National Diabetes and Digestive and Kidney Diseases (NIDDK) Advisory Council Meeting

Division of Kidney, Urologic, and Hematologic Diseases Advisory Subcouncil Meeting
September 11, 2024

Advisory Council KUH Subcommittee Members:

Dr. Arthur Burnett (Ad Hoc) (Johns Hopkins University)
Dr. Lilia Cervantes (Ad Hoc) (UC Health University of Colorado Hospital)
Dr. Velia Fowler (SME) (University of Delaware)
Mr. Alfred Grasso (SME) (The MITRE Corporation)
Dr. Keith Norris (University of California at Los Angeles)
Dr. Aylin R. Rodan (Ad Hoc) (University of Utah)
Dr. Ian Stewart (ex-Officio, USAF; Walter Reed National Military Medical Center)
Dr. Hunter Wessells (SME) (University of Washington)

NIH/NIDDK/KUH Staff:

Dr. Kevin Abbott
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Ms. Aretina Perry-Jones
Dr. Matt Portnoy
Dr. Tracy Rankin
Mr. Griffin Rodgers
Dr. Cindy Roy
Dr. Anna Sadusky
Dr. Ivonne Schulman
Ms. Aliecia Shepherd
Dr. Robert Star
Mr. Jonathan Teinor
Dr. Ken Wilkins

Welcome and Introductions

Dr. Star welcomed council members and attendees to the 226th KUH subcouncil meeting. Dr. Star welcomed Drs. Rodan and Cervantes as Ad Hoc Advisory Council Members and Drs. Burnett, Fowler, and Wessells as well as Mr. Grasso as subject matter experts. Dr. Norris led the motion to approve the meeting minutes from May subcouncil and Dr. Burnett seconded this motion.

Upcoming Meetings and Workshops

Dr. Star noted several upcoming meetings and workshops and commented that this information is available on the ECB for future reference.

U2C/ TL1 Concept Clearance

Dr. Rankin discussed a concept renewal for the KUH Research Training Network (KUHR-TN) and requested approval from Councilors to continue this Consortium for another five years**,** which will allow staff to continue to solicit new and renewal programs and gather evaluation data towards the efficacy of this new training approach.

Councilors provided the following feedback:

- Dr. Rodan noted that it would be helpful to discuss what is going well and what is going poorly for the next iteration of this program at the consortium meeting in August. Dr. Sadusky noted that trainees expressed enthusiasm to hold a meeting prior to this year and commented that many expressed enthusiasm for this meeting to establish connections and expand networks, using professional development resources. Dr. Maric-Bilkan noted plans to engage trainees in the structure of the U2C/TL1 program in addition to recruiting them as part of the planning committee. She noted that PIs provided positive feedback about this program versus their experience with the T32 program.
- Dr. Norris emphasized the importance of this program for retaining career development individuals looking to enter the workforce.
- Dr. Wessells noted that as a PI on a TL1, the types of trainee expertise are broader due to the K, U, and H collaboration; this broadens the cache of innovative people.
- Dr. Burnett noted historically black, colleges and universities (HBCUs) that have come into the program and queried what challenges were involved. Dr. Rankin noted that the partnerships with HBCUs in NC that recruit from various areas to partner institutions.
- Dr. Fowler commented that retention of individuals in the workforce also encompasses the process of getting tenured and/or a grant; however, many leave before entering it due to discouragement. Dr. Maric-Bilkan noted that the goal is to create a training community and added that a new initiative, KUH FAMILY, will become a coordinating center. Dr. Norris noted it would be helpful to retain some of these trainees at the sites.

Councilors expressed strong enthusiasm to approve this concept.

Councilor Presentations

Dr. Fowler began her presentation by noting that non-malignant hematology encompasses a large number of diseases and conditions such as hemoglobin disorders, inherited and acquired anemias, disorders of iron metabolism and iron deficiency anemias. Dr. Fowler emphasized that research in non-malignant hematology has long been a leader in biomedical science, from early studies of sickle hemoglobin to red cell membrane structure, to molecular biology of gene regulation, to genetics and genomics, and in gene therapy.

Dr. Fowler emphasized the need to improve recruitment and success of new and early-stage investigators in non-malignant hematology research as the number of researchers has been declining over the last decade. She commented on the need to support investigators in transition to independence by building on existing NIDDK hematology training programs (T-, F- and K-award mechanisms) and highlighted the need to recruit new investigators that include diverse perspectives and pose new study questions. Dr. Fowler noted that while a majority of researchers study malignant hematology, a large population in the US is affected by non-malignant hematology conditions, particularly in underserved populations.

To recruit more researchers into benign hematology, she suggested that NIDDK employ a model such as the IDeA State Center of Biomedical Research Excellence (COBRE). COBRE objectives serve to: (1) “strengthen an institution’s biomedical research infrastructure through the establishment of a thematic multidisciplinary center and to (2) enhance the ability of investigators to compete independently for NIH individual research grants or other external peer-reviewed support." She proposed that NIDDK create career development program(s) to recruit and support new investigators in relevant areas of NIDDK Hematology mission which would provide program support for 3-4 investigators via a research project and pilot funding for early-stage investigators (junior faculty), and a mentoring program for research and career development. The overarching goal of this initiative would be for investigators to transition to independent funding, such as receiving an NIH/NIDDK R01 and/or to establish a career progression with investigators to be promoted/tenured.

Dr. Fowler noted that this could be accomplished through institutional partnerships; NIH funding support; faculty mentoring teams; peer-to-peer networking and collaborations; funds for travel to other institutions, conferences; and grant proposals for mentoring and development. Progress in this area could be tracked through program evaluation and improvement, investigator progress and outcomes, and through an external advisory committee.

Meeting participants provided the following feedback:
- Dr. Norris noted support for the COBRE example and commented that this is something NIDDK could consider.
- Dr. Rodan also commented that she was supportive of a COBRE-like mechanism and noted this could apply to the kidney space.
- Dr. Fowler noted that this could be a post-K mechanism or as a way to recruit someone into the field using a complementary pipeline.
- Dr. Roy queried how the science excels without a medical center nearby. Dr. Fowler commented that mentorship can be collaborative while using remote resources; however, she detailed it is likely more difficult to recruit researchers in states without a medical center.

Dr. Burnett discussed critical areas and questions within the urology field, including where the field is going, guiding principles for progress, promising subdisciplinary areas of progress, subdisciplines which need advancement, and opportunities for inter- and intradisciplinary collaborations. Dr. Burnett noted three guiding resources and their recommendations:

- Urologic Diseases of America (2007): Salient areas of attention include epidemiology (clinical), population studies; pathogenesis/risk factors; urologic disease associations; prevention
- NIDDK Strategic Plan (2020): Strategies:
    - \Advance understanding of biologic pathways and environmental contributors to health and disease (health disparities, behavioral links)
    - Advance pivotal clinical studies and trials for prevention, treatment, and cures in diverse populations (data science)
- AUA National Quality Agenda & Strategies for Urologic Practice (2024): Salient areas of attention include health disparities, diagnostic excellence, and person-centered care.

Dr. Burnett detailed the following recommendations for future urology initiatives:
- Urologic conditions as markers/sentinels/correlates for other diseases
- Treatment based on disease course, not just symptoms at presentation
- "Precision" management of urologic conditions

Meeting participants provided the following feedback:

- Dr. Abbott queried what are the unique challenges for data science in benign urology. Dr. Burnett noted there is a need to recognize institutions and registries to capture all the data. He also emphasized the importance of capturing clinical and pathology data as well as tissue and lab samples. This data should be kept as expansive as possible for analysis.
- Dr. Wessells noted that benign urology does not generally have registries like cancer. Dr. Star queried what could NIDDK do over 10-15 years to improve the LURN question harmonization and asked what other systems need to be developed and harmonized. Dr. Burnett noted a lack of precision about disease states that should be improved and added it would also be helpful to know what kinds of measurements are needed to move the field forward. Dr. Burnett commented that technology is evolving and commented on the evolution of prostate imaging. Dr. Wessells noted imaging for kidney stones is frequently used to manage care. Dr. Star asked councilors to consider the utility of "stress tests" rather than the use of a static measurement.

Dr. Cervantes' began her presentation on kidney disease and pregnancy, noting that she is focusing primarily on acute kidney injury (AKI) during pregnancy and chronic kidney disease (CKD) and end-stage kidney disease (ESKD) among reproductive people. She detailed that while AKI can be caused by conditions like preeclampsia, placental abruption, or maternal sepsis, CKD and ESKD can pose significant challenges during pregnancy, as kidney disease can lead to complications for both the mother and developing fetus. Although the incidence of AKI during pregnancy is underestimated due to the challenges associated with the definition of AKI, it disproportionately affects Black people. She added that it is challenging to diagnose because of the renal physiology of pregnancy and because people infrequently have a baseline serum creatinine or urine studies. There are consensus guidelines; however, these are not validated or consistently used. Pregnancy-related causes of AKI include the following statistics:

- Preeclampsia and eclampsia—Affects 3-5% of pregnancies, risks include hypertension (HTN), diabetes or CKD, diagnosis made by new onset HTN and proteinuria at 20 weeks, and accounts for 20% of AKI.
- HELLP (hemolysis, elevated liver enzymes, and low platelets), AKI in 3-15% of patients with HELLP
- Acute fatty liver of pregnancy
- Thrombotic microangiopathies such as thrombotic thrombocytopenic purpura (TTP) and Hemolytic Uremic Syndrome (HUS)

Dr. Cervantes cited a paper titled "Characteristics and Outcomes of Patients With Pregnancy-Related End-Stage Kidney Disease" and emphasized that AKI during pregnancy is a major cause of morbidity and mortality. Treatment of AKI (when AKI is due to preeclampsia, eclampsia, or HELLP) is based on expert opinion and small case series that can include renal replacement therapy (RRT) and prompt delivery of fetus (once >34 weeks) or glucocorticoids for 48 hours to accelerate fetal pulmonary maturity. Follow-up efforts include nephrology and primary care consultations, beginning angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) medications, avoiding nonsteroidal anti-inflammatory drugs (NSAIDS), and routine assessment of estimated glomerular filtration rate (eGFR).

Transitioning to her second topic, CKD and ESKD in reproductive-age people, Dr. Cervantes commented that 1-4% of pregnant people have chronic kidney disease (CKD) and added that this is increasing due to increasing rates of diabetes mellitus (DM)/HTN. This incidence is underestimated because pregnancy is often the first time a pregnant person seeks medical care so there is no baseline. Additionally, people of reproductive age with kidney failure constitute 30% of the U.S. population with kidney failure; however, pregnancy is rare due to dysregulation of the hypothalamic-pituitary-gonadal axis and menstrual cycle. Clinicians, specifically nephrologists, are not well trained in providing family planning education and many of their patients are on teratogens. Adverse outcomes in CKD and ESKD for mothers include cesarean section, preeclampsia, worsening kidney function, postpartum hemorrhage and cardiovascular issues and for babies include preterm birth, low birth weight, perinatal mortality, and congenital anomalies. Among pregnant people with CKD, there is a significant decline in kidney function during pregnancy and in the post-partum period and those with more advanced CKD have greater decline. In a retrospective study of 67 women with 82 pregnancies and CKD, the decline was higher among women with a serum Cr>2mg/dL compared to those with a serum Cr <2mg/dL. Dr. Cervantes cited the paper "Pregnancy in young women with kidney disease — a most worthwhile journey," noting that the pregnancy rate among women with ESKD on dialysis in the U.S. is 17.7 pregnancies per 100 patient years. By race and ethnicity, the rate is higher among American Indians, followed by Hispanics, Blacks and then Whites. A systematic review of primarily retrospective studies shows that intensive dialysis improves maternal outcomes. In terms of family planning, the rate of contraceptive use is low and in qualitative interviews of women with ESKD, patient participants expressed that more research was needed in reproductive and women's health as it relates to kidney disease.

In closing, she presented the following opportunities for NIDDK in AKI during pregnancy and post-partum ESKD:

- Longitudinal collection of clinical data to improve the detection/diagnosis of AKI, to predict or identify the drivers of poor outcomes including ESKD, and to better inform treatment
- Research on biomarkers to improve our ability to prevent, diagnose, and treat AKI during pregnancy
- Community participatory research--Racial and ethnic minoritized individuals are disproportionately burdened with CKD, with AKI during pregnancy, and with postpartum ESKD.
    - Longitudinal data to understand -- are pregnant people evaluated by nephrology during pregnancy and referred postpartum? Of those referred and seen by nephrology or primary care provider, are they started on an ACE-I or ARB? Are they referred but miss nephrology appointments, what challenges are they experiencing? Opportunities for community participatory research and qualitative/mixed methods.
    - What services are needed since the majority are racial and ethnic minoritized individuals who may experience social challenges (e.g., testing community interventions)?
    - Using implementation science to ensure interventions can be implemented in low-resource settings and among diverse communities.
- Research to restore fertility in patients with CKD and ESKD, to improve family planning, and to understand the outcomes that are most important among people of child-bearing age

Meeting participants provided the following feedback:

- Dr. Rodan commented that this is an important topic and queried what the awareness rate was of women suffering from AKI while pregnant (disease process). Dr. Cervantes noted there is a dearth of research and noted the need for the community to lead research in this space. Dr. Schulman noted the epidemiology group within KUH has looked at this area of research.

Mr. Grasso began his talk, noting that he was trained as a computer scientist/electrical engineer and practiced system engineering for over 30 years. He commented that he retired six years ago as CEO of The MITRE Corporation. His familiarity with health and healthcare came from the creation of a Health Federally Funded Research Center sponsored by the Centers for Medicare and Medicaid Services (CMS).

He described his journey with AKI resulting from an adverse reaction to Nonsteroidal anti-inflammatory drugs (NSAIDs). He was immediately diagnosed with AKI and put on dialysis. Following a week of hospitalization, he was released into a dialysis unit and assigned a Nephrologist.

Mr. Grasso noted that he found himself somewhat helpless and was dissatisfied with the standard of care and reached out for a second opinion and was guided differently through the process, eventually coming off dialysis.

Following this consultation and negative patient experience, he reached out to National Center for Advancing Translational Sciences (NCATs) staff who connected him to Dr. Star. Based on his patient experience and system background, he noted the following observations:

- Education is critically important and recognized the importance of self-advocacy or to have another person advocate for the patient
- Communication and coordinated care plan among providers (i.e. Hospitalist, Nephrologist, Pharmacist, Nursing) from hospital to dialysis unit is lacking
- He observed no difference between AKI and CKD patient care in the dialysis center. He was taking daily vitals to measure his progression towards recovery, but there was little interest in these details in the dialysis center
- He suggested that CMS should take high interest in differentiating quality and type of care.

Dr. Star noted NIDDK is looking for patient input on their e-Care and other research programs. Dr. Fowler commented that if patients have tools, they may be able to better advocate for themselves.

Dr. Star thanked Councilors and subject matter experts for their informative presentations.

KUH Closed Session

Dr. Star commented on the importance of confidentiality during closed session. Council members approved several closed business items.