Dialysis Therapies: A National Dialogue

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Abstract
The National Institute of Diabetes, Digestive, and Kidney Diseases–supported Kidney Research National Dialogue asked the scientific community to formulate and prioritize research objectives that would improve our understanding of kidney function and disease. Kidney Research National Dialogue participants identified the need to improve outcomes in ESRD by decreasing mortality and morbidity and enhancing quality of life as high priority areas in kidney research. To reach these goals, we must identify retained toxins in kidney disease, accelerate technologic advances in dialysate composition and devices to remove these toxins, advance vascular access, and identify measures that decrease the burden of disease in maintenance dialysis patients. Together, these research objectives provide a path forward for improving patient-centered outcomes in ESRD.

Introduction
The National Institute of Diabetes, Digestive, and Kidney Diseases recently asked the community to identify research objectives that, if addressed, would improve our understanding of basic kidney function and aid in the prevention, treatment, and reversal of kidney disease. The Kidney Research National Dialogue (KRND) welcomed all interested parties to submit, discuss, and prioritize ideas through an interactive website. Over 1600 participants posted more than 300 ideas covering all areas of kidney disease, including ESRD.

High morbidity and mortality disproportionately burden people with ESRD, whereas their lost productivity and health care expenditures are significant national problems. High-priority objectives identified by KRND participants (Figure 1) for research regarding maintenance dialysis include investigating health-related quality of life (HR-QOL) and patient-centered outcomes, determining the best nutritional treatments, decreasing deleterious cardiovascular, vascular access, and other outcomes, identifying uremic toxins, and determining best technical practices, especially for distinct ESRD populations.

Since the expansion of Medicare coverage in 1972 to provide RRT to people with ESRD, researchers have made enormous advances. Additional data show that, since 1980, the adjusted annual mortality rate of dialysis–dependent ESRD has declined by 23% (1). Although this result represents significant improvement in the care of people who otherwise would not have survived, challenges remain. People in the United States initiating dialysis therapy continue to have impaired HR-QOL, have an adjusted median life expectancy of just over 3 years, and spend an average of 12 days in the hospital every year (1,2).

Although key goals for improving the lives of people with ESRD comprise enhancing quantity and quality of life (QOL) and decreasing the occurrence of complications necessitating hospitalizations, realistic assessments must be made regarding this population (3). A large proportion of this population is elderly, and many patients have severe comorbid chronic illness, which might limit longevity and QOL, even in the absence of CKD. The research objectives for dialysis therapies as identified by KRND are given below.

Enhance Patient-Centered Outcomes
Refine the instruments used to measure the HR-QOL of people undergoing maintenance dialysis.

Test assumptions suggesting that current and emerging technologies that allow self-dialysis and/or home dialysis care might improve HR-QOL.

Consider the broad and vexing set of symptoms within ESRD. Determine the efficacy of psychosocial interventions on meaningful patient-centered outcomes using state of the art clinical trials tools, including cognitive behavioral therapy, treatment of depression and anxiety with pharmacologic therapies, and treatment of sleep disorders with either continuous airway pressure devices or alternative approaches.

Study shared decision-making, motivation, and education techniques to increase people’s engagement in aspects of their care, such as selection of dialysis modality, timely placement of dialysis access, and adherence to diet and treatment.

Improve the HR-QOL of special ESRD populations, such as the elderly, children, and adolescents making the transition to adulthood, using distinct research approaches.

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Ascertain the value of nondialytic approaches to advanced kidney disease, as well as how best to deliver palliative care for people with ESRD nearing the end of life.

Decrease the Cardiovascular Risk of People Undergoing Maintenance Dialysis

Determine the safety and efficacy of BP control and drugs used for this purpose to reduce cardiovascular risk for people on dialysis.

Determine whether achieving euvoe-mia mitigates the cardiovascular risk of people undergoing maintenance dialysis. This task will require refining approaches to evaluating volume status and comparing the efficacy and safety of achieving volume goals by dietary, behavioral, or dialytic techniques.

Test the efficacy and safety of β-blockers and/or automatic implantable cardioverter defibrillators and antifibrotics to reduce the risk of sudden cardiac death, the single most common cause of mortality during maintenance dialysis. Identify effective interventions that reduce the extremely high risk of death in the first 3–4 months of treatment with maintenance dialysis.

Identify vascular access hemodynamic monitoring, anatomic imaging, and evaluation of genetic and biologic markers of risk for vascular access failure.

Test the efficacy of arteriovenous access creation (such as the use of individualized and hemodynamically predesigned anastamotic devices and hybrid catheter–graft catheter devices) for selected clinical circumstances.

Reduce morbidity and mortality associated with central venous catheters by minimizing their use, decreasing catheter-associated blood stream infections with currently available devices, and fostering innovations in biomaterials, design, and implantation of central venous catheters.

Identify Uremic Toxins and Optimize Their Clearance

Validate the measurement and determine the clinical relevance of different uremic toxins with the goal of identifying new markers for better prediction of clinical risk and efficacy of novel treatments for maintenance dialysis patients.

Evaluate therapies that decrease the synthesis and increase the clearance of uremic toxins to improve outcomes.

Improve Vascular Access Outcomes

Improve the maturation, preservation, thrombosis, and infection-free patency of arteriovenous vascular accesses to reduce morbidity.

Fistulae may be impractical or inappropriate for some people. Investigate the systemic hemodynamic effects of higher blood flow in upper arm fistulae and determine best practices for vascular access and survival by clinical trials methods.

Reduce morbidity and mortality associated with central venous catheters by maximizing their use, decreasing catheter-associated blood stream infections with currently available devices, and fostering innovations in biomaterials, design, and implantation of central venous catheters.

Initiate Innovative Approaches to Reduce the Burden of Hemodialysis Treatments

Establish wearable artificial kidney or implantable bioartificial kidney technology for widespread clinical use...
and address problems with biomaterials, dialysate regeneration, and anticoagulation.

**Establish What Works and What Might Not—and for Whom**

Determine whether different traditional modalities of ESRD therapy and alternative regimens—such as short daily or long nocturnal hemodialysis at a dialysis facility or home—provide differential benefits related to physical function, HR-QOL, and, perhaps, long-term morbidity and mortality. Test modalities using randomized controlled trials or the less costly comparative effectiveness research (CER) techniques, such as propensity score matching and marginal structural modeling.

Determine the risks and benefits of different dosing strategies for erythropoiesis-stimulating agents and the role of checklists or changes in procedures to optimize different aspects of dialysis care using traditional clinical trials or less costly CER techniques.

Determine the optimal therapies for special populations, such as the elderly, children, and adolescents making the transition to adulthood, using traditional clinical trials or less costly CER techniques.

**Optimize the Composition of Dialysate**

Determine the optimal characteristics of dialysate (concentrations of potassium, sodium, bicarbonate, and calcium) for people treated with maintenance hemodialysis.

Determine the clinically relevant benefits of alternative solutions for people treated with peritoneal dialysis (such as those people with low concentrations of glucose degradation products or low-sodium dialysate).

**Evaluate Nutritional and Metabolic Therapies**

Determine definitively the risks associated with vitamin D deficiency and benefits of vitamin D supplementation.

Determine the best methods to optimize phosphate balance in people undergoing RRT.

Understand the roles of micronutrients, antioxidants, and trace minerals in determining meaningful outcomes.

Determine optimal diets and the role of protein-energy supplementation in people (and subgroups) treated with RRTs.

Evaluate the role of the microbiome in generating uremic toxins and the associations of the microbiome with clinically meaningful outcomes in people treated with different dialytic modalities.

**Discussion**

We hope that the identification of these broad themes will help focus the research agenda for dialysis therapies. The objectives captured by the KRND hold potential for improving the physical and emotional wellbeing of people with ESRD undergoing maintenance dialysis and reducing the associated morbidity and mortality. Using feedback from the broader community to shape this discussion will add value to future outcomes and policies. Priority areas (Figure 1) include increasing our knowledge of uremic toxins and nutrition to parallel technological improvements. These findings, in turn, will reduce morbidity and increase QOL, leading to improved outcomes.

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