and Neil Powe, MD.

Disclosures: The authors reported no financial disclosures.

The article, entitled “High dietary acid load predicts ESRD among adults with CKD,” is available at <http://jasn.asnjournals.org/content/early/2015/02/11/ASN.2014040332>.



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#### IMPORTANT DATES (2015)

##### ABSTRACTS

**Wednesday, April 8**  
Abstract Submission Site Opens

**Wednesday, June 3**  
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Late-Breaking Clinical Trial Submission Site Closes  
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Please note that ALL abstract authors (including co-authors) must have current disclosures on file with ASN at time of submission.



# Findings

## Time-Updated BP Shows Stronger Association with CKD Progression

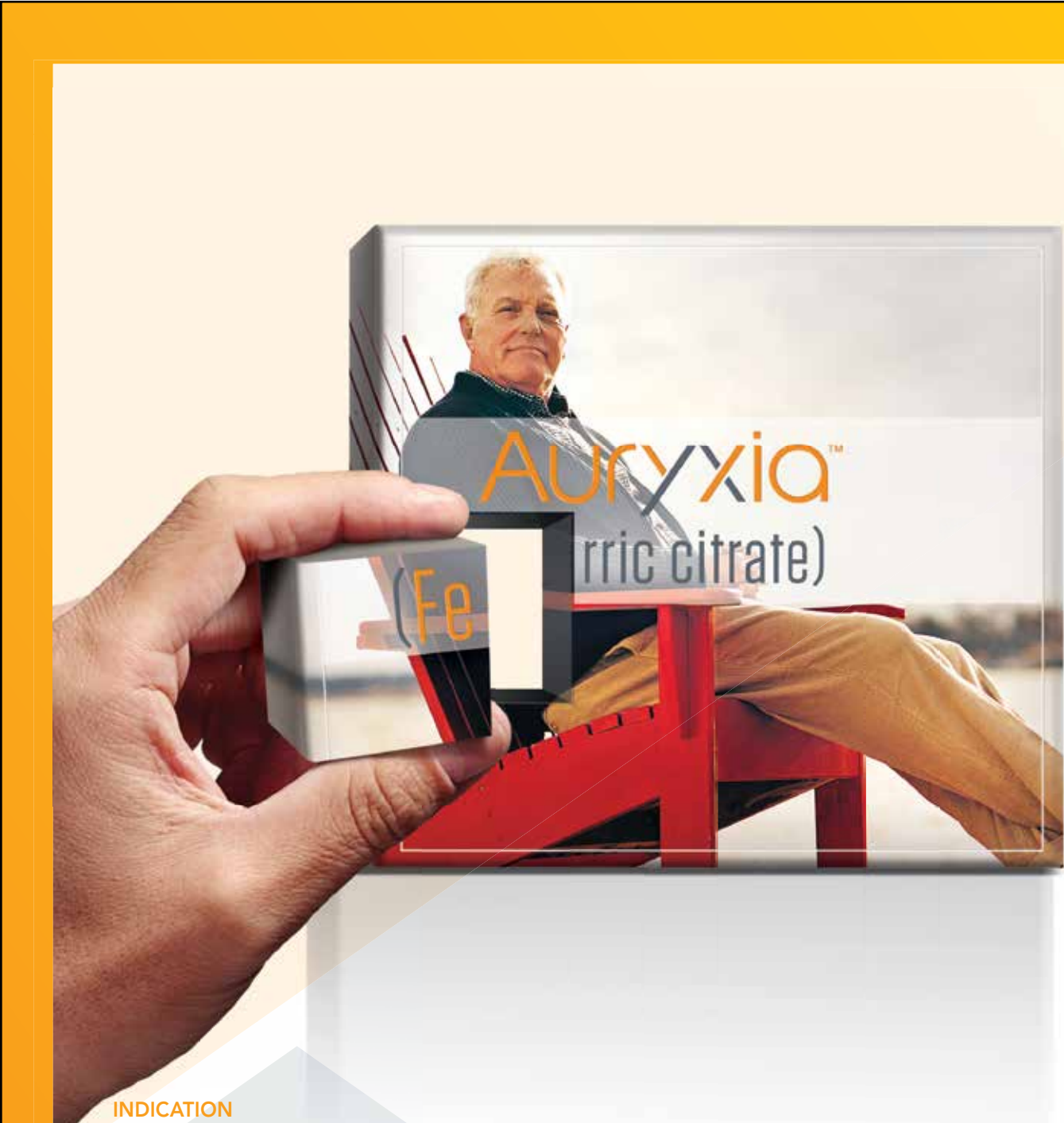
Compared with one-time measurement, time-updated BP values are a stronger predictor of chronic kidney disease (CKD) progression, reports a study in the *Annals of Internal Medicine*.

The prospective Chronic Renal Insufficiency Cohort Study included 3708 patients with mild to moderate CKD who were enrolled at seven centers in the United States between 2003 and 2008. At annual clinic visits, the visit-specific systolic BP (SBP) was determined as the mean of three seated SBP measurements. Time-updated

SBP was calculated as the mean of that value and all previous visit-specific values.

Visit-specific and time-updated SBPs were compared for association with progression to ESRD and with a composite endpoint of ESRD or halving of the estimated GFR. Analyses were adjusted for time-updated covariates.

Over a median 5.7 years of follow-up, 19.2 percent of patients had an SBP of 130 mm Hg or greater at all visits. When baseline data only were used, the hazard ratio for ESRD associated with SBP of 130 to 139 mm Hg was 1.46 (compared with SBP less than 120 mm Hg). For a time-updated SBP of 130 to 139 mm Hg, the HR was 2.37.



### INDICATION

AURYXIA is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

### IMPORTANT SAFETY INFORMATION

**Contraindication:** AURYXIA is contraindicated in patients with iron overload syndromes.

**Iron Overload:** Iron absorption from AURYXIA may lead to excessive elevations in iron stores. Assess iron parameters, serum ferritin and TSAT, prior to and while on AURYXIA. Patients receiving IV iron may require a reduction in dose or discontinuation of IV iron therapy.

**Overdose:** AURYXIA contains iron. Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant IV iron is used.

**Accidental Overdose of Iron:** Accidental overdose of iron containing products is a leading cause of fatal poisoning in children under 6 years of age. Keep this product out of the reach of children.

**Patients with Gastrointestinal Bleeding or Inflammation:** Safety has not been established.

**Pregnancy Category B and Nursing Mothers:** Overdosing of iron in pregnant women may carry

Time-updated BP measurements are more strongly linked to risk of progressive CKD than are baseline SBP values. “[P]rolonged exposure to SBP greater than 130 mm Hg may portend increased risk for progressive loss of kidney function among persons with CKD regardless of diabetes or proteinuria sta-

tus,” the researchers write. They call for further studies to assess the relevance of time-updated BP for clinical practice guidelines [Anderson AH, et al. Time-updated systolic blood pressure and the progression of chronic kidney disease: a cohort study. *Ann Intern Med* 2015; 162:258–265]. ●

## Good Outcomes with HIV-Positive Kidney Donors and Recipients

At up to 5 years of follow-up, HIV-positive recipients of kidney transplants from HIV-positive donors have good graft survival and other outcomes, reports a study in the *New England Jour-*

*nal of Medicine*.

The experience included kidney transplants in 27 HIV-infected patients at a South African transplantation center from 2008 to 2014. All patients were receiving antiretroviral therapy (ART), with a CD4 T cell count of at least 200 mm<sup>3</sup> and undetectable plasma HIV RNA.

*Continued on page 8*

For the control of serum phosphorus levels in patients with chronic kidney disease on dialysis

## AURYXIA™ (ferric citrate) IS THE FIRST AND ONLY ABSORBABLE-IRON–BASED PHOSPHATE BINDER CLINICALLY PROVEN TO MANAGE HYPERPHOSPHATEMIA<sup>1-6</sup>

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### References:

1. Fosrenol [package insert]. Wayne, PA: Shire US, Inc.; 2014. 2. Phoslyra [package insert]. Waltham, MA: Fresenius Medical Care North America; 2011. 3. PhosLo Gelcaps [package insert]. Waltham, MA: Fresenius Medical Care North America; 2012. 4. Renagel [package insert]. Cambridge, MA: Genzyme Corporation; 2014. 5. Renvela [package insert]. Cambridge, MA: Genzyme Corporation; 2014. 6. Velphoro [package insert]. Waltham, MA: Fresenius Medical Care North America; 2014. 7. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis*. 2003;42(4 Suppl 3):S1-S201. 8. Data on File 1, Keryx Biopharmaceuticals, Inc.

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.

**Pediatric:** The safety and efficacy of AURYXIA have not been established in pediatric patients.

**Adverse Events:** The most common adverse events with AURYXIA were diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). Gastrointestinal adverse reactions were the most common reason for discontinuing AURYXIA (14%).

**Drug Interactions:** Doxycycline should be taken at least 1 hour before AURYXIA. Consider separation of the timing of the administration of AURYXIA with drugs where a reduction in their bioavailability would have a clinically significant effect on safety or efficacy.

**Please see Brief Summary on following page.**

**You may report side effects to Keryx at 1-844-44KERYX (844-445-3799).**



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# Findings

## Good Outcomes

Continued from page 7

Kidneys were obtained from 23 deceased donors, all positive for HIV by fourth-generation enzyme-linked immunosorbent assay. The donors had received no or only first-line ART. The surviving recipients were followed up for a median of 2.4 years. Patient survival was 84 percent at 1 and 3 years and 74 percent at 5 years. Graft survival rates were 93 percent, 84

percent, and 84 percent, respectively. Five patients had a total of eight confirmed episodes of acute rejection; the rejection rate was 8 percent at 1 year and 22 percent at 3 years. The patients’ HIV disease remained well controlled, with continued suppression of viral load. The successful rollout of ART in South Africa has led to an increased number of patients with diagnoses of HIV nephropathy. Kidneys from HIV-infected donors provide a promising alternative to dialysis for these patients.

The new experience shows good graft functioning and patient survival after kidney transplantation from HIV-positive deceased donors to HIV-positive recipients. The outcomes appear similar to those in high-risk kidney transplant patients without HIV infection. The authors discuss the challenges related to interactions between antiretroviral and immunosuppressant drugs [Muller E, et al. HIV-positive–to–HIV-positive kidney transplantation: results at 3 to 5 years. *N Engl J Med* 2015; 372:613–620]. ●

### BRIEF SUMMARY

AURYXIA™ (ferric citrate) tablets contain 210 mg of ferric iron equivalent to 1 g ferric citrate for oral use.

### INDICATIONS AND USAGE

AURYXIA is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

### CONTRAINDICATIONS

AURYXIA is contraindicated in patients with iron overload syndromes (eg, hemochromatosis).

### WARNINGS AND PRECAUTIONS

**Iron Overload:** Iron absorption from AURYXIA may lead to excessive elevations in iron stores. Increases in serum ferritin and transferrin saturation (TSAT) levels were observed in clinical trials. In a 56-week safety and efficacy trial in which concomitant use of AURYXIA and IV iron was permitted, 55 (19%) patients treated with AURYXIA had a ferritin level >1500 ng/mL as compared with 13 (9%) patients treated with active control. Assess iron parameters (eg, serum ferritin and TSAT) prior to initiating AURYXIA and monitor iron parameters while on therapy. Patients receiving IV iron may require a reduction in dose or discontinuation of IV iron therapy. **Accidental Overdose of Iron:** Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6 years of age. Keep this product out of the reach of children. In case of accidental overdose, call a doctor or poison control center immediately. **Patients with Gastrointestinal Bleeding or Inflammation:** Patients with inflammatory bowel disease or active, symptomatic gastrointestinal bleeding were excluded from clinical trials. Safety has not been established in these populations.

### ADVERSE REACTIONS

Adverse reactions to a drug are most readily ascertained by comparison with placebo, but there is little placebo-controlled experience with AURYXIA, so this section describes adverse events with AURYXIA, some of which may be disease-related, rather than treatment-related. A total of 289 patients were treated with AURYXIA and 149 patients were treated with active control (sevelamer carbonate and/or calcium acetate) during the 52-week, randomized, open-label, active control phase of a trial in patients on dialysis. A total of 322 patients were treated with AURYXIA for up to 28 days in three short-term trials. Across these trials, 557 unique patients were treated with AURYXIA; 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. In these trials, adverse events reported for AURYXIA were similar to those reported for the active control group. Adverse events reported in more than 5% of patients treated with AURYXIA in these trials included diarrhea (21%), nausea (11%), constipation (8%), vomiting (7%), and cough (6%). During the 52-week active control period, 60 patients (21%) on AURYXIA discontinued study drug because of an adverse event, as compared to 21 patients (14%) in the active control arm. Patients who were previously intolerant to any of the active control treatments (calcium acetate and sevelamer carbonate) were not eligible to enroll in the study. Gastrointestinal adverse events were the most common reason for discontinuing AURYXIA (14%). AURYXIA is associated with discolored feces (dark stools) related to the iron content, but this staining is not clinically relevant and does not affect laboratory tests for occult bleeding, which detect heme rather than non-heme iron in the stool.

### DRUG INTERACTIONS

Doxycycline is an oral drug that has to be taken at least 1 hour before AURYXIA. Oral drugs that can be administered concomitantly with AURYXIA are: amlodipine, aspirin, atorvastatin, calcitriol, clopidogrel, digoxin, doxercalciferol, enalapril, fluvastatin, levofloxacin, metoprolol, pravastatin, propranolol, sitagliptin, and warfarin. There are no empirical data on avoiding drug interactions between AURYXIA and most concomitant oral drugs. For oral medications where a reduction in the bioavailability of that medication would have a clinically significant effect on its safety or efficacy, consider separation of the timing of the administration of the two drugs. The duration of separation depends upon the absorption characteristics of the medication concomitantly administered, such as the time to reach peak systemic levels and whether the drug is an immediate release or an extended release product. Consider monitoring clinical responses or blood levels of concomitant medications that have a narrow therapeutic range.

### USE IN SPECIFIC POPULATIONS

**Pregnancy:** Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women. It is not known whether AURYXIA can cause fetal harm when administered to a pregnant woman. Animal reproduction studies have not been conducted. The effect of AURYXIA on the absorption of vitamins and other nutrients has not been studied in pregnant women. Requirements for vitamins and other nutrients are increased in pregnancy. An overdose of iron in pregnant women may carry a risk for spontaneous abortion, gestational diabetes, and fetal malformation. **Labor and Delivery:** The effects of AURYXIA on labor and delivery are unknown. **Nursing Mothers:** Data from rat studies have shown the transfer of iron into milk by divalent metal transporter-1 (DMT-1) and ferroportin-1 (FPN-1). Hence, there is a possibility of infant exposure when AURYXIA is administered to a nursing woman. **Pediatric Use:** The safety and efficacy of AURYXIA have not been established in pediatric patients. **Geriatric Use:** Clinical studies of AURYXIA included 106 subjects aged 65 years and older (33 subjects aged 75 years and older). Overall, the clinical study experience has not identified any obvious differences in responses between the elderly and younger patients in the tolerability or efficacy of AURYXIA.

### OVERDOSAGE

No data are available regarding overdose of AURYXIA in patients. In patients with chronic kidney disease on dialysis, the maximum dose studied was 2,520 mg ferric iron (12 tablets of AURYXIA) per day. Iron absorption from AURYXIA may lead to excessive elevations in iron stores, especially when concomitant IV iron is used. In clinical trials, one case of elevated iron in the liver as confirmed by biopsy was reported in a patient administered IV iron and AURYXIA.

### PATIENT COUNSELING INFORMATION

**Dosing Recommendations:** Inform patients to take AURYXIA as directed with meals and adhere to their prescribed diets. Instruct patients on concomitant medications that should be dosed apart from AURYXIA. **Adverse Reactions:** Advise patients that AURYXIA may cause discolored (dark) stools, but this staining of the stool is considered normal with oral medications containing iron. AURYXIA may cause diarrhea, nausea, constipation, and vomiting. Advise patients to report severe or persistent gastrointestinal symptoms to their physician.



# Introducing KSAP

The Kidney Self-Assessment Program (KSAP) is a new CME and Part 2 MOC product designed to help you review the essentials of nephrology. The program is composed of challenging, clinically-oriented questions that will refresh your understanding of the core elements of nephrology.

Based on the American Board of Internal Medicine (ABIM) nephrology examination blueprint, KSAP provides excellent preparation for fellows preparing for initial certification or practicing nephrologists preparing for recertification.

Refresh your nephrology knowledge and earn 25 Maintenance of Certification (MOC) points and 15 *AMA PRA Category 1 Credits*™.

Learn more and get started at [www.asn-online.org/ksap](http://www.asn-online.org/ksap)

## ASN Partners with Harold Amos Medical Faculty Development Program to Create ASN-AMFDP Award

In February 2015, ASN announced the creation of the American Society of Nephrology–Harold Amos Medical Faculty Development Program (ASN-AMFDP) Award. Through a partnership with the Harold Amos Faculty Development Program (Amos Scholars), this initiative will support the research and career development of a kidney research scholar and future health care leader, and extend ASN's commitment to advancing diversity and inclusion.

The Amos Scholars program of the Robert Wood Johnson Foundation (RWJF) began in 1983 and is now one of the foundation's longest running programs. The program was renamed in January 2004 to honor Harold Amos, PhD, the first African American to chair a department at Harvard Medical School. Dr. Amos recruited and mentored minority and disadvantaged students and faculty throughout his career.

The Amos Scholars Program is designed to increase the number of historically disadvantaged faculty who achieve senior rank in academic medicine and dentistry and to foster the development of succeeding classes of such physicians and dentists. Many of the 250 alumni of the Amos Scholars Program are full professors, chairs of departments, leaders of institutes within the National Institutes of Health (NIH), and individuals widely known for valuable contributions to biomedical research, health services research, clinical investigation, and leadership in the medical profession.

More than three-quarters of Harold Amos scholars remain in academic medicine, including 57 professors, 76 associate professors, and 56 assistant professors. Three alumni are directors at the NIH, and 10 have been elected to the Institute of Medicine.

Out of the 250 scholars, 23 have focused on kidney care. Griffin P. Rogers, MD, the director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is a former Amos Scholar. Many of these scholars have gained influence far beyond nephrology. Placing kidney experts in key leadership positions in

medicine and science is vital to supporting and building the profession over time. "ASN is honored to partner with the Robert Wood Johnson Foundation to support the Harold Amos Medical Faculty Development Program, an outstanding initiative that has greatly enriched medicine and science," said ASN President Jonathan Himmelfarb, MD, FASN.

### Ties to ASN's mission

ASN's participation in the Amos Program was initiated by a recommendation from ASN's Diversity and Inclusion Work Group. The Work Group evaluated the program's history, the impressive achievements of Amos Scholars and the involvement of Amos Scholars in mentoring others from groups underrepresented in medicine.

The Work Group and ASN Council recognize that advancing diversity and inclusion is essential to mitigating disparities in kidney medicine. Many Amos Scholars are engaged in research that has advanced knowledge related to disparities in care and access to care.

"Promoting diversity and inclusiveness to enhance nephrology and improve patient care is key to ASN's mission," Dr. Himmelfarb noted. The ASN-AMFDP program will increase diversity among future leaders in nephrology, promoting the innovation, creativity, and sensitivity that will advance health for all people living with kidney disease."

The ASN-AMFDP program is one of several recommendations of the Diversity and Inclusion Work Group approved by ASN Council. These include support of participants at the NIDDK Network of Minority Health Research Investigators meeting, exhibiting at the Student National Medical Association Annual Meeting, developing an online curriculum for nephrology mentors and mentees, and hosting an event at Kidney Week focused on promoting sponsorship and networking opportunities for underrepresented students, trainees, and young professionals. ●

### The Amos Scholars Program

Amos Scholars are individuals committed to pursuing an academic career, serving as a role model for students and faculty from historically disadvantaged backgrounds, as well as improving the health status of underserved populations and/or furthering the understanding and elimination of health disparities.

Each scholar receives an annual stipend of up to \$75,000, complemented by a \$30,000 annual grant toward support of research activities. Each scholar studies and conducts research in association with a senior faculty member located at an academic medical center or dental school noted for the training of young faculty. The application process for the award cycle for nephrology closed on March 18, 2015.

The excellent and influential core of mentors on RWJF National Advisory Committee, with many years of experience in medicine, academia, and industry provide counseling, career advice, and have helped many scholars navigate the promotion process and challenging institutional situations. This helps scholars position themselves as mentors. Amos scholars also receive media training, including skill building around presenting scientific data and conducting interviews, which are highly valuable and marketable skills.

## Kidney Transplantation Practice Improvement Module

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### Meaningfully improve patient care

The Kidney Transplantation PIM has been planned and implemented through the joint providership of American Society of Nephrology (ASN) and American Society of Transplantation (AST). The program is designed to help you improve care for post-kidney transplant patients.

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To learn more, visit [asn-online.org/pim](http://asn-online.org/pim)



# Q and A: National Institute on Minority Health and Health Disparities

***This year marks the five-year anniversary of the establishment of the National Institute on Minority Health and Health Disparities (NIMHD). ASN Kidney News interviewed NIMHD Acting Director Yvonne Maddox, PhD, about the institute's mandate to coordinate minority health and health disparities research at NIH.***



Yvonne Maddox, PhD

***Prior to becoming an NIH institute in 2010 with passage of the Patient Protection and Affordable Care Act, NIMHD was an NIH center—the National Center on Minority Health and Health Disparities. What impact did that change have on the institute's focus, agendas, and programs?***

It is exciting to look back on where the health disparities initiative has come and where it is going since passage of the *Minority Health and Health Disparities Research and Education Act of 2000* (Public Law 106-525).

The US Department of Health and Human Services in 2000 designated the National Center on Minority Health and Health Disparities (NCMHD) to be a focal point for coordinating minority health and health disparities research at the NIH through “the conduct and support of research, training, dissemination of information, and other programs with respect to minority health conditions and other populations with health disparities.” Three legacy programs were established under this new law to expand upon research within NCMHD’s mission and build a diverse research workforce:

- The Centers of Excellence (COE) for Research Education and Training, which establishes centers within colleges and universities to address health disparities through three main core areas: research, research training and education, and community engagement.
- The Loan Repayment Program for Minority Health Disparities Research, which promotes

research careers in basic, clinical, and behavioral research especially for young scientists underrepresented in research.

- The Research Endowment Program, which promotes minority health and health disparities research capacity building at eligible COE funded by the Health Resources and Services Administration (HRSA) under sections 736 of the Public Health Service Act.

With passage of the *Patient Protection and Affordable Care Act* (Public Law 111-148) NCMHD was re-designated an institute, NIMHD, on March 23, 2010. The law transferred all of the responsibilities of the center to NIMHD and expanded eligibility for Research Endowment grants to also include eligible COE funded by NIMHD. The expanded eligibility criterion was incorporated in the NIMHD Research Endowment Program in FY 2010. With a focus on research capacity building, the NIMHD Research Endowment Program is unique to NIH. (Table 1).

ers, we have been leading a “visioning initiative” to better define minority health and health disparities issues and to identify the needs of the various populations who experience grave disparities in health status.

The science of health disparities research examines the etiology of health differences and research interventions to specifically identify and address the factors contributing to various health disparities. These factors, or health determinants, such as biological risk factors (including genetic and microbial), behavioral risk factors, social/economic factors, health systems, resiliency/protective factors, quality of life experiences, and environmental/physical factors affect various population groups in different ways and may contribute to differential consequences and unequal health burdens. Once the interactions and contributions of the various health determinants are understood through scientific research, tailored interventions can be designed, tested, and implemented widely to reduce the health burden. So we need to be mindful of population health and the science of behavioral change.

**Table 1**  
**NIMHD Research Endowment Program**

## Goals

1. Establish an income-producing asset within institutions to support development of the next generation of diverse health disparities researchers.
2. Develop and enhance the infrastructure for research.
3. Enhance the academic environment to overcome educational and financial resource barriers to promote a diverse scientific workforce.
4. Recruit and retain faculty/scientists currently underrepresented in the biomedical, clinical, behavioral, and social sciences.

## Initiatives

- The *Research and Institutional Resources Health Disparities Endowment Grants-Capacity Building* initiative (S21 mechanism) is designed to strengthen the research and training infrastructure of the institution, while addressing current and emerging needs in minority health and other health disparities research.
- The *Research and Student Resources Health Disparities Endowment Grants-Educational Programs* initiative (S22 mechanism) is designed to increase the investment in student-centered programs to improve the academic success of individuals underrepresented in the biomedical, clinical, behavioral, and social sciences and those from socioeconomically disadvantaged backgrounds.

***You were recently appointed acting director of NIMHD. Tell us about your vision for the future direction of the institute.***

As acting director of NIMHD, I have been working with the NIMHD staff and across the other NIH institutes and centers (ICs) to continue to advance our programs. With the support and collaboration of the many NIMHD intramural and extramural stakehold-

It is also important to recognize that minority health and health disparities are not the same, and that the terms must be properly defined. NIMHD is establishing a trans-NIH approach to define these critical areas. *Health disparities* are differences in the incidence, prevalence, mortality, and burden of diseases and other adverse health conditions that exist among specific population groups in the United States owing

*Continued on page 12*

to social, economic, and environmental disadvantage. *Minority health* refers to health outcomes associated with a particular population group and is often correlated with race and ethnic differences.

**What role does NIMHD play in fostering research in kidney disease health disparities? Does NIMHD collaborate with any other institutes or federal agencies on kidney-related studies?**

NIMHD plays a significant role in supporting and conducting research in minority health and health disparities for all diseases and conditions that disproportionately affect health disparity populations (such as racial, ethnic, low socioeconomic status, and rural populations). This includes addressing research in kidney disease and disparities. Diabetes is one of the six health disparities areas NIH identified in its first strategic plan in 2001 as a high priority area, especially when it relates to social determinants of health, health promotion, and disease prevention.

Kidney disease impacts the health of underserved populations and its effects are disproportionately high. For example, African Americans are five times more likely to develop glomerular disease, such as focal segmental glomerulosclerosis (FSGS), than Caucasians. Glomerular disease remains a focus of the NIMHD research agenda through the COE Program, which supports biomedical, clinical, behavioral, and community-based participatory research; research training; and community outreach in minority health and health disparities. One NIMHD-supported study is investigating the progression of end-stage renal disease (ESRD) in African Americans, with a focus on the genetic risk factors for ESRD and the role of the sympathetic nervous system in the progression of kidney disease. NIMHD co-sponsored a conference with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) on the potential biological and social impact of the discovery of genetic variations that appear to predispose African Americans to certain forms of kidney disease, including FSGS. Staff from NIDDK, NIMHD and other NIH ICs reviewed genetic, public health, ethical, and social implications of these new findings. With input from conference participants, NIMHD has now identified glomerular disease and nephrotic syndrome as priority research areas in our Notice of Participation in the NIH Parent R01 (investigator-initiated) Program Announcement.

NIMHD also supports diabetes research both in its extramural programs and in its intramural laboratory. An important focus is the testing of culturally tailored social support intervention for individuals of different ethnic backgrounds with type 2 diabetes. The NIMHD intramural program continues to study health disparities in diet and eating habits and their influence on obesity as a contributing factor to diabetes development in children and young adults.

**How do institute programs help trainees and researchers balance the need for addressing health disparities with regard to both prevention and treatment of disease?**

The institute has developed and implemented a full range of programs from the prevention of disease to the comparison of different treatment regimens. While prevention has the potential for creating a windfall in improving the health of indi-

viduals, determining the best treatment interventions to reach underserved populations is critical to improving the lives of all Americans. For example, NIMHD is collaborating with other institutes and centers to support research to develop, adapt, and test the effectiveness of health promotion and disease prevention interventions in many community settings, including the American Indian and Alaska Native communities. Our Community-Based Participatory Research Initiative establishes collaborations with the community to identify health priorities and implement interventions designed to improve health. As true partners, the community embraces an “ownership” role in the research and helps to develop ways to disseminate and implement the evidence-based information.

Health disparities research includes basic, applied, clinical, social and behavioral, and translational research. NIMHD supports programs that provide opportunities for research training and career development in all of these areas. A new focus for the institute is population health and health disparities. The programs in this priority area also increase the evidence base for interventions to reduce health disparities and seek to improve the quality and length of life for all populations (Table 2).

**Table 2**  
**Objectives of the NIMHD basic, social and behavioral science programs**

- Support systems research strategies to investigate the role that health determinants (including biological, social, cultural, and environmental factors) play in driving or sustaining health disparities.
- Use validated results from systems research etiology studies to design and to test tailored interventions targeting the reduction of health disparities.
- Foster sustainable programs that improve health behaviors and health outcomes in disparity populations through culturally tailored interventions.

As part of NIMHD’s role in coordinating and facilitating health disparities research across NIH, we continue to work with the other ICs to conduct scientific portfolio reviews and evaluations to identify priority areas that include efforts aimed at disease prevention, early detection, risk reduction efforts, and targeted treatment interventions to improve population health.

**What strategies for attracting trainees into health disparities research have you found successful at NIMHD?**

NIMHD is one of the lead NIH institutes to conduct and support research training particularly in the field of minority health research and health disparities research.

A successful program for recruiting trainees into research, leading to a reduction and elimination

of disparities in population health, has been the NIMHD Loan Repayment Program (LRP) that offers loan repayment awards of up to \$35,000 per year to health professionals with doctorate degrees (e.g., MD, PhD, DrPh) while conducting health disparities or clinical research in non-federal research settings for at least two years. Since its inception, the NIMHD LRP has supported more than 2400 scholars, many of whom have gone on to receive R01 funding from NIMHD and other NIH ICs, including the NIDDK.

The LRP has two tracks:

- **The NIMHD Loan Repayment Program for Health Disparities Research** supports qualified health professionals engaged in basic, clinical, behavioral, social sciences, or health services research addressing health disparities. At least 50% of recipients must be from a health disparity population, as required in the Minority Health and Health Disparities Research and Education Act of 2000 (P.L. 106-525).
- **The NIMHD Extramural Clinical Research Loan Repayment Program for Individuals from Disadvantaged Backgrounds** supports health professionals from financially disadvantaged backgrounds who conduct clinical research. Clinical research involves direct patient interaction and usually studies the origins or effects of a disease or health condition.

Another recruitment initiative has been to encourage participation in the NIH Diversity Supplement Program. This program provides an opportunity for grantees, including those working in the health disparities field, to apply for administrative supplements to allow support for trainees/early career investigators to work within the scope of the parent health disparities research project.

NIMHD also offers a competitive, annual two-week intensive, on-site training in the principles and practices of health disparities research through the NIMHD Translational Health Disparities Course held on the NIH campus in Bethesda, MD. Since its launch in 2010, roughly 264 scholars have gone through the course. The course has Continuing Medical Education accreditation through Johns Hopkins University.

As an additional training mechanism, NIMHD staff provide information on institute programs at various meetings and workshops across the US and abroad throughout the year.

**Are there plans for offering mentored career development awards (i.e., K awards) from the NIMHD?**

NIMHD believes early training programs may be the best models to address the immediate pipeline issues. The institute is investing in the National Research Service Award Institutional (T32) and individual fellowship (F31, F32) training programs in FY 2015 and FY 2016. Specifically, we will be seeking to develop a training portfolio in population health science. Working with the NIH Office of Behavioral and Social Sciences Research (OBSSR), NIMHD will co-sponsor an Institute of Medicine Workshop on *Training in Interdiscipli-*

nary Population Health Science: A Vision for the Future, Institute of Medicine Roundtable in June 2015.

Population health science is an interdisciplinary science that develops an integrated understanding of the determinants of health and health disparities, and therefore holds promise for advancing the science of health disparities. It is essential that other ICs recognize that training in population health is critical to the science of health disparities. Therefore, we are pleased that OBSSR is advancing a trans-disciplinary approach to this area of training.

#### **In addition to attracting trainees, what insights can NIMHD offer regarding actively fostering the careers of young faculty?**

Providing structured mentoring and professional development can help foster the careers of young faculty. Most important is protected time for junior faculty. Developing bridge-plans for moving successful postdoctoral researchers into junior faculty positions and junior faculty into tenured track positions is important, as is developing a schema to help junior faculty choose mentors and institutions that support them and providing visibility to the success stories of professional advancement of those early career faculty members.

#### **How does the institute support training of a diverse research workforce?**

NIMHD plays an active role in the three new NIH Common Fund initiatives that support programs with the potential to dramatically affect biomedical research by achieving a set of high impact goals within a defined time frame. In these interrelated initiatives, awardees will work together as part of the Diversity Program Consortium (Table 3).

Another catalyzing, trans-NIH initiative that NIMHD supports is the Big Data to Knowledge (BD2K) program, which aims to facilitate broad use of biomedical big data, develop and disseminate analysis methods and software, enhance training for disciplines relevant for large-scale data analysis, and establish centers of excellence for biomedical big data. NIMHD has a lead role on the BD2K Enhancing Diversity in Biomedical Data

Science research program (RFA-MD-15-005). The over-arching goal of this education grant program is to support educational activities that enhance the diversity of the biomedical, behavioral, and clinical research workforce. To achieve this goal, this Funding Opportunity Announcement will support creative educational activities with a primary focus on research experiences and curriculum development.

#### **Are there programs that are under-utilized that students and young investigators should know about?**

NIH offers a diverse range of research training and career development programs for all degree levels and for early career investigators. This includes Summer Internships in Biomedical Research, the Biomedical Engineering Summer Internship Program, the Introduction to Cancer Research Careers program, the Summer Internship Program for Veterinary Medical Students, and the Recruitment and Training Program for Under-Represented Populations. Training also includes the Post-Baccalaureate Intramural Research Training Award program and the NIH Academy.

Many of the NIH institutes have their own special training programs, which are often discipline specific. However, one program that is not well known is the NIH intramural Medical Research Scholars Program (MRSP), which is co-funded by NIMHD, and engages scholars in a one-year research intensive, mentored basic, translational, or clinical research project in an area that matches their personal interests and career/research goals. This is a comprehensive residential research enrichment program for medical, dental, and veterinary students. The program highlights understanding of clinical protocol development and the conduct of human subjects' research, focusing on clinical teaching rounds with patients participating in research protocols at the NIH Clinical Center, and academic leadership development.

#### **What do you consider the greatest research opportunities of NIMHD in the short and long-term?**

NIMHD science spans fundamental understanding of the basic biological processes and epigenetic

mechanisms associated with health disparities to applied, clinical and translational research, and population science studies and interventions that seek to address disparities. Our existing knowledge provides a useful basis for critical scientific activities and innovation needed to address the research and population health needs in transition, but it falls short of integrated solutions to eliminating health disparities. An objective of our current health disparities science visioning process is to focus on these unanswered research questions and processes to address racial/ethnic minority health and eliminate health disparities.

Following are NIMHD research goals to build upon current observations/advances to mature the field of health disparities research:

- Utilize multidisciplinary systems approaches and encourage team science;
- Identify rigorous scientific methods/tools, measurements, metrics, etc.;
- Identify gaps in research areas and determine priority areas for action;
- Establish some basic foundations or principles for the health disparity community to consider when addressing health disparities;
- Create training opportunities to develop a robust health disparities and population health research workforce; and
- Collaborate with federal and non-federal research organizations to identify partnerships in critical areas to more effectively and efficiently advance the field of health disparities research and population health.

NIMHD will continue to collaborate with the other NIH ICs to develop a health disparities research framework to explore the following questions:

- What are some core attributes and expectations for a transformative discipline of health disparities science?
- What are some of the key research questions that should be given high priority on a health disparities research agenda, because knowledge in those areas might inform translation efforts that could have a high impact on reducing health disparities?
- Which scientific disciplines and/or approaches are needed to address critical knowledge gaps in health disparities research?
- What will be the basic, applied, clinical, and translational health disparities research questions to address?
- What research tools, methods, and approaches are needed to adequately address health disparities science?
- What are the infrastructure, resources, training, and capacity-building needs and opportunities?

Among the important scientific areas expected to advance health disparities research are: model systems; life-course science; the science of behavior change; and population science, including increasing the recruitment and retention of diverse populations in clinical trials, while being mindful that effective clinical studies must consider all ethnicities, as exclusions can endanger populations; along with precision medicine; behavior and cognitive development, with a focus on mental health; the analysis of big data; and the translation, dissemination, and implementation of interventions.

**Table 3**  
**NIH Common Fund Program: Enhancing the diversity of the NIH-funded workforce**

Program	Description	Goals
Building Infrastructure Leading to Diversity (BUILD) Program	Will provide support for under-resourced institutions with high concentrations of students from disadvantaged backgrounds.	Implement transformative approaches to train students to undertake biomedical and behavioral research.
National Research Mentoring Network (NRMN)	Will build a nationwide network of mentors and mentees spanning all disciplines relevant to the NIH mission.	Establish an interconnected set of skilled mentors linked to students and faculty across the country.
Coordination and Evaluation Center (CEC)	Will coordinate consortium-wide activities and assess efficacy of the training and mentoring approaches developed by the BUILD and NRMN awardees.	Develop both short- and long-term measures of efficacy, allowing the consortium to continuously gather data and respond accordingly.



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## Mortality Predictors in Dialysis Patients with Atrial Fibrillation

For hemodialysis patients with atrial fibrillation (AF), antiplatelet drugs are associated with increased mortality, and oral anticoagulants may be associated with better survival, reports a study in *Nephrology Dialysis Transplantation*.

In the prospective study, all patients with documented AF at 10 Italian hemodialysis centers were followed up for 2 years. The use of oral anticoagulant and antiplatelet drugs and the percentage of time spent in the target international normalized ratio range (TTR) were assessed as predictors of death,


thromboembolic events, and bleeding. The predictive value of age, dialytic age, and comorbid conditions was also assessed.

Of 290 patients with AF enrolled in the study, 134 were taking oral anticoagulants at baseline. There were 115 deaths during follow-up, including three deaths resulting from hemorrhagic stroke and one resulting from thromboembolic stroke. Patients taking antiplatelet drugs were at increased risk of death: hazard ratio (HR) 1.71. Other significant risk factors were age 75 years or older, permanent

AF, heart failure, and history of bleeding episodes.

The estimated survival was 68.6 percent for patients who always took oral anticoagulants versus 49.6 percent for patients who stopped taking these medications. The risk of thromboembolism was unaffected for patients taking oral anticoagulants, but the risk of bleeding was increased: HR 3.96. Patients with a higher TTR had a lower risk of bleeding: HR 0.09. The risk of bleeding was higher for those with previous hemorrhagic events: HR 2.17.

This study documents the 2-year mortality of about 40 percent in dialysis patients with AF. Patients taking antiplatelet drugs may be at increased risk of death. Mortality appears lower for patients taking oral anticoagulants; the bleeding risk is higher, although the risk of hemorrhagic stroke is unaffected. More time in the TTR is associated with a lower risk of bleeding among hemodialysis patients with AF [Genovesi S, et al. Warfarin use, mortality, bleeding and stroke in haemodialysis patients with atrial fibrillation. *Nephrol Dial Transplant* 2015; 30:491–498]. ●



## What's really behind your patient's hyponatremia?

**Excess vasopressin may be complicating your patient's treatment**

Elevated vasopressin levels can cause abnormal water retention, leading to hyponatremia (serum sodium <135 mEq/L).<sup>1,2</sup>

Hyponatremia may increase mortality risk and length of hospital stay and adversely affect outcomes for patients with various medical conditions.<sup>1,3</sup>

**Pull back the curtain on hyponatremia**

**hypo Na<sup>+</sup> tremia**  
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## Policy Update

### Bipartisan Kidney Legislation Aims to Improve Research and Treatment

By Congressman Tom Marino



Rep. Tom Marino

**K**idney failure was a death sentence in the 1960s. Since then, remarkable scientific advances and a landmark commitment to the millions of Americans affected by kidney disease have reversed that fact. Today, more than 600,000 Americans are living with kidney failure—and a large majority of those lives are sustained by life-saving dialysis treatments. I represent Pennsylvania's 10th District in the U.S. House of Representatives, and in my home state, more than 17,000 people rely on dialysis therapy, and another 8000 have received the gift of life through a kidney transplant.

In 1972, Congress developed the Medicare End-Stage Renal Disease benefit. This vitally important program ensures that every American, regardless of age or income, has access to life-saving dialysis care. The time has come for Congress to sustain this commitment by modernizing kidney health policies, intensifying research, improving care coordination, and expanding patient choice.

I recently introduced legislation—the Chronic Kidney Disease Improvement in Research and Treatment Act (HR

1130)—that I am confident will be instrumental in accomplishing these goals. I am very proud to be the bill's lead sponsor and honored to have my friends and colleagues John Lewis (D-GA) and Peter Roskam (R-IL) standing by me in this effort. We are joined by our colleagues in the Senate, Mike Crapo (R-ID) and Ben Cardin (D-MD), who introduced corollary legislation, S. 598.

In April 2015, I hosted a roundtable discussion with fellow Pennsylvanians to hear their thoughts about this legislation. I had the opportunity to learn how these patients and their families, physicians and health professionals, and other constituents are affected by kidney disease, and how my fellow members of Congress and I can best advocate for them—through this bill and in other aspects of our work in Washington. I was gratified that ASN Board of Advisors member and Biosciences Research Advisory Group chair Larry Holzman, MD, participated in this roundtable discussion to share his perspectives, and to reiterate the American Society of Nephrology's support and enthusiasm for this legislation: "I was pleased to participate in Congressman Marino's roundtable on his kidney legislation," Holzman said. "Clearly, he is dedicated to kidney care issues and was sincerely interested in what I and the other participants had to say about the bill and about other opportunities to improve the lives of people with kidney disease—as well as the scientific understanding of kidney disease."

The legislation is built on three primary tenets. First, investments in medical research can lead to a deeper understanding of kidney disease prevention and to innovations in treatment that reduce cost and improve patients' lives. Second, coordinating care is essential to bettering their outcomes and reducing health care costs for individuals living with chronic diseases—including kidney failure. Third, ensuring stability in the Medicare program is central to an ESRD program that guarantees patients' access to kidney care and delivers optimal results.

HR 1130 would improve research efforts to prevent, treat, and cure chronic kidney disease and kidney failure in the future by helping to develop a strategic plan to better direct biomedical research funding. The legislation also asks the Government Accountability Office (GAO) to develop a comprehensive report to Congress that assesses the adequacy of federal investments in kidney research given the

prevalence of kidney disease in the population and the cost of care. The United States is the undisputed leader in medical innovation, and with adequate investments in kidney research I am confident we will continue to lead the global fight against kidney disease.

Studies show that promoting collaboration between primary care physicians and specialists treating the same patients improves outcomes and reduces the cost of care. Coordinated care is especially important for kidney patients, many of whom are living with multiple chronic conditions and have to juggle numerous health care providers and health care settings. To spur the creation of a workable coordinated care program for dialysis patients, HR 1130 would establish a voluntary program to incentivize kidney doctors and dialysis facilities to better align treatment.

While many seniors—particularly those with multiple co-morbidities—rely on Medicare Advantage plans to coordinate their care, Medicare beneficiaries who develop ESRD are prohibited from enrolling in this kind of plan. If we want health care delivery to be more efficient through care coordination, this prohibition is an outdated relic. HR 1130 would lift this restriction and allow people with kidney failure the option to choose a Medicare Advantage plan.

Our bill expands options for patients to dialyze at home by facilitating home dialysis treatment options through telemedicine, especially in rural and underserved regions. The legislation would also help improve access to care for patients in rural and medically underserved areas by helping ensure that there are enough kidney doctors and other kidney specialists practicing in these regions. Every American deserves ready access to highly trained medical professionals, and HR 1130 aims to make this a reality for kidney patients nationwide. ●

*Rep. Tom Marino (R-PA) represents Pennsylvania's 10th congressional district. He serves as co-chair of the Congressional Kidney Caucus and received the ASN President's Medal at ASN Kidney Week 2014.*

*To join ASN in supporting this legislation, please visit ASN's Legislative Action Center to send a pre-composed message to your Congressional delegation at <https://www.asn-online.org/policy/lac.aspx>.*

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## Looking Ahead: VA Kidney Research

By Grant Olan and Michael Fischer, MD, FASN

Not many people know about the US Department of Veterans Affairs' (VA) research program outside the Washington beltway. The lack of recognition may in part be because the program is dwarfed by the National Institutes of Health (NIH) budget (\$589 million vs. \$29.4 billion in 2015). Yet the VA is a leader in a number of research fields, including vision and hearing loss, orthopedics and prosthetics, and mental health issues such as posttraumatic stress disorder and traumatic brain injury. VA investigators—half of whom are clinician-scientists—have won three Nobel Prizes and seven Lasker Awards, the US equivalent of a Nobel Prize in medicine.

Similar to the NIH, VA research proposals are peer-reviewed and merit-based. Unlike the NIH, however, the VA research program is strictly intramural. Therefore, investigators generally must be employed at least five-eighths of the time by the VA to compete for research funding awards. Moreover, VA research must be veteran-focused. VA research program priorities today include women's health, polytrauma, and the Million Veteran Program (MVP)—but the agency also conducts veteran-focused research in many other areas, including nephrology.

As the name implies, MVP's goal is to collect health information and blood samples from one million veterans to enable researchers to study how genes affect health and disease, in order to improve healthcare for veterans. The VA has many advantages for conducting research like MVP, including a stable patient population, integrated electronic medical records, and numerous clinical research centers.

According to Veterans Health Administration (VHA) National Program Director for Kidney Disease and Dialysis Susan T. Crowley, MD, FASN, "The Million Veteran Program could help unlock the biological mechanisms that cause kidney disease, helping determine who is most susceptible to developing kidney disease and evaluating the most effective therapies for preventing progression of kidney disease based on an individual's genetic makeup."

Kidney disease is naturally a concern to the VA, considering the population it serves. Veterans are at especially high risk for chronic kidney disease (CKD) and end-stage kidney disease (ESKD). Nearly 11% of patients using healthcare services have moderate and severe CKD, and VA enrollees make up approximately one-tenth of the annual US incident ESKD population.

The VA recently completed studies such as the Diabetes in Nephropathy (NEPHRON-D) Study and Acute Renal Failure Trial Network (ATN) Study (co-sponsored with the NIH). These studies have helped shed light on combined angiotensin inhibition for the treatment of diabetic nephropathy and renal replacement therapy for acute kidney injury in critically ill patients, respectively. Another VA clinical trial is currently underway to evaluate preventive strategies for reducing adverse events following angiography (Prevention of Serious Adverse Events Following Angiography Study).

The VHA is the largest provider of kidney care in the nation. Similar to that for non-veterans, mortality rates and healthcare resource utilization for veterans on dialysis remain notably high, and the cost of caring for patients with kidney disease in the VA is substantial. In fact, among the 30 most common chronic conditions in the VA, CKD and ESKD care accounted for the second highest mean VA total costs per person and similarly the second largest percentage of total VA annual medical costs, according to prior reports.

Despite the significant and growing cost of kidney care, VA dollars and awards for kidney research have been flat in recent years, at about \$20 million



Grant Olan (right) represents ASN at a Friends of VA Medical Care and Health Research briefing on March 25, 2015, with VA Chief Research and Development Officer Timothy O'Leary, MD, PhD (third from right).

for 95 awards. Recognizing the disparity between the cost of kidney care and its investments in kidney research, the VHA Kidney Disease and Dialysis Program Office delineated high-priority areas of kidney research in its recent strategic plan, including investigating barriers, facilitators, and outcomes associated with home dialysis.

The outlook for VA research funding may be looking brighter: In his 2016 budget, President Barack Obama requested \$622 million for the VA research program, an increase of 5.6% over the program's 2015 budget (Table 1). ASN serves on the executive committee of the Friends of VA Medical Care and Health Research advocacy coalition, which has been meeting with the offices of members on the House and Senate Veterans Affairs Committees and appropriators in Congress over the past few months in support of the president's request.

"ASN commends the president's 2016 budget request for the VA research program," ASN Research Advocacy Committee Chair Frank "Chip" Brosius, MD, stated. "The additional funds will provide the VA the resources it needs to maintain funding for current projects and bolster support for exciting new initiatives like the Million Veteran Program."

*Michael J. Fischer, MD, FASN, is Research Health Scientist at the VA Center of Innovation for Complex Chronic Healthcare. Grant Olan is ASN Senior Policy and Government Affairs Associate.*

**Table 1. VA research funding**

Millions of Dollars					
2012 Actual	2013 Actual	2014 Actual	2015 Actual	President's 2016 budget request	% change over 2015 Actual
\$581	\$583	\$586	\$589	\$622	5.60%

# Something to Say?

ASN Kidney News accepts correspondence in response to published articles. Please submit all correspondence to [kidneynews@asn-online.org](mailto:kidneynews@asn-online.org)



## In Memoriam: Winnie Tapper

### *Reached milestone of 40 years on dialysis*

***“Be the best that you can be. Make your life count,”***

was the motto of Winifred “Winnie” Yuri Tapper, who passed away on February 4, 2015, at the age of 70. She was perhaps one of the longest surviving patients on continuous hemodialysis, having undergone the procedure for more than 40 years. A memorial service was held on March 7, 2015.

Born in Hawaii on May 18, 1944, Winnie was of Japanese descent. Owing to her father’s job transfer in 1949, the family moved to California, where she spent the remainder of her childhood. She attended California State University, Northridge, and the University of California, Los Angeles, where she studied psychology and later discovered a love for teaching children. She worked as a kindergarten teacher for 31 years.

Her extraordinary story began in 1972, when at the age of 27, Winnie learned she had gone into kidney failure. Her doctors

believed a serious strep infection that attacked her kidneys may have been the cause. At the time, kidney dialysis was still in its infancy, and Winnie had not even heard of the procedure. Nevertheless, she found she qualified for treatment. Because she did not want to stop teaching, her doctors agreed to train her to perform dialysis at home.

“She was smart and determined,” said Marc Tapper, her long-time friend and husband at the time, who was also trained to be her assistant. “She was ready to roll with a very positive attitude.”

Despite this, Winnie’s best friend, Sachi Stark, wrote that her first year on dialysis was “filled with much anxiety and a lot of tears.” However, with perseverance and determination, she became stronger and stronger, and even was able to maintain her teaching schedule while undergoing dialysis after school three times a week.

Over time, Winnie was able to see a significant change in the way dialysis was per-

formed. Early dialysis sessions lasted eight hours, but over the course of her many years of treatment, the time was reduced to three hours per session. “They have greatly improved the process,” she told the *Ventura County Star* in 2013 for the 40th anniversary of her continuous hemodialysis treatment. The National Kidney Foundation (NKF) also gave her a certificate for that milestone. NKF reported it knew of no one else in the country who had achieved that record.

Winnie had considered a kidney transplant at one point and was placed on the transplant waiting list, but ultimately decided against it.

Although dialysis was a large part of her life, Winnie was still able to enjoy her favorite things, such as the arts, outdoor activities, and traveling, by making arrangements in advance for treatments. “People feel that they have to give up the things they love, but you don’t have to stop your life,” she told the *Ventura County Star*. “You just have to make different arrangements.” ●

## Industry Spotlight

### Strongest FDA Warning for Anemia Drug

The anemia drug Feraheme (ferumoxytol (AMAG Pharmaceuticals, Waltham, MA) will now carry the FDA’s strongest warning. The FDA has stipulated that the drug must carry a boxed warning that states “serious, potentially fatal allergic reactions can occur with the anemia drug Feraheme (ferumoxytol).”

In a Drug Safety Communication issued on March 31, 2015, The FDA said it will continue to monitor and evaluate the risk of serious allergic reactions with all IV iron products, and will provide updates as new information becomes available. All IV iron products carry a risk of potentially life-threatening allergic reactions, the communication stated.

When Feraheme was approved in 2009, this risk was described in the Warnings and Precautions section of the drug label. Since then, serious reactions, including deaths, have occurred despite the proper use of therapies to treat these reactions and emergency resuscitation measures (more information is available at the Drug Safety Communication/Data Summary).

The data summary shows that 79 anaphylactic reactions have occurred since 2009, 18 of which were fatal. In nearly half of the 79 cases, anaphylactic reactions occurred with the first dose of Feraheme. In

75 percent of cases, the reaction began during the infusion or within 5 minutes of the administration being completed.

“Frequently reported symptoms included cardiac arrest, hypotension, dyspnea, nausea, vomiting, and flushing,” the Data Summary reported. “Of the 79 cases, 43 percent of the patients had a medical history of drug allergy, and 24 percent had a history of multiple drug allergies.”

Among the FDA’s recommendations for the drug:

- Only administer IV iron products to patients who require IV iron therapy.
- Do not administer Feraheme to patients with a history of allergic reaction to Feraheme or other IV iron products.
- Only administer diluted Feraheme as an IV infusion over a minimum of 15 minutes. Feraheme should not be given as an undiluted IV injection.
- Closely monitor patients for signs and symptoms of serious allergic reactions, including monitoring blood pressure and pulse during Feraheme administration and for at least 30 minutes after each infusion.
- Carefully consider the potential risks and benefits of Feraheme administration in patients with a history of multiple drug allergies. Patients with



multiple drug allergies, as with older patients, may also be at higher risk.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA’s MedWatch Safety Information and Adverse Event Reporting Program at [www.fda.gov/MedWatch/report](http://www.fda.gov/MedWatch/report). ●

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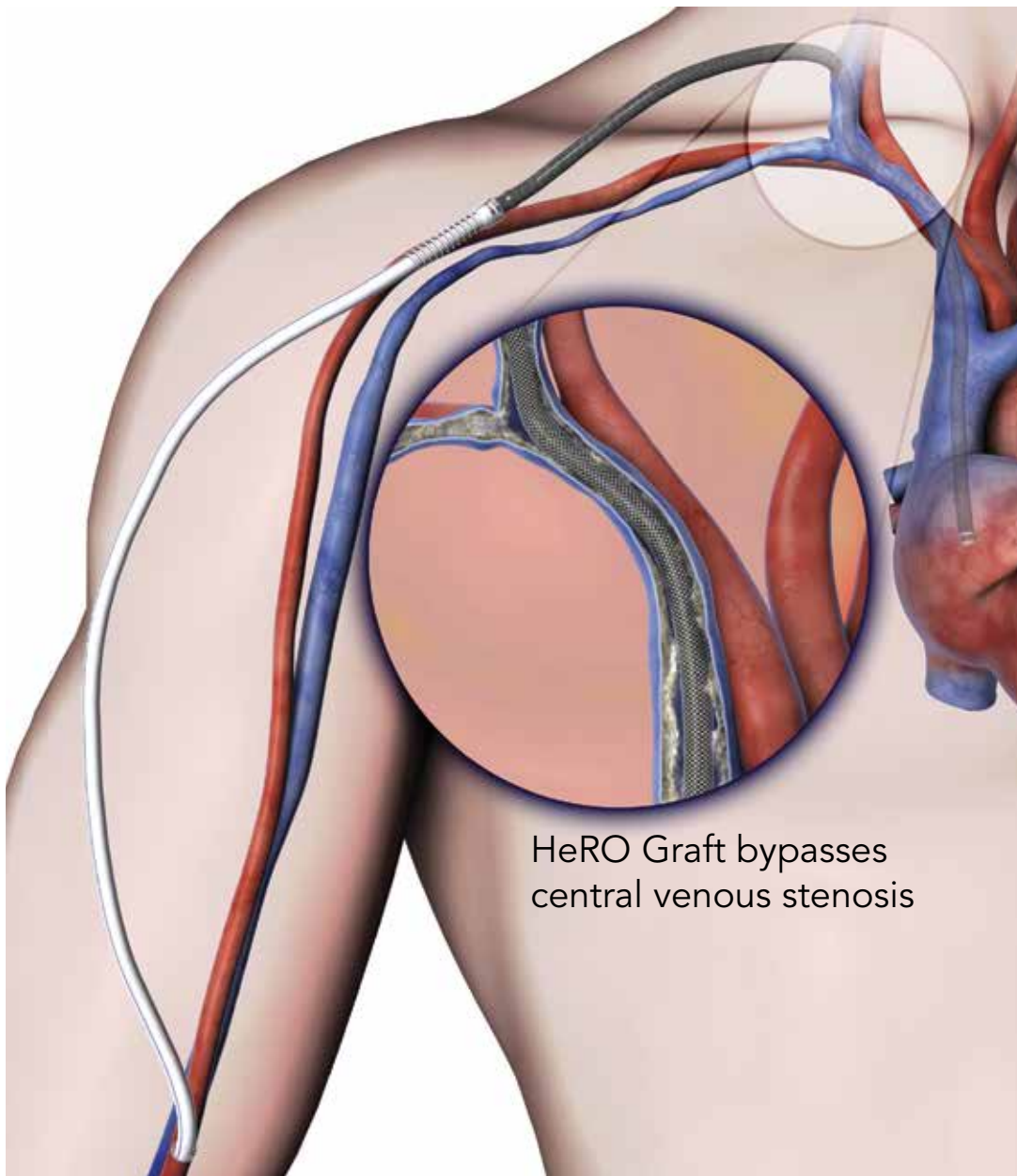
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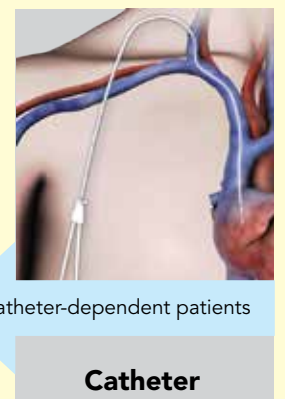
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1) Katzman et al., J Vasc Surg 2009. 2) Gage et al., EJVES 2012. 3) Dageforde et al., JSR 2012.

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