Research Prioritization Topic Brief

Topic 13: “Chronic Kidney Disease”

Comparative effectiveness of treatment and prevention options for patients with chronic kidney disease.

PCORI Scientific Program Area: Assessment of Prevention, Diagnosis and Treatment Options

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<th>Criteria</th>
<th>Brief Description</th>
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<td><strong>Overview/definition of topic</strong></td>
<td><strong>DESCRIPTION OF CONDITION</strong>&lt;br&gt;• Chronic kidney disease (CKD) is a condition in which the kidneys are damaged and cannot filter blood as well as in normal functioning kidneys.¹&lt;br&gt;• There are five stages of CKD based on level of functional impairment.</td>
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<td><strong>Relevance to patient-centered outcomes</strong></td>
<td><strong>SYMPTOMS</strong>&lt;br&gt;• CKD is usually asymptomatic in the early stages.¹&lt;br&gt;• In more advanced kidney disease stages, symptoms can include lack of energy, difficulty concentrating, poor appetite, insomnia, muscle cramping, edema (swelling), dry skin, increased urinary frequency, bruising, shortness of breath, and bone pain.²&lt;br&gt;<strong>OUTCOMES</strong>&lt;br&gt;• CKD can cause wastes to build up in the body and lead to other health problems, including cardiovascular disease, anemia (low red blood cells), and bone deformities and weakening.¹&lt;br&gt;• CKD is usually irreversible and progressive.&lt;br&gt;• If not treated, over time it can lead to kidney failure, also called end-stage kidney disease (ESKD).¹</td>
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<td><strong>Burden on Society</strong></td>
<td><strong>INCIDENCE (NEW CASES)</strong>&lt;br&gt;• The incidence of CKD is increasing most rapidly in people aged 65 and older—more than doubling in this age group between 2000 and 2008, to nearly 4.5%.³&lt;br&gt;• The incidence of recognized CKD among 20-64 year olds is 0.5%.³&lt;br&gt;**PREVALENCE (PROPORTION OF POPULATION LIVING WITH THE CONDITION)**¹&lt;br&gt;• In the United States, more than 20 million people aged 20 years or older (&gt;10%) have CKD.&lt;br&gt;• CKD is more common among women than men.&lt;br&gt;• African Americans were nearly four times more likely to develop ESKD than whites in 2007; however, this disparity in ESKD incidence had narrowed from 1998 to 2005.&lt;br&gt;• The Hispanic population has 1.5 times the rate of kidney failure compared to the non-Hispanic white population.</td>
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<td><strong>Effects on patients’ quality of life, productivity, functional capacity, mortality, use of health care services</strong></td>
<td><strong>QUALITY OF LIFE</strong>&lt;br&gt;• Multiple studies have shown that CKD is associated with decreased health-related quality of life (QOL), most showing a worse QOL decreasing with progressive kidney disease.⁴-⁶&lt;br&gt;<strong>PRODUCTIVITY</strong>&lt;br&gt;• One study showed that patients with CKD reported 18% absenteeism and 35% productivity loss.⁷&lt;br&gt;<strong>MORTALITY</strong>&lt;br&gt;• Premature death from both cardiovascular disease and from all causes is higher in adults with CKD compared to adults without CKD.¹&lt;br&gt;• Individuals with CKD are 16-40 times more likely to die before progressing to ESKD.¹&lt;br&gt;• The number of annual deaths from ESKD increased from 10,478 in 1980 to 90,118 in 2009.³&lt;br&gt;<strong>COST</strong></td>
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*PCORI Topic Brief: Assessment of Prevention, Diagnosis and Treatment Options*
- The overall medical and economic cost of CKD in the United States was approximately $82.9 billion in 2007.8
- Expenditures for patients with CKD accounts for nearly 28% of all Medicare spending.8

### How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?

CKD is an increasingly common medical condition, which results in significant economic costs to society and impact on the quality of life of individual who have it. High priority should be given to this research topic.

### Options for Addressing the Issue

#### Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?

- For CKD patients with large amounts of protein in their urine—nearly all with diabetes and hypertension—angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) significantly reduced the risk of progressing to ESKD compared with placebo.9
- For CKD patients with small amounts of protein in their urine who have cardiovascular disease or diabetes with other cardiovascular risk factors, ACEIs treatment reduced mortality risk compared with placebo.9
- In randomized controlled trials that directly compared different treatments for hypertension, diabetes, and high cholesterol, it was unclear whether increasing treatment improves clinical outcomes.9
- Despite substantial focus on the early identification and proactive management of CKD in the last few years, there are significant areas where more research is needed in order to know how best to manage people with CKD.10

#### What could new research contribute to achieving better patient-centered outcomes?

- Examining different strategies to screen for CKD or monitor CKD progression could lead to earlier detection of kidney disease, faster initiation of preventive medicine, and better patient-centered outcomes (such as QOL and delayed progression of CKD).
- Evaluating the comparative effectiveness of various treatments for CKD risk factors such as hypertension, diabetes, and high cholesterol could help to determine the best treatment of these conditions to prevent progression of CKD and improve patient-centered outcomes.
- Evaluating available treatment for slowing progression of CKD at different stages could help determine the optimal timing for initiation of treatment to slow CKD progression and improve patient-centered outcomes.
- Evaluating available treatment for slowing progression of CKD among patients in different demographic subgroups and with different comorbidities could lead to more effective and better tolerated treatment, thus improving patient-centered outcomes.
- Evaluating harms of treatments to slow progression of CKD could potentially improve patient adherence and quality of life.
- Although research exists showing improvement in diabetes treatment (a known risk factor for CKD) with medical nutrition therapy (MNT), additional research assessing the
comparative effectiveness of MNT vs. (or in addition to) other treatments for diabetes may provide useful information for determining how to best manage diabetes in order to optimize kidney functioning.

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<th>Have recent innovations made research on this topic especially compelling?</th>
<th>Newer drug classes, several of them “first-in-class” drugs (i.e., drugs which, for example, use a new and unique mechanism of action for treatment) that are being tested have less supportive data and would make compelling areas for additional research.</th>
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| How widely does care now vary? | VARIABILITY IN CARE  
• Among people with CKD in the United States, lower socioeconomic status is associated with greater risk of disability. This is found regardless of a patient’s race or ethnicity, health care access, and comorbid conditions.\(^{11}\)  
• The mechanisms by which socioeconomic status influences the development of risk factors for CKD throughout the course of an individual’s life are not entirely clear.\(^{11}\) |
| What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)? | Clinicaltrials.gov:  
• Total ongoing trials: 548  
• Completed trials: 778  
NIH Reporter:  
• Projects: 250  
• Publications: 596 |
| How likely is it that new CER on this topic would provide better information to guide clinical decision making? | KEY UNCERTAINTIES IN CLINICAL DECISION MAKING  
• Does systematic CKD screening improve clinical outcomes?  
• Does systematic CKD monitoring for worsened kidney function or damage improve clinical outcomes?  
• What medications used to treat diabetes, hypertension, and high cholesterol have an effect on progression of renal disease?  
• Does the effectiveness of available medical treatments differ based on severity of CKD stage?  
• Do medical treatments have different risks vs. benefits in clinical outcomes for patients with recently worsened kidney function or damage (as detectable by monitoring) compared with those with stable CKD?  
• Do medical treatments improve outcomes in CKD subgroups for which treatment is not already indicated?  
• How effective is MNT alone or in combination with other treatment in preventing or slowing progression of CKD?  
• What is the effect of MNT on clinical outcomes in patients with CKD stages 1–3 vs. later stage CKD?  
• Does effectiveness of medical treatments vary based on stage of kidney disease?  
• What is the optimal timing (stage of kidney disease) of referral to a nephrologist (kidney specialist) for management of CKD?  
LIKELIHOOD THAT CER WOULD BE ABLE TO REDUCE THESE UNCERTAINTIES  
• New research would likely be able to identify ideal screening and monitoring strategies.  
• New research could clarify ideal treatment for those risk factors such as diabetes, hypertension, and high cholesterol that would prevent progression of kidney disease.  
• New research could clarify effectiveness of treatment in different stages of kidney disease.  
• New research could clarify the comparative effectiveness of MNT in preventing or
slowing progression of kidney disease.

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<th>Potential for New Information to Improve Care and Patient-Centered Outcomes</th>
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<td>What are the facilitators and barriers that would affect the implementation of new findings in practice?</td>
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<tr>
<td>FACILITATORS</td>
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<td>• Diabetes, hypertension, and high cholesterol are all already high-priority conditions.</td>
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<td>• Many medications exist to treat these conditions and potentially prevent complications.</td>
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<td>• MNT is covered by Medicare.</td>
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<td>• Most patients with kidney disease are on Medicare and/or Medicaid, so some information may be able to be obtained from their databases.</td>
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<td>BARRIERS</td>
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<td>• Studies of earlier stage CKD would require years of follow-up, which could be expensive.</td>
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<td>• The number of available treatments and many different patient subgroups could make designing generalizable studies challenging.</td>
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<td>• There is a potential lack of workers to provide MNT to all qualified patients.</td>
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<td>• There is a potential lack of coverage for MNT by insurance plans other than Medicare.</td>
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<td>• Providers lack knowledge about MNT.</td>
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<td>• Providers lack knowledge about current CKD management guidelines.</td>
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<td>How likely is it that the results of new research on this topic would be implemented in practice right away?</td>
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<td>• It is likely that new information regarding optimal treatments for diabetes, hypertension, and high cholesterol in patients with CKD could be implemented quickly with education.</td>
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<td>• If MNT were shown to be effective in preventing or slowing progression of kidney disease, it is likely that new information could be implemented quickly if there is an adequate number of trained workers to provide nutrition counseling.</td>
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<td>Would new information from CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?</td>
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<td>It is likely that new information from comparative-effectiveness research (CER) would remain current for several years.</td>
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REFERENCES

APPENDIX: Topic Questions

Nominated by ‘Web’

1) What are the best strategies for delaying the progression of chronic kidney disease, maintaining the patient's quality of life, and decreasing morbidity?

**Importance:** Chronic kidney disease (CKD) is common, affecting approximately 20 million (one out of every nine) people in the United States.

2) Is Diabetes Self-Management Training (DSMT) and/or dietetic consultation (including, but not limited to, Medicare Medical Nutrition Therapy) effective in empowering patients to avoid morbidity/mortality from chronic kidney disease (CKD) associated with diabetes?

**Population:** The burden of CKD is greatest among senior citizens, including Medicare beneficiaries, as well as among members of racial and ethnic minority groups, and among populations with lower socioeconomic status. The growth of CKD in the United States is related to the increase in both diabetes and hypertension at the population level.

**Importance:** Medical Nutrition Therapy (MNT) is Medicare coverage for consultation with a nutritionist that was authorized by the Benefits Improvement and Protection Act of 2000 and is available to individuals with diabetes and/or impaired kidney function (eGFR below 50). Utilization of MNT benefits has been far below expectations. However, MNT and DSMT provide excellent opportunities for patient empowerment. Proof that DSMT and MNT are effective in improving outcomes (eg, preventing/delaying End Stage Renal Disease, improving blood pressure control, enhancing glycemic control, reducing avoidable hospitalizations from CKD associated with diabetes) should enhance utilization of these benefits. In addition, this kind of research could incentivize group health plans to include similar initiatives as part of the wellness programs they provide pursuant to the Affordable Care Act.