National Institute of Diabetes and Digestive and Kidney Diseases

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Pre-receipt Webinar for Caring for OutPatiEnts after Acute Kidney Injury (COPE-AKI) Research Consortium FOAs

A forum to bring together investigators in the AKI field interested in applying for this funding opportunity and answer questions.

August 18, 2020 at 3pm EST

Agenda

3:00 – 3:15 p.m.	Welcome and Introduction (NIDDK)
3:15 – 3:50 p.m.	Question and Answer Session
3:50 – 4:00 p.m.	Concluding Comments (NIDDK)

Caring for OutPatiEnts after Acute Kidney Injury (COPE-AKI) – (U01 Clinical Trial Required)

- The Caring for OutPatiEnts after Acute Kidney Injury (COPE-AKI) Consortium composed of 3 to 4 Clinical Centers (CCs) and a Scientific and Data Research Center (SDRC) will **develop and test interventions that aim to reduce morbidity compared with usual care in patients after hospitalization with Stage 2 and 3 AKI**.
- Improving outcomes of AKI survivors is of high significance to patients as well as healthcare organizations.
- Both **clinical outcomes** and **patient-centered outcomes** should be assessed.
- This FOA is **not intended to test novel drug therapies**, such as Phase 1-3 drug studies.
- **Delayed onset studies** that are data gathering in one aim to support a clinical study in another aim are **not considered responsive** to this FOA.

Knowns

- Acute kidney injury (AKI) is associated with high morbidity, including increased risk of chronic kidney disease (CKD), end-stage kidney disease (ESKD), cardiovascular disease, and mortality.
- Severity, duration, and frequency of episodes of AKI as well as age, pre-existing CKD, and other comorbidities are associated with greater risks of CKD progression and death.

Unknowns

- There is limited evidence to inform recommendations for processes of care or therapeutic interventions targeting progression of kidney disease and the associated morbidity and mortality in adult, Stage 2 and 3 AKI survivors.
- Can a medical intervention in AKI survivors, such as nephrology clinic follow-up education and clinical care and/or therapy with available treatments, improve outcomes is this population?
- What are potential designs for a study to follow up post-hospitalization AKI patients in the outpatient setting?
- In whom (inclusion/exclusion) or when (early or late) might intervention be effective?
- What are possible primary outcome(s) (that might respond to intervention)?
- Adequate power?
- Number of available patients that meet inclusion/exclusion criteria?

Important gaps in knowledge and care in AKI survivors that could be addressed include, but are not limited to:

- Management of risk factors for developing CKD, ESKD, and cardiovascular complications
- Blood pressure goals
- Fragmentation and heterogeneity of care, poor communication among providers, and other socioeconomic barriers

Interventions might include, but are not limited to:

- Primary care or nephrology outpatient follow up and coordination of care using bundled processes of care
- Use of telemedicine, social media, or digital mobile platforms for implementation and evaluation of processes of care
- Pharmacologic or non-pharmacologic methods to prevent recurrent AKI
- Targeting established pathways of progression in CKD [e.g. inhibition of the renin-angiotensin-aldosterone system (RAAS)]
- Physical and psychological rehabilitation

Clinical outcomes to consider include but are not limited to:

- Recurrent AKI hospitalization
- All-cause hospitalizations
- A composite endpoint of events or event-free days (for example, recurrent AKI hospitalization, all cause hospitalizations or ER visits, congestive heart failure, and/or adverse drug events),
- Major adverse kidney events (MAKE; composite of death, disability, dialysis, and persistent kidney dysfunction)
- Congestive heart failure
- Magnitude and change in albuminuria or proteinuria and hypertension
- Incident or progressive CKD
- Cardiovascular events
- Death

Patient-centered outcomes to consider include but are not limited to:

- Patients' perceptions of health-related quality of life and functional status
- Patients' knowledge
- Patients' symptom control
- Patients' psychosocial status
- Proposed trials could include study of patients with COVID-19 related AKI.

The COPE-AKI Consortium Structure

- The COPE-AKI FOA will establish 3 to 4 Clinical Centers (CCs) to work collaboratively with a Scientific and Data Research Center (SDRC) in a Consortium.
- The Consortium is expected to comprise a wide range of expertise, including but not limited to nephrologists, primary care physicians, intensivists, biostatisticians, ethicists, data scientists, and patient advisor participants.
- **Studies proposed by the successful applicants will be the starting point for discussions regarding the research to be undertaken by the Consortium.**
- **The final study protocol will be designed by the CC and SDRC Principal Investigators and approved by the Steering Committee, and then the DSMB and the NIDDK.**
- Consortium study results are expected to provide evidence for management approaches to improve outcomes after hospitalization with AKI.
- **It is envisioned that a successful applicant for a Clinical Center will have a large population of patients with AKI that can be identified and followed as outpatients after hospitalization.**
- The CC and SDRC investigators will work collaboratively on the design, planning, execution, and analysis of the intervention.

The COPE-AKI Consortium Structure

- The CCs will be responsible for screening and recruiting study participants, conducting interventions, obtaining biological samples and clinical information from all participants at baseline and during follow-up, and transmission of those data and samples to the SDRC, which will accept and manage the data. **Each CC will be required to enroll and follow between 300-500 patients in the study.** Each CC will **submit a plan for screening hospitalized AKI patients** to identify patients being discharged and a proposed outpatient intervention.
- The SDRC will be primarily responsible for ensuring the scientific integrity, comprehensiveness, and robustness of the research design, biostatistics, implementation, data quality, analysis, storage, and availability for study both within and eventually outside the Consortium. **The SDRC investigators, including biostatisticians, will work with the CC investigators to develop the scientific design of the study.**
- The Consortium Program Directors/Principal Investigators (PD/PIs) will have the primary responsibility for ensuring that the design of the study, including the primary outcome, is scientifically sound, comprehensive, with sufficient statistical power to study the primary outcomes.
- The SDRC will provide biostatistical and analytic expertise and conduct analyses and interpretation of the data in conjunction with the investigators at the CCs. The SDRC and CCs will work closely together to achieve the goals of the Consortium.
- The CCs will work in a collaborative, harmonious and efficient manner with the SDRC to comprehensively maximize the number of participants and collect initial and longitudinal data and information on clinical outcomes on all participants during the study period, within the purview of the Consortium**. A CC can propose satellite hospital sites to work together under its direction to fulfill recruitment requirements.**

Administration and Meetings

- The **Steering Committee (SC) will serve as the governing body of the Consortium**. Its actions and decisions will be determined by majority vote. The SC will be **composed of the SDRC and CC Program Directors/Principal Investigators (PDs/PIs), other key investigators and the NIDDK Project Scientist, as well as patient participant representatives, appointed by the NIDDK**. The SC will meet regularly in-person in the Bethesda MD / Washington DC metropolitan area, and by telephone or webinar, as necessary, as a full committee and in working groups to develop and implement study protocols.

- **SC responsibilities** include: providing input on and approval of all studies developed by the Consortium members prior to study implementation; review and approval of all data analyses, public presentations and publications of research conducted within the consortium; and development of policies and procedures for submission and approval of research applications using Consortium resources. The NIDDK will select a chair of the SC (Steering Committee Chair [SCC]) either from the PDs/PIs of the CC's, or outside the study group.

- An **Executive Committee (EC) will be comprised of the Steering Committee Chair, the SDRC PDs/PIs, and the NIDDK Project Scientist.** Additional CC investigators, NIDDK Program Officers and other NIH officers, patient participant representatives and support personnel may participate in the EC as needed. The Executive Committee will make operational decisions for the Consortium between SC meetings by means of weekly telephone conference calls.

- The **NIDDK Project Scientist** will assist the SC in the development of Consortium study protocols, will monitor the progress of projects and functioning of all consortial activities, will assist investigators in the analysis and interpretation of consortial data, and will participate in all aspects of the research and in preparation and writing of all manuscripts from consortial studies for publication.

Administration and Meetings

- SDRC and CC Investigators will devise studies that will be reviewed by a Data and Safety Monitoring Board (DSMB) and approved by the NIDDK. **The final study protocol will be designed by the CC and SDRC PDs/PIs and approved by the Steering Committee, and then the DSMB and the NIDDK.**

- A **DSMB will be appointed by the NIDDK at the beginning of the funding period, to provide input on the design of studies prior to their implementation**. The DSMB will monitor the research efforts and the progress of the studies and advise primarily the NIDDK as well as the Consortium investigators. The DSMB may include biostatisticians, pharmacologists, nephrologists, ethicists, and CKD and AKI patients. The DSMB will review study protocols prior to implementation and will monitor progress and safety of the studies. CC applicants must not suggest potential participants for the DSMB in their applications.

- The **CCs and SDRC will each identify two representatives of the patient population** to be studied to serve on a Community Advisory Council, which will provide feedback to the Consortium regarding the design and conduct of the study. One NIDDK and one SDRC member will staff this committee.

- Awardees will meet to finalize the Consortium study protocol(s). **Both CC and SDRC awardees should be prepared to participate in conference calls immediately after funding and should plan to attend the first Steering Committee meeting in the Bethesda, Maryland / Washington DC area, or virtually if necessary, on July 26-27, 2021.**

RFA-DK-20-011 - COPE-AKI – Clinical Centers (U01 Clinical Trial Required)

- **Funds Available and Anticipated Number of Awards**
  - NIDDK intends to commit $2 Million in FY 2021 to fund up to 4 awards.
- **Award Budget**
  - Application budgets are limited to $500,000 direct costs in the first year and should reflect the actual needs of the proposed project.
- **Award Project Period**
  - The maximum project period is 5 years

RFA-DK-20-012 - COPE-AKI – Scientific and Data Research Center (U01 Clinical Trial Required)

- **Funds Available and Anticipated Number of Awards**
  - NIDDK intends to commit up to $750,000 in FY 2021 to fund one award.

- **Award Budget**
  - Application budgets are limited to $500,000 direct costs in the first year and should reflect the actual needs of the proposed project.

- **Award Project Period**
  - The maximum project period is 5 years.

Frequently Asked Questions

- Is the NIDDK CKD eCare plan developed and will it be available to be utilized in the study? How do we access it?
  - Jenna Norton will address.
- Does the SDRC have to propose a specific clinical trial design in the application?
  - Yes
- The RFA states the first year budget for direct costs is $500K. Is this the annual amount for the SDRC or does it increase in subsequent years and if so to what amount?
  - This is the annual amount for subsequent years.

Frequently Asked Questions

- Will the NIDDK be receptive to a single center applying as both a DCC site and a clinical site? Is there any concern about this (assuming the PIs would be different for each application)?
  - PIs must be different and there must be no budgetary overlap.
- May investigators listed on Clinical Center proposals also have a role in an SDRC?
  - Yes but there must be no budgetary or effort overlap.
- The RFA allows for multiple-PIs. Will the NIDDK be receptive to a clinical site submission recruiting from multiple sites?
  - Yes. Multiple local or out-of-state sites are allowed.

NIH resources

- **CALL US:** Ivonne H. Schulman, MD
  - Program Director, Translational and Clinical Studies of Acute Kidney Injury
  - KUH, NIDDK
  - Tel: 301-385-5744
  - Email: ivonne.schulman@nih.gov
- https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-20-011.html
- https://grants.nih.gov/grants/guide/rfa-files/rfa-dk-20-012.html