



Defining, Understanding, and Addressing Postdialysis Fatigue

Takeaways from a Scientific Workshop Hosted by the National Institutes of Health

Yuvaram N.V. Reddy^{1,2,3}, Ann M. O'Hare^{4,5,6}, Dawn Edwards⁷, and Rasheeda Hall^{8,9,10}

JASN 35: 1130–1133, 2024. doi: <https://doi.org/10.1681/ASN.0000000000000409>

Background

Although fatigue is common among patients with chronic health conditions (such as CKD), postdialysis fatigue is highly prevalent and debilitating, affecting 60%–97% of patients receiving in-center hemodialysis.^{1–6} Despite its prevalence, postdialysis fatigue is not routinely or reliably measured as part of dialysis care and there is little research on this topic.³ As a result, little is known about why postdialysis fatigue occurs and how it should be diagnosed and treated.¹

To stimulate research interest in postdialysis fatigue, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) hosted “A Scientific Workshop on Post-Dialysis Fatigue” in May 2023.⁷ NIDDK staff recruited and worked with an external organizing committee—comprising clinicians, researchers, and a patient—to convene an online meeting of over 175 participants. Before the workshop, patient representatives from the American Association of Kidney Patients developed and administered a patient-facing survey to guide the workshop discussion. Patients also presented and moderated several sessions, marking one of the first NIDDK workshops to be co-hosted by patients.

This Perspective—written by four members of the external organizing committee—summarizes the structure of the workshop, describes key insights that we identified during the workshop, and highlights research priorities for postdialysis fatigue. Table 1 summarizes challenges and opportunities for postdialysis fatigue research.

NIDDK Workshop—Overview

The 2-day virtual NIDDK workshop included six scientific sessions. The sessions provided an opportunity for people

with lived experience in postdialysis fatigue to describe the burden and impact of postdialysis fatigue on their lives, for clinicians to outline major challenges in diagnosing and treating postdialysis fatigue, and for researchers to describe methodologies and content areas (e.g., Gulf War syndrome) with potential relevance to postdialysis fatigue. During the breakout sessions, patients, researchers, and clinicians came together to identify several research priorities, which are described in detail in the full NIDDK report (available on NIDDK's website).⁷ This Perspective describes three of these priorities that the authors identified as being central to addressing postdialysis fatigue.

Key Priority 1: What Is Postdialysis Fatigue? What Is the Case Definition of Postdialysis Fatigue? Why Does Postdialysis Fatigue Occur?

Patients and clinicians described a range of different symptoms that occur during or after dialysis. Some patients voiced that postdialysis fatigue was more than feeling tired and should include a range of mental and physical impairments that occur during and after dialysis. One patient speaker discussed the results of a survey that was created and distributed by the American Association of Kidney Patients to collect information about the patient experience of postdialysis fatigue. The survey revealed that approximately half of surveyed people undergoing dialysis experience a decline in their stamina and energy levels, reinforcing the notion that postdialysis fatigue is pervasive.⁷

Some patients participating in the workshop expressed concern for the unintended consequences of labeling

¹Renal-Electrolyte and Hypertension Division, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

²Center for Health Equity Research and Promotion, Corporal Michael J. Crescenz VA Medical Center, Philadelphia, Pennsylvania

³Leonard Davis Institute of Health Economics, University of Pennsylvania, Philadelphia, Pennsylvania

⁴Health Services Research & Development Center of Innovation for Veteran-Centered and Value-Driven Care, VA Puget Sound Health Care System, Seattle, Washington

⁵Hospital and Specialty Medicine and Geriatrics and Extended Care Services, VA Puget Sound Health Care System, Seattle, Washington

⁶Department of Medicine, University of Washington, Seattle, Washington

⁷Rogosin Institute, New York, New York

⁸Renal Section, Durham Veterans Affairs Healthcare System, Durham, North Carolina

⁹Division of Nephrology, Department of Medicine, Duke University, Durham, North Carolina

¹⁰Center for the Study of Aging and Human Development, Duke University, Durham, North Carolina

Correspondence: Dr. Yuvaram N.V. Reddy, email: yuvaram.reddy@pennmedicine.upenn.edu

Published Online Ahead of Print: May 9, 2024

Table 1. Challenges and opportunities to address postdialysis “fatigue”

Area	Challenges	Opportunities
What is postdialysis fatigue?	Postdialysis fatigue lacks a formal definition Patients experience a heterogeneous constellation of symptoms during or after dialysis	Include research designs, such as mixed methods, ecological momentary assessments, and anchor-based methods to better understand postdialysis fatigue Leverage mixed methods to characterize the depth and breadth of postdialysis fatigue. Conduct interviews to describe the temporal course of postdialysis fatigue and develop a case definition
Is postdialysis fatigue the right term?	The term “fatigue” could stigmatize patients and minimize the burden of the disease	Consider a modified Delphi panel to identify a more appropriate term that better reflects how people with postdialysis fatigue feel and to avoid stigma
Where do we start?	There are no biological, radiological, or other markers associated with postdialysis fatigue	Encourage community-based participatory research where patients work collaboratively to help researchers understand how postdialysis fatigue feels and how postdialysis fatigue impacts functional and cognitive capacity
Why does postdialysis fatigue occur?	Little is known about the pathophysiology of postdialysis fatigue Some participants hypothesize that postdialysis fatigue may be caused by the dialysis machine and prescription	Mechanistic discovery could include prospective collection of biomarkers, imaging (<i>e.g.</i> , neurological, ultrasonography), functional testing (physical and cognitive), and clinical/epidemiological data for omics platform-based discovery Timing these data collections before, during, and after dialysis may help facilitate the development of individualized postdialysis fatigue treatments
How do we assess postdialysis fatigue?	No universal tool exists to assess postdialysis fatigue Symptoms often occur after dialysis is completed, when clinicians are not always present to observe symptoms	Evaluate existing fatigue measurement tools for postdialysis fatigue ^{8–10} or develop a new tool Develop a uniform standard to diagnose postdialysis fatigue, even after dialysis is completed
How do we diagnose postdialysis fatigue in the real world?	Patients and clinicians are concerned that tools to diagnose postdialysis fatigue may be too cumbersome and burdensome to implement in dialysis units	When evaluating new diagnostic tools for postdialysis fatigue, assess implementation outcomes (acceptability, feasibility, and ease of use) of these tools Develop short-form versions of postdialysis fatigue tools to improve real-world adoption
How do we treat postdialysis fatigue?	There are no data on postdialysis fatigue treatment options. Yet, patients strongly advocated for near-term research that tests and implements treatments of postdialysis fatigue Patients and clinicians felt that postdialysis fatigue may improve with home dialysis, less aggressive ultrafiltration, and enhanced patient autonomy. But these strategies lack evidence for postdialysis fatigue and are difficult to implement in the current clinical and regulatory environment	Conduct hybrid effectiveness-implementation trials for postdialysis fatigue that not only measure effectiveness outcomes but also measure implementation outcomes Health services research could help understand and address the barriers that limit implementation of the strategies outlined by patients and clinicians Consider the close and frequent input of regulatory bodies (<i>e.g.</i> , FDA, CMS) to identify outcomes that could align with current or future quality metrics in dialysis care delivery and improve adoption of postdialysis fatigue treatments
How do we ensure postdialysis fatigue treatments are equitably implemented?	Researchers noted dialysis unit characteristics (<i>e.g.</i> , staffing ratios) may impact delivery of treatments of postdialysis fatigue	Research should ensure adequate representation of historically excluded or underrepresented patient populations in clinical trials Novel therapies for postdialysis fatigue should be evaluated to ensure implementation is feasible, irrespective of dialysis unit performance ratings or staffing ratios

This table represents a summary of key challenges and opportunities identified by the authors. Please refer to the comprehensive National Institute of Diabetes and Digestive and Kidney Diseases workshop report for additional challenges, opportunities, and suggested research designs.⁷ CMS, Centers for Medicare & Medicaid Services; FDA, US Food and Drug Administration.

postdialysis fatigue as “fatigue.” People with lived experience in other chronic illnesses noted that “fatigue” minimizes the true burden of the illness and can be stigmatizing. For example, the initial use of the term chronic fatigue syndrome to describe what is now referred to as myalgic encephalomyelitis led the medical community to stigmatize and dismiss those affected with this condition.⁷ Workshop participants advocated for a thoughtful approach to renaming postdialysis fatigue that embraces the complexity of the condition and minimizes these unintended consequences.

There emerged a clear need for a case definition of postdialysis fatigue that accurately and precisely identifies postdialysis fatigue symptoms. To illustrate how to develop a case definition, one speaker discussed their experience studying Gulf War syndrome¹¹ (a cluster of chronic symptoms affecting veterans). The speaker discussed using a systematic approach to formulate a highly specific case definition based on interviews and surveys.

Workshop attendees also discussed the mechanistic pathways that might cause or exacerbate postdialysis fatigue. Although prior studies are inconsistent, postdialysis fatigue has been associated with the dialysis modality and dialysis prescription. Several patients shared their belief that postdialysis fatigue is closely tied to volume removal, noticing that their symptoms were worsened by aggressive ultrafiltration and were alleviated by switching to home dialysis (both peritoneal dialysis and home hemodialysis). Patients also felt that postdialysis fatigue is a biological phenomenon and strongly discouraged studies designed to establish a link between postdialysis fatigue and social determinants of health. Patients felt that such research could unintentionally marginalize underrepresented groups, much like how the inclusion of race in the eGFR equation affected the Black community and biased the practice of medicine. Their experiences suggest that initial research in postdialysis fatigue should prioritize studying factors intrinsic to the modality and prescription of in-center hemodialysis.

Key Priority 2: How Do We Assess the Multidimensional Aspects of Postdialysis Fatigue? How Can Postdialysis Fatigue Be Diagnosed in Routine Clinical Practice?

Patients, clinicians, and researchers discussed tools needed to accurately diagnose and measure postdialysis fatigue in research and routine clinical settings. Workshop attendees advocated for adapting and testing existing measures of fatigue to develop instruments that measure the effect of postdialysis fatigue. Given the multidimensional and debilitating nature of postdialysis fatigue, it was recommended that these instruments should measure the effect of postdialysis fatigue across several domains, including physical, emotional, social, and functional well-being.^{8–10}

An overriding concern among workshop attendees was that tools to assess postdialysis fatigue should be minimally burdensome for patients and clinicians to facilitate uptake in the clinical setting. Several patients who participated in the workshop expressed worry about having to conduct extensive and burdensome tests with little immediate benefit to them. Clinicians were concerned that dialysis units

are understaffed, and that staff lack the bandwidth to add cumbersome tools into routine clinical practice. Overall, it was felt that research to develop postdialysis fatigue measures should incorporate a human-centered design approach guided by patient and clinician input to ensure that tools are easy to understand, use, and implement into routine practice.

Key Priority 3: How Do We Treat Postdialysis Fatigue? How Do We Ensure Treatments Developed for Postdialysis Fatigue Are Delivered Equitably to All People Experiencing Postdialysis Fatigue?

While workshop attendees acknowledged that there is a need to understand postdialysis fatigue to inform novel treatments, some patients expressed worry that research focused on the etiology of postdialysis fatigue could come at the expense of developing treatments in real time. Some patients strongly advocated for research that prioritized fast-paced development and adoption of treatments for postdialysis fatigue within the next decade.

Patients and clinicians also noted that strategies may already exist to alleviate or eliminate postdialysis fatigue, including increasing home dialysis use (both peritoneal dialysis and home hemodialysis), minimizing aggressive volume removal for symptomatic patients, and encouraging patient involvement in care so that patients feel better supported during their dialysis treatment. However, some participants also acknowledged these interventions needed more robust evidence and were difficult to implement in current practice. For example, in-center hemodialysis is currently seen as the “default pathway,” with few patients receiving home dialysis. Furthermore, it was also noted that the rigidity of dialysis unit schedules along with unfavorable staffing ratios make it challenging to individualize care, such as by tailoring the duration and frequency of dialysis sessions.

These concerns conveyed the importance of incorporating implementation science principles to accelerate the adoption of new evidence-based treatments into practice. Specifically, when developing new diagnostic and treatment strategies for postdialysis fatigue, researchers should evaluate implementation outcomes during clinical trials and should consider the feasibility and acceptability of implementing these strategies into routine practice after the trial ends. By working with dialysis units and regulatory bodies (such as the Centers for Medicare & Medicaid Services and the US Food and Drug Administration), researchers can strive for new treatments to receive regulatory approval and secure reimbursement pathways for dialysis units, which will facilitate adoption of treatments into practice. Furthermore, researchers should consider how new treatments can be equitably adopted into practice to serve all patients with kidney disease, including people who have historically been excluded or underrepresented in clinical research.

Postdialysis fatigue is a debilitating, pervasive, and understudied condition that affects many patients receiving in-center hemodialysis. Patients, clinicians, and researchers met through a 2-day NIDDK-hosted virtual workshop to identify research priorities to address what is currently

known as postdialysis fatigue. We call upon the scientific community to partner with patients and clinicians to address several research domains, including (1) defining, understanding, and renaming postdialysis fatigue; (2) diagnosing and measuring postdialysis fatigue with a lens toward implementing diagnostic tools in routine clinical practice; and (3) developing treatments for postdialysis fatigue alongside developing implementation strategies to equitably deliver treatments to all people experiencing postdialysis fatigue.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at <http://links.lww.com/JSN/E697>.

Funding

Y.N.V. Reddy: Agency for Healthcare Research and Quality (K12HS026372). R. Hall: National Institute of Aging (K76AG059930 and R01AG076918).

Acknowledgments

The authors would like to thank the internal and external organizing committees of the “Scientific Workshop on Post-Dialysis Fatigue,” including Kevin Chan, Kevin Abbott, Daniel Gossett, Susan Mendley, Christopher Mullins, Jenna Norton, Afshin Parsa, Griffin Rodgers, Ivonne Schulman, Neha Shah, and Robert Star (from the internal organizing committee) and Kord Kober, Vanessa Merker, and Mark Unruh (from the external organizing committee). In particular, the authors would like to thank the lead organizer, Dr. Kevin Chan, and the >175 workshop attendees. This content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality, the Department of Veterans Affairs, or the American Society of Nephrology.

The content of this article reflects the personal experience and views of the authors and should not be considered medical advice or recommendation. The content does not reflect the views or opinions of the American Society of Nephrology (ASN) or JASN. Responsibility for the information and views expressed herein lies entirely with the authors.

Author Contributions

Conceptualization: Rasheeda Hall, Yuvaram N.V. Reddy.

Writing – original draft: Rasheeda Hall, Yuvaram N.V. Reddy.

Writing – review & editing: Dawn Edwards, Rasheeda Hall, Ann M. O’Hare, Yuvaram N.V. Reddy.

References

- Jacobson J, Ju A, Baumgart A, et al. Patient perspectives on the meaning and impact of fatigue in hemodialysis: a systematic review and thematic analysis of qualitative studies. *Am J Kidney Dis*. 2019;74(2):179–192. doi:10.1053/j.ajkd.2019.01.034
- Jhamb M, Pike F, Ramer S, et al. Impact of fatigue on outcomes in the hemodialysis (HEMO) study. *Am J Nephrol*. 2011;33(6):515–523. doi:10.1159/000328004
- Jhamb M, Weisbord SD, Steel JL, Unruh M. Fatigue in patients receiving maintenance dialysis: a review of definitions, measures, and contributing factors. *Am J Kidney Dis*. 2008;52(2):353–365. doi:10.1053/j.ajkd.2008.05.005
- Sklar A, Newman N, Scott R, Semenyuk L, Schultz J, Fiacco V. Identification of factors responsible for postdialysis fatigue. *Am J Kidney Dis*. 1999;34(3):464–470. doi:10.1016/s0272-6386(99)70073-9
- Sklar AH, Riesenberger LA, Silber AK, Ahmed W, Ali A. Post-dialysis fatigue. *Am J Kidney Dis*. 1996;28(5):732–736. doi:10.1016/s0272-6386(96)90256-5
- Bossola M, Hedayati SS, Brys ADH, Gregg LP. Fatigue in patients receiving maintenance hemodialysis: a review. *Am J Kidney Dis*. 2023;82(4):464–480. doi:10.1053/j.ajkd.2023.02.008
- National Institute of Diabetes and Digestive and Kidney Diseases. *A Scientific Workshop on Post-Dialysis Fatigue: Executive Summary*. 2023. <https://www.niddk.nih.gov/news/meetings-workshops/2023/scientific-workshop-on-post-dialysis-fatigue>
- Kodama H, Togari T, Konno Y, et al. A new assessment scale for post-dialysis fatigue in hemodialysis patients. *Ren Replace Ther*. 2020;6(1):1. doi:10.1186/s41100-019-0252-5
- Ju A, Teixeira-Pinto A, Tong A, et al. Validation of a core patient-reported outcome measure for fatigue in patients receiving hemodialysis: the SONG-HD fatigue instrument. *Clin J Am Soc Nephrol*. 2020;15(11):1614–1621. doi:10.2215/CJN.05880420
- Cella D, Lai JS, Stone A. Self-reported fatigue: one dimension or more? Lessons from the functional assessment of chronic illness therapy-fatigue (FACIT-F) questionnaire. *Support Care Cancer*. 2011;19(9):1441–1450. doi:10.1007/s00520-010-0971-1
- Haley RW, Kurt TL, Hom J. Is there a Gulf War syndrome? Searching for syndromes by factor analysis of symptoms. *JAMA*. 1997;277(3):215–222. doi:10.1001/jama.277.3.215