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Nonprofit Kidney Care Alliance

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On behalf of the Nonprofit Kidney Care Alliance (NKCA), I write to offer our comments regarding the Draft Technology Assessment (TA) JHE51000, "End Stage Renal Disease in the Medicare Population: Frequency and Duration of Hemodialysis and Quality of Life Assessment."

NKCA represents six nonprofit dialysis providers: Centers for Dialysis Care; Dialysis Center of Lincoln; Dialysis Clinic, Inc.; Independent Dialysis Foundation, Inc.; Northwest Kidney Centers; and The Rogosin Institute. Collectively, we serve more than 21,000 patients at more than 300 facilities in 30 states. We also serve more than 5,700 patients with chronic kidney disease (CKD) with the goal of avoiding, or at least delaying, the onset of end-stage renal disease (ESRD) and maximizing the quality of life for our patients. We are committed to promoting kidney transplantation, eliminating barriers to access, and reducing organ discards. To that end, many of our member companies participate in value-based care arrangements such as the Comprehensive ESRD Care (CEC) model and will likely continue to expand their participation in such arrangements under new models as part of the Administration's Advancing American Kidney Health Initiative. Through the CEC model, many of our member companies are pursuing partnerships with various providers and suppliers, not only in nephrology, but across the care continuum, from primary care to hospice.

NKCA appreciates the need for evaluating the evidence to assess the clinical outcomes and Quality of Life (QoL) outcomes in Medicare patients treated with hemodialysis and believe this draft report can be an important first step in this evaluation. While we support the draft report's conclusion that more rigorous studies are needed, we believe that an evaluation of this topic and any policy discussions should not be limited to randomized controlled trials (RCTs) and should also include studies and clinical practice guidelines focused on subpopulations.

Simply put, while randomized controlled trials (RCTs) are the "gold standard," there is a paucity of such studies that address either or both of the twin issues of frequency and duration of hemodialysis. A significant constraint on conducting rigorous RCTs with sufficient follow up (such as the six-month standard applied in the draft report) is patient recruitment, particularly for RCTs studying whether more frequent dialysis will yield better outcomes. The increased demand on patients' time cannot be overlooked, particularly for in-center hemodialysis, where the travel and treatment time for even one additional session poses a significant burden.

Moreover, as dialysis providers we believe that a 4 hour session is well within usual care in the US, and that extended dialysis should be considered more than 4 hours as defined in Table 3 in the report. As noted throughout the report, the current standard dialysis time in the US is up to 4 hours per session and 12 hours per week. This is discussed in the background, where it is stated that "the current practice (is) thrice-weekly hemodialysis for 3 to 4 hours per session." However, within the KQs, the text is inconsistent regarding inclusion of the 4 hour threshold as extended or standard duration. For example, in Table 1 and Table 2 usual care is described as "3 times/week and 3 to 4 hours per treatment" for KQs 1 and 4 while increased duration is defined as "≥12 hours/week" for KQ 3. In Table 3, duration is stratified at "less than or equal to 4 hours" and "more than 4 hours." Further evidence of the inconsistency regarding the definition of extended dialysis is apparent from Table 1 of the Protocol document which, unlike Table 3 of the report, defines extended dialysis as "4 hours and more."

The mean dialysis duration in the US is 220 minutes, a duration lower than much of the rest of the world, and, based on DOPPS Practice Monitor Data, at least a third of US hemodialysis patients are prescribed 4 hour sessions. The TiME Trial for example had a >4 hour rather than ≥4 hour threshold for "longer dialysis" This is a very important factor as our understanding is that the goal of this review is not to evaluate the current common US dialysis prescribing practices but rather to evaluate extended duration or increased frequency dialysis.

In addition, it is important to acknowledge that the current practice standards are not based on "rigorous studies" but instead are based on a trial and error process that began 50 years ago and has been subsequently updated to find the right balance between clinical efficacy and financial efficiency. Thus, while the draft report poses good questions, its assumptions about the clinical validity of current policy undercut its conclusions.

The draft report also acknowledges the marked heterogeneity of ESRD patients treated with dialysis including differences in age, comorbidity and social determinants and seems to recognize the difficulty both of arriving at positive findings related to the effects of more frequent or longer dialysis and of making broad-based conclusions generalizable across the entire, roughly 500,000-person population on maintenance dialysis in the United States. However, the draft report does not acknowledge that the lack of strong conclusive evidence applicable to all, or even most, patients does not imply that there is also lack of strong evidence within subpopulations. Given the large number of dialysis patients in the U.S., significant subpopulations do exist, and the effects of additional dialysis treatments within these groups is worthy of investigation. Moreover, evidence that the ESRD population is forecast to increase by 260 percent in the coming decade (McCullough et. al (2019)) suggests that subpopulations will grow significantly.

In addition, given the heterogeneity of this population, we think it would be appropriate to compare subpopulations receiving the current standard of treatment to a similar subpopulation receiving longer dialysis treatment. Further, the draft report's focus on comparing research study populations to the USRDS general population forgoes an opportunity to identify the potential effects of longer dialysis relative to comparable populations treated thrice weekly. Critically as well, if comparing to the USRDS, it is important to compare studies that utilize incident patients to USRDS data on incident patients and studies that utilize prevalent patients to USRDS data on prevalent patients. It is also essential to account for whether Hispanic ethnicity was reported as a race or whether race and ethnicity were reported separately, as differences across studies have a marked impact on the generalizability conclusions.

We are also concerned that the inclusion criteria for the systematic review are inconsistently adhered to throughout the process and likely too stringent for an evaluation of a heterogeneous population. Specifically, there is inconsistent inclusion of patients outside the U.S. Medicare ESRD population. This appears to have been revised in a subsequent amendment but the language has not been clarified in the primary document, such that the emphasis on Medicare in the US remains. This amendment was focused on changing criteria to allow inclusion specifically of the two FHN trials. Given the similarities throughout North America in population and the joint conduct of the FHN trials in the US and Canada, it would be sensible to include all North American studies, including those that have North American patients as a minority. This step would allow inclusion of Culleton et al. (2007), which is one of the very few RCTs of at least 6 months in length that directly evaluates this question, and inclusion would follow the precedent that the evidence review team established in modifying the protocol to allow the specific FHN trials to be included. Given the overall lack of data in this space and the presence of well performed international cohort studies and clinical trials, a more inclusive approach would be more informative in approaching an answer to this important question for patients. We would also note that, based on our reading of the amendments, other cohort studies should have been included, such as Tentori et al. (2012).

In addition, we urge AHRQ to take a closer look at the inclusion of the TiME trial particularly on the critical matter of treatment times which differ by only nine minutes between the treatment arms, with a mean treatment duration of 216 minutes in the 'extended dialysis' group. The AHRQ draft report refers to this problem, noting that the trial was terminated, but then it appears to include this trial as part of the report's conclusions. Also, while the Miller et al. (DVA) study had a large sample size, it was focused only on incremental hemodialysis duration, not more frequent hemodialysis. We think these are important distinctions that need to be accounted for in the AHRQ final report.

We are also concerned with the draft report's focus on the control of phosphorous levels by patients who receive longer dialysis, rather than the issue of improving treatment of their uremia, which can improve patients' functional status and quality of life. When considering the consequences of greater dialysis frequency and/or duration, it is important to consider basic physiology: normal kidneys function 168 hours per week while hemodialysis patients typically receive 12 hours of dialysis per week; and, blood flow to healthy kidneys is approximately 1 liter per minute, whereas blood flow to the dialyzer is roughly 500 ml per minute. Given these dramatic differences and the consequences of urea and creatine in the blood stream, it is critically important to consider the potential gains associated with more frequent dialysis in these regards as well and observe improvements in the patients' functional status instead of on one laboratory number.

We concur with the draft report's conclusions on the four KQs that "more rigorous studies are needed." But in their absence, AHRQ, and by extension CMS in considering Medicare coverage policy, should incorporate findings and recommendations from clinical and quality experts. For example, the KDOQI Clinical Practice guideline for Hemodialysis Adequacy—which is based on a panel of experts—states that additional or longer hemodialysis should be considered for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight or poor metabolic control. Although patient experience may not be determinative, it can inform the setting of parameters that can contribute to improved outcomes based on real life experiences and not just what might be the findings from research. Ironically, in its June 2019 report setting out the background and parameters for the TA report, AHRQ states: " Finally, patient perspective is essential

to put outcome data in context." While KQ 4 addresses quality of life studies, the patient perspective seems to have been largely compartmentalized. In light of the challenges in patient recruitment to RCT's noted above, future research reports should seek to inform broader conclusions.

In closing, we hope that this draft report will be but a first step in a thoughtful and transparent process. Notwithstanding the limitations of this report, it does represent a cautionary message about proceeding to new national coverage policy at this time. In posting the report, AHRQ acknowledges that CMS may host a public meeting and that this TA may inform deliberations regarding a national coverage decision. We hope that prior to any public meeting that the lists of Key Informants, Technical Experts and Peer Reviewers will be posted.

We also hope that future opportunities to comment, whether to AHRQ or CMS, on this matter will not be subject to the compressed timetable that was applied to this TA. AHRQ justifies the compressed comment period on this report as necessary to accommodate CMS coverage timetable. However, we are unaware of any open NCD on which the CMS coverage "clock" is running. AHRQ, through its Technical Assessments, plays an important role related to CMS coverage policy and the short timeline for public review on the 100 page report and the over 600 pages of Appendices—particularly over the holidays—represents a process shortcoming, which we hope will be addressed through further opportunity for stakeholder input.

Thank you for the opportunity to comment on the Draft Technology Assessment (TA) JHE51000, "End Stage Renal Disease in the Medicare Population: Frequency and Duration of Hemodialysis and Quality of Life Assessment." We would be pleased to discuss any of these comments in greater detail at any time. If you have any questions, please feel free to contact Martin Corry at 202-580-7707 or info@nonprofitkidneycare.org.

Sincerely,

Martin Corry
Executive Director