May 7, 2018

Palmetto Government Benefits Administrators
Leland Garrett, Chief Medical Director
Jurisdiction J
Attn: Medical Policy Department
P.O. Box 100305 AG-275
Columbia, SC 29202-3238

Re: Proposed LCD 34575: Frequency of Hemodialysis

Dear Dr. Garrett:

Thank you for the opportunity to comment on your recently proposed Local Coverage Determination (LCD) regarding more frequent hemodialysis (HD). NxStage Medical, Inc. (NxStage) is a Lawrence, Massachusetts based developer of innovative HD device technology, as well as a provider of dialysis services in 20 Medicare-certified dialysis clinics across 12 states. We are the worldwide leader in home HD, and have led significant clinical research efforts and publications regarding alternative treatment regimen, including more frequent HD.

We appreciate that this proposed LCD, for administrative reasons given that Palmetto GBA has only recently taken over responsibility for this MAC jurisdiction from Cahaba, is virtually identical to the proposed LCDs from the other Medicare Administrative Contractors (MACs) that were released in the second half of 2017. In our responses to each of the MACs on their respective proposals, we have been clear that we support the efforts to address local coverage for more frequent HD through a formal process, but we have deep concerns with the substance of the proposed LCD and that the factual and procedural inaccuracies must be corrected to ensure that patients are not harmed. We submitted comments and a compendium of publications to support the case-by-case medical necessity for more frequent HD. We are including the most recent version of this comment letter, sent to CGS Administrators on December 19, 2017, for your review and your records. We note also that we submitted a comment letter to Palmetto GBA on the LCD (DL 34575) on November 17, 2017.

In addition to the attached comment letter, we would like to point out several important contemporaneous developments that further support the arguments we are making:

1. *Renal Physicians Association (RPA) position paper*: On January 20, 2018, the RPA board approved the position paper "Increasing Dialysis Options for Patients with End Stage Renal Disease."[1] With respect to improved clinical outcomes associated with longer and/or more frequent HD treatments, the Executive Summary of this document states "The studies presented vary in sample size and in quality of evidence, but the RPA believes that in aggregate they strongly suggest that patient benefits exist. Although longer or more frequent treatments may not be needed for all dialysis patients, there is consensus among the specialty that for certain conditions…longer or more frequent schedules are justified." This clear public contemporaneous support from the leading nephrologist organization is highly significant.

2. *Recently published review article on more frequent dialysis from the Frequent Hemodialysis Network lead investigators in Seminars in Dialysis:* Earlier this year, the Suri and Kliger article

[1] https://c.ymcdn.com/sites/www.renalmd.org/resource/resmgr/Position_Papers/Increasing_Hemodialysis_Opti.pdf.

"When is more frequent hemodialysis beneficial?" was published.[2] The article is relevant because it a) was written by two of the principal investigators and leaders of the Frequent Hemodialysis Network (FHN) study, the largest randomized study of more frequent HD ever conducted, b) summarized the evidence of the potential benefits and adverse effects of more frequent HD, and c) offered opinion on when frequent HD is likely to be most beneficial. Importantly, in the "Introduction" section the authors state "While optimal dialysis frequency and duration remains uncertain, it has become clear that a one-size-fits-all approach is not suitable for all patients", and in the "Our Opinion" section the authors offer further clarification on the 5 situations where they believe frequent HD to be "most beneficial."[3] Clearly, given the authors' stature in the academic nephrology community, it is appropriate and expected that they would highlight the need for additional future well-designed studies as well as the need for physicians to consider potential adverse effects. Given this context and their deep experience in this field, the fact that they explicitly articulate 5 potential indication categories is highly relevant. We note that these indication categories are echoed in the referenced RPA position paper and in the literature provided with our prior comment letters, as attached.

3. *NxStage Medical Meeting with CMS:* On November 20, 2017, NxStage met with leadership of the coverage and payment groups of CMS at CMS headquarters in Baltimore to review the substance of our comment letters on the proposed LCDs. In this meeting, Laurence Wilson (Director of the Chronic Care Policy Group) confirmed that CMS payment policy authorizes payment for more frequent hemodialysis where medically justified, and imposes no categorical restriction based on the content of the plan of care, the chronic or acute nature of the condition, or the duration of the hemodialysis session. (Indeed, as Laurence and his team noted during the meeting, CMS's articulations of its payment policy have included illustrative examples of both chronic and acute conditions with respect to which payment for medically justified more frequent hemodialysis may be available, based on a MAC's proper determination of medical justification.) So, even setting aside the fact that payment policy is never a proper basis for a MAC's coverage restriction, this confirms our assertion that CMS's payment policy in no way supports the proposed restrictions of the draft LCDs (e.g., that there can never be coverage for more frequent dialysis that is in a patient's plan of care).

4. *CVS home dialysis announcement in April*: On April 4, 2018, CVS publicly announced its intent to make a medical device for at-home dialysis.[4] In the announcement, the senior leader of the company's effort, a cardiologist, said both "Customers [commercial insurance companies] often tell him that dialysis is one of their bigger costs, though outcomes are poor," and "Dialysis done longer and more frequently could make patients healthier, but realistically that can only happen if it's easier to do at home." This announcement is relevant for two reasons: first, because it is another reference point supporting the medical benefits of more frequent hemodialysis, and, second, that it reiterates the point that more frequent HD is only practically administered in the home setting. We understand that a potential concern driving the proposed LCD effort may be cost implications of dramatically increased utilization of more frequent HD in the in-center setting. CVS's statement echoes our previous assertions that this is highly unlikely for myriad reasons, and is supported by extended follow-up of FHN study participants: after the formal study ended, less than 30% of patients assigned to 6 HD sessions per week in the center continued to dialyze at least 4 times per

[2] Suri RS, Kliger AS. When is more frequent hemodialysis beneficial? *Semin Dial*. 2018;00:1-11.
[3] The noted five situations are: 1) For reduction of left ventricular hypertrophy, especially in patients with minimal to no urine output; 2) refractory volume overload and/or high interdialytic fluid gains; 3) pregnancy; 4) for patients wanting to try frequent HD for potential lifestyle or quality of life benefits; and 5) severe hypertension and/or severe hyperphosphatemia.
[4] https://www.prnewswire.com/news-releases/cvs-health-announces-plans-to-focus-on-kidney-care-and-dialysis-treatment-300624063.html, https://www.marketwatch.com/story/cvs-is-making-a-medical-device-showing-how-health-care-companies-are-doing-more-2018-04-05

week; the majority of patients assigned to 6 nocturnal HD sessions in the home continued their regimen; and a large minority of patients assigned to 3 nocturnal HD sessions in the home converted to frequent nocturnal HD[5]).

Again, NxStage appreciates the opportunity to review the draft LCD. We support the LCD process and streamlining coverage decisions in a way that facilitates the patient-physician relationship and delivery of medically necessary care.

The long-standing policy for medical justification for more frequent dialysis has led to innovations in care and impressive patient benefits over the last decade; we believe that nephrologists and the rest of the community have been good stewards of the policy. The coverage restrictions in the proposed LCDs, including Palmetto GBA's, are inappropriate, and would undermine the practice of medicine and beneficiary access to the care they deserve. However, with some modifications, we believe that the proposed LCD could be made consistent with the breadth of clinical evidence, local and international standards of care, CMS payment policies, and the articulate objectives of the Medicare program. To illustrate the modesty of changes to the language to redress the concerns we have identified, we have attached a red-lined document with annotations supporting the rationale in the side margin.

We welcome the chance to work with Palmetto GBA to explain our perspectives further, and to discuss any concerns that you have not addressed by our recommendations. Please do not hesitate to contact us if you have any question or would like to set up a meeting to review what we have submitted.

Sincerely

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Attachments:

Redlined and Annotated Draft Local Coverage Determination

RPA Position Paper: "Increasing Dialysis Options for Patients with End-Stage Renal Disease"

Seminars in Dialysis Article: "When is more frequent hemodialysis beneficial?"

CVS ***Insights*** *feature:* "Life-Changing Options: CVS Health to Focus on Improving Care for Patients with Kidney Disease," April 4, 2018.

Comment letter to CGS Administrators, submitted December 19, 2017, with all attachments
(A folder containing the relevant clinical literature was submitted electronically)

[5] Chertow GM, Levin NW, Beck GJ, Daugirdas JT, Eggers PW, Kliger AS, Larive B, Rocco MV, Greene T; Frequent Hemodialysis Network (FHN) Trials Group. Long-Term Effects of Frequent In-Center Hemodialysis. J Am Soc Nephrol. 2016 Jun;27(6):1830-6. Rocco MV, Daugirdas JT, Greene T, Lockridge RS, Chan C, Pierratos A, Lindsay R, Larive B, Chertow GM, Beck GJ, Eggers PW, Kliger AS; FHN Trial Group. Long-term Effects of Frequent Nocturnal Hemodialysis on Mortality: The Frequent Hemodialysis Network (FHN) Nocturnal Trial. Am J Kidney Dis. 2015 Sep;66(3):459-68.

Redlined and Annotated Draft Local Coverage Determination

Local Coverage Determination (LCD): Frequency of Hemodialysis (DL34575)

The Jurisdiction "J" Part A and Part B Contracts for Alabama (10111/10112), Georgia (10211/10212) and Tennessee (10311/10312) are now being serviced by Palmetto GBA. This draft LCD was presented for comment in Jurisdiction “M” in October 2017. It is being presented for comment for Jurisdiction “J” beginning March 26, 2018 and will end comment on May 10, 2018. Once the formal comment period ends for Jurisdiction “J”, this LCD will be published for notice in both Jurisdictions "J" and Jurisdiction “M” simultaneously. Please note the following contract numbers are being added to the LCD via Sticky Note: 10111, 10112, 10211, 10212, 10311 and 10312.

Please Note: **This is a Proposed/Draft policy.**
Proposed/Draft LCDs are works in progress that are available on the Medicare Coverage Database site for public review. Proposed/Draft LCDs are not necessarily a reflection of the current policies or practices of the contractor.

CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Palmetto GBA	A and B and HHH MAC	11201 - MAC A	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11202 - MAC B	J - M	South Carolina
Palmetto GBA	A and B and HHH MAC	11301 - MAC A	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11302 - MAC B	J - M	Virginia
Palmetto GBA	A and B and HHH MAC	11401 - MAC A	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11402 - MAC B	J - M	West Virginia
Palmetto GBA	A and B and HHH MAC	11501 - MAC A	J - M	North Carolina
Palmetto GBA	A and B and HHH MAC	11502 - MAC B	J - M	North Carolina

Document Information

Proposed/Draft LCD

Source LCD ID
L34575

Proposed LCD ID
DL34575

Original ICD-9 LCD ID
L31578

Proposed LCD Title
Frequency of Hemodialysis

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

CMS National Coverage Policy

CMS National Coverage Policy Language quoted from the Centers for Medicare and Medicaid Services (CMS) National Coverage Determinations (NCDs) and coverage provisions in interpretive manuals is italicized throughout the policy. NCDs and coverage provisions in interpretive manuals are not subject to the Local Coverage Determination (LCD) Review Process (42 CFR 405.860[b] and 42 CFR 426 [Subpart

Commented [SPF1]: In response to the request that stakeholders provide comments on specifically proposed LCD language, we are providing this annotated document. It is intended to demonstrate the modesty of the changes to the language that would need to made to redress the concerns that we have identified in our comment letter. It illustrates the ease with which the proposed LCD could be revised to be brought in line the clinical evidence, CMS payment policies, and the objectives of the Medicare program.

D]). In addition, an administrative law judge may not review a NCD. See §1869(f)(1)(A)(i) of the Social Security Act.
This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for additional hemodialysis sessions. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for additional hemodialysis sessions and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies may be found in the following Internet-Only Manuals (IOMs) published on the CMS Web site:
Title XVIII of the Social Security Act, §1862(a)(1)(A) allows coverage and payment for only those services that are considered to be reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.
Title XVIII of the Social Security Act, §1862 (a)(1)(D) limits payment for services that are investigational or experimental.
Title XVIII of the Social Security Act, §1833(e) prohibits Medicare payment for any claim which lacks the necessary information to process the claim.
CMS Internet-Only Manual, Pub 100-01, Medicare General Information, Eligibility and Entitlement Manual, Chapter 1, §§10 General Program Benefits
CMS Internet-Only Manual, Pub 100-01, Medicare General Information, Eligibility and Entitlement Manual, Chapter 2, §§10 Hospital Insurance Entitlement

CMS Internet-Only Manual, Pub 100-02, Medicare Benefit Policy Manual, Chapter 11, End Stage Renal Disease (ESRD)
CMS Internet-Only Manual, Pub 100-03, Medicare National Coverage Determinations Manual, Chapter 1, Part 2, §110.10 Intravenous Iron Therapy
CMS Internet-Only Manual, Pub 100-03, Medicare National Coverage Determinations Manual, Chapter 1, Part 2, §110.15 Ultrafiltration, Hemoperfusion and Hemofiltration
CMS Internet-Only Manual, Pub 100-03, Medicare National Coverage Determinations Manual, Chapter 1, Part 4, §260.6 Dental Exam Prior to Kidney Transplantation

CMS Internet-Only Manual, Pub 100-04, Medicare Claims Processing Manual, Chapter 8, Outpatient ESRD Hospital, Independent Facility, and Physician/Supplier Claims
CMS Internet-Only Manual, Pub 100-05, Medicare Secondary Payer Manual, Chapter 2, §20 Medicare Secondary Payer Provisions for End Stage Renal Disease (ESRD) Beneficiaries
CMS Internet-Only Manual, Pub 100-08, Medicare Program Integrity Manual, Chapter 13, §13.5.1 Reasonable and Necessary Provisions in LCDs
CMS Internet-Only Manual, Pub 100-09, Medicare Contractor Beneficiary and Provider Communications Manual, Chapter 5, Correct Coding Initiative
CMS Manual System, Pub 100-04, Medicare Claims Processing, Transmittal 1084, Change Request 5039, dated October 27, 2006
CMS Manual System, Pub 100-20, One-Time Notification, Transmittal 1849, Change Request 9989, dated May 12, 2017
42 Code of Federal Regulations, Chapter IV, Subchapter G, Part 494, Subpart C, §494.80 Condition: Patient assessment and §494.90 Condition: Patient plan of care
Federal Register, Volume 81, No 214, dated November 4, 2016

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Notice: It is not appropriate to bill Medicare for services that are not covered (as described by this entire LCD) as if they are covered. When billing for non-covered services, use the appropriate modifier. Compliance with the provisions in this policy may be monitored and addressed through post payment data analysis and subsequent medical review audits.

This LCD sets out medical conditions likely to meet medical justification for additional payments.

Providers establish parameters for treatment of any given patient through a Patient Plan of Care (POC). It is defined in the Conditions of Coverage for ESRD Services 42 CFR 494.90. Among other items, the POC developed by the Interdisciplinary Team must provide the necessary care and services to manage the patient's volume status; and achieve and sustain the prescribed dose of dialysis to meet a hemodialysis Kt/V of at least 1.2 for patients treated thrice weekly and a peritoneal dialysis weekly Kt/V of at least 1.7 or meet an alternative equivalent professionally-accepted clinical practice standard for adequacy of dialysis. (i.e., for hemodialysis schedules other than thrice weekly to meet a minimum delivered target stdKt/V dose of 2.1). The prescription for chronic hemodialysis therapies includes the type of dialysis access, the type and amount of anticoagulant to be employed, blood flow rates, dialysate flow rate, ultrafiltration rate, dialysate temperature, type of dialysate (acetate versus bicarbonate) and composition of the electrolytes in the dialysate, size of hemodialyzer (surface area) and composition of the dialyzer membrane (conventional versus high flux), duration and frequency of treatments, the type and frequency of measuring indices of clearance, and intradialytic medications to be administered.

Those treatment sessions established in the POC are paid by Medicare as up to 3 X per week. without the need for a secondary diagnosis to justify payment. Establishment of more sessions in the POC, such as 4 - 6 sessions per week, are still reimbursed at the 3 X per week amount, unless accompanied with one of the diagnoses set forth below and otherwise meeting the requirements of this LCD.

~~However, on occasion, acute conditions may require additional sessions during the month outside the POC. These~~ Extra hemodialysis sessions ordered in excess of 3 X per week (whether on an acute or chronic basis) may be considered for additional payment. This LCD provides a list of diagnoses felt to be consistent with such clinical conditions that could establish medical justification for payment. Use of these diagnoses should be verified in the medical records to support any payment made. Clinical Conditions not seen in the list below may still be appropriate to allow payment. However, these claims may require additional review through the appeals process.

Modifier KX will be appended to CPT 90999 to signify ~~an additional session was needed for an acute clinical condition.~~sessions ordered consistent with this policy. It will be appended on each line for each additional session within the claim for each month billed.

Medicare will monitor the frequency of additional sessions which may trigger Medical Review.

The POC reassessment is noted in CFR 42 494.80(d) as below:

494.80(d) Standard: Patient reassessment. In accordance with the standards specified in paragraphs (a)(1) through (a) (13) of this section, a comprehensive reassessment of each patient and a revision of the plan of care must be conducted-(1) At least annually for stable patients; and (2) At least monthly for unstable patients including, but not limited to, patients with the following: (i) Extended or frequent hospitalizations; (ii)

Commented [SPF2]: KDOQI Adequacy Guideline: 2015 Update, Guideline 3.1

Commented [SPF3]: K-DOQI HD Adequacy Guideline: 2015 Update, Guideline 3.3

Commented [SPF4]: Medicare payment policy has been consistent for decades. CMS pays for medically justified hemodialysis sessions in excess of three per week, irrespective of whether these sessions are ordered under a POC. CMS payment policy is clearly articulated in Medicare Manuals. See e.g., Chapter 11, Section 50.A of the Medicare Benefit Policy Manual.

Commented [SPF5]: Revisions made to clarify that the prescription of additional dialysis sessions are not limited to acute clinical conditions.

Marked deterioration in health status; (iii) Significant change in psychosocial needs; or (iv) Concurrent poor nutritional status, unmanaged anemia, and inadequate dialysis. ~~Repeated need~~Need for additional dialysis sessions as noted by 90999-KX is expected to be ~~subsequently~~ addressed in the ~~monthly~~ POC and medical documentation. (See medical documentation requirements below.)

Commented [SPF6]: Revision made to clarify that all patients receiving medically appropriate more frequent hemodialysis sessions are not unstable, and monthly POC updates may not be necessary in order to comply with the POC requirements of the ESRD Conditions for Coverage.

Summary of Evidence

According to the Kidney Disease Outcomes Quality Initiative (KDOQI) Practice Guideline for Hemodialysis Adequacy: 2015 update, over 400,000 patients are currently treated with hemodialysis (HD) in the United States, with Medicare spending approaching $90,000 per year of care in 2012. They note mortality rates remain higher than age-matched individuals in the general population. They also experience an average of 2 hospitalizations per year. Attempts to improve outcomes have included initiation dialysis at higher glomerular filtration rates (GFRs), increasing dialysis frequency and/or duration, using newer membranes, and employing supplemental or alternative hemofiltration. Efforts to increase the dose of dialysis ~~administration above~~administered 3 times ~~per week~~weekly have not improved survival, indicating that something else needs to be addressed. This guideline was also cited in the most recent Federal Register, Volume 81, No 214, dated November 4, 2016.

Commented [SPF7]: The draft LCD misquotes this reference from the KDOQI 2015 update; and this misquote changes its meaning. More importantly, this quote is not presented here within the context in which it appears – which is as an introductory statement of a guideline update under which KDOQI actually recommends the use of more frequent hemodialysis as a treatment alternative.

HD at 3 times (3 X) per week is noted to be 'conventional' treatment. Conventional HD remains the most common treatment modality for ESRD worldwide and is usually performed for 3 to 5 hours, 3 days per week. CMS established payment for hemodialysis based on conventional treatment.

Hence, Medicare reimburses HD treatments 3 times per week (13/14 sessions per month depending on length of month). In the Federal Register, Volume 81, No 214, dated November 4, 2016, CMS outlines the process for medical justification for additional treatment payments. The following statements are made:

Under this policy, the MACs determine whether additional treatments furnished during a month are medically necessary and when the MACs determine that the treatments are medically justified, we pay the full base rate for the additional treatments. While Medicare does not define specific patient conditions that meet the requirements of medical necessity, the MACs consider appropriate medical conditions that would result in the medical need for additional dialysis treatments (for example, excess fluid). When such patient conditions are indicated on the claim, we instruct MACs to consider medical justification and the appropriateness of payment for the additional sessions.

Analysis of Evidence
(Rationale for Determination)

KDOQI Clinical Practice Guideline for Hemodialysis Adequacy:2015 Update Guidelines 4.1.1 states to 'Consider additional hemodialysis sessions or longer hemodialysis treatment times for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor metabolic control (such as hyperphosphatemia, metabolic acidosis, and/or hyperkalemia).'

This specific recommendation was 'Not Graded' in the Guidelines but based on expert opinions. However, these guidelines are determined by a panel of experts and are felt to have a STRONG level of evidence to follow.

National experts were also contacted for input during development of this policy.

Based on KDOQI Practice Guidelines as well as Kidney Disease: Improving Clinical Outcomes (KDIGO) Guidelines, the listed conditions in the LCD may be considered reasonable and necessary to have created medical justification for additional payments.

Based on local collaborative data, Medicare contractors expect the list of diagnoses in this LCD would represent the great majority of claims for which additional payment might be medically justified.

Facilities with sites in multiple states should be able to submit claims in a unified approach.

However, this LCD would not be the appropriate approach to change the payment methodology by CMS and reconsiderations to this LCD to potentially try to change the CMS payment process will be denied as invalid reconsideration to this LCD.

Covered Indications

Metabolic acidosis

1. Fluid positive status not controlled with routine dialysis
2. Hyperkalemia
3. Pregnancy
4. Heart Failure
5. Pericarditis
6. Incomplete dialysis secondary to hypotension or access issues

Limitations

The following are considered not reasonable and necessary and therefore will be denied as not medically justified for payments.

~~1. POC number of sessions above 3 times per week (for example the POC states 5 times per week) those above 3 times per week are not medically justified for additional payment~~

~~2. Planned inadequate or short~~ dialysis

1. Convenience of patient or staff

There are documentation requirements in this LCD which if not followed will generate denials. Please refer to the ***Documentation Requirements*** section below.

While there are no set frequency limitations for these services, continued use of additional sessions by a given provider or for a given beneficiary or unusual patterns of billing, verification of need for services will generate reviews. Please refer to the ***Utilization Guidelines*** section below.

For coding guidelines, please refer to the related article.

As published in CMS Internet-Only Manual, 100-08, Chapter 13, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary. When appropriate, contractors shall describe the circumstances under which the proposed LCD for the service is considered reasonable and necessary under Section 1862 (a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- *Safe and effective.*
- *Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary).*
- *Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:*
  - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member.*
  - *Furnished in a setting appropriate to the patient's medical needs and condition.*
  - *Ordered and furnished by qualified personnel.*
  - *One that meets, but does not exceed, the patient's medical needs.*

Commented [SPF8]: Medicare policy does not support this construction. This is inconsistent with payment policy, as articulated in the 2011 ESRD PPS Final Rule (establishing the per treatment unit of payment) as well as the 2015 and 2017 ESRD PPS Final Rules, reaffirming Medicare's long-standing policy of paying for medically justified hemodialysis sessions in excess of three treatments per week, irrespective of whether the sessions are part of a POC.

Commented [SPF9]: These limitations are vague, at best. At worst, they are invalid blanket restrictions on coverage not allowed under CMS payment policy or supported by clinical evidence.

- CMS pays on a per treatment basis, not by duration or by planned adequacy. Significantly, in the 2017 ESRD PPS Final Rule, CMS noted that commenters suggested that CMS should pay for dialysis by the hour, and CMS declined to do so. 81 Fed. Reg. 77846.

Characterizing shorter, more frequent hemodialysis as de facto medically unnecessary is inconsistent with the best clinical evidence. One arm of the Frequent Hemodialysis Network (FHN) Trial randomly assigned patients to undergo hemodialysis 6 times per week in a short (1.5 to 2.75 hours) treatment with lower dose delivery per session (per treatment Kt/V of 0.9) versus conventional thrice weekly dialysis. The study results, published in *The New England Journal of Medicine*[1], showed significant benefits associated with short more frequent hemodialysis in reduction of left ventricular mass and physical-health composite score, important surrogate endpoints selected for their historical correlation with mortality and hospitalization outcomes. Short frequent hemodialysis was also associated with improved control of hypertension and hyperphosphatemia, and in a subsequent publication was shown to significantly reduce post-dialysis recovery time.[1] Importantly, this study was jointly supported by the NIH, the NIDDK, and CMS. These results were the primary driver of the K-DOQI recommendations (2.1) that short frequent HD sessions should be considered for selected patients. Given these important results from a study with regulatory agency participation, along with the K-DOQI recommendations, characterizing shorter more frequent hemodialysis broadly as medically unnecessary is logically inconsistent.

- *At least as beneficial as an existing and available medically appropriate alternative.* **The redetermination process may be utilized for consideration of services performed outside of the reasonable and necessary requirements in this LCD.**

Synopsis of Changes

CHANGES	FIELDS CHANGED
Under Proposed LCD Title the title was changed to Frequency of Hemodialysis. The LCD was made an A/B MAC LCD. Under CMS National Coverage Policy updated the regulations. While coverage remains the same, verbiage throughout the entire LCD was revised for clarification. Information regarding the CG and KX modifiers was added. Under Bill Type Codes added 72X and under Revenue Codes added 0821 and 0881. Under ICD-10 Codes That Support Medical Necessity deleted A18.84, E83.31, I95.89, N25.89, N28.81, O09.A0, O09.A1, O09.A2, O09.A3, O26.90, R60.0, and R60.9. Under ICD-10 Codes That Support Medical Necessity added E87.2, I30.0, I30.1, I30.8, I30.9, I50.810, I50.811, I50.812, I50.813, I50.814, I50.82, I50.83, I50.84, I50.89, I77.0, I95.3, R63.5, T82.898A, T82.898D, and T82.898S. Under Sources of Information and Basis for Decision updated the Bibliography to reflect current citations.	CMS National Coverage Policy Sources of Information and Basis for Decision Bill Type Codes Revenue Codes ICD-10 Codes that Support Medical Necessity

Associated Information

Documentation Requirements

All documentation must be maintained in the patient's medical record and made available to the contractor upon request.

1. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient.
2. The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.
3. The medical record documentation must support the medical necessity of the services as directed in this policy.
4. The medical records documentation should include the order from the prescribing physician for the additional sessions. This should be available for ~~each and every~~all additional ~~session~~sessions outside the usual 13/14 treatments per month with the CG modifier appended, as well as those described in this LCD with the KX modifier appended. Should the records not show the order and evaluation leading to additional ~~session~~sessions, denials will occur.
5. POC should be available upon request and should be the annual update or monthly depending on the guidelines above and the stability of the patients. Should a patient require consistent additional dialysis sessions, the POC should ~~show changes in~~note the ~~dialysis prescription or other parameters~~medical justification to address the repeated need for additional sessions and be updated on at least a quarterly basis, for stable

Commented [SPF10]: Revision made to clarify that the physician does not need to write a new prescription each time a patient receives an additional session of hemodialysis per week. Physicians may write prescriptions for medically appropriate more frequent hemodialysis on a chronic basis. As long as progress notes, medical records and POC reviews support the ongoing prescription, there should be no need for the physician to rewrite a prescription every week and for each additional treatment.

Commented [SPF11]: Even though patients receiving more frequent HD as part of their plan of care may be stable, we appreciate that the MAC may desire confirming documentation of medical necessity more regularly, but the provision of such support should not be overly inefficient or burdensome.

patients, or at least monthly for unstable patients. Lack of this documentation will lead to denials.

Utilization Guidelines

In accordance with Federal Register, Volume 81, No 214, dated November 4, 2016 utilization of these services should be consistent with locally acceptable standards of practice.
With continued utilization of additional sessions by a specific provider generally, or for a given beneficiary, the provider should expect medical review of medical records by contractors.

Sources of Information
N/A

Bibliography
KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3(1):1-150.
National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 Update. *Am J Kidney Dis*. 2012;60(5):850-886.
National Kidney Foundation. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 Update. *Am J Kidney Dis*. 2015;66(5):884-930.
Frequency of Dialysis LCD L35014 Novitas Solutions, Inc.
Contractor Medical Director ESRD Workgroup

Open Meetings/Part B MAC Contractor Advisory Committee (CAC) Meetings

MEETING DATE	MEETING TYPE	MEETING STATE(S)	MEETING INFORMATION
10/09/2017	Open Meeting	Virginia	Richmond
10/09/2017	Carrier Advisory Committee (CAC) Meeting	Virginia	Richmond

Comment Period Start Date
10/09/2017

Comment Period End Date
11/27/2017

Released to Final LCD Date
Please Note: This is not the LCD Effective Date.
N/A

Reason for Proposed LCD
- Automated Edits to Enforce Reasonable & Necessary Requirements
- Creation of Uniform LCDs With Other MAC Jurisdiction

Proposed Contact
Part B Policy
PO Box 100238 (JM) or PO Box 100305 (JJ)
AG-275
Columbia, SC 29202-
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Proposed/Draft LCD

Bill Type Codes:
Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

072x	Clinic - Hospital Based or Independent Renal Dialysis Center

Revenue Codes:
Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

0821	Hemodialysis - Outpatient or Home - Hemodialysis Composite or Other Rate
0881	Miscellaneous Dialysis - Ultrafiltration

CPT/HCPCS Codes

Group 1 Paragraph:
***NOTE: 90999KX is required for treatments billed in excess of 13.**

Group 1 Codes:

90999	UNLISTED DIALYSIS PROCEDURE, INPATIENT OR OUTPATIENT

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:
Medicare is establishing the following limited coverage for **CPT/HCPCS code 90999KX:**

Group 1 Codes:

ICD-10 CODES	DESCRIPTION
E83.30	Disorder of phosphorus metabolism, unspecified
E83.39	Other disorders of phosphorus metabolism
E87.2	Acidosis
E87.5	Hyperkalemia

E87.70	Fluid overload, unspecified
E87.71	Transfusion associated circulatory overload
E87.79	Other fluid overload
I30.0	Acute nonspecific idiopathic pericarditis
I30.1	Infective pericarditis
I30.8	Other forms of acute pericarditis
I30.9	Acute pericarditis, unspecified
I32	Pericarditis in diseases classified elsewhere
I50.1	Left ventricular failure, unspecified
I50.20	Unspecified systolic (congestive) heart failure
I50.21	Acute systolic (congestive) heart failure
I50.22	Chronic systolic (congestive) heart failure
I50.23	Acute on chronic systolic (congestive) heart failure
I50.30	Unspecified diastolic (congestive) heart failure
I50.31	Acute diastolic (congestive) heart failure
I50.32	Chronic diastolic (congestive) heart failure
I50.33	Acute on chronic diastolic (congestive) heart failure
I50.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
I50.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
I50.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.810	Right heart failure, unspecified
I50.811	Acute right heart failure
I50.812	Chronic right heart failure
I50.813	Acute on chronic right heart failure
I50.814	Right heart failure due to left heart failure
I50.82	Biventricular heart failure
I50.83	High output heart failure
I50.84	End stage heart failure
I50.89	Other heart failure
I50.9	Heart failure, unspecified
I77.0	Arteriovenous fistula, acquired
I95.3	Hypotension of hemodialysis

J81.0	Acute pulmonary edema
M32.12	Pericarditis in systemic lupus erythematosus
N25.81	Secondary hyperparathyroidism of renal origin
O09.211	Supervision of pregnancy with history of pre-term labor, first trimester
O09.212	Supervision of pregnancy with history of pre-term labor, second trimester
O09.213	Supervision of pregnancy with history of pre-term labor, third trimester
O09.219	Supervision of pregnancy with history of pre-term labor, unspecified trimester
O09.891	Supervision of other high risk pregnancies, first trimester
O09.892	Supervision of other high risk pregnancies, second trimester
O09.893	Supervision of other high risk pregnancies, third trimester
O09.899	Supervision of other high risk pregnancies, unspecified trimester
R60.1	Generalized edema
R63.5	Abnormal weight gain
T82.898A	Other specified complication of vascular prosthetic devices, implants and grafts, initial encounter
T82.898D	Other specified complication of vascular prosthetic devices, implants and grafts, subsequent encounter
T82.898S	Other specified complication of vascular prosthetic devices, implants and grafts, sequela

ICD-10 Codes that DO NOT Support Medical Necessity

Group 1 Paragraph:
~~All diagnoses~~N/A. Diagnoses with a KX modifier which are not listed in the "ICD-10 Codes That Support Medical Necessity" section of this LCD~~.~~ will be considered as supporting payment on a case by case basis.

Commented [SPF12]: Revision made to indicate that the ICD-10 code list is not exclusive, allowing for the use of other diagnoses codes, on a case by case basis, based upon the individualized documentation of medical justification submitted

Group 1 Codes: N/A

ICD-10 Additional Information

Attachments
N/A
Related Local Coverage Documents
Article(s)
A55354 - Coding for Hemodialysis Sessions opens in new window
Related National Coverage Documents
N/A

- Dialysis

- Hemodialysis

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RPA Position Paper: “Increasing Dialysis Options for Patients with End-Stage Renal Disease”

RPA
Renal Physicians Association

POSITION PAPER

Approved by RPA Board
1.20.18

Increasing Dialysis Options for Patients with End-Stage Renal Disease

Executive Summary

Despite decades of experience and peer-reviewed literature supporting clinical and quality of life benefits of more frequent dialysis, the vast majority of end-stage renal disease (ESRD) patients in the United States receive in-center hemodialysis (HD) for 3-4 hours, three days a week. Not only does this schedule simply not provide optimal clinical benefit for some patients, it has a negative effect on quality of life for many others. RPA believes that one size does not fit all in this regard and that a more patient-centered approach to the care of people with ESRD is needed. Delivery of care structures, reimbursement models and payment policies must evolve and move forward to meet this need.

Overall mortality rates in dialysis patients have declined over the past 15 years, but adjusted rates of all-cause mortality are still 6.5-7.9 times greater for dialysis patients than for the general population [1]. Recent peer-reviewed literature suggests that clinical benefits are associated with longer and/or more frequent hemodialysis (HD). Furthermore, associations between longer treatment times (TT) and better patient outcomes have been documented by multiple investigators, in a variety of patient populations in the United States and elsewhere [2,3,4]. A greater number of hours of HD per week has been shown to result in improvements in several parameters, including hypertension, phosphorus control, erythropoiesis, quality of life, nutrition, and perhaps most notably, left ventricular hypertrophy (LVH) [5,6], the latter a key intermediate outcome associated with cardiac death [7]. A recent clinical trial randomized 200 adult maintenance hemodialysis patients to extended weekly (>24 hours) or standard (target 12-15 hours, maximum 18 hours) hours of hemodialysis for 12 months [6]. Patients in the extended weekly arm had lower phosphorus levels, lower potassium levels, and higher hemoglobin levels, and achieved these results with fewer BP-lowering agents and phosphate-binding medications.

It is also notable that longer TT has been associated with fewer hospitalizations, and decreased use of anti-hypertensives and phosphorus binders, suggesting the potential for global savings. [6,8]. A reduction in hospitalizations alone would impart significant savings to Part A Medicare and while the provision of more frequent dialysis would increase expenditures in Part B, a net savings to the system is suggested by experience elsewhere. RPA posits that this net savings alone offers a compelling argument for the desegregation of Medicare Part A and B, with the relative success of early alternative payment model demonstration projects in kidney disease supporting such change.

In addition to the clinical and fiscal benefits, more convenient dialysis schedules can improve quality of life for some patients [9]. Alternate treatment schedules allow patients to work, care for relatives, or go to school during the day. Quality of life scores in the randomized trial noted above were not higher in the extended weekly arm, but this may be because the majority of patients received eight or more hours of dialysis during the day. Eight hours of dialysis three days a week during the day is a hassle. If the eight hours are delivered at night when the patient can sleep, or in more frequent and shorter treatments of 2-3 hours 4-5 days a week, then the treatments interfere less with activities during the day, and a higher quality of life is possible. It is also crucial to recognize that the same patient may benefit from transitioning between different schedules and modalities throughout the course of their clinical ESRD trajectory.

This RPA position paper presents some of the evidence associating longer and/or more frequent treatments with improved clinical outcomes. The studies presented vary in sample size and in quality of evidence, but RPA believes that in aggregate they strongly suggest that patient benefit exists. Although longer or more frequent treatments may not be needed for all dialysis patients, there is consensus among the specialty that for certain conditions, such as congestive heart failure (CHF), pregnancy, and calciphylaxis, longer or more frequent schedules are justified [10]. While coverage policies currently support provision of more frequent hemodialysis for many, though not all, of the medical indications considered necessary and appropriate, barriers still exist with regard to the frequency with which additional treatments outside of the traditional thrice-weekly schedule will be covered. RPA strongly believes that payment policies that facilitate patient access to these alternative, more frequent and/or longer therapies should be expanded in both Medicare and Medicaid as well as by commercial payors. To realize the potential of these therapies, nephrologists should assess their patients who might benefit from more intensive hemodialysis. Funding in the forms of Medicare reimbursement and kidney-specific health services research should be provided to advance technologies that make longer and more frequent HD including those provided at home, more convenient, safe, and cost effective.

Background

Hemodialysis began as a treatment for patients with acute renal failure. Maintenance hemodialysis evolved into three sessions per week of 3-5 hours per session for chronic renal failure [11]. In the 1970s the demand for HD increased, legislation funding HD through the Medicare program was passed, and the time per session was shortened [12,13].

The landmark National Cooperative Dialysis Study (NCDS) was performed in the 1970s and published in 1981 [14]. In the NCDS, patients were randomized using a 2x2 study design into 4 groups by treatment time, 4.5 to 5 hours vs. 2.5 to 3.5 hours, and by time averaged blood urea concentration (TAC). The NCDS looked at the clinical effects of each of the four dialysis prescriptions. There was no difference in mortality between the groups during the study. However, TAC_{urea} essentially determined the clinical outcomes of patient morbidity or withdrawal from the study. In addition, after the intervention portion of the study ended and patients returned to their usual treatment schedules, the dose of dialysis delivered during the study had a “lasting effect”, in that patients who received a lower TAC_{urea} during the study had a higher mortality, even after the study ended. There was also a non-significant trend toward lower morbidity and hospitalization in the groups that received longer

treatment times. The groups in the NCDS were relatively small, and the study may not have been powered to detect a difference in survival.

Following the NCDS, clinicians focused on small solute clearance to assess adequacy. The development of high efficiency dialyzers allowed for greater small solute clearance in shorter amounts of time, adequacy goals based on urea clearance could be achieved more quickly, and TT subsequently decreased. Shorter TT were favored by commercial providers because they allowed for more treatments per day. However, studies performed over time indicated that shorter TT were associated with poorer patient outcomes, which led to the development of guidelines stipulating the delivery of a minimum target Kt/V_{urea}, usually 1.2 delivered in thrice weekly treatments [15].

Kt/V_{urea} as a measure of dialysis adequacy, or dose, has remained the standard practice because it is easy to calculate even when using variable volume formulae or shorter dialysis times. Also, Kt/V_{urea} is assumed to be a reasonable surrogate for clearance of low-molecular weight uremic “toxins”, other than urea [14]. The HEMO trial studied the effects of dialysis dose and level of dialyzer membrane flux on mortality and morbidity [16]. The HEMO trial found no major patient benefit to either higher dialysis dose (single pool Kt/V_{urea} 1.71, equilibrated Kt/V_{urea} 1.53 vs. standard dose single pool Kt/V_{urea} 1.32, equilibrated Kt/V_{urea} 1.16), or high flux vs. low flux membranes. These results suggested that the high mortality associated with HD could not be reduced by relatively small increases in solute clearance.

The motivation for careful, intense study of practice patterns such as adequacy metrics and dialyzer flux, is that mortality in dialysis patients in the United States has always been remarkably high. Although overall mortality rates have declined over the past 15 years, adjusted rates of all-cause mortality are still 6.5-7.9 times greater for dialysis patients than for the general population [1].

This high mortality rate for patients on dialysis as compared to the general population is chiefly cardiovascular (CV) [17-20]. Non-traditional CV risk factors such as metabolic bone disease, chronic inflammation, and oxidative stress contribute [21-23]. The high mortality rate has persisted despite a progressive increase in average Kt/V_{urea} over the past two decades, from 1.11 in 1991 to 1.52 in 2002. In addition, the proportion of patients with a Kt/V_{urea} less than 1.2 decreased from 34% in the period 1996-2001 to 10% in the period 2002-2004 [24]. Even with these notable increases in small solute clearance, the complications of hypertension [18, 25], malnutrition [26,27], congestive heart failure [18], and bone and mineral disorders [24, 28] remain unabatedly high, suggesting that dialysis adequacy cannot be measured simply in terms of Kt/V_{urea}. Indeed, many of the identified toxins that accumulate in chronic kidney disease are highly protein bound and can only be cleared with the clinical approach of more dialysis time per week [29]. It is likely that in order to truly improve survival and quality of life, adequacy measures must take into account additional clinical factors impacted by dialysis treatments, such as extracellular volume (ECV) control, phosphorus control, removal of protein bound toxins, and nutrition. Finally, according to the USRDS, the major cause of mortality remains sudden cardiac death (SCD). SCD likely occurs because of arrhythmias related to large and rapid shifts in potassium. Rapid potassium shifts are minimized by longer treatments with slower blood flows which may decrease the risk for SCD.

Many believe that at least part of the high morbidity in prevalent HD patients can be attributed to the non-physiologic nature of the conventional thrice-weekly hemodialysis schedule, and thus there is continued interest in modification of the current standard thrice-weekly dialysis treatment schedule, during the day. Intermittent hemodialysis allows toxins, salts, and water to accumulate in the body during the interdialytic period, some of which accumulate and deposit in tissues, exacerbating tissue damage. The intermittency of thrice-weekly hemodialysis also permits large fluctuations in the levels of these toxins and in extracellular volume, commonly referred to as the "unphysiology of dialysis." Such imbalances may be particularly hazardous in patients with underlying cardiomyopathy, cardiac arrhythmias, and coronary disease. More frequent renal replacement therapy is believed by many as necessary to achieve better body homeostasis, improved elimination of toxins, and better outcomes. Finally, the reduction in LVH associated with more hours of dialysis/week, shown in the FHN trial with a relatively small sample size and only one year of follow-up, suggests that modification of standard HD regimens with increased time, increased frequency, and perhaps adequacy evaluation by metrics other than Kt/V_{urea}, could reduce cardiac mortality. Several alternative dialysis strategies such as short daily hemodialysis [SDHD], long nocturnal daily hemodialysis [LNDHD], long conventional hemodialysis [LHD], in-center nocturnal hemodialysis [INHD], long intermittent dialysis [LID], and hemodialfiltration [HDF], both in a conventional three times a week and in a daily modality, are being actively investigated.

Terminology

- Conventional hemodialysis (CHD): intermittent hemodialysis (IHD) performed in a dialysis center for 3-5 hours per session, three times weekly
- Quotidian dialysis: daily hemodialysis treatments that can be performed as:
    - Nocturnal hemodialysis (NHD): performed while a patient sleeps for sessions lasting as long as 8-9 hours
    - Short-daily hemodialysis (SDHD): performed daily but with a shortened duration of 2-3 hours
- In-center nocturnal hemodialysis [INHD]: performed for 7-8 hours overnight 3 nights a week
- Long intermittent dialysis (LID): includes either nocturnal or daytime sessions that are long (6-9 hours) but performed 3 sessions/week

Quantification of Solute Removal

Comparisons of solute clearance between peritoneal dialysis (PD) and CHD have demonstrated roughly equivalent patient survival, especially in the first years of dialysis, despite the fact that weekly solute clearances with PD are lower than with CHD [30]. The standardized Kt/V (stdKt/V) was formulated to give a uniform measure of dialysis dose across different modalities [31,32]. The stdKt/V is calculated based on mid-week pre-dialysis blood urea nitrogen (BUN) level. In this formulation, dialysis regimens with the same mid-week pre-dialysis BUN have the same weekly stdKt/V. The differences in the stdKt/V among the various modalities are outlined below:

- CHD and PD: weekly stdKt/V is roughly 2.0 (corresponds to a single session IHD spKt/V of 1.2)
- NHD: weekly stdKt/V of 4-5 (spKt/V of about 1.8-2.5/treatment)
- SDHD: weekly stdKt/V of 2.0 (spKt/V of 0.53-0.56/treatment, eKt/V of 0.38/treatment)

An important effect of dialysis is the removal of middle molecular weight molecules that may represent uremic toxins (such as β-2 microglobulin) not measured by urea kinetics [33]. Longer treatment times may remove a greater amount of these potential toxins. For example, in one study the weekly dialysate β-2 microglobulin mass clearance increased from 127 to 585 mg when the patient was switched from CHD to NHD [34]. Furthermore, removal of smaller, protein-bound substances such as indole-3-acetic acid and acid indoxy sulfate are increased on SDHD as compared to CHD [35].

Clinical Benefits of More Intensive Hemodialysis

RPA believes that in aggregate the relevant literature indicates clear clinical benefit to the provision of more intensive dialysis to certain sub-populations of ESRD patients. The following discussion provides a partial listing of these clinical benefits, broken out by organ system or clinical indication.

<u>Cardiovascular Benefits</u>

Several studies, including one randomized controlled trial, have examined the changes in cardiovascular parameters associated with more intensive dialysis therapies. The effects studied have included surrogate outcome measures for mortality such as blood pressure control and left ventricular hypertrophy.

Blood pressure control
Several studies performed in patients undergoing both SDHD as well as NHD have clearly demonstrated that blood pressure goals are more readily met by patients receiving dialysis through these modalities as compared to patients on CHD [36-41]. These studies include one randomized controlled trial (RCT) [36]. In many cases, blood pressure control was achieved with either fewer medications or with cessation of all blood pressure medications. While the mechanism of improved blood pressure control is uncertain, one study in patients undergoing SDHD showed improved control in extracellular fluid volume [42].

Left Ventricular Mass and Geometry
Four separate studies, including a RCT, have shown reduction in left ventricular mass index (LVMI) as measured by either echocardiography or magnetic resonance imaging [6,36,40,42,43]. In several of these studies CHD patients were converted to either SDHD or NHD and then followed prospectively. In an additional smaller study, patients with impaired left ventricular function on CHD were switched to NHD with subsequent modest improvements in left ventricular ejection [44].

Slower ultrafiltration rates (UFR), made possible by longer treatment times, have been linked to lower mortality [45]. One group of researchers found associations between frequent hemodialysis schedules and reduced levels of dialysis-induced cardiac injury [46].

Longer and/or more frequent dialysis treatments may minimize LVH by minimizing cardiac stunning and thus damage from rapid UFRs, and these findings are consistent with the FHN results.

Other cardiovascular effects
Small studies have also demonstrated partial restoration of heart rate variability during sleep when patients were converted to NHD [47] as well as improvement in baroreceptor sensitivity and decreases in sympathetic nervous system activity [48].

Malnutrition and Inflammation

Several studies have investigated the effects of more intensive dialysis on markers of nutrition and inflammation. This is critical as the loss of amino acids into the dialysate with more intensive dialysis can be as high as 10 grams per day [49].

Two studies have demonstrated increases in appetite, weight gain and increases in muscle mass when patients are converted to daily dialysis [50,51]. A more detailed study of nitrogen kinetics in patients on NHD revealed that despite the larger amounts of amino acids lost in the dialysate, there was no decline in total body nitrogen as measured by in-vivo neutron activation [49]. However, studies looking at serum albumin levels have been conflicting, with several studies showing an improvement in serum albumin levels and others showing no effect [37,50-52].

Mechanistically, the improvement in nutritional parameters may be secondary to improved appetite, more regular eating schedule, and the liberalization of diet that often occur when patients are switched to either SDHD or NHD [50,53,54]. There may also be an effect of more intensive dialysis to decrease the inflammatory milieu associated with ESRD as levels of interleukin (IL)-6 and C-reactive protein have been shown to decrease in one study of patients undergoing daily hemodialysis [55].

Phosphate and Bone Metabolism

Overall, daily hemodialysis is associated with significant improvements in net phosphate removal. With NHD delivered 4-7 nights a week, phosphate removal is approximately twice that of CHD. Many, if not the majority, of patients no longer require phosphate binders or dietary phosphorus restriction. In fact, many patients require supplementation of phosphate in the dialysate [36,38,56,57]. There is evidence that NHD delivered only 3 nights a week for 7-8 hours also leads to a decline in phosphorus levels [58]. With SDHD, serum phosphate levels tend to fall when the daily sessions are longer than 2 hours and most of these patients still require phosphate binders [52, 59]. It should also be mentioned that in one study, patients converted from CHD to NHD demonstrated improved levels of both 1-25 $(OH)_2$ and 25-(OH) vitamin D independent of supplementation [60].

The benefits of more intensive hemodialysis on serum phosphate control have led to the proposal that NHD may be a treatment for tumoral calcinosis or calciphylaxis. A single case report demonstrated significant improvement in tumoral calcinosis in a patient transitioned from CHD to daily nocturnal home HD [61].

Anemia and Erythropoietin Dosage

There has been conflicting data on whether intensification of hemodialysis is associated with either increases in serum hemoglobin or increased responsiveness to erythropoietin (EPO). In this regard, many of the studies are small and likely underpowered to detect any difference [62, 52, 63, 36, 64].

Sleep Disorders

Patients with ESRD have a high prevalence of sleep disorders, and it has been proposed that this may reflect suboptimal dialysis and may impact on quality of life as well as cardiovascular mortality [65]. The greatest effects of NHD on sleep disorders have been seen in patients with sleep apnea. Significant reductions in the apnea-hypopnea index have been shown in patients converted from CHD to NHD [66,67]. Mechanistically, this improvement may be due to two effects of NHD: (1) improvements in ventilatory instability associated with ESRD that leads to increased ventilatory sensitivity to hypercapnia and (2) improvements in pharyngeal cross-sectional area that may be due to improved fluid balance and decreased neck edema.

Fertility

Patients with ESRD undergoing CHD have reduced rates of fertility and a high rate of fetal complications [68]. More intensive hemodialysis is recommended for those pregnant females on CHD based on several observational studies showing better outcomes with longer treatment times [69-71].

Quality of Life

Patients on CHD typically report relatively poor quality of life and the majority do not work. Several studies have examined the changes in quality of life when patients make the switch from CHD to more intensive therapy [36,50,72-74]. Despite receiving more dialysis with its attendant time and labor demands, the majority of studies have reported improved cognition, improved psychomotor efficiency, and improved quality of life parameters using several different survey instruments (such as the Beck Depression Index, SF-36, and Sickness Impact Profile) [36,50,72]. These studies may be influenced by modality-selection bias as healthier patients with better baseline quality of life may opt for NHD at a higher rate than CHD [75].

Hospitalization Rates

In one study, high-comorbidity patients with ESRD who were converted from CHD to SDHD while maintaining the same total weekly dialysis time were studied prospectively over 72 months. SDHD was associated with a significant 34% decrease in hospitalization days with, notably, no increase in vascular access hospitalizations [52].

In another study, 32 NHD patients were studied 1 year before and 2 years after conversion to NHD and compared to 42 CHD patients (matched for age, dialysis vintage and controlled for comorbidities) during the same time period [74]. While hospitalization rates were stable for the CHD group, the group that was converted to NHD experienced a fall in dialysis or

cardiovascular admission rates from 0.50 +/- 0.15 to 0.17 +/- 0.06 admissions per patient year (p = 0.04).

Survival

Abundant observational data spanning over three decades of investigation consistently shows associations between longer treatments times and improved outcomes, when compared to thrice-weekly HD for 3-4 hours [1,2,3]. The challenge in interpreting this data has always been the potential for selection bias, as it is usually the healthier, more functional patients that can dialyze multiple times a week, or do their own, more frequent dialysis at home [75]. It must also be noted that selection bias is but one of multiple potential biases that might be present in both observational and sometimes randomized controlled trial data. Great care must be taken in interpreting the results of these studies. Cohort studies, case controls and propensity scoring help in interpretation, but do not remove the multiple biases that surely can and do affect outcomes such as survival.

To reduce selection bias, as well as other sources of bias, the FHN trial randomized patients to hemodialysis six times per week (frequent HD, 125 patients) or three times a week (conventional HD, 120 patients) and followed them for one year [6]. The pre-determined outcomes for the FHN trial were (a) death, and for survivors, change in LVM, and (b) death, and for survivors, change in Physical Health Composite of the RAND 36 scale. The Daily FHN study did show a significant effect of daily dialysis on both of these - and thus satisfied a positive result on these pre-determined primary outcomes. It is notable that in this randomized, controlled trial, frequent HD was associated with a statistically significant reduction in LVH, as well as improvements in hypertension and phosphorus control. These findings are consistent with another previous, smaller randomized controlled trial, in which 52 patients were randomized to receive either nocturnal HD 6 times weekly, or conventional HD 3 times weekly [36]. In this study, frequent HD was also associated with a statistically significant reduction in LV mass, and with a reduction in the need for blood pressure and oral phosphate binder medications. Finally, the nocturnal arm of the FHN trial compared outcomes in 45 patients who received nocturnal home hemodialysis six times a week to outcomes in 42 patients who received conventional thrice weekly HD [76] and showed improved control of hyperphosphatemia and hypertension in patients in the nocturnal arm.

The number of vascular access interventions was higher in the frequent dialysis group, but there were no significant differences in failure rates of vascular access between the frequent and standard dialysis groups. It must also be noted that in the Nocturnal FHN study, patients treated with frequent hemodialysis had a significantly higher and faster rate of endogenous kidney function loss. It is not clear whether this association was causal, or what the implications might be for patients.

Patient Selection for Intensive Hemodialysis

Given benefits such as reducing extremes of solute fluctuations, decreased ultrafiltration rate, increase in dialysis dose and consistent improvements in clinical parameters, there are sub-groups of patients with ESRD who may be particularly good candidates for more intensive hemodialysis. These include:

- Patients with poor quality of life on current renal replacement modalities
- Patients who want to work or go to school during the daytime
- Patients who would benefit from a liberalized diet
- Patients who have disabling intra- or inter-dialytic complications
    - Unstable blood pressure during dialysis
    - Severe cramping during dialysis
    - Uncontrollable hypertension
    - Impaired left ventricular function or congestive heart failure
    - Persistent hyperphosphatemia
    - Calciphylaxis
- Patients with sleep apnea
- Patients who would benefit from and wish to stay with a home therapy after transition from peritoneal dialysis
- Patients who may not be candidates for kidney transplantation
- Patients who have difficulty in controlling uremic symptoms
- Obese patients
- Patients with an arteriovenous fistula that can consistently deliver blood flows of at least 250ml/min as needed for longer, slower treatments such as nocturnal HD, but not 350ml/min as needed for CHD. It must be noted that for patients with an access that cannot supply higher blood flows, a shorter therapy such as SDHD, that requires BFRs of 500ml/min, would not be a good option.

For these patients, the ability to tailor a hemodialysis therapy to specific patient needs is critically important to ensure good outcomes and optimize quality of life.

Cost Effectiveness of More Intensive Hemodialysis

As noted, RPA believes that the current system where savings accrued to Medicare Part A have no relationship to the activities of Part B providers confounds the ability to accurately assess the cost-effectiveness of medical innovations such as advancements in more intensive hemodialysis. Accordingly, RPA believes that analysis of the cost-effectiveness of more intensive or alternate dialysis schedules must include the cost-savings from decreased hospitalizations, reduction in medications such as anti-hypertensives and phosphate binders, reduced need for transportation to and from a dialysis unit for those patients doing home dialysis, and the ability of the dialysis patient to work and provide child or elder care.

The London Daily/Nocturnal Hemodialysis Study compared the economics of short daily HD (n = 10), long nocturnal HD (n = 12), and conventional thrice-weekly HD (n = 22) in patients over 18 months [77]. A retrospective analysis of patients' conventional HD costs during the 12 months before study entry was conducted to measure the change in cost after switching to quotidian HD. Because of the increase in number of treatments, treatment supply costs per patient for the daily HD and nocturnal HD study groups were approximately twice those for conventional HD patients. However, average costs for consults, hospitalization days, emergency room visits, and laboratory tests for quotidian HD patients tended to decline after study entry. The major cost saving in home quotidian HD derived from the reduction in direct nursing time, excluding patient training. Total annualized cost per quality-adjusted life-

year for the daily HD and nocturnal HD groups were 85,442 Can dollars (2003) and 120,903 Can dollars, which represented a marginal change of - 15,090 Can dollars and - 21,651 Can dollars, respectively, as compared to conventional thrice-weekly HD. Overall, the authors conclude that their economic analysis points toward both improved quality of life and reduced costs for quotidian HD patients.

Another cost analysis study from Canada revealed that NHD was associated with a net 20% decrease in weekly mean total health care cost [78]. Cost categories found to be less expensive for NHD included: staffing, overhead, hospital admissions and procedures, and medications. Cost categories that were more expensive for NHD included hemodialysis materials and other capital costs and laboratory tests.

An economic evaluation comparing short daily or nocturnal hemodialysis with thrice-weekly conventional in-center dialysis was performed in the United States [79]. In this study, costs are sensitive to assumptions about the effect of daily dialysis on hospital days. Reductions of at least 8% in hospital days are required for these more intensive modalities to be cost saving.

It is important to understand that cost analyses such as these presume that patient outcomes with a new intervention are as good or better than those outcomes achieved with conventional care. If the emerging data on the benefits of more intensive hemodialysis are integrated into this analysis, then more intensive dialysis may be considered a “dominant” therapy in that it is both less expensive and more effective than conventional in-center hemodialysis.

Summary

Over one hundred abstracts and peer-reviewed journal articles have demonstrated clear and consistent clinical benefits of longer and/or more frequent HD treatments. This is the case whether the therapy is performed as SDHD or as NHD. Reported benefits include improvements in cardiovascular outcomes, bone and mineral metabolism, nutrition, sleep, fertility, and quality of life. Furthermore, observational data consistently shows associations between lower hospitalization rates and better survival. The benefits may be particularly robust in patients with comorbidities that are improved with consistent, gentle, and overall greater fluid removal, such as congestive heart failure, hypertension, and obstructive sleep apnea. In addition to many clinical benefits, quality of life can be optimized for some patients with a schedule that allows them to do their treatments at night, leaving their days free for school, work, or caring for family.

Individualized therapy is key to providing patient-centered care and provision of more frequent and/or intensive dialysis exemplifies this approach for patients with dialysis-dependent ESRD. Moving this from conversation to standard of care will require active changes in delivery of care structures, reimbursement models and payment policies of CMS and other third-party payors to support therapies other than the dominant in-center, thrice-weekly, 3-4 hours treatment paradigm. The is the essence of patient-centered care for people with ESRD.

Recommendations

1. Longer and more frequent dialysis should be an option available to all patients for whom there is potential for clinical and quality of life benefits.
2. Nephrologists should assess their patient population for those patients who might benefit from more intensive hemodialysis and offer them that option.
3. Medicare, Medicaid, and commercial health insurers should adopt payment policies that increase the availability of more intensive dialysis therapies (either SDHD or NHD) to patients as prescribed by the patient's nephrologist.
4. Funding both in the form of Medicare reimbursement for dialysis through the ESRD Prospective Payment System (PPS) and research funding to NIH should be provided to advance technologies that promote the practice of more intensive hemodialysis, whether at home or in-center, for its convenience and cost effectiveness, but mostly for the clinical benefits it provides to patients.
5. Continued study of the benefits of more frequent dialysis is appropriate but should not preempt the provision of the best care possible based on current evidence.

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Glossary

BFR	Blood flow rate
BUN	Blood urea nitrogen
CHD	Conventional hemodialysis
CV	Cardiovascular
ECV	Extracellular volume
FHN	Frequent Hemodialysis Network Trial
HD	Hemodialysis
HDF	Hemodiafiltration
HEMO	The Hemodialysis Study
IHD	Intermittent hemodialysis
INHD	In-center nocturnal hemodialysis
LHD	Long conventional hemodialysis
LID	Long Intermittent dialysis
LNDHD	Long nocturnal daily hemodialysis
LVH	Left ventricular hypertrophy
LVMI	Left ventricular mass index
NCDS	National Cooperative Dialysis Study
NHD	Nocturnal hemodialysis
PD	Peritoneal dialysis
RCT	Randomized controlled trial
RRT	Renal replacement therapy
SDHD	Short daily hemodialysis
TAC	Time averaged blood urea concentration, used in the NCDS as a measured of delivered dialysis dose
TT	Treatment time
UFR	Ultrafiltration Rates

Seminars in Dialysis Article: “When is more frequent hemodialysis beneficial?”

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UNRESOLVED ISSUES IN THE CARE OF DIALYSIS PATIENTS

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WILEY Seminars in Dialysis

When is more frequent hemodialysis beneficial?

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Abstract

The use of frequent hemodialysis (HD) is growing, with the hope of improving outcomes in end-stage renal disease. We narratively review the three randomized trials, 15 comparative cohort studies, and several case series of frequent HD that empirically demonstrate the potential efficacy and adverse effects of these regimens. Taken together, the randomized studies suggest frequent HD may result in left ventricular mass regression. This effect is most pronounced when left ventricular mass is abnormal, but attenuated by significant residual urine output. Both frequent short and long HD consistently improved blood pressure control and reduced antihypertensive use, despite greater weekly interdialytic weight gains. Serum phosphate was lowered. Frequent short daytime HD improved health-related quality of life, while frequent long overnight HD did not. Regarding adverse effects, frequent HD patients underwent significantly more procedures to salvage arteriovenous vascular accesses. An absolute increase in hypotensive episodes was observed with frequent short HD, while frequent long HD accelerated residual renal function loss and increased perceived caregiver burden. The effect of frequent HD on mortality is controversial, due to conflicting results and limitations of published studies. Finally, pregnancy outcomes may be substantially better with frequent long HD. On the basis of these data, we suggest frequent HD is most likely to benefit patients with left ventricular hypertrophy particularly if there is minimal urine output, those unable to attain dry weight on a thrice weekly schedule, and pregnant women. All patients receiving frequent HD should be advised of and monitored for potential risks.

1 | INTRODUCTION

Despite significant advances in general medicine and technology over the last four decades, nephrologists remain agonizingly aware of the grim prognosis for patients with end-stage renal disease, particularly amongst those receiving dialysis. Although mortality has improved in the last decade, it remains high: the median life expectancy of a patient starting hemodialysis is just over 3 years.[1] The average adult hemodialysis patient is hospitalized 1.73 times per year,[2] endures multiple unrelenting symptoms, and has substantially reduced quality of life.[3] In-center three times weekly hemodialysis (HD) remains the dominant dialysis therapy for ESRD in the United States, accounting for 90% of patients, with the remainder receiving some sort of home dialysis (peritoneal or home HD).[4]

Therapies to further improve the prognosis of patients receiving chronic hemodialysis have been limited. More programs are now offering the option of increasing HD frequency and/or intensity either in-center or at home in an effort to improve long-term outcomes and quality of life. Currently, it is estimated that <2% of all US ESRD patients receive frequent HD, defined as at least 5 treatments per week, but this proportion is growing.[5] While optimal dialysis frequency and duration remains uncertain, it has become clear

that a one-size-fits all approach is not suitable for all patients. In this review, we will summarize the evidence of the potential benefits and adverse effects of more frequent HD. We end by offering our opinion on when frequent HD is likely to be most beneficial.

2 | EVOLUTION OF DIALYSIS FREQUENCY

In 1960, Scribner and colleagues are credited with reporting the first successful use of intermittent HD for the treatment of chronic renal failure in two patients using a Teflon arterio-venous forearm shunt.[6] The initial dialysis treatments were delivered for 24-60 hours every 5-9 days. As the patients' renal function declined to almost zero, it was noticed that their uremic symptoms of lethargy, anorexia, and vomiting would return 1 or 2 days prior to the next dialysis, and their hemodialysis frequency was accordingly increased to twice weekly.[6] This twice weekly long-duration regimen, combined with a low-protein and sodium-restricted diet, allowed the patients to experience improvement in anorexia and nausea, regain lost weight, remain free of pruritus and muscle cramps, and even return to work part-time[6].

These two patients, along with five others, are reported to have survived on 12-16 hours twice weekly HD for at least 2 years, with continued general well-being and ability to function in their daily activities.[7] Major ongoing problems included recurrent gout, metastatic calcifications with high calcium-phosphate product, hyperparathyroidism and related bone disease, predialysis hypertension from extracellular volume overload, transfusion dependent anemia with iron deficiency, and recurrent malnutrition due to under-dialysis when the arteriovenous access failed. An eighth patient (the oldest, age 48), died after 12 months of dialysis from coronary artery disease.[7] It is remarkable how these early reports, based on just a few patients, so clearly and accurately identified the complications experienced by patients receiving HD, which continue to afflict patients in the current era.

In the 1960s, demand for HD exceeded supply and in-hospital dialysis was restricted to patients approved by a special committee.[8] Some centers thus began to prescribe HD at home, delivered more conveniently as 8 hours, three nights per week, with favourable results.[9] The first report of home "daily" HD (delivered as 2 hours, 6 days per week) was also around this time, reported by de Palma in 1969.[10] It was recognized that more intense dialysis was required to better ameliorate peripheral neuropathy,[11] with 6 hours, three times per week preferable to 6 hours twice weekly.[12] In the ensuing years, technology for "high-efficiency" HD was developed, including larger surface area dialyzers, better water purification systems, and improved arteriovenous access, allowing treatments to be further shortened. When in-center HD was finally approved for Medicare coverage in 1973, short, three times weekly schedules became the norm to accommodate the most patients at the least cost.[13] The prevalence of home HD fell from 40% to 13% over the next 5 years.[14]

Based on these early reports, there was widespread belief that as long as patients were not having uremic symptoms, dialysis was probably "adequate." It was only later appreciated that while conventional three times weekly hemodialysis was sufficient to prevent the acute uremic syndrome, more intense dialysis might be required to improve long-term prognosis and complications for ESRD patients the United States, particularly for those with little to no residual renal function. From 1981 to 2002, focus was shifted to measuring and obtaining higher urea clearances within the three times weekly schedule, with disappointing results. A minimum *Kt/V* threshold of 0.9 was initially identified based on a randomized trial,[15,16] but many hypothesized that much higher clearances may be more beneficial.[17,18] However in 2002, the large randomized HEMO study of 1846 patients definitively showed that increasing urea clearances modestly on a three times weekly schedule did not improve mortality.[16] Since then, there has been renewed interest in schedules of more frequent and longer dialysis duration to improve outcomes.[19-23]

3 | WHY CONSIDER FREQUENT HEMODIALYSIS?—PHYSIOLOGICAL RATIONALE

The normal kidney functions 24 hours per day, 7 days per week, delivering clearances of over 1000 L per week. In comparison, three times weekly conventional hemodialysis delivers urea clearances of <200 L per week. It should also be noted that the intermittent nature of HD is inherently inefficient compared to the continuous clearance of the native kidney. Thus, 200 L per week with intermittent HD is not equivalent to 200 L per week of continuous native kidney function. This is because the rate of urea and other small toxic solute removal with HD is proportional to the solute's concentration. Consequently, most solute removal occurs at the start of the HD session when concentrations are highest, with decreasing removal rates as the HD session proceeds. Dialyzing 6 days rather than 3 days per week allows more time to be spent on the steepest part of the urea removal curve, allowing greater weekly small solute removal.

Another major problem with conventional HD is related to chronic extracellular volume overload, which contributes to hypertension, congestive heart failure, and cardiovascular risk.[24,25] Interdialytic fluid gains can be particularly pronounced after the long 2-day interdialytic interval, especially in anuric patients. As high ultrafiltration rates can result in hypotension,[26] patients are often unable to achieve their "dry weight." Intradialytic hypotension not only results in symptoms, but has been associated with end-organ damage such as myocardial stunning,[27] and cerebral ischemia.[28] Furthermore, high ultrafiltration rates >10 mL/kg/hr have been shown to be associated with greater all-cause and cardiovascular mortality.[29,30] Increasing dialysis frequency from 3 to 6 days per week halves the interdialytic interval for fluid accumulation, theoretically allowing for reduced ultrafiltration rates and better hemodynamic stability.[26] Consequently, the patient may be better able to attain dry weight, with reduced risk of left ventricular hypertrophy, hypertension, and congestive heart failure.

Significantly increasing the duration of dialysis as well as the frequency (eg, nocturnal dialysis, 8 hours 5-6 nights per week) has added benefits of greater phosphate removal. Long duration dialysis of >5 hours allows time for stores of intracellular phosphate to be transferred to the blood compartment, where it is accessible to the dialyzer.[31] This can help ameliorate hyperphosphatemia, which has been associated with vascular calcification[32] and death.[33,34]

Finally, the large fluctuations in phosphate, potassium, volume, blood pressure, etc. that occur due to long periods without dialysis have been termed the "unphysiology" of intermittent HD.[35] It has been well demonstrated that patients on three times weekly HD are ~20% more likely to die on Mondays and Tuesdays following the long 48 hour interdialytic interval.[36] The increased deaths were mostly cardiovascular-related, and may be the consequence of worse hyperkalemia and/or fluid overload on these days. With more frequent dialysis, this long interdialytic interval and its potential deleterious consequences are avoided.

4 | NOMENCLATURE

In 2015, the KDOQI Hemodialysis Adequacy Guideline Update proposed using a descriptive nomenclature for intensive dialysis therapies.[37] Briefly, frequent HD refers to 5 or more dialysis treatments per week, and can be either of short (<3 hours), standard (3-5 hours), or long (>5 hours) duration. The first two regimens are often referred to in the literature as "daily" HD, and can be performed either in-center or at home. The latter regimen is referred to as "nocturnal" HD, as it is almost exclusively performed overnight at home. Many programs are now also offering long duration (>5 hours) 3 times weekly or every other night dialysis. This regimen, often referred to as "extended-hours" conventional dialysis, is not discussed in this review.

5 | WHAT DOES THE EVIDENCE SHOW?

From 1998 to 2004, the publication of numerous small studies empirically supporting some of the theoretical benefits of frequent HD discussed above led to a renewed interest in these regimens. In two systematic reviews summarizing this evidence, it was found that 35 studies described 28 unique populations of <500 patients in total. Each of these studies showed significant, and often dramatic, improvements in at least one outcome, including blood pressure, left ventricular mass, phosphate, nutritional markers, and/or health-related quality of life with frequent HD.[19,20] Frequent HD could deliver up two times more weekly small solute clearances (weekly standard Kt/V = 2.35 vs 3.01 vs 4.65 with three times weekly, frequent short, and frequent long HD, respectively).[38] Interdialytic weight gains decreased.[19] These studies had serious methodological limitations, however, including inadequate control groups, selection and dropout bias, small sample size, and unadjusted confounding. Potential adverse effects were not addressed.[19,20] Since then, additional studies have been conducted to address some of these limitations. These are summarized below.

5.1 | Randomized Trials of Frequent Hemodialysis

5.1.1 | Efficacy—quality of life and surrogate outcomes

To date, there have been three parallel-arm randomized trials of frequent HD (Table 1). A fourth trial, ACTIVE dialysis, was predominantly a trial of long three times weekly or every other day HD, and is not discussed here.[39] In the largest trial, known as the Frequent Hemodialysis Network (FHN) *Daily Trial*, 245 patients from 11 centers in North America were randomized to receive conventional HD (3-5 hours, three times weekly) or *frequent short* HD (1.5-2.75 hours, six times weekly) for 12 months. Frequent short HD *significantly improved health-related quality of life* and several surrogate outcomes, associated with cardiovascular risk, including *left ventricular mass VM), blood pressure, and phosphate.*[22] Measures of cognitive and physical function, depression, and albumin did not change (Table 1).[22]

Simultaneously, the FHN *Nocturnal Trial* randomized 87 patients from eight centers in North America to receive conventional HD (<5 hours, 3 days per week), or *frequent long* HD (≥6 hours, 6 nights weekly) for 12 months.[23] Notably, both groups performed their dialysis treatments at home. Unlike the Daily trial, this trial was unable to show a statistically significant change in the two coprimary outcomes of left ventricular mass and quality of life, despite >2.5 times the number of treatment hours (31 vs 13 hours per week).[23] In contrast, in the *Alberta Trial* of 52 patients from 2 Canadian centers, patients randomized to *frequent long* HD at home (≥6 hours, 5-6 nights per week) experienced a *statistically significant reduction in their LVM* after 6 months of treatment, compared to those remaining on 3 days per week dialysis in-center.[21] Patients receiving frequent long HD in both these trials did show *statistically significant reductions in systolic blood pressure, antihypertensive use, and serum phosphate*, but not in quality of life (Table 1).[21,23]

How can we explain the statistically nonsignificant results of the FHN Nocturnal trial on LVM? There are several potential explanations. Previous studies have shown that the effect of pharmacological interventions on left ventricular anatomy and function is correlated with the baseline LVM.[40] The baseline LVM of patients in the Alberta and Nocturnal trials was ~180 g and ~140 g, respectively. A 7%-8% regression in left ventricular mass was observed with frequent HD in each trial, translating to absolute changes of −15.3 (P<.05) and −10.9 (P = .09), respectively[21,41] Limited patient enrollment in the Nocturnal Trial resulted in lack of statistical power to detect the smaller treatment effect. Post-hoc analysis of the FHN Trials showed that observed improvements in left ventricular mass were indeed correlated with the baseline left ventricular mass,[42] and that only the subgroup with abnormal left ventricular mass at baseline showed statistically significant improvements with frequent long HD.[42] The mechanism of LVM regression with frequent HD is

TABLE 1 Summary of randomized trials of frequent hemodialysis, 2007-2011

Trial	Intervention	Control group	Follow-up	Main findings with frequent hemodialysis	Limitations

Culleton et al[21] (Alberta Trial)	• N = 27
	• 5-6 nights/week
	• ≥6 hours/night
	• at home
		• N = 25
		• 3 days/week
		• spKt/V>1.2
		• in-center
			• 6 months	• ***Primary:***
				  • *Left-ventricular mass change* −15.3 g (−29.6 to −1.0) (p<0.05)
				• ***Secondary:***
				  no change in quality of life (EQ5D index)
				  • decrease in SBP and antihypertensive use
				  • decrease in serum phosphate
					• Intervention was at home, while control was in-center
					• Mostly prevalent cohort (mean ESRD duration >5 y)
					• Short follow-up
					• Not powered for mortality or hospitalisations

Chertow et al[22] (FHN Daily)	• N = 125
	• 6 days/week
	• 1.5-2.75 hrs
	• target eKt/V>0.9
	• in-center
		• N = 120
		• 3 days/week
		• 2.5-4.0 hours
		• target eKt/V>1.1
		• in-center
			• 12 months	• ***Co-Primary***[a]***:***
				  • *Left-ventricular mass change* −13.8 g (−21.8 to −5.8) (p<0.001)
				  • *Quality of life (PHC) change* +3.2 points (1.0 to 5.4) (*P* = .004)
				• ***Secondary and Tertiary*:**
				  • decrease in pre-dialysis SBP/ antihypertensive use
				  • decrease in serum phosphate
				  • no change in albumin, ESA dose, depression, objective physical function, or cognitive tests
				• ***Adverse effects*:**
				  • more arteriovenous vascular access interventions
				  • increased intradialytic hypotensive events
					• Selected patients
					• Mostly prevalent cohort (45% ESRD duration >5 y)
					• Short follow-up
					• Not powered for mortality or hospitalizations

Rocco et al[23] (FHN Nocturnal)	• N = 45
	• 6 nights/week
	• ≥6 hours/night
	• at home
		•N = 42
		•3 days/week
		•<5.0 hours
		•target eKt/V>1.1
		•at home
			• 12 months	• ***Co-Primary***[a]***:***
				  • *Left-ventricular mass change* −10.9 g (23.7 to 1.8) (*P* = .09)
				  • *Quality of life (PHC) change* +0.6 (3.4 to 4.7) (*P* = .75)
				• ***Secondary and Tertiary*:**
				  • decrease in pre-dialysis SBP/ antihypertensive use
				  • decrease in serum phosphate
				  • no change in albumin, ESA dose, depression, objective physical function, or cognitive tests
				• ***Adverse effects*:**
				  • more arteriovenous vascular access interventions
				  • accelerated loss of residual renal function
				  • increased perceived caregiver burden
					• Selected patients
					• Short follow-up
					• Limited statistical power
					• Significant baseline residual renal function may have attenuated response to frequent therapy

[a]In the FHN trials, the two coprimary outcomes were actually composite outcomes, ie: i) death, or change in left ventricular mass, and ii) death, or combined with change in physical health composite score. There were no meaningful differences in deaths between groups during the first 12 months.
Alb, albumin; ESA, erythropoiesis stimulating agent; ESRD, end-stage renal disease; FHN, Frequent Hemodialysis Network; PHC, physical health composite score of the RAND-36; SBP, systolic blood pressure.

unclear. LVM regression correlated with the change in predialysis systolic blood pressure, but not the interdialytic weight gain or ultrafiltration rate.[42]

The presence of significant residual renal function in incident patients the Nocturnal trial may also have decreased their response to frequent HD treatment. More than half of patients recruited to the Nocturnal trial were new to dialysis (incident patients), producing >500 mL of urine a day. Participants in the Daily and Alberta trials were largely prevalent patients, treated with hemodialysis for >3-4 years.[21,22] Only 27% of Nocturnal patients were anuric, compared with 66% anuria in the Daily trial.[23] Re-examination of the FHN trial data revealed that the effect of frequent dialysis on left ventricular mass was more pronounced when residual urine output was low, and the majority of patients who experienced a marked reduction in

left ventricular mass had negligible baseline residual urine volume.[42] The authors thus concluded that with higher urine output, the differential benefits of more frequent hemodialysis are likely attenuated.[42] Finally, it should be noted that the adherence to therapy in the Nocturnal Trial was nonideal, with only 73% of patients performing >80% of their prescribed treatments.[23]

These landmark trials, which were difficult to execute and cost millions, provide critical information on the effects of frequent hemodialysis, and are unlikely to be repeated soon.[43] Notwithstanding, the trials had some limitations. Each of these trials enrolled a highly select, motivated group of patients; <10% of those screened were eventually randomized.[44] In the 3 trials, the mean age ranged 49-55 years, and between 55%-81% had arteriovenous fistulae or grafts, suggesting they were healthier than the general hemodialysis population.[21-23] The effectiveness of frequent hemodialysis to reduce LVM may not apply to incident patients with significant residual renal function, nor to patients with normal LVM at baseline. Some measures used to assess secondary outcomes may not have been adequately sensitive (eg, cognitive function). Long-term effects were not studied, as treatment duration was limited to 6 to 12 months. Finally, the trials were not powered to examine mortality or other hard outcomes. Post-hoc analyses of mortality are discussed below.

5.1.2 | Adverse effects

Patients receiving frequent short HD experienced a clinically and significantly increased risk of *vascular access complications*, particularly those with arteriovenous accesses at randomization (Daily Trial, HR = 1.90, 95% CI 1.12-3.23, $P = .020$; Nocturnal Trial HR = 3.23, 95% CI 1.07-10.3, $P = .038$).[45] This increased risk was primarily explained by an increase in procedures to salvage arteriovenous accesses. Access losses and access-related hospitalizations were similar between groups. In the Daily trial, the access repairs were not just limited to increased angioplasties (which could arguably have been the result of heightened surveillance), but frequent short HD patients also required twice as many surgical revisions and thrombectomies. This information suggests that without intervention, the accesses most likely would have been lost.

One controversial result of the FHN Daily trial was that related to intradialytic hypotension. While *the rate of intradialytic hypotension per dialysis session* was observed to be significantly lower with frequent (724 episodes/6667 sessions = 10.9%) than with conventional HD (470 episodes/3440 sessions = 13.6%),[22] the *absolute exposure* to intradialytic hypotension was higher with the frequent short HD due to having twice as many dialysis sessions per week (~0.6 vs ~0.4 episodes per week).[46] In fact, the hazard ratio for severe intradialytic hypotension requiring administration of intravenous saline with frequent HD was 1.53 (95% CI 1.11-2.09, $P = .0086$). Given that every intradialytic hypotensive episode may theoretically result in sequelae such as myocardial stunning and cerebral ischemia,[27,28] the latter measure is likely most clinically relevant. From a physiological standpoint, however, the fact that frequent HD did not result in a doubling of hypotensive episodes despite a doubling of treatments is somewhat surprising as ultrafiltration rates were similar between groups (conventional 14.5 vs frequent 13.9 mL/min).[46] (The hypothesis that frequent HD would result in a halving of interdialytic weight gain (due to halving the interdialytic interval) did not hold true as patients receiving frequent HD liberalized their fluid intake from 9 to 10.6 L/week ($P < .001$)).[22] It is possible that the frequent short HD patients had a lower per session risk of hypotension due to less antihypertensive use and/or better left ventricular function during follow-up, but this requires further study. Whether the risk of intradialytic hypotension was also increased with frequent long HD is unclear, as patients in the Nocturnal trial did not measure their blood pressures routinely while they were sleeping.

A major unexpected adverse effect in the Nocturnal trial was the finding the frequent long HD *accelerated the loss of residual renal function*.[47] At the beginning of the trial, 72% (63/87) of patients had some urine production. By 12 months, 67% of patients assigned to frequent long HD became anuric, compared with 36% of patients who remained on conventional HD ($P = .06$). It is possible that increased exposure to lower intradialytic blood pressures may have lead to anuria. In post-hoc analyses, the observed change in the lowest intradialytic blood pressure between baseline and 12 month follow-up periods was associated with decrease in urine volume at 12 months.[47] Adherence to therapy appeared to be correlated with loss of urine volume, although confounding by indication cannot be ruled out; it is possible that patients who were losing their residual function may have been more likely to stay adherent to frequent HD to remove their fluid gains. The number of patients in the Daily trial with nonzero urine volume was too low to draw any conclusions regarding the impact of frequent short HD on residual renal function.

Finally, patients assigned to frequent long HD overnight at home experienced a significant *increase in the burden they perceived on their unpaid caregivers*. Although causality cannot be inferred from association, it is troubling that increases in perceived burden were significantly correlated with adherence to treatment.[48] In the Daily Trial, increases in perceived burden on unpaid caregivers were not observed, suggesting that perceived burden may be related to reliance on unpaid caregivers who help with performing frequent HD treatments at home. This finding is particularly important as patients receiving frequent long HD at home did not experience the same beneficial effects on quality of life as those assigned to frequent short HD in-center. One limitation of this study was that it evaluated the patients' perception of burden on their unpaid caregivers, and not the burden perceived by the caregivers themselves.[48]

5.1.3 | Mortality

Two papers provided the long-term survival of patients enrolled in the FHN trials up to 5 years after they completed their randomized treatment assignments.[49] In the Daily Trial, patients who were randomized to frequent short HD for 12 months experienced a significantly reduced risk of death after a median follow-up of 3.6 years

(intent-to-treat analysis HR = 0.54, 95% CI 0.31-0.93, $P = .024$).[50] In the Nocturnal Trial, patients who were randomized to frequent long HD for 12 months experienced a significantly increased risk of death after a median follow-up of 3.7 years (intent-to-treat analysis HR = 3.9, 95% CI 1.3-11.8, $P = .010$).[50] It should be noted that there were a high number of crossovers in the Nocturnal Trial, such that only 61% of patients assigned to frequent long HD were adherent during the first year, while 33% of patients assigned to three times weekly HD were receiving frequent long HD by 4 years.[50] The hazard ratio was similar in the as-treated analysis that defined groups by the treatment received during the previous 12 months. The authors concluded that Daily dialysis appeared to improve mortality, an effect not seen in the Nocturnal trial. The mortality results from both of these trials should be interpreted with great caution due to few numbers of observed events and low statistical power. No definitive conclusions can be drawn regarding the effect of frequent short or long HD on long-term mortality from the FHN trials.

5.2 | Comparative Cohort Studies of Frequent Hemodialysis

5.2.1 | Mortality

Several comparative cohort studies have attempted to evaluate the effect of frequent HD regimens on survival. The main results of these studies, along with their limitations, are summarized in Table 2.

We found four comparative studies of in-center frequent HD evaluating mortality.[49,51-53] The Daily Trial mortality results have been discussed above.[49] Kjellstrand et al compared 150 patients receiving in-center frequent short HD in Europe to USRDS expected mortality rates, and found a hazard ratio of 0.73 in favour of frequent HD.[51] The main limitation of this study was that it did not adequately match for country or comorbid conditions. In contrast, Suri et al compared 318 in-center frequent short HD patients to propensity-score and country matched controls receiving in-center three times weekly HD, and found that frequent short HD was associated with a 60% higher mortality risk.[52] Despite matching, these results may have been subject to indication bias—that is, patients may have been prescribed frequent HD because they were ill. Marshall et al compared mortality amongst several modalities using adjusted marginal structural models, treating modality as a time-varying covariate. They found a 30% increased mortality risk with in-center frequent (short and long) compared to in-center three times weekly HD, though this was not statistically significant.[53] Incidentally, this same study suggested a mortality benefit with "quasi-intensive" in-center HD (ie longer and more frequent HD but <5 days per week) (results not shown).[53]

We found eight comparative studies evaluating mortality with home frequent vs three times weekly HD.[50,53-58] Six cohort studies each found frequent HD to be associated with substantial mortality benefit (HR 0.36-0.87); four of these six studies were statistically significant (Table 2). However, each of these studies compared patients receiving frequent HD at home, to patients receiving three times weekly HD in-center. Because patients who dialyze at home tend to be more motivated and healthier than those dialyzing in-center, each of these studies is limited by potential selection bias. A Canadian study comparing home frequent short and long HD to home three times weekly HD found similar mortality between the modalities, although this study may have been underpowered.[58] There were also substantial center and patient differences between groups that may not have been fully mitigated by the multivariable adjustment model.[58] Finally, in the FHN Nocturnal trial, the control group received their HD treatments at home[50]; the mortality results of this trial are discussed above.

We found two papers that compared home frequent long HD with transplantation[59,60]; the second of these is an update of the first. In the updated matched analysis, all types of transplant recipients (ie living donor, standard criteria donor, expanded criteria donor) had a reduced risk of treatment failure and death compared to patients receiving home frequent long HD.[60]

In summary, the mortality data regarding frequent short and long HD is conflicting and controversial, and is based on studies with important methodological limitations. Thus, to date, no definitive conclusions can be made on the effect of frequent HD on survival.

5.2.2 | Frequent Short HD with Very Low Dialysate Flow Rates

The above studies compared frequent HD and three times weekly HD delivered by traditional HD machines. Dialysate flow rates were 300 mL/min with frequent long HD, and up to 800 mL/min with frequent short HD. There is a new device being increasingly used for home frequent short HD that uses very low dialysate flow rates (~20 L/treatment).[61] While ultrafiltration is performed daily, weekly small solute clearances with this device are the same or just slightly higher than with three times weekly HD (weekly standard *Kt/V* 2.3).[61] Given the substantial differences in machine characteristics, results from the studies described above cannot be necessarily extrapolated to patients using this new device.

We found five papers describing mortality, hospitalizations, and modality failure on overlapping cohorts who received home frequent HD using this new device.[56,62-65] These matched analyses found frequent short HD was associated with reduced mortality risk compared to in-center three times weekly HD (Table 2),[56] as well as compared to home peritoneal dialysis (HR 0.75-0.80; 95% CI 0.68-0.87).[63,65] The authors provided the comparison of home frequent HD to home peritoneal dialysis to help reduce potential confounding associated with patients' ability to dialyze at home. Interestingly, frequent short HD was associated with reduced hospitalizations compared to peritoneal dialysis (HR 0.73; 95% CI 0.67-0.79),[62] but not compared to in-center three times weekly HD (0.92; 95% CI 0.85-1.00).[62] This latter result was due to less cardiovascular but more infection-related hospitalizations with frequent short HD.[62] Finally, frequent short HD using this device was associated with significantly less modality failure than home peritoneal dialysis (HR 0.29; 95% CI 0.25-0.34).[62] An additional prospective cohort study of this device is currently being conducted.[66,67]

TABLE 2 Summary of comparative studies evaluating mortality with frequent vs. three times weekly hemodialysis, 2006-2016

Study	Subject group	N	Control group N, matching methods	Mean follow-up	Mortality rate Freq. vs Control (/100 pt-y)	Risk estimate	Potential limitations
IN-CENTER FREQUENT							
Kjellstrand et al 2008[51]—Europe	**Short**	150	Expected USRDS death rate (unmatched)	2.4 y	NR	**SMR = 0.73** [0.69-0.81]	• Europe vs US • ***unmatched***
Suri et al 2013[52]—France/US/Canada	**Short**	318	575 PS matching	1.6 y	15.6 vs 10.9	**HR = 1.6** [1.1-2.3]	• ***potential indication bias***
FHN Daily 2016[49]—US/Canada	**Short**	125	120 Randomized	3.6 y (median)	4.3 vs 8.2	**HR = 0.54** [0.31-0.93]	• ***few events*** (20 frequent, 34 control) • treatment period 12 months
Marshall et al 2015[53]—Australia/New Zealand[b]	**Mixed**[c]	484	32823 MSM	2.7 y	NR	HR = 1.30 [0.92-1.84]	• mixed population, as treated analysis • ***not matched for ESRD duration***
HOME FREQUENT							
Blagg et al 2006[54]—Europe	**Short**	117	Expected USRDS death rate (unmatched)	1.1 y	NR	**SMR = 0.39** [0.19-0.51]	• ***home vs center*** • ***unmatched***, Europe vs US
Johansen et al 2009[55]—US	**Short**	43	430PS matching	2.7 y	9.1 vs 13.9	HR = 0.64 [0.31-1.31]	• ***home vs center*** • potential immortal time bias
Weinhandl et al 2012[56]—US[a]	**Short**	1873	9365 matching algorithm	1.7 y	11.0 vs 12.7	**HR = 0.87** [0.78-0.97]	• ***home vs center*** • incomplete match for ESRD duration
Tennankore et al 2017[58]—Canada	**Short**	202	600 **(home)** adjusted (unmatched)	2.2 y	4.3 vs 5.6	HR = 1.10 [0.65-1.85]	• ***substantial group and center differences*** • small sample size, very low event rates
Marshall et al 2015[53]—Australia/New Zealand[b]	**Mixed**[c]	375	32823 MSM	2.7 y	NR	HR = 0.59 [0.32-1.10]	• ***home vs center*** • mixed population, as treated analysis • not matched for ESRD duration
Johansen et al 2009[55]—US	**Long Nightly**	94	940 PS matching	2.7 y	7.5 vs 15.4	**HR = 0.36** [0.22-0.61]	• ***home vs center*** • potential immortal time bias
Nesrallah et al 2012[57]—France/US/Canada	**Long Nightly**	338	1388 PS matching	1.7 y	6.1 vs 10.5	**HR = 0.55** [0.34-0.87]	• ***home vs center***
FHN Nocturnal 2015[50]—US/Canada	**Long Nightly**	42	45 **(home)** Randomized	3.7 y (median)	9.9 vs 3.3	**HR = 3.9** [1.3-11.8]	• ***few events*** (14 frequent, 5 control) • treatment 12 months, high crossover
Tennankore et al 2017[58]—Canada	**Long Nightly**	508	600 **(home)** adjusted (unmatched)	2.2 y	5.4 vs 5.6	HR = 0.96 [0.64-1.42]	• ***substantial group and center differences*** • very low event rates

Bold values indicate statistically significant results ($P < .05$, 95% confidence intervals do not include the value 1.0). Control patients received 3 times weekly HD in-center, unless otherwise indicated.

[a]This study evaluated frequent short HD using a newer device with low dialysate flow rates.

[b]This group published another study based on the same cohort in 2011[74]; only the updated results from 2015 are presented here.

[c]Frequent HD (≥5 treatments per week), any number of hours.

ESRD, end-stage renal disease, HD, hemodialysis; HR, hazard ratio; SMR, standardized mortality ratio; MSM, marginal structural models; PS, propensity-score; USRDS, United States Renal Data System.

TABLE 3 Summary of volume-related parameters from the FHN trials[22,23,46]

	Three-times weekly HD (Baseline → 12 month)	Frequent HD (Baseline → 12 month)	Difference[a] or ratio (frequent vs control) [95% CI]	*P*-value
Nocturnal Trial				
Per week IDWG (kg)	9.0 (3.0)	10.6 (3.8)	**Ratio = 1.18**	**<.001**
Per session IDWG (kg)	3.1 (1.0) → 3.1 (1.0)	3.16 (0.99) → 2.11 (0.86)	**−1.0 [−1.1, −0.8]**	**<.001**
UF rate (mL/hr)	888 (246) → 870 (258)	900 (330) → 834 (282)	−36 [−90, 18]	NS
Post HD weight (kg)	78.9 (19.8) → 79.2 (19.9)	77.0 (20.8) → 78.2 (21.2)	0.79 [−0.1, 1.68]	NS
Daily Trial				
Per week IDWG (kg)	7.4 (3.0)	9.1 (3.3)	**Ratio = 1.23**	**.01**
Per session IDWG (kg)	2.4 (1.2) → 2.6 (1.0)	1.72 (0.77) → 2.04 (0.87)	**−0.46 [−0.77, −0.15]**	**<.01**
UF rate (mL/hr)	654 (372) → 624 (228)	606 (384) → 360 (216)	**−246 [−324, −168]**	**<.001**
Post HD weight (kg)	83.5 (24.1) → 84.1(25.6)	88.6 (28.2) → 89.1 (28.6)	+0.6 [−1.9, 3.1]	NS

[a]Between group differences adjusted for baseline values.
Bold text indicates statistically significant values.
FHN, Frequent Hemodialysis Network; HD, hemodialysis; IDWG, interdialytic weight gain; UF, ultrafiltration.

5.3 | CASE SERIES OF FREQUENT HD IN SPECIFIC SETTINGS

There are several case series describing often dramatic benefits with frequent HD in specific settings. One study compared outcomes for 22 pregnant patients receiving frequent long HD in Canada to USRDS data, and found that frequent long HD was associated with an increase in the live birth rate (86% vs 61%, $P = .03$), and longer gestational age (36 vs 27 weeks, $P = .002$).[68] Findings from this report were confirmed in a meta-regression that suggested that pre-term delivery and small for gestational age correlated inversely with weekly dialysis hours received.[69] Other case series suggest that frequent long HD may result in complete resolution of calciphylaxis[70,71] and substantial improvements in sleep apnea.[72,73] We acknowledge the methodological limitations of these studies lacking appropriate control groups; further study of frequent HD in these settings is needed.

6 | OUR OPINION

Due to its high cost, logistical constraints (whether related to difficulties with scheduling in-center, or to patient training and implementation of home treatment), increased burden of therapy, and potential adverse effects, frequent HD is likely not suitable for all patients with ESRD. Yet the noted improvements in surrogate and quality of life outcomes cannot be ignored. Recent clinical practice guidelines do not provide solid recommendations on when to use frequent HD.[37] They *suggest* that in-center frequent short HD be offered "after considering individual patient preferences, potential quality of life and physiological benefits, and the risks of these therapies (2C)," while long frequent HD be *considered* for patients "who prefer this therapy for lifestyle considerations (not graded)." There is also an ungraded statement that pregnant women "*should receive*" frequent long HD. The only strong recommendations are with respect to informing all patients considering frequent HD about the potential risks (increase in vascular access procedures, intradialytic hypotension, caregiver burden, and residual renal function loss (1B/C).[37] While we generally agree with these guidelines, we offer further clarification on the situations where we believe frequent hemodialysis is likely to be most beneficial. *This opinion is based on our review and interpretation of the totality of evidence given above, in combination with our clinical experience.*

1). *For reduction of left ventricular hypertrophy, especially in patients with minimal to no urine output*. In our opinion, this indication may be particularly pertinent for patients being considered for renal transplantation, in whom the main contraindication is cardiomyopathy of uncertain etiology. It is possible that frequent HD may improve a patient's cardiac status sufficiently such that he/she may be wait-listed, but this requires further study.
2). *Refractory volume overload and/or high interdialytic fluid gains* that cannot be controlled on three times weekly HD. In the FHN trials, a significant increase in total weekly interdialytic weight gain was observed with both frequent short and long HD, indicating that frequent HD patients liberalized their fluid intake. Despite this, however, *the gains between each session significantly decreased* (table 3). It should be noted that *ultrafiltration rates were reduced only with frequent long HD* due to the substantial increase in weekly dialysis time (table 3).
3). *Pregnancy*. We recognize the limited evidence base for this indication. However, we believe that the temporary inconvenience and extra costs of frequent long HD are worth undertaking in this setting, given the potential of intensive therapy to prevent the catastrophic outcomes for foetuses of women receiving HD or peritoneal dialysis.
4). *For patients wanting to try frequent HD for potential lifestyle or quality of life benefits*. As individual quality of life responses will vary, we suggest regular re-evaluation of the patient's desire to continue frequent HD as well as the burden on caregivers.

Importantly, in this instance, we would suggest avoiding frequent HD if there is significant urine output, as the burden of therapy combined with the risk of residual function loss likely outweighs any benefits.

5). *Severe hypertension and/or severe hyperphosphatemia* that are uncontrollable with three times weekly HD. In our opinion, this may be particularly important in patients with ongoing end-organ damage from hypertension, or calciphylaxis.

All patients should be informed about and monitored for adverse effects of frequent HD, particularly vascular access complications and residual function loss. Caregivers should be informed about the potential increase in burden. Patients should be carefully monitored carefully for adherence to therapy. Finally, whether to perform frequent HD in-center or at home will depend on the center's capabilities and patient preference. It should be noted that home HD likely carries quality of life benefits above and beyond those of dialyzing more frequently. In the FHN Nocturnal Trial, both groups received similar quality of life benefits after switching from in-center to home HD.[23] Absence of a caregiver at home is not, in our opinion, itself a contraindication to home HD.

7 | CONCLUSION

In summary, it is plausible that while conventional HD may be insufficient to maintain physiological homeostasis, the potential for adverse effects may outweigh intended benefits if HD is "overly intense." Indeed the answer likely lies somewhere in the middle. Further research in the way of rigorously conducted, adequately powered, prospective studies is needed to determine the optimal dialysis frequency and time that will optimize outcomes while minimizing adverse effects for patients with ESRD receiving dialysis.

CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to declare.

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CVS ***Insights*** *feature:* “Life-Changing Options: CVS Health to Focus on Improving Care for Patients with Kidney Disease,” April 4, 2018.

Insightsfeature

April 4, 2018

Life-Changing Options

CVS Health to Focus on Improving Care for Patients with Kidney Disease

CVSHealth®

CVS Health is bringing its unique integrated model and holistic patient care to an area of significant, unmet clinical need — chronic kidney disease (CKD) and end-stage renal disease (ESRD). Our proven, in-market programs have enabled us to improve health outcomes — including for patients with complex, chronic conditions. Now we are leveraging our experience and expertise to help disrupt and reshape care for patients with kidney disease.

CVS Health's approach to this expensive, complex disease has two main components.

The first is early identification through advanced analytics of patients with CKD before they require dialysis. Our highly trained AccordantCare nurses will work with these patients to help them with comorbidity management and nutritional counseling, which can delay the need for dialysis.

Specially trained nurses will also provide the support needed for a smooth transition to renal replacement therapy. Given the scarcity of donor kidneys for transplantation this generally means some form of dialysis.

The second pillar of our approach is to make home dialysis the modality of choice for patients and nephrologists.

Currently, most ESRD patients in the U.S. receive hemodialysis treatments three times a week in dedicated treatment centers. Unfortunately, these patients have relatively poor outcomes with high mortality rates and significantly lower quality of life.

The medical literature is clear that longer, more frequent hemodialysis treatments can improve outcomes in appropriate patients.[1] For many reasons, this type of dialysis is best provided in the convenience of the patient's home.

There are many current barriers to home hemodialysis and our program will be designed to mitigate nearly all of them. Central to our approach is the development of innovative new technology intended to make self-treatment with hemodialysis at home easy and safe. We expect this to allow more patients, for whom this treatment is appropriate, to achieve the better outcomes seen with longer, more frequent hemodialysis.

Our home hemodialysis device in development has:

- Fewer steps than traditional devices and a simple, animated interface to guide patients through set-up, treatment and cleaning
- Advanced technology intended to help reduce the likelihood of adverse clinical events
- Cloud connectivity to share treatment information between patients and nephrologists

Over the next few months we will be initiating a clinical trial intended to demonstrate the safety and efficacy of the new device to support U.S. Food and Drug Administration clearance.

~$100B
combined Medicare expense for ESRD and CKD[2]

up to 10X
higher mortality rates among patients with ESRD†

6X
higher hospitalization rate for people with ESRD/CKD†

+700K
cases of ESRD in the U.S.[2]

~120K
new cases are diagnosed each year[2]

>500K
patients receive dialysis[2]

Kidney Disease: The Silent Killer

Kidneys are the primary way the human body flushes toxins from the body. Every day the kidneys process about 200 quarts of blood to filter out about two quarts of waste products and extra water, which are flushed out of the body through urination.[3]

Patients with CKD or ESRD lose kidney function, which leads to fluid retention, electrolyte imbalance, and accumulation of certain toxins.

This often results in high blood pressure, heart disease, muscle wasting, general feeling of fatigue and weakness, and other symptoms and side effects which can be severe or life-threatening.

Unfortunately, in the early stages, CKD has no symptoms and so can go undetected until it is very advanced. That's why it is often called the "silent killer."

48%
of those with severely reduced kidney function are not aware they have CKD[4]

96%
of people with kidney damage or mildly reduced kidney function are not aware they have CKD[4]

Current Treatments: Poor Outcomes, High Costs

There are two types of dialysis — hemodialysis and peritoneal dialysis. With hemodialysis, a patient's blood is circulated through an artificial filter outside the body, to "clean" it and then returned to the patient. While hemodialysis can be done at home, nearly all patients receive treatment in-center. Typically, patients receive hemodialysis three times a week with each treatment lasting three to four hours. This leaves a two-day interval each week without treatment, which has been linked to a significant increase in risk of hospitalization and death.[5]

Peritoneal dialysis requires a flexible catheter to be surgically implanted within the abdominal cavity of the patient with one end of the catheter brought through the skin overlying the lower abdomen. Sterile dialysis fluid is instilled into the patient's abdominal cavity through the catheter, allowed to rest, then drained several hours later. This procedure removes waste products and normalizes electrolytes such as sodium and potassium. Peritoneal dialysis can be administered throughout the day, each day, or every night while the patient is sleeping. About 9 percent of ESRD patients in the U.S. utilize peritoneal dialysis.[2]

Kidney transplantation is the gold standard of treatment for patients on dialysis. However the wait list is long — more than 3,000 patients are added each month — and not all patients are medically suitable to receive a transplant.[6]

For a majority of patients on the waitlist, or those not medically eligible for a transplant, dialysis is a life-saving treatment that performs some of the activities of normally functioning kidneys.[7] Treatment outcomes for in-center dialysis — currently the standard for a vast majority of patients on dialysis — tend to be poor. One in five dialysis patients dies in the first year after starting treatment — mainly from infection or cardiovascular disease.[2] Overall mortality rates among ESRD patients are four- to 10-fold higher than the general Medicare population and hospitalization rates, six-fold higher.[2]

+50%
of nephrologists would prefer their patients receive at-home dialysis treatment[8]

69%
of nephrologists said longer dialysis performed nocturnally would result in significantly better clinical outcomes[8]

up to **45%**
lower mortality rate when patients receive longer, more frequent dialysis[9]

Improving Outcomes

Eliminating gap days and enabling longer, more frequent dialysis, in appropriate patients, has been shown to improve outcomes, most notably lower mortality.[5] The risk of death from cardiac arrest is 36 percent higher and that from heart failure or arrhythmia is nearly double on the day after the two-day interval in treatment.[10]

Patients who receive more frequent hemodialysis also have better metabolic and blood pressure control.[1] Patients receiving more frequent dialysis report having a better quality of life. Logistically and economically the home is generally the best setting for these treatments.

Patients can opt for more frequent, shorter daytime or evening treatments or longer treatments overnight — all without traveling to a center or taking time off work. Patients receiving in-home dialysis report being more satisfied with their treatment.[11]

In one survey, 63 percent of nephrologists said they would recommend at-home treatment for close friends and family.[5] A majority — 59 percent — agreed that increasing the frequency of dialysis beyond three times a week significantly improves clinical outcomes. However, only a small percentage of patients are offered home hemodialysis today.[8]

Better for Patients and Payors

Our comprehensive patient care solution for kidney disease will address significant challenges to at-home dialysis treatment by:

- Helping identify and diagnose advanced kidney disease before urgent dialysis is required
- Educating patients about at-home treatment options before they start dialysis
- Providing comprehensive patient training to enable a smooth transition to home with ongoing support
- Developing a home hemodialysis device that is simple to use, as well as safe and effective

Caring for members with kidney disease is expensive for payors and can be highly complex. Payors need better patient care solutions, as well as effective cost management strategies to mitigate the trend impact. Our goal is to help make convenient, at-home peritoneal dialysis and hemodialysis a reality for as many patients with kidney disease as possible.

At CVS Health we are continually looking for opportunities to help patients on their path to better health and to help payors improve outcomes and reduce costs for their members. We are excited to bring our resources to bear on one of the most challenging areas in health care — chronic kidney disease.

Alan Lotvin, M.D.
Executive Vice President Specialty Pharmacy, CVS Health

You can subscribe to *Insights* by visiting
payorsolutions.cvshealth.com

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† Than general Medicare population.

CVSHealth®

Comment letter to CGS Administrators, submitted December 19, 2017, with all attachments
(A folder containing the relevant clinical literature was submitted electronically)

December 19, 2017

CGS Administrators
Earl Berman, MD
Attn: Medical Review
Two Vantage Way
Nashville, TN 37228

Re: Proposed LCD ID DL37575 Frequency of Hemodialysis

Dear Dr. Berman:

Thank you for the opportunity to comment on your recently proposed Local Coverage Determination (LCD) regarding more frequent hemodialysis (HD) LCD ID DL37575. NxStage Medical, Inc. (NxStage) is a Lawrence, Massachusetts-based developer and manufacturer of innovative HD device technology for patients with kidney failure. NxStage is also a provider of dialysis services, with 20 Medicare-certified dialysis clinics across 12 states. As the leader in home hemodialysis (home HD) and in clinical research regarding alternative treatment regimens that improve dialysis outcomes both in the short and long term, we have unique insight into how CGS Administrators (CGS) proposed coverage policy would impact beneficiary access to medically necessary services.

The need for continued innovation in the delivery of dialysis care for patients suffering from end stage renal disease ("ESRD") is without question. In the National Kidney Foundation ("NKF") Kidney Disease Outcomes Quality Initiative ("KDOQI") 2015 Clinical Practice Guideline Update, the KDOQI workgroup acknowledged the limitations of existing treatment paradigms, stating:

> *"Efforts to increase the dose of dialysis administered 3 times weekly have not improved survival, indicating that something else needs to be addressed", and*
> *"What we have seen over time is a lack of evidence for a one-size-fits-all approach to hemodialysis."*[i]

These two realities, combined with evolving clinical evidence, led that workgroup to recommend the consideration of high frequency dialysis in certain, but not all, ESRD patients. Specifically, in a NKF press release announcing the new 2015 guidelines, Dr. Thomas Depner, Co-Chair of the Guidelines Workgroup, stated that:

> "*The workgroup found evidence to support high frequency dialysis in certain patients, but the guidelines do not include blanket recommendations for high frequency hemodialysis in all patients.*"[ii]

[i] Introductory Press Release to NKF's 2015 Update to Clinical Practice Guidelines for HD. https://www.kidney.org/news/nkf-releases-update-clinical-practice-guideline-hemodialysis.
[ii] Id.

The press release and the clinical practice guidelines go on to describe a number of temporary (e.g., pregnancy or metabolic derangements) or ongoing (e.g., uncontrolled hypertension or sleep disturbances) patient conditions where the consideration of high frequency hemodialysis is recommended.

We support CGS' effort to address local coverage for more frequent (> 3 times per week) HD through a formal LCD process. However, the substance of the proposed LCD and its factual inaccuracies must be corrected to ensure patients are not harmed. More frequent HD has become a valuable therapeutic option for delivery of innovations in individualized patient care, both in its proven clinical benefits for certain patients and in its role as a catalyst for home HD consistent with the Congressional mandate to support maximal utilization of home based therapies.[iii]

We appreciate the policy's recognition that more frequent HD sessions may be medically necessary for a number of patient conditions; there are, however, several additional patient conditions that should also be considered based upon current clinical literature and locally accepted standards of care. In addition, we are deeply concerned with the assertions of blanket non-coverage of more frequent HD treatments administered as part of a plan of care ("POC") addressing chronic conditions (as well as non-coverage for treatments characterized as "short or planned inadequate"). Finally, CGS misrepresentation of CMS payment policy and the proposed burdensome and inefficient documentation requirements must be addressed.

Pursuant to the above, we make the following specific observations on the proposed LCD:

1. The absolute coverage restriction that additional HD sessions are not medically necessary when delivered routinely as part of a patient plan of care to address chronic conditions is not supported by the clinical evidence, locally accepted standards of care, and even the proposed LCD's own ICD-10 Codes that Support Medical Necessity. This restriction should be eliminated.
2. Declaring "short" or "planned inadequate" HD treatments as medically unnecessary is an unfair characterization of current medical practice and the clinical adequacy goals of HD. These inappropriate declarations, inconsistent with CMS payment policy and clinical evidence, should be eliminated.
3. The assertion that CMS payment policy never allows for payment for more frequent HD sessions that are part of a POC (even if medically justified) is incorrect, and should be eliminated.
4. Additional codes reflecting uncontrolled hypertension, dialysis-induced post-treatment fatigue, and specific manifestations of low quality of life should not be excluded from the list of "ICD-10 Codes Supporting Medical Necessity"; these should be added, or, in the alternative, the proposed LCD should be revised to allow for the MAC's individualized consideration of the medical necessity of more frequent HD prescribed to treat such conditions.
5. Documentation requirements should not be so burdensome to dissuade a physician from prescribing medically necessary care, and should reasonably correspond with CMS' POC review requirements.

[iii] *"The maximum practical number of patients who are medically, socially, and psychologically suitable candidates for home dialysis . . . should be so treated."* SSA § 1881(c)(1)(A)(i)(6).

6. The ramifications of this policy, if adopted, would be catastrophic to beneficiary access and health, inconsistent with CMS policy, and contrary to objectives of the Medicare system.

Implementation of this LCD would lead to denial of payment for the modest number of stable Medicare patients receiving HD at home and in-center patients that are currently receiving this therapy with their doctor's medical justification to manage specific chronic or acute diagnoses, the majority of whom are receiving payment for extra prescribed sessions. Without payment for the additional treatments, many patients would be forced back into a conventional treatment regimen, adversely impacting their health. This is unacceptable and must be addressed.

We will discuss the above points in greater detail, and include specific recommended changes to the LCD language as an attachment ("Redlined and Annotated Draft Local Coverage Determination").

1. **The absolute coverage restriction that additional HD sessions are not medically necessary when delivered routinely as part of a patient POC to address chronic conditions is not supported by the clinical evidence, locally accepted standards of care, or even the proposed LCD's own ICD-10 Codes that Support Medical Necessity. This restriction should be eliminated.**

Without citing any applicable supporting clinical evidence, the proposed LCD would establish a restriction on more frequent HD called for in a POC where the "number of sessions [is] above 3 times per week." The proposed LCD also suggests a restriction on dialysis not involving "acute conditions," which similarly appears to be related to the proposed POC restriction. These proposed restrictions (collectively, "POC-related restrictions") are not supported by valid evidence and must be withdrawn. Worse yet, the meager evidence cited by the LCD is misquoted, and the content of the evidence cited is actually supportive of the medical necessity of additional HD sessions prescribed to treat chronic patient conditions.

In "Summary of the Evidence," the LCD states "Efforts to increase the dose of dialysis ***administration above*** 3 times per week have not improved survival, indicating that something else needs to be addressed." As mentioned in the introduction to this comment letter, the *KDOQI Clinical Practice Guidelines for Hemodialysis Adequacy: 2015 Update* actually states in its Executive Summary "Efforts to increase the dose of dialysis ***administered 3 times weekly*** have not improved survival, indicating something else needs to be addressed." (emphasis added). The draft LCD language changes the meaning of the KDOQI statement, which was intended as an introduction to a guidelines document that contains recommendations on when more frequent hemodialysis might be considered medically appropriate. It is also within the context of a paragraph where the National Kidney Foundation's Workgroup notes that "interventions that can improve outcomes in dialysis are urgently needed." Although this MAC quoted this paragraph from the KDOQI Executive Summary nearly verbatim, it omitted this sentence only, which was a call to action for improved care.

CGS directly references three publications in the proposed LCD: (i) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease, (ii) NKF's KDOQI Clinical Practice Guidelines for Diabetes and CKD: 2012 Update, and (iii) KDOQI Clinical Practice Guidelines for Hemodialysis Adequacy: 2015 Update. It also indirectly references an additional 10 manuscripts through citing Palmetto (L34575) and Novitas (L35014) LCDs. None of these

references support restricting coverage to "occasion[al] "acute conditions", as suggested by the POC-related restrictions. Rather, most of the cited publications discuss patient conditions in which more frequent dialysis may be indicated on a routine basis, and one of the cited KDOQI manuscripts provides adequacy guidelines for more frequent HD.[iv] Interestingly, in referring to the 2015 update to the KDOQI Guidelines, the proposed LCD notes that the recommendations under Guideline 4.1.1 referenced in the proposed LCD although 'Not Graded' "are determined by a panel of experts and are felt to have a STRONG level of evidence to follow." The MAC then "follows" this evidence and indicates that "the listed conditions in the LCD may be considered reasonable and necessary to have created medical justification for additional payments." Unfortunately, the POC-related restrictions completely eviscerate the clinical integrity of the coverage proposed, and render these conditions, most of which are chronic in nature, uncovered, creating a nonsensical interpretation of the strong, but limited, evidence cited.

It is unclear whether the references to Palmetto GBA L34575 and Novitas Solutions, Inc. L35014 in CGS' Bibliography are meant to also incorporate the literature referenced in those LCDs. Again, we note that none of those references support the proposed restrictions on coverage set forth in this proposed LCD either. Novitas Solutions, Inc. L35014, which did *not* contain the same limitations on coverage imposed by this proposed LCD, references under "Sources of Information and Basis for Decision" six articles[v] discussing HD frequency, none of which Novitas, within L35014, or [Palmetto GBA] within this proposed LCD, discuss in any way. One of the six cited articles is the Kidney Disease Outcomes Quality Initiative (KDOQI) HD adequacy clinical practice guidelines, which were since updated in 2015 to specifically address the frequency of HD. It is even more telling that the references actually discuss the clinical benefits of additional HD sessions as prescribed for ongoing or chronic therapy, and that these findings were associated with statistical significance. The National Institutes' of Health Frequent Hemodialysis Network Daily Trial (which will be discussed in greater detail below) showed statistically significant improvements in its co-primary endpoints of the composite of change in left ventricular mass or death and the composite of change in physical quality of life and death with short daily HD in nearly 250 patients, and during extended follow-up, showed statistically significant improvement in mortality with short daily HD in a subsequent publication[vi]. Foley, et al., and Kalantar-Zadeh, et al., which in aggregate studied 64,000 patients, demonstrated substantially increased risks of cardiovascular death and

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[iv] A summary of the 13 directly or indirectly cited manuscripts and clinical practice guidelines is included as an attachment to this comment letter. 9 relevant references support the medical necessity of more frequent HD for selected patients (4 references are not relevant to more frequent HD). Importantly, not one of the referenced manuscripts supports any categorical restriction.

[v] L35014 references: Foley RN, Gilbertson DT, Murray T, Collins AJ. Long interdialytic interval and mortality among patients receiving hemodialysis. N Engl J Med. 2011;365(12):1099-107. FHN Trial Group, Chertow GM, Levin NW, Beck GJ, Depner TA, Eggers PW, Gassman JJ, Gorodetskaya I, Greene T, James S, Larive B, Lindsay RM, Mehta RL, Miller B, Ornt DB, Rajagopalan S, Rastogi A, Rocco MV, Schiller B, Sergeyeva O, Schulman G, Ting GO, Unruh ML, Star RA, Kliger AS. In-center hemodialysis six times per week versus three times per week. N Engl J Med. 2010;363(24):2287-300. Kalantar-Zadeh K, Regidor DL, Kovesdy CP, Van Wyck D, Bunnapradist S, Horwich TB, Fonarow GC. Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis. Circulation. 2009;119(5):671-9. Kumar VA, Ledezma ML, Rasgon SA. Daily home hemodialysis at a health maintenance organization: three-year experience. Hemodial Int. 2007;11(2):225-30. National Kidney Foundation. Guidelines and Commentaries. https://www.kidney.org/professionals/guidelines/guidelines_commentaries, date accessed: 8/5/13. Weinhandl ED, Liu J, Gilbertson DT, Arneson TJ, Collins AJ. Survival in daily home hemodialysis and matched thrice-weekly in-center hemodialysis patients. J Am Soc Nephrol. 2012;23(5):895-904. The LCD also references undefined "Other Contractor Policies" that cannot possibly be relied upon as a reference source for purposes of evaluating the clinical evidence relied upon as a "source of information and basis for decision".

[vi] Chertow GM, Levin NW, Beck GJ, Daugirdas JT, Eggers PW, Kliger AS, Larive B, Rocco MV, Greene T; Frequent Hemodialysis Network (FHN) Trials Group. Long-Term Effects of Frequent In-Center Hemodialysis. J Am Soc Nephrol. 2016;27(6):1830-6.

hospitalization after long interdialytic intervals, as mediated by high interdialytic fluid gain, thus supporting the rationale for more frequent dialysis. Weinhandl, et al., demonstrated 13% (intent-to-treat) to 18% (as-treated) all-cause mortality reductions with daily home HD (1,873 patients) versus conventional in-center HD (9,365 matched patients), and both findings were statistically significant. Finally, Kumar, et al., in a much smaller study, demonstrated that daily home HD (5 to 7 sessions per week, for an average of 147 minutes per session) improved nutritional status and decreased hospital admissions in dialysis-dependent patients. The references included within Palmetto GBA L34575[vii] similarly fail to support the proposed restrictions. Again, none of these references are discussed within L34575 or in this proposed LCD and the relevance of many of the citations is unclear. Brenner and Rector is a medical textbook and includes one chapter regarding hemodialysis. The IDEAL trial (Cooper, et. al.) tested the effect of early versus late initiation of dialysis, and has no relevance to hemodialysis frequency. In the New England Journal of Medicine, Himmelfarb penned an editorial about the HEMO trial, which likewise did not address hemodialysis frequency. However, given the negative findings of the trial, he suggested that the National Institutes of Health should be encouraged to sponsor a trial to assess the potential benefits of daily dialysis. The 2006 Clinical Practice Guidelines for Hemodialysis Adequacy relied on what was then relatively little evidence regarding hemodialysis frequency, but nonetheless stated in guidelines 4.5, 4.6, 4.7 and 4.8 that patients who "might benefit from more frequent hemodialysis" include malnourished and/or underweight patients, patients with hyperphosphatemia, and patients with chronic fluid overload (with or without refractory hypertension). Additionally, the guidelines stated that more frequent hemodialysis may reduce sleep apnea. So it is inexplicable that these sources would be used as references to support non-medical justification of additional hemodialysis sessions for ongoing or chronic therapy prescription, as suggested by the POC-related restrictions set forth in the proposed LCD. Importantly, these references were used within L34575 to support an LCD which did not contain the significant POC-related restrictions set forth in this proposed LCD.

Congress itself recently reinforced the need for accountability, reasoned explanation, and rigorous evidence in the LCD process — when it passed the 21st Century Cures Act by an overwhelming majority in December 2016. Pub. L. No. 114-225 § 4010, 130 Stat. 1033, 1185 (2016). In section 4010 of the Act, Congress established new guarantees aimed to ensure that contractors adequately "expl[ain] . . . the rationale" supporting their LCD determinations and include competent evidence justifying their reasoning. *See id.* CGS ignores Congress's objective of accountability in the LCD process when it proposes blanket restrictions unsupported by valid evidence.

Indeed, the failure to appropriately cite *any* supporting clinical evidence, let alone *the strongest* clinical evidence, in support of the proposed POC-related restrictions on more frequent HD is "in direct conflict with the plain language of [what] the law" and CMS policy require in adopting LCD restrictions. *See* Medicare Program Integrity Manual (MPIM), ch. 13, § 13.7.1; *see also* SSA §

[vii] L34575 references: Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, Harris A, Johnson DW, Kesselhut J, Li JJ, Luxton G, Pilmore A, Tiller DJ, Harris DC, Pollock CA; IDEAL Study. A randomized, controlled trial of early versus late initiation of dialysis. N Engl J Med. 2010;363(7):609-19. Himmelfarb J et al. Hemodialysis. In Brenner BM, Rector FC, eds., *Brenner and Rector's The Kidney.* Vol. 2, 8th ed. Philadelphia: Saunders Elsevier, 2008: 1957-2006. Himmelfarb J. Success and challenge in dialysis therapy. N Engl J Med. 2002;347(25):2068-70. FHN Trial Group, Chertow GM, Levin NW, Beck GJ, Depner TA, Eggers PW, Gassman JJ, Gorodetskaya I, Greene T, James S, Larive B, Lindsay RM, Mehta RL, Miller B, Ornt DB, Rajagopalan S, Rastogi A, Rocco MV, Schiller B, Sergeyeva O, Schulman G, Ting GO, Unruh ML, Star RA, Kliger AS. In-center hemodialysis six times per week versus three times per week. N Engl J Med. 2010;363(24):2287-300. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis. 2006;48 Suppl 1:S2-90.

1869(f). This is *conclusively fatal* to the proposed policies and is grounds for invalidating these LCD restrictions as unreasonable as a matter of law. 68 Fed. Reg. 63,692, 63,704 (Nov. 7, 2003); *see also* 42 C.F.R. § 426.425 (unreasonable LCD interpretations cannot be upheld).

As a foundational matter, any restriction established by an LCD must be appropriately rooted in *coverage* policy. In the absence of any nationwide CMS coverage policy,[viii] a coverage restriction established in an LCD must be based on the strongest clinical evidence available. *See* MPIM, ch. 13, § 13.7.1. Absolute coverage restrictions, such as proposed in this LCD, require especially "strong clinical justification"[ix] to "refute evidence presented in support of coverage."[x] Yet, the proposed LCD does not cite *any* clinical evidence that supports, or even materially addresses, the proposed POC-related restrictions on more frequent HD — in direct contravention of this clear mandate. Nor could the proposed LCD cite any such clinical evidence, given that the available clinical evidence, in fact, refutes the propriety of a categorical restriction on more frequent HD administered to patients with chronic conditions on an ongoing basis to manage the conditions and mitigate negative outcomes.

The MPIM, ch. 13, § 13.7.1 lists the evidence MACs should consider, in order of preference, as:

- "Published authoritative evidence derived from definitive randomized clinical trials [and] other definitive studies,
- General acceptance by the medical community (standard of practice) as supported by sound medical evidence based on:
    - Scientific data or research studies published in peer-reviewed medical journals;
    - Consensus of expert medical opinion (i.e. recognized authorities in the field); or
    - Medical opinion derived from consultations with medical associations or other healthcare experts."

None of the above – none – support CGS' restriction on coverage. Published authoritative evidence derived from the largest randomized clinical trial on dialysis frequency, the Frequent Hemodialysis Network Trial published in the *New England Journal of Medicine*, showed significant benefits associated with short more frequent HD in reduction of left ventricular mass and physical health composite score, important surrogate endpoints selected for their historical correlation with mortality and hospitalization outcomes. Short[xi] frequent HD was also associated with improved control of hypertension and hyperphosphatemia, and in a subsequent publication was shown to significantly reduce post-dialysis recovery time[xii]. Also, both hospitalization in 12-month follow-up and mortality in extended follow-up were lower in the frequent arm of this study. General acceptance by the medical community is also strongly supported by sound medical evidence based on research studies on more frequent dialysis prescription, published in peer-reviewed medical journals. Consensus expert medical opinion (such as the National Kidney Foundation's KDOQI Workgroup, which CGS actually references, as well as other leading international nephrology societies) recommend that short frequent HD sessions should be considered for selected patients

[viii] The LCD does not purport to rely on CMS *coverage* policy as its justification. Nor could it. CMS has disavowed having *any* national coverage policy on more frequent hemodialysis. *See, e.g.*, 81 Fed. Reg. at 77,847 ("[T]here is no national coverage decision for additional [hemodialysis] sessions.").
[ix] MPIM, ch. 13, §13.5.3.
[x] *Id.* § 13.7.1
[xi] Short in this context takes the KDIGO definition of <3 hrs; for this study each session was targeted between 1.5 and 2.5 hours.
[xii] Garg AX, Suri RS, Eggers P, *et al.* Patients receiving frequent hemodialysis have better health-related quality of life compared to patients receiving conventional hemodialysis. *Kidney Int* 2017;91(3):746-754.

(without any restriction on POC, based nearly exclusively on evidence derived from the treatment of chronic patient conditions with additional HD sessions prescribed routinely for a period typically exceeding 6 months). Finally, medical opinion derived from consultations with medical associations or health care experts further support the medical justification of additional HD sessions prescribed to treat a number of chronic patient conditions, as evidenced by comment letters provided separately from the National Kidney Foundation, Renal Physicians Association, the American Society of Nephrology, American Society of Pediatric Nephrology, the Kidney Care Council, Kidney Care Partners and others. The evidence is **actually overwhelming** in all categories, yet none of this is referenced. Indeed, nothing refuting this mountain of evidence is even put forth to justify this LCD.

This collective assemblage of clinical literature, best practices, international guidelines, and expert opinion recognizes that certain patients with chronic diseases may benefit from, if not require, more than three treatments per week on an ongoing basis. An *American Journal of Kidney Diseases* Supplement on Intensive HD published in November 2016[xiii] catalogs the peer-reviewed literature supporting the prescription of additional HD sessions for the treatment of a number of different chronic patient conditions. In addition to the benefits of additional HD sessions to treat patients with large weight gains, high ultrafiltration rates, hypotension, difficulty achieving dry weight, or poor metabolic control that are already proposed in the draft LCD, published studies report that patients prescribed to receive more than three treatments per week have been able to achieve reductions in, among other things, left ventricular hypertrophy, heart failure hospitalizations, hypertension (using fewer medications), depressive symptoms, sleep disturbances, restless leg syndrome, and post-treatment fatigue. We are submitting this journal supplement, each of the articles referenced in it, new articles published after the date of this journal supplement, as well as applicable international guidelines as part of our comment letter (see the "Evidence Matrix" that accompanies this letter submission).

Clinical Practice Guidelines for the United States[xiv], Japan[xv], the United Kingdom[xvi], Canada[xvii] and Europe[xviii] all suggest an increase in frequency of treatments be considered, as part of a standard dialysis prescription (rather than one-time acute need), to address a number of acute and chronic patient conditions. In aggregate, the conditions that could benefit from a chronic more frequent dialysis regimen included fluid overload, uncontrolled hypertension, cardiac failure, hemodynamic instability during dialysis, and poor metabolic control including hyperphosphatemia and hyperkalemia (see attached "INCREASED HD TIME AND FREQUENCY: Guidelines from 5 Medical Societies in North America, Europe, and Asia"). The KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 Update Guidelines 4.1.1 instructs physicians to "Consider additional HD sessions or longer HD treatment times for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor

[xiii] http://www.ajkd.org/issue/S0272-6386(16)X0004-2
[xiv] *KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 update.* Am J Kidney Dis, 2015. **66**(5): p. 884-930.
[xv] Watanabe, Y., et al., *Japanese society for dialysis therapy clinical guideline for "Maintenance hemodialysis: hemodialysis prescriptions".* Ther Apher Dial, 2015. **19 Suppl 1**: p. 67-92.
[xvi] Mactier, R., N. Hoenich, and C. Breen, *Renal Association Clinical Practice Guideline on haemodialysis.* Nephron Clin Pract, 2011. **118 Suppl 1**: p. c241-86.
[xvii] Tattersall, J., et al., *EBPG guideline on dialysis strategies.* Nephrol Dial Transplant, 2007. **22 Suppl 2**: p. ii5-21.
[xviii] Jindal, K., et al., *Hemodialysis clinical practice guidelines for the Canadian Society of Nephrology.* J Am Soc Nephrol, 2006. **17**(3 Suppl 1): p. S1-27.

metabolic control (such as hyperphosphatemia, metabolic acidosis, and/or hyperkalemia)." The workgroup that drafted the NKF-KDOQI guidelines noted that "[c]onsiderations for initiating high-frequency HD include: sleep apnea, pregnancy, metabolic derangements, uncontrolled hypertension and left ventricle hypertrophy and/or congestive heart failure."[xix] In addition, Section 2.1 of the KDOQI Guidelines states that "patients with end-stage kidney disease be offered in-center short frequent HD as an alternative to conventional in-center thrice weekly HD after considering individual patient preferences, the potential quality of life and physiological benefits, and the risks of these therapies." While an acute episode may be the initial trigger for a physician prescribing more than three treatments per week, the success of the additional treatments in preventing additional acute incidents and the desire to treat chronic conditions such that patients do not progress to acute episodes may justify the more frequent sessions on an ongoing basis. Lastly, even the Frequent Hemodialysis Network trial investigators suggested that ". . . changes in LVM associated with more frequent dialysis were likely caused by volume load and ECF expansion directly, …" thereby supporting the guideline recommendation that more frequent HD may be useful to treatment of chronic volume overload.[xx]

Even the diagnoses that have been initially proposed as part of this LCD are inconsistent with the acute vs. chronic limitation to coverage. As conditions such as "Chronic systolic [or diastolic] (congestive) heart failure" indicate in their title, as well as others without the modifier of "chronic" suggest, not all of these conditions are acute in nature. Moreover, it is contrary to best medical practices to treat chronic conditions in patients when they have an acute episode, only to stop the treatment that has addressed the situation so that it occurs as another acute episode later on. Conceptually, this would be as illogical as discontinuing insulin once diabetes control was achieved, or removing a pacemaker once cardiac rhythm is stabilized.

Importantly, there is ample evidence that more frequent HD has benefited individual patients. As part of annual CMS's annual rulemaking, over 1,000 patients submitted comments in support of the home training payment over the last few years. Most of these letters in some way articulated the real clinical improvements that they had achieved through performing more frequent dialysis at home on an ongoing basis, echoing the published benefits. Significantly, since this and other similar LCDs were published only weeks ago, hundreds of patients have already submitted comments to MACs across the country, all encouraging MACs to continue to support their access to a therapy that has truly improved their health and ability to live a more normal life, despite their chronic disease. These provide direct testimonial to the benefits of ongoing individualized care as deemed medically appropriate by their physicians.

As established by CMS's own regulations, these patients have a right to continue to receive the necessary more frequent HD called for in their POCs. *See* 42 C.F.R. § 494.70(a)(12) (right to receive necessary care in the POC). CGS' unsupported restriction would infringe upon this right, as well as CMS's regulations.

In summary, the conclusion that chronic administration of more frequent HD treatments is never medically necessary is completely unsupported by the clinical literature and global standards of

[xix] https://www.kidney.org/news/nkf-releases-update-clinical-practice-guideline-hemodialysis
[xx] Raimann et al, Blood Purif 2016

care, so this limitation must be removed with respect to the LCD in general as well as its application to the diagnosis codes listed.

2. **Declaring "short" or "planned inadequate" HD treatments as medically unnecessary is an unfair characterization of current medical practice and the clinical adequacy goals of HD. These inappropriate declarations, inconsistent with CMS payment policy and clinical evidence, should be eliminated.**

As a threshold matter, physicians do not prescribe "planned inadequate" therapy for their patients. To do so would be inconsistent with medical practice and the requirements of the ESRD conditions for coverage.[xxi] These already dictate that a patient's plan of care "must address, but not be limited to, the … necessary care and services to manage the patient's volume status; and achieve and sustain the prescribed dose of dialysis to meet a HD Kt/V of at least 1.2 and a peritoneal dialysis weekly Kt/V of at least 1.7 or meet an alternative equivalent professionally accepted clinical practice standard for adequacy of dialysis."[xxii] NKF KDOQI guidelines (which define the very Kt/V standards referenced in the ESRD Conditions for Coverage, and the manuscripts referenced in this draft LCD) suggest this alternative standard for adequacy as a weekly target minimum standardized weekly Kt/V dose of 2.1 for HD and the per-treatment minimum dose requirements to achieve this based upon the number of treatments per week. The single treatment Kt/V adequacy requirement of 1.2 only applies to thrice weekly HD therapy; for 4x and 6x weekly therapy the KDOQI requirements are 0.8 and 0.5, respectively, as these mathematically and kinetically are what is required to deliver adequate weekly small solute clearance under these various intermittent dialysis schedules **independent of the other treatment goals**.[xxiii] These clinical practice standards are readily achievable and easily understood. Even taking aside the fact that physicians are not in the business of prescribing "planned inadequate" care, centers will not, by definition, plan to deliver "inadequate" dialysis (meaning, dialysis not meeting professionally accepted clinical practice standards) if they wish to continue in their business.

In addition, CMS chose to pay by treatment, and explicitly chose to not link payment to time in recent rulemaking. Nowhere in CMS regulation, rulemaking or manuals does CMS require a minimum number of hours of dialysis per treatment or a minimum or maximum number of treatments as a precondition to payment. The basis of payment under the ESRD entitlement is set forth in 42 CFR 413.215(a). That section states: "effective January 1, 2011, ESRD facilities receive a predetermined *per treatment payment* amount described in §413.230 of this part, for renal dialysis services, specified under section 1881(b)(14) of the Act and as defined in §413.217 of this part, furnished to Medicare Part B fee-for-service beneficiaries."[xxiv] And the per treatment unit of payment is agnostic as to duration. Thus, it matters only whether medical justification supports more frequent HD, not the treatment length. See, e.g., 79 Fed. Reg. 66,120, 66,145 (Nov. 6, 2014) ("We codified the per-treatment unit of payment under the ESRD PPS at 42 CFR 413.215(a) . . . . Our policy is that ESRD facilities treating patients on home [HD] will be paid for up to three [HD]-equivalent sessions for each week of dialysis, unless there is medical justification for furnishing

[xxi] 42 CFR Parts 405, 410, 413, 414, 488, and 494.
[xxii] 42 CFR Part 494.90.
[xxiii] Outlined specifically in the *2006 NKF KDOQI Clinical Practice Guidelines*; the 2015 Update contained the weekly target and the clinician can calculate the adequate per treatment dose.
[xxiv] 42 CFR 413.215(a) (emphasis added)

additional treatments."). The proposed LCD's *de facto* limitation on coverage for "short" dialysis is, therefore violative of CMS payment policy, and must be removed.

Finally, and of most clinical relevance, to characterize "short" additional HD sessions as *de facto* medically unnecessary is also inconsistent with the best clinical evidence. As referenced earlier, one arm of the Frequent HD Network (FHN) Trial randomly assigned patients to undergo HD 6 times per week in a short (1.5 to 2.75 hours) treatment with lower dose delivery per session (per treatment Kt/V of 0.9) versus conventional thrice weekly dialysis. Although the per treatment time was shorter than in the conventional arm, the total treatment time per week was 30% higher (796 min/week versus 613 min/week).[xxv] As discussed earlier in this document, the study was published in *The New England Journal of Medicine* and showed significant benefits across multiple dimensions including its primary endpoints selected for their important correlation with mortality and hospitalization outcomes. Importantly, this study was jointly supported by the NIH, the NIDDK, and CMS. These results were the primary driver of the K-DOQI recommendations (Guideline 2.1) that short frequent HD sessions should be considered for selected patients. Given these important convincingly positive results from a study with regulatory agency participation, along with the associated K-DOQI recommendations, characterizing shorter more frequent HD broadly as universally medically unnecessary is logically inconsistent.

Characterizing "short" additional HD sessions as *de facto* medically unnecessary also constitutes undue interference with medical practice and the direct patient physician relationship in delivering care individualized to their needs. *See* SSA § 1801 (prohibiting such interference). The duration of any treatment is defined, purely at the discretion of the prescribing physician, based upon the patient's fluid volume, amount of fluid to remove, residual renal function, number of sessions per week, vascular access capabilities (relating to commanded blood flow rate), dialyzer size, dialysate flow, dialysate concentration, the patient's electrolyte status, dietary and fluid intake between sessions, and ability to tolerate fluid volume removal, among other elements. If there is a clinical decision to dialyze additional sessions per week in order to limit interdialytic weight gain, there may be no clinical rationale to dialyze for the same number of hours per session as under a less frequent schedule. Why force a patient to remain tethered to the machine for marginal hours that confer limited or no benefit, particularly when the total weekly treatment time has been significantly increased (as described above)? CGS must appreciate the essential role physician's play and not dictate the practice of medicine in the absence of compelling evidence that could ever warrant such a restriction on a physician's ability to prescribe medically necessary individualized care.

[xxv] This 30% increase in weekly time also corresponds with treatment times observed in the NxStage home patient population performing more frequent HD vs. conventional thrice weekly peers (14 vs. 11 weekly hours). Treatment times for patients on more frequent HD are derived from an analysis of Nx2me Connected Health data. Nx2me Connected Health is a telehealth platform that collects NxStage System One cycler data and patient factors and transmits data to providers after each dialysis session, enabling providers to review data regularly. This platform enables the collection of precise information, such as treatment times. Information for conventional thrice-weekly treatment times is derived from *The DOPPS Practice Monitor*. http://www.dopps.org/DPM/. Accessed May 20, 2015.

3. The assertion that CMS payment policy never allows for payment for more frequent HD sessions that are part of a POC (even if medically justified) is incorrect, and should be eliminated.

We agree that a POC that calls for more frequent HD, in and of itself, does not provide sufficient documentation to support medical necessity. It is also clear that it is the MAC's responsibility for making the decision on the appropriateness of extra treatments. However, the fact that a POC includes more than three treatments per week should not act as an automatic trigger for denying payment for medically justified additional treatments.

CMS payment policy simply does not support the proposed POC-related restrictions on more frequent HD. CMS payment policy on more frequent HD is entirely straightforward. CMS's manual provides:

> ESRD PPS payment is made on a per treatment basis. . . . ESRD facilities furnishing dialysis treatments in-facility are paid for up to 3 treatments per week. ESRD facilities treating patients at home regardless of modality receive payment for 3 HD (HD) equivalent treatments per week. *Payment for additional treatments may be considered when there is medical justification for more than 3 weekly treatments* . . . . ESRD facilities furnishing dialysis in-facility or in a patient's home are paid for a maximum for 13 treatments during a 30 day month and 14 treatments during a 31 day month *unless there is medical justification for additional treatments.*
>
> Regardless of dialysis modality or treatment setting, payments for additional treatments may be made when they are medically justified. The A/B MAC (A) reviews the medical justification and is responsible for making the decision on the appropriateness of the extra treatment.
>
> . . . . If the ESRD facility bills for any treatments in excess of [3 times per week], medical justification is required to be furnished to the . . . MAC . . . and must be *based upon an individual patient's need*.
>
> MPIM, ch. 11, § 50(A) (emphasis added).[xxvi]

CMS payment policy does not impose any categorical restriction on payment for more frequent HD called for in a POC, more frequent HD for chronic conditions, or shorter more frequent HD. To the contrary, it expressly directs that payment is available for more frequent HD in *any* circumstance in which there is medical justification based on *individual need*. If a MAC seeks to impose a categorical restriction on *coverage* of more frequent HD, it may seek to do so via an assessment of the strongest available clinical evidence under an LCD process, if that evidence leads the MAC to conclude that there is no medical justification for treatment under the restricted circumstances. But it cannot impose a categorical restriction on more frequent HD by pointing to CMS *payment* policy, which imposes no such restriction.

[xxvi] By contrast, "three sessions per week [or below] . . . is paid *without* the need for a secondary diagnosis to justify payment." Medicare Claims Processing Manual, ch. 8, § 50.6.2.

Like all manual provisions, this is guidance that *binds* the MAC. *Catholic Health Initiatives v. Sebelius*, 617 F.3d 490, 491 & n.1 (D.C. Cir. 2010) ("The Manual does bind Medicare's 'fiscal intermediaries'"); 52 Fed. Reg. 15,560, 15,562 (Apr. 28, 1987); *see also* 70 Fed. Reg. at 11,439 (May 8, 2005) (context of redeterminations). It also is unambiguous. Without limitation or qualification, CMS policy is to pay for more frequent HD *whenever* it is justified by adequately documented medical necessity based on individual need, MPIM, ch. 11, § 50, as evidenced by "specific comorbid diagnoses" (i.e., secondary diagnoses) in the medical record "that necessitate additional treatment[]" sessions. *See* 81 Fed. Reg. 77,834, 77,856 (Nov. 4, 2016).

Thus, CMS payment policy clearly does not impose the categorical restrictions on more frequent HD asserted by the MAC. To the contrary; and this CMS policy is binding on the MAC. It is unambiguous, and it has not been modified.[xxvii]

a. *Despite some ambiguous language in the preambles of CMS 2014 and 2016 ESRD PPS rulemaking, there is no ambiguity as to CMS's payment policy on more frequent HD*

The MAC cannot credibly suggest that CMS has modified the payment policy on more frequent HD articulated in its manual.

Since the current manual provision was last amended in 2015, CMS has addressed its payment policy on more frequent HD only in 2016 guidance.[xxviii] In that guidance, CMS reiterated the importance of individualized care and physician and patient choice as well as its consistently held belief (which forms the basis of its current payment policy) that there are certain patient conditions that can benefit from more than 3 HD sessions per week (of importance, CMS did not say an extra session, if needed):

> We believe that the choice of modality and frequency of treatments for a patient are decisions that are made by the physician and the patient[xxix]. … We continue to believe that patients should have access to various treatment options and schedules and facilities should offer various treatment options to meet the needs of its patients[xxx]. … While the majority of ESRD patients are prescribed conventional 3-times-per-week HD, we have always recognized that some patient conditions benefit from more than 3 HD sessions per week and as such, we developed a policy for payment of medically necessary dialysis treatments beyond the 3-treatments-per-week payment limit[xxxi].

[xxvii] Medicare Article MM9989, effective 10/1/17, provides another, even more recent, expression of this point. That article states that when a beneficiary's plan of care requires more than three weekly dialysis treatments, whether HD or daily PD, CMS applies payment edits to ensure that Medicare payment on the monthly claim is consistent with the 3-times weekly dialysis treatment payment limit. Thus, for a 30-day month, payment is limited to 13 treatments, and for a 31-day month payment it is limited to 14 treatments, **with exceptions made for medical justification.** *Note, the exceptions made for medical justification are not limited to when the extra treatments are ordered outside of a plan of care.*

[xxviii] This guidance was issued on November 4, 2016, in the preamble to the ESRD PPS final rule for calendar year 2017. *See generally* 81 Fed. Reg. 77,834.

[xxix] 81 Fed. Reg. 77844.

[xxx] *Id.*

[xxxi] *Id.* at 77843.

In the same guidance, CMS also repeatedly stated that, when the "additional treatments furnished during a month are medically necessary and when the MACs determine that the additional treatments are medically justified, we pay the full base rate for the additional treatments," without establishing any further restriction on payment. 81 Fed. Reg. at 77,843.

To the extent the MAC would point to any select passage for support, any ambiguity generated by an isolated passage in the guidance must be resolved by looking to CMS's guidance as a whole. *See King v. St. Vincent's Hosp.*, 502 U.S. 215, 221 (1991).[xxxii] Here, the overall context of any isolated passage is CMS's repeated statements, without limitation, that "[p]ayment for HD treatments that exceed 3 treatments per week occurs when those treatments are medically justified, as indicated by diagnosis codes." 81 Fed. Reg. at 77,842. CMS clearly did not intend to establish any restriction on payment for more frequent dialysis called for in a POC or more frequent dialysis for chronic conditions.

Indeed, in the 2016 guidance, virtually all of CMS's references to more frequent HD called for in a POC came in the context of CMS's proposed-but-never-finalized equivalency payment for *non-medically necessary* more frequent HD. *See* 81 Fed. Reg. at 77,842 (stating such an adjustment could be beneficial because CMS does not have a mechanism to pay for "more than 3 [HD] treatments per week that *do not have medical justification*," because CMS's payment policy supports reimbursement only when medical justification *does* exist) (emphasis added). Thus, these references are simply irrelevant to whether payment is available for *medically necessary* more frequent HD.

b. *CMS expressly stated that it has not modified its payment policy on more frequent HD for decades; and the practice of medicine has evolved in reliance upon this fact*

That CMS has not modified the payment policy on more frequent HD articulated in its manual is clear not only from context. CMS *itself* has expressly and repeatedly disavowed doing so. In fact, CMS has stated that it has not changed this policy in more than thirty years. In the 2016 guidance, the agency observed that the policy had remained unchanged "[s]ince the composite rate payment system was implemented in the 1980s." 81 Fed. Reg. at 77,841. CMS went on to say that it has "always" recognized that "some patients benefit from more than 3 [HD] sessions per week" and, as such, CMS policy has been to pay for "medically necessary dialysis treatments beyond the 3-treatments-per-week payment limit" when there is documented medical justification. *Id.* at 77,843.

CMS's express disavowal that it has modified the payment policy articulated in its manual definitively settles any dispute over whether any isolated passage in the 2016 guidance alters the analysis. Indeed, CMS's position that its payment policy has remained the same "[s]ince the composite rate payment system was implemented" over thirty years ago, *id.* at 77,841 — i.e., to pay for more frequent HD when the extra sessions are supported by adequately documented medical justification demonstrating medical necessity based on individual need — resolves any ambiguity presented by any isolated passage in *any* guidance over the past thirty years.

[xxxii] *See also NLRB v. Federbush Co.*, 121 F. 2d 954, 957 (2d Cir. 1941) ("'Words are not pebbles in alien juxtaposition; they have only a communal existence; and not only does the meaning of each interpenetrate the other, but all in their aggregate take their purport from the setting in which they are used . . . .'").

Even setting aside CMS's express statements that it has not modified its payment policy on more frequent HD, CGS cannot credibly suggest that CMS has adopted new restrictions on more frequent HD. To be sure, CMS can establish and amend payment policies under the ESRD PPS, *see* SSA § 1881(b), but CMS's authority to do so is not unlimited. Rather, CMS's payment policy authority is restricted by statute and CMS's regulations. CMS would have exceeded this authority if it had adopted the restrictions imputed to the agency by the proposed LCD without first undertaking a notice-and-comment rulemaking. CMS has never undertaken such a rulemaking.

The following results of the rulemaking process support the straightforward reading of CMS' payment policy on this issue:

- CMS has dispositively established the basis of payment under Medicare's ESRD benefit as "per treatment." In 2010 rulemaking, finalizing the new bundled payment system, CMS stated:

  > "Under section 1881(b)(14)(C) of the Act, as added by section 153(b) of MIPPA, the ESRD PPS may provide for payment on the basis of renal dialysis services furnished during a week, or month, or such other appropriate unit of payment as the Secretary specifies. We proposed to establish an ESRD PPS which relies on a per treatment unit of payment (74 FR 49931). We proposed to continue the present per treatment basis of payment in which ESRD facilities would be paid for up to three treatments per week, unless there is medical justification for more than three weekly treatments (74 FR 49931). ESRD facilities treating patients on PD or home HD would also receive payments for up to three treatments for each week of dialysis, unless there is medical justification for the furnishing of additional treatments."[xxxiii]

  Treatments found to be "reasonable and necessary" under Medicare standards are to be paid at the full base rate. Changing this methodology, such as by the imposition of a weekly rate for POC sessions in excess of three treatments per week as this MAC proposes, would require explicit rulemaking at the federal level, which CMS has not done, and which this MAC may not do.
- CMS has expressly affirmed that there is no national coverage decision for more frequent HD sessions, and, therefore, every session prescribed by a physician and submitted by an ESRD facility for payment MUST be evaluated by the MAC for its medical necessity, in the absence of an LCD based upon the strongest evidence imposing a jurisdiction-wide restriction on coverage.[xxxiv]
- Finally, CMS evaluated a HD equivalent payment method for medically unnecessary sessions ordered in excess of three treatments per week in 2016 rulemaking, as referenced above, and this proposal was rejected in final rulemaking.[xxxv]

[xxxiii] 75 Fed. Reg. 49200.
[xxxiv] In 2014 ESRD PPS Rulemaking, CMS expressly reaffirmed that "CMS has no national policy for medical justification for additional dialysis treatments, and we rely upon either a MAC's local coverage determination (LCD) policy or medical review by a physician working under the direction of the MAC's medical director." 79 Fed. Reg. 66,146.
[xxxv] 81 Fed. Reg. at 77,842

It would be unlawful for CMS to repeatedly insist that its policy has not changed "[s]ince the inception of the composite payment system in 1983," 74 Fed. Reg. at 49,922, 49,931 (Sept. 29, 2009), *accord* 81 Fed. Reg. at 88,841, while simultaneously effectuating new restrictions on more frequent HD and refusing to acknowledge that this represents a change in policy. CGS can neither plausibly nor reasonably ascribe such unlawful conduct to the agency when a far more straightforward reading of CMS's guidance exists: namely, that CMS actually means what it says when it states that it has not changed its policy and that it "pay[s] the full base rate for the additional treatments" whenever the "MACs determine the additional treatments are medically justified," *id.* at 77,843, as has been the agency's "policy since the . . . 1980s." *Id.* at 77,841.

This straightforward reading of CMS's guidance is also completely consistent with payment practices in the years prior to this proposed to the LCD which were not administered in a vacuum. We are aware of MAC reviews of claims seeking payment for more frequent HD prescribed for the treatment of chronic patient conditions. We also note that CMS referenced its own review of MAC payment practices relating to more frequent HD in 2015 ESRD PPS rulemaking. In guidance for that year, CMS noted that:

> "[p]ayments provided by MACs for additional HD weekly dialysis treatments that are furnished in-facility or in the home, have been audited by CMS. We recognize that some MACs were not requiring documented patient conditions for medical justification for additional weekly treatments and were inappropriately authorizing Medicare payment for additional dialysis services where no medical justification was included in the claim. Thus, our intent in clarifying our policy was to remind facilities and MACs of the Medicare ESRD benefit, which only allows for the payment of three weekly dialysis treatments, and that additional weekly dialysis treatments may be paid for if there's documented medical justification. We believe that our policy clarification will result in a consistent Medicare benefit for all beneficiaries and eliminate the regional payment differences."[xxxvi]

These audits did not lead either MACs or CMS to stop paying for more frequent HD ordered as part of a POC or to treat chronic patient conditions. These audits did not lead either MACs or CMS to stop paying for "short" more frequent HD. From the plain reading of CMS' guidance, CMS only intended to ensure that appropriate documentation of medical justification was required to allow payment for "additional weekly dialysis treatments". Of note, CMS didn't describe medically necessary additional treatments as "rare" or "acute". CMS instead simply referenced "additional weekly dialysis treatments" (without further qualification).

An unsupported POC restriction on care also runs counter to basic common sense that informed the imposition of POC requirements in the ESRD Conditions for Coverage. Sound policy dictates that — when feasible — medically appropriate treatment for all relevant clinical diagnoses (and other issues bearing on a patient's care) be in the POC. The entire point of a POC is to provide the most realistically comprehensive plan possible, which is capable of facilitating a coordinated response from a patient's interdisciplinary team based on the particularized needs of that patient. Forcing more frequent HD to be outside of the POC serves only to hamper the ability of the interdisciplinary team to develop a coordinated response that meets all the individualized needs of a patient. Such a

[xxxvi] 79 Fed. Reg. 66147.

restriction is fundamentally inconsistent with the objectives of individually-tailored coordination and responsiveness that undergird CMS's adoption of a POC requirement. See generally 42 C.F.R. § 494.90(a). Worse still, the proposed restriction on more frequent HD called for in a POC is in tension with CMS regulations granting patients an affirmative "right" to "[r]eceive the necessary services outlined in the patient [POC]." Id. § 494.70(a)(12). The proposed LCD would improperly restrict this right by inhibiting medically necessary more frequent HD from appearing in the POC.

Importantly, what should also not be lost is that CMS' long-standing policy of paying for medically necessary HD sessions in excess of three treatments per week has allowed for the evolution of the practice of medicine, truly individualized care, and the development of peer-reviewed clinical evidence supporting the statistically significant benefits of more frequent HD for the treatment of certain patient conditions. It has stimulated innovation in patient care. Providers and patients alike have come to rely upon this payment policy in their prescription and receipt of care, including within this MAC jurisdiction. In the absence of a change in payment policy, which as articulated above has not occurred, it is unconscionable to revoke coverage for what has consistently been covered in the past to the clinical benefit of patients. This is particularly true at a time when the evidence supporting the medical necessity of more frequent HD as a tool to treat chronic certain patient conditions has never been stronger.

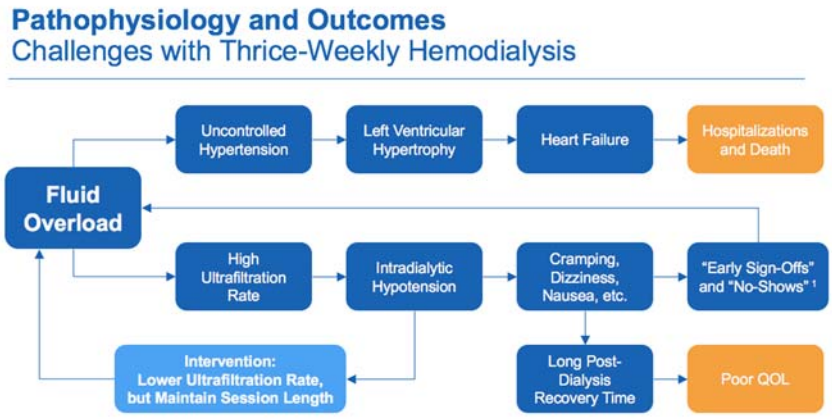
In conclusion, CMS payment policy sits on top of any coverage policy properly established by an LCD. But such payment policy is not the domain of the MAC. Indeed, NxStage agrees with CGS' admonishment to stakeholders that an "LCD would not be the appropriate approach to change [CMS's] . . . payment methodology." But this is exactly what CGS is proposing to do. Indeed, CGS is not merely improperly relying on payment policy to justify the proposed POC-related restrictions; it is affirmatively *misstating* CMS payment policy and then invoking that misstated policy as the sole justification for new POC-related restrictions on more frequent HD. It is also using this misstatement to *revoke* coverage for treatments that have been paid for by all MACs previously. This must be eliminated.

4. **Additional codes reflecting uncontrolled hypertension, dialysis-induced post-treatment fatigue, and specific manifestations of low quality of life should not be excluded from the list of "ICD-10 Codes Supporting Medical Necessity"; these should be added, or, in the alternative, the proposed LCD should be revised to allow for the MAC's individualized consideration of the medical necessity of more frequent HD prescribed to treat such conditions.**

The proposed LCD already includes a reasonable list of diagnosis codes that could provide medical justification for additional HD sessions; provided those codes are not read to limit payment to additional HD sessions prescribed to treat acute-only conditions, not part of a patient's POC. As the publications and standards included in the enclosed binder of clinical evidence support, the inclusion of numerous diagnosis codes regarding heart failure and fluid overload is appropriate and truly necessary, as acute care encounters to address both chronic and acute manifestations of heart failure and fluid overload are both common and costly in the dialysis population. The inclusion of diagnosis codes regarding hyperphosphatemia is also appropriate, as it is widely understood that increased treatment length and/or frequency results in increased clearance of phosphate, excess levels of which may encourage vascular calcification. Furthermore, inclusion of diagnosis codes

regarding pregnancy is appropriate, as clinical practice guidelines indicate that intensive HD should be prescribed to women who are pregnant.

However, there are three missing domains that should be added to the proposed ICD-10 Codes that Support Medical Necessity claims, as evidenced in the published clinical literature and/or published clinical practice guidelines of both domestic and international bodies. These include uncontrolled hypertension, dialysis-induced post-treatment fatigue (*i.e.*, long recovery time), and specific manifestations of poor physical and mental health-related quality-of-life. Each of these domains can be linked to the fundamental problem of chronic fluid overload that more frequent HD can address, as depicted below:



The problem, the etiology, the published effects of more frequent HD, and recommended additions to the list of ICD-10 diagnosis codes supporting medical necessity claims are discussed below. Literature references identified in brackets are listed at the end of this document in "Clinical References to Section 4".

Uncontrolled Hypertension
Highly elevated blood pressure is associated with poor outcomes in dialysis patients. In both dialysis facility-level and patient-level studies, pre-dialysis systolic blood pressure exceeding 160 mm Hg was associated with significantly higher risk of death.[1, 2] Furthermore, an increasing volume of literature indicates that ambulatory blood pressure is linearly associated with risks of cardiovascular mortality and morbidity in dialysis patients.[3, 4] The epidemic of hypertension cannot be readily attributed to underutilization of oral medications: 70%, 50%, and 40% of contemporary HD patients use beta blockers, calcium channel blockers, and renin-angiotensin system inhibitors, respectively.[5]

Hypertension is multifactorial, but key causes include persistent hypervolemia and elevated peripheral resistance. With three HD sessions per week, blood pressure climbs during the interdialytic interval, in step with interdialytic weight gain, particularly among elderly patients and those with higher dry weight.[6] Elevated peripheral resistance can be attributed to inappropriate activation of the sympathetic nervous system, due to higher concentration of plasma norepinephrine.

Multiple randomized clinical trials show that frequent HD reduces blood pressure and the need for oral medications indicated for hypertension. In the first two months of the Frequent HD Network (FHN) trial, the short daily schedule reduced pre-dialysis systolic and diastolic blood pressures by 7.7 and 3.9 mm Hg, respectively, while the nocturnal schedule reduced corresponding pressures by 7.3 and 4.2 mm Hg, all relative to three sessions per week. These improvements in blood pressure were sustained after 12 months.[7] Both the short daily and nocturnal schedules reduced use of antihypertensive medications.[7] In the Following Rehabilitation, Economics, and Everyday-Dialysis Outcome Measurements (FREEDOM) study, a large prospective cohort study of short daily HD, the percentage of patients not using antihypertensive agents increased from 21% to 47% in one year, while the mean number of prescribed agents decreased from 1.7 to 1.0.[8] Interestingly, nocturnal HD appears to markedly reduce total peripheral resistance and plasma norepinephrine and to restore endothelium-dependent vasodilation.[9]

Frequent HD reduces blood pressure and the need for antihypertensive medications. Clinical practice guidelines in the United States,[10] Japan,[11] the United Kingdom,[12] Europe,[13] and Canada[14] all suggest that increased treatment time and/or frequency should be considered in patients with poorly controlled or uncontrolled hypertension. In addition, a recent European consensus statement about hypertension on dialysis indicates that non-pharmacologic measures should be prioritized to correct the primary pathogenetic mechanism, sodium and volume excess. Such measures include increased treatment time and/or frequency, as well as achievement of dry weight and avoidance of intradialytic (dialysate) and interdialytic (dietary) sodium gain.[15]

Dialysis-Induced Post-Treatment Fatigue

Dialysis treatment can be difficult to tolerate. Recurrent complications during and after the HD session may limit treatment persistence and engender withdrawal, which is the primary cause of death in 10% to 15% of cases. Common complications are intradialytic hypotension and dialysis-induced post-treatment fatigue, or long recovery time. In DOPPS, recovery time was between 2 and 6 hours for 41% of HD patients and greater than 6 hours for 27%; recovery time greater than 6 hours was associated with substantially higher risks of death and hospitalization.[16] More aggressive ultrafiltration is strongly associated with longer recovery time.[17]

Frequent HD clearly addresses post-treatment fatigue. In the FHN trial, both the short daily and nocturnal schedules significantly reduced recovery time, relative to three sessions per week.[18] Moreover, in the FREEDOM study of short daily HD, recovery time was sharply reduced after 12 months of treatment, from roughly eight hours at baseline to merely one hour in per-protocol analysis.[19] Remarkably, recovery time after nocturnal HD may be only minutes in duration.[20] This effect may ultimately contribute to reduction in the incidence of withdrawal from dialysis. In a matched cohort study, daily home HD was associated with almost 40% lower risk of death due to withdrawal or cachexia, relative to thrice-weekly in-center HD.[21]

Specific Manifestations of Low Quality of Life

"The ultimate goal of treatment for patients with CKD stage 5 is improvement in quality of life, with prolongation of life often an additional goal."

KDOQI Clinical Practice Guideline for HD Adequacy: 2015 Update[10]

Conventional HD patients may report substandard health-related quality of life (HRQOL). Characteristics of poor physical HRQOL include limitations in physical, self-care, and social

activities; severe bodily pain; frequent tiredness; and low self-rating of physical health. Mean physical HRQOL in HD patients is almost 2 standard deviations below the US general population norm. Poorer physical HRQOL, as measured by the Kidney Disease Quality of Life (KDQOL) Short Form, is associated with higher risks of both death (21% higher adjusted risk per 10-point decrement) and hospitalization (9% higher adjusted risk) in HD patients in DOPPS.[22] Characteristics of poor mental HRQoL include frequent psychological distress; social disability due to emotional problems; and low self-rating of mental health. Poorer mental health, as measured by the KDQOL Short Form, was associated with increased risks of both death (13% higher adjusted risk per 10-point decrement) and hospitalization (5% higher adjusted risk) in HD patients in DOPPS.[22]

Although the causes of poor physical HRQOL are numerous, specific symptoms are commonly reported. According to a systematic review of 59 studies, fatigue is reported by 71% of patients, sleep disorders by 44%, and restless legs by 30%.[23] The pathogenesis of restless legs is uncertain, but may be related to an insufficient quantity of HD.[24] Sleep disorders may be motivated by restless legs themselves, as well as sleep apnea, which is common in HD patients and may be related to hypervolemia and azotemia.[25] Sleep disorders also associate with depression and hyperphosphatemia.[26] On the other hand, depression is an important feature of poor mental health. The prevalence of clinical depression in dialysis patients is between 35% and 40% and is similar with HD and peritoneal dialysis.[27] Depression, when it is self-reported, is associated with markedly higher risk of death and modestly higher risk of hospitalization.[28] Notably, depression is strongly associated with higher risk of withdrawal from dialysis.[29] In patients with a recent myocardial infarction, depression is independently associated with increased incidence of recurrent cardiac events, possibly due to the association of altered serotonin concentration with platelet activation and vasoconstriction.[30] Importantly, the efficacy of antidepressant medications in moderate or severe chronic kidney disease is not clearly established.[31]

In both randomized clinical trials and prospective cohort studies, frequent HD improves physical HRQOL. In the Frequent HD Network trial, the short daily schedule improved self-reported physical health, relative to three sessions per week; the nocturnal schedule similarly improved physical health, albeit not significantly more than three sessions.[32] In the FREEDOM study of short daily HD, self-reported physical health improved significantly during 12 months of treatment.[33] Short daily HD also associated with improvements in restless legs, especially in patients with severe symptoms, and sleep disturbances, including daytime somnolence.[34] In an earlier trial of nocturnal HD, apnea and hypopnea episodes per hour decreased by almost 70% after conversion from three dialysis sessions per week.[35]

Frequent HD can also address depression and improve mental HRQOL. Both short daily and nocturnal schedules in the Frequent HD Network trial lowered Beck Depression Inventory (BDI) scores by clinically significant margins, relative to three sessions per week, although differences lacked statistical significance.[36, 37] In the FREEDOM study of short daily HD, prevalence of severe depression (BDI score > 15) decreased from 25% to 16% during 12 months of treatment.[19] Short daily HD also led to improvement in overall mental health, including large improvements in vitality and social functioning.[33] In an earlier trial, nocturnal HD in the home setting significantly relieved the effects and the burden of kidney disease, as measured by the KDQOL Short Form.[38] Because frequent HD is often prescribed in the home setting, the treatment may be an effective way

by which to increase patient engagement in the delivery of dialysis; accumulating health services research suggests improved outcomes with higher patient activation.[39]

In summary, we believe that, in addition to the ICD-10 codes already proposed by CGS in this draft LCD, a strong base of current clinical evidence supports the medical necessity of additional treatments for the diagnoses of uncontrolled hypertension, dialysis-induced post-treatment fatigue (*i.e.*, long recovery time), and specific manifestations of poor physical and mental health-related quality-of-life (attached to this document as "Proposed Additional ICD-10 Codes Supporting Medical Necessity"). If CGS is not ready to include additional diagnosis codes to support the medical necessity of the above conditions, we ask, in the alternative, that CGS modify the language of the proposed LCD to make clear that the list of codes provided is not exclusive, and that the MAC will consider, on an individualized basis, the medical necessity of additional dialysis sessions prescribed to treat conditions not included within the LCD's listed set of codes. This is best accomplished by a modest change to the section of the proposed LCD entitled "ICD-10 Codes that DO NOT Support Medical Necessity", indicating that there are no codes that *per se* do not support medical necessity, and that other codes would be considered on a case by case basis depending upon their merit, as would happen outside of the context of an LCD. This less prescriptive approach will allow for the development of evidence, further encouraging innovation in care delivery.

5. **Documentation requirements should not be so burdensome to dissuade a physician from prescribing medically necessary care, and should reasonably correspond with CMS' POC review requirements**

In 2016 ESRD PPS rulemaking, CMS articulated the documentation requirements for establishing the medical necessity of HD sessions ordered in excess of three times a week. CMS stated:

> The medical necessity for additional dialysis sessions must be documented in the patient's medical record at the dialysis facility and available for review upon request. The documentation should include the physician's progress notes, the dialysis records and the results of pertinent laboratory tests. The submitted medical record must support the use of the diagnosis code(s) reported on the claim and the medical record documentation must support the medical necessity of the services. This documentation would need to be available to the contractor upon request[xxxvii].

We support these documentation requirements, and note that, when combined with the documentation requirements for POCs under the ESRD Conditions for Coverage, they provide for appropriate medical records documentation.

By contrast, the proposed LCD provides that medical documentation should include "the order from the prescribing physician for the additional sessions," which "should be available for each and every additional session outside the usual 13/14 treatments per month." The proposed LCD also provides that "the POC should show changes in the dialysis prescription or other parameters to address the repeated need for additional sessions."

[xxxvii] 81 Fed. Reg. 77843.

We ask that these incremental documentation requirements proposed under this LCD, be eliminated—particularly if they contemplate a completely new prescription for *each* individual session of more frequent HD (rather than a prescription of more frequent HD for a reasonable fixed period of time) or require modifications to the POC on a more frequent basis than that required under CMS's Conditions for Coverage. This process would be burdensome, inefficient, and could result in delays to essential care. It also seems inconsistent with RFIs in CMS's 2018 rulemaking process in which administration asked for suggestions regarding limiting burden across all payment systems.

As the LCD notes, 42 C.F.R. § 494.80 of the ESRD Conditions for Coverage requires that POCs must be revised at least monthly for unstable patients and yearly for stable patients. Requiring anything more than a monthly care plan reevaluation, particularly for stable patients, is unjustifiable, and unduly burdensome to both providers and patients in practice. We believe that a quarterly update to the POC when more frequent dialysis is administered to a *stable* patient is clinically and operationally justified.

6. **The ramifications of this policy, if adopted, would be catastrophic to beneficiary access and health, inconsistent with CMS policy, and contrary to objectives of the Medicare system.**

As discussed above, payment for more frequent HD has enabled innovation in patient care to a very modest number of patients who medically benefit from the therapy. The number of extra treatments paid in excess of 3 per week nationally by Medicare was very small in 2014-2015, totaling only 366,000 treatments at home and 201,000 treatments in-center. This represents less than 0.7% of the 80.9 million treatments paid by Medicare Part B in the same period.[xxxviii]

More frequent HD is most often prescribed in the home setting, mostly because delivering additional treatments in a center is impractical. Even though it is "easier" to refer patients in-center, more frequent dialysis disrupts the operational schedule and economics of centers structured for thrice-weekly care. Out of necessity, clinicians must consider the home setting for patients that they believe will benefit from more treatments. For patients and their families, it takes the noticeable clinical and quality-of-life benefits of more frequent HD to make the additional efforts of home HD worthwhile. Given this, the practical access to more frequent HD is important in support of the long-standing statutory mandate to encourage home as a setting for dialysis care. This is particularly true when operating within the understanding that peritoneal dialysis, which is the most prevalent home therapy choice, is not clinically appropriate for all patients. Taking away this therapeutic choice for patients WILL reduce patient access to home therapy, which cannot be an objective of ANYONE: CGS or CMS.

There is absolutely no evidence of overutilization of more frequent HD sessions, in-center or at the home. In addition to its clinical findings, the seminal FHN study also shed light on the potential utilization of more frequent HD in-center. Only 6% of screened patients enrolled in the study, and of the 125 patients in the daily HD arm, only 26 of those (21%, or 1% of those originally screened) were still undergoing HD for 4+ sessions/week at 14 months (hemodialysis session frequency was

[xxxviii] Internal analysis of Medicare Limited Data Sets: Outpatient Standard Analytic Files (100% Sample), 2014-2015. Data obtained under Data Use Agreement 51218 with CMS.

not regularly tracked thereafter). With respect to home HD, penetration has grown to only 1.7% of total patients over the last decade, with the total percentage levelling over the last few years.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
US Dialysis Population* (Cumulative)	357,943	371,094	386,830	402,067	414,177	427,460	442,218	460,675	479,409	496,556
US Home HD Population (Cumulative)	3,370	4,123	4,889	5,860	6,366	7,111	7,685	8,041	8,150	8,425
Home HD Penetration Rate	0.9%	1.1%	1.3%	1.5%	1.5%	1.7%	1.7%	1.7%	1.7%	1.7%

* 2007 - 2014 from USRDS Annual Report
* 2015-2016 from Dialysis Network Reports

Even in countries such as Australia and New Zealand, whose public policies are highly supportive of home HD and have approximately 11% of patients on the modality, only slightly more than 9% of all HD patients dialyze more than 3 times per week.[xxxix]

Previous CMS analysis showed that MACs' payment practices for more frequent HD positively correlated with utilization of home HD in the respective jurisdictions.[xl] Clear evidence exists that modifying the long-standing policy of paying for medically necessary HD sessions in excess of three treatments per week will have an immediate and dramatic negative effect on patient access and innovations in home care. In 2014, Noridian issued a coverage article articulating similar but less severe restrictions versus the proposed LCD. Following this, one large dialysis organization ("LDO") completely stopped their practice of billing for more frequent dialysis in Noridian's jurisdiction. Within one year, the LDO saw their Medicare home HD patient population fall from a high of 677 prior to the article to 577 one year after publication, a 15% reduction.[xli] More dramatically, patient training, the indicator of new patient access, dropped from approximately 51 patients per month to approximately 39 patients per month, a 24% reduction. This effect was not seen elsewhere in the country in other MAC jurisdictions at this LDO. This implied revocation of coverage had clearly negative impact on patient access; however, the impact would be even more catastrophic if similar change were implemented through binding LCD (as proposed) with the substantial majority of MAC jurisdictions having similar coverage restrictions (as MACs representing nearly 90% of the beneficiary population are currently undertaking the same LCD proposal process).

[xxxix] ANZDATA Registry. 39th Report, Chapter 4: Haemodialysis. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2017. Available at: http://www.anzdata.org.au.

[xl] Hirth R, Sleeman K, Wheeler JRC, Turenne M, Zhang W, Wilk A, Messana J, Kidney Epidemiology & Cost Center, University of Michigan, Arbor Research: Frequency of Payments for More Than Thrice Weekly Dialysis for Home Hemodialysis (HHD). J Am Soc Nephrol 22, 2011: Page 804

[xli] Internal analysis of Medicare Limited Data Sets: Outpatient Standard Analytic Files (100% Sample), 2014-2015. Data obtained under Data Use Agreement 51218 with CMS.

Importantly, these coverage restrictions are completely inconsistent with the objectives of Medicare to maximize utilization of home therapies[xlii], to support individualized care and the physician/patient relationship[xliii], and to foster innovation in care models. It is naive and unfair to assert that this therapeutic choice will continue to be offered to patients if the incremental treatments are not paid. The cost of delivering additional HD sessions are simply higher, and the savings that may be achieved, including with respect to anti-hypertensive medicines or hospitalizations, are not realized by the ESRD facilities shouldering those incremental treatment costs. This is not a case of winners and losers on the margin, such as may be seen with patient treatment times that may vary between 3 and 5 hours under a conventional thrice weekly schedule. This is a case of stifling better care and innovations in care delivery that could ultimately lead to even greater numbers of patients treated at home (a Medicare and Congressional objective) as well as greater savings to the ESRD program over the longer term.

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Again, NxStage appreciates the opportunity to review the draft LCD. We support the LCD process, and streamlining coverage decisions in a way that facilitates the patient-physician relationship and delivery of medically necessary care.

During the open forums that MACs initiating their individual LCD processes on this topic have held, it has been stressed that commenters should provide specific comments on specific language in the LCD. Pursuant to this request, we have attached a red-lined, annotated document. We provide this document to illustrate the modesty of the changes to the language that would need to be made to redress the concerns that we have identified. Such modest modifications would suffice to make the proposed LCD consistent with the breadth of clinical evidence, local and international standards of care, CMS payment policies, and the articulated objectives of the Medicare program. With each change, we have annotated in the side margin the rationale for the specific modifications consistent with points outlined in this letter.

The long-standing policy for medical justification for more frequent dialysis has led to innovations in care and impressive patient benefits over the last decade; we believe that nephrologists and the rest of the community have been good stewards of the policy. Going forward, we do understand the administrative efficiencies of clarifying local coverage policy through the LCD process. The draconian and abrupt nature of the restrictions in this draft LCD, however, suggest concerns with either inappropriate current utilization or a perception of the potential for abuse rather than a desire to clarify coverage based on medical evidence. We don't believe the concerns are founded, based upon our observations of actual practice shared in this document and the compelling evolution of the clinical evidence and practice standards. In any event, any perceived risk would be better addressed through claims and medical record audits than through coverage restrictions that would undermine the practice of medicine and beneficiary access to the care they deserve.

[xlii] SSA § 1881(c)(1)(A)(i)(6).

[xliii] It is well settled that, when a coverage determination is made through adjudicatory processes, without an applicable regulation or other semi-formal and class-wide quasi-rulemaking (e.g., LCD or NCD), the medical necessity determination should be individualized. See 68 Fed. Reg. at 63,693 ("In circumstances when there is no published policy on a particular topic, decisions are made based on the individual's particular factual situation.") (citing Heckler v. Ringer, 466 U.S. 602, 617 (1984))

We welcome the chance to work with CGS to explain our perspectives further, and to discuss any concerns that you have not addressed by our recommendations. Please do not hesitate to contact us if you have any questions or would like to set up a meeting to review what we have submitted.

Sincerely,

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Attachments:

Clinical References to Section 4 (pg. 25)

Redlined and Annotated Draft Local Coverage Determination (pg. 29)

Summary of Relevance of References in Proposed Noridian LCD Regarding Medical Necessity of More Frequent HD (pg. 38)

Evidence Matrix – Clinical Indications by Published Study with Study Type, Duration, Patient Count and Binder Containing References (pg. 42)

INCREASED HEMODIALYSIS TIME AND FREQUENCY: Guidelines from 5 Medical Societies in North America, Europe, and Asia (pg. 51)

CLINICAL REFERENCES TO SECTION 4

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REDLINED AND ANNOTATED LOCAL COVERAGE DETERMINATION

Source LCD ID
N/A

Proposed LCD ID
DL37575

Proposed LCD Title
Frequency of Hemodialysis

AMA CPT / ADA CDT / AHA NUBC Copyright Statement

CMS National Coverage Policy

This LCD supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for additional hemodialysis sessions. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this LCD. Neither Medicare payment policy rules nor this LCD replace, modify or supersede applicable state statutes regarding medical practice or other health practice professions acts, definitions and/or scopes of practice. All providers who report services for Medicare payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for additional hemodialysis sessions and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies may be found in the following Internet-Only Manuals (IOMs) published on the CMS Web site:

IOM Citations:

- CMS IOM Publication 100-01, *Medicare General Information, Eligibility and Entitlement Manual*
  - Chapter 1, Section 10: General Program Benefits.
  - Chapter 2, Section 10: Hospital Insurance Entitlement.
- CMS IOM Publication 100-02, *Medicare Benefit Policy Manual*, Chapter 11, End Stage Renal Disease (ESRD).

Commented [A1]: In response to the request that stakeholders provide comments on specifically proposed LCD language, we are providing this annotated document. It is intended to demonstrate the modesty of the changes to the language that would need to made to redress the concerns that we have identified in our comment letter. It illustrates the ease with which the proposed LCD could be revised to be brought in line with the clinical evidence, CMS payment policies, and the objectives of the Medicare program.

- CMS IOM Publication 100-03, *Medicare National Coverage Determinations (NCD) Manual,* Chapter 1
  - Part 2, Section 110.10: Intravenous Iron Therapy; Section 110.15: Ultrafiltration, Hemoperfusion and Hemofiltration.
  - Part 4, Section 260.6: Dental Examination Prior to Kidney Transplantation.
- CMS IOM Publication 100-04, *Medicare Claims Processing Manual*, Chapter 8: Outpatient ESRD Hospital, Independent Facility, and Physician/Supplier Claims.
- CMS IOM Publication 100-05, *Medicare Secondary Payer Manual*, Chapter 2, Section 20: Medicare Secondary Payer Provisions for End Stage Renal Disease (ESRD) Beneficiaries.
- CMS IOM Publication 100-08, *Medicare Program Integrity Manual*, Chapter 13, Section 13.5.1: Reasonable and Necessary Provisions in LCDs.
- CMS IOM Publication 100-09, *Medicare Contractor Beneficiary and Provider Communications Manual*, Chapter 5, Correction Coding Initiative.

Change Request References:

- Change Request 5039, Transmittal 1084, October 27, 2006: Line Item Billing Requirement for Type of Bill 72X.
- Change Request 9989, Transmittal 1849, May 12, 2017: Implementation of Modifier CG for Type of Bill 72X.

Social Security Act (Title XVIII) Standard References:

- Title XVIII of the Social Security Act, Section 1862(a)(1)(A) states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury.
- Title XVIII of the Social Security Act, Section 1862 (a)(1)(D) limits payment for services that are investigational or experimental.
- Title XVIII of the Social Security Act, Section 1833(e) states that no payment shall be made to any provider for any claim that lacks the necessary information to process the claim.

Federal Register References:

- 42 CFR, Chapter IV, Subchapter G, Part 494, Subpart C,
  - Section 494.80 Condition: Patient assessment.
  - Section 494.90 Condition: Patient plan of care.
- CMS Final Rule CMS-1651-F published November 4, 2016.

Note: *Italicized font* represents CMS manual titles, journal titles and/or CMS national NCD language/wording copied directly from CMS Manuals or CMS Transmittals. Contractors are prohibited from changing national NCD language/wording.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

Notice: It is not appropriate to bill Medicare for services that are not covered (as described by this entire LCD) as if they are covered. When billing for non-covered services, use the appropriate modifier.
Compliance with the provisions in this policy may be monitored and addressed through post payment data analysis and subsequent medical review audits.

History/Background and/or General Information

According to the Kidney Disease Outcomes Quality Initiative (KDOQI) Practice Guideline for Hemodialysis Adequacy: 2015 update, over 400,000 patients are currently treated with hemodialysis (HD) in the United States, with Medicare spending approaching $90,000 per year of care in 2012. They note mortality rates remain higher than age-matched individuals in the general population. They also experience an average of 2 hospitalizations per year. Attempts to improve outcomes have included initiation dialysis at higher glomerular filtration rates (GFRs), increasing dialysis frequency and/or duration, using newer membranes, and employing supplemental or alternative hemofiltration. Efforts to increase the dose of dialysis ~~administration above~~administered 3 times ~~per week~~weekly have not improved survival, indicating that something else needs to be addressed. This guideline was also cited in the most recent CMS Final Rule CMS-1651-F published November 4, 2016.

Commented [A2]: The draft LCD misquotes this reference from the KDOQI 2015 update; and this misquote changes its meaning. More importantly, this quote is not presented here within the context in which it appears – which is as an introductory statement of a guideline update under which KDOQI actually recommends the use of more frequent hemodialysis as a treatment alternative.

Covered Indications

1. Metabolic acidosis
2. Fluid positive status not controlled with routine dialysis
3. Hyperkalemia
4. Pregnancy
5. Heart Failure
6. Pericarditis
7. Incomplete dialysis secondary to hypotension or access issues

Limitations

The following are considered not reasonable and necessary and therefore will be denied as not medically justified for payments.

1. ~~POC number of sessions above 3 times per week (for example the POC states 5 times per week)-those above 3 times per week are not medically justified for additional payment~~
2. ~~Planned inadequate or short dialysis~~
3. 1. Convenience of patient or staff

There are documentation requirements in this LCD which if not followed will generate denials. Please refer to the 'Documentation Requirements' section below.

While there are no set frequency limitations for these services, continued use of additional sessions by a given provider or for a given beneficiary or unusual patterns of billing, verification of need for services will generate reviews. Please refer to the Utilization Guidelines section below.

For Coding Guidelines, please refer to the companion article A55723.

Notice: This LCD imposes diagnosis limitations that support diagnosis to procedure code automated denials. However, services performed for any given diagnosis must meet all of the indications and limitations stated in this policy, the general requirements for medical necessity as stated in CMS payment policy manuals, any and all existing CMS national coverage determinations, and all Medicare payment rules.

As published in CMS IOM 100-08, Chapter 13, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary. When appropriate, contractors shall describe the circumstances under which the proposed LCD for the service is considered reasonable and necessary under Section 1862 (a)(1)(A). Contractors shall consider a service to be reasonable and necessary if the contractor determines that the service is:

- Safe and effective.
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September19, 2000, that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary).
- Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:
  - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member.
  - Furnished in a setting appropriate to the patient's medical needs and condition.
  - Ordered and furnished by qualified personnel.
  - One that meets, but does not exceed, the patient's medical needs.
  - At least as beneficial as an existing and available medically appropriate alternative.

The redetermination process may be utilized for consideration of services performed outside of the reasonable and necessary requirements in this LCD.

Summary of Evidence

HD at 3 times (3 X) per week is noted to be 'conventional' treatment. Conventional HD remains the most common treatment modality for ESRD worldwide and is usually performed for 3 to 5 hours, 3 days per week. CMS established payment for hemodialysis based on conventional treatment.

Hence, Medicare reimburses HD treatments 3 times per week (13/14 sessions per month depending on length of month). In CMS-1651-F (November 4, 2016), CMS outlines the process for medical justification for additional treatment payments. The following statements are made:

Under this policy, the MACs determine whether additional treatments furnished during a month are medically necessary and when the MACs determine that the treatments are medically justified, we pay the full base rate for the additional treatments. While Medicare does not define specific patient conditions that meet the requirements of medical necessity, the MACs consider appropriate medical conditions that would result in the medical need for additional dialysis treatments (for example, excess fluid). When such patient conditions are indicated on the claim, we instruct MACs to consider medical justification and the appropriateness of payment for the additional sessions.

This LCD sets out medical conditions likely to meet medical justification for additional payments.

Providers establish parameters for treatment of any given patient through a Patient Plan of Care (POC). It is defined in the Conditions of Coverage for ESRD Services 42 CFR 494.90. Among other items, the POC developed by the Interdisciplinary Team must provide the necessary care and services to manage the patient's volume status; and achieve

Commented [A3]: This POC restriction is inconsistent with payment policy, as articulated in the 2011 ESRD PPS Final Rule (establishing the per treatment unit of payment) as well as the 2015 and 2017 ESRD PPS Final Rules, reaffirming Medicare's long-standing policy of paying for medically justified hemodialysis sessions in excess of three treatments per week, irrespective of whether the sessions are part of a POC.

Commented [A4]: The limitations on "inadequate or short dialysis" are vague, at best. At worst, they are invalid blanket restrictions on coverage not allowed under CMS payment policy or supported by clinical evidence.

- CMS pays on a per treatment basis, not by duration or by planned adequacy. Significantly, in the 2017 ESRD PPS Final Rule, CMS noted that commenters suggested that CMS should pay for dialysis by the hour, and CMS declined to do so. 81 Fed. Reg. 77846.

Characterizing shorter, more frequent hemodialysis as de facto medically unnecessary is inconsistent with the best clinical evidence. One arm of the Frequent Hemodialysis Network (FHN) Trial randomly assigned patients to undergo hemodialysis 6 times per week in a short (1.5 to 2.75 hours) treatment with lower dose delivery per session (per treatment Kt/V of 0.9) versus conventional thrice weekly dialysis. The study results, published in *The New England Journal of Medicine*[1], showed significant benefits associated with short more frequent hemodialysis in reduction of left ventricular mass and physical-health composite score, important surrogate endpoints selected for their historical correlation with mortality and hospitalization outcomes. Short frequent hemodialysis was also associated with improved control of hypertension and hyperphosphatemia, and in a subsequent publication was shown to significantly reduce post-dialysis recovery time.[1] Importantly, this study was jointly supported by the NIH, the NIDDK, and CMS. These results were the primary driver of the K-DOQI recommendations (2.1) that short frequent HD sessions should be considered for selected patients. Given these important results from a study with regulatory agency participation, along with the K-DOQI recommendations, characterizing shorter more frequent hemodialysis broadly as medically unnecessary is logically inconsistent.

and sustain the prescribed dose of dialysis to meet a hemodialysis Kt/V of at least 1.2 for patients treated thrice weekly and a peritoneal dialysis weekly Kt/V of at least 1.7 or meet an alternative equivalent professionally-accepted clinical practice standard for adequacy of dialysis. (i.e., for hemodialysis schedules other than thrice weekly to meet a minimum delivered target stdKt/V dose of 2.1).

The prescription for chronic hemodialysis therapies includes the type of dialysis access, the type and amount of anticoagulant to be employed, blood flow rates, dialysate flow rate, ultrafiltration rate, dialysate temperature, type of dialysate (acetate versus bicarbonate) and composition of the electrolytes in the dialysate, size of hemodialyzer (surface area) and composition of the dialyzer membrane (conventional versus high flux), duration and frequency of treatments, the type and frequency of measuring indices of clearance, and intradialytic medications to be administered.

Those treatment sessions established in the POC are paid by Medicare ~~a~~up to 3 X per week without the need for a secondary diagnosis to justify payment. Establishment of more sessions in the POC, such as 4 - 6 sessions per week, are still reimbursed at the 3 X per week amount.

~~However, on occasion, acute conditions may require additional sessions during the month outside the POC. These~~Extra hemodialysis sessions ordered in excess of 3 X per week (whether on an acute or chronic basis) may be considered for additional payment. This LCD provides a list of diagnoses felt to be consistent with such clinical conditions that could establish medical justification for payment. Use of these diagnoses should be verified in the medical records to support any payment made.

Clinical Conditions not seen listed in this policy may still be appropriate to allow payment. However, these claims may require additional review through the appeals process.

Modifier KX will be appended to CPT 90999 to signify ~~an additional session was needed for an acute clinical condition.~~sessions ordered consistent with this policy. It will be appended on each line for each additional session within the claim for each month billed.

Medicare will monitor the frequency of additional sessions which may trigger Medical Review.

The POC reassessment is noted in 42 CFR 494.80(d) as below:

494.80(d) Standard: Patient reassessment. In accordance with the standards specified in paragraphs (a)(1) through (a)(13) of this section, a comprehensive reassessment of each patient and a revision of the plan of care must be conducted-(1) At least annually for stable patients; and (2) At least monthly for unstable patients including, but not limited to, patients with the following: (i) Extended or frequent hospitalizations; (ii) Marked deterioration in health status; (iii) Significant change in psychosocial needs; or (iv) Concurrent poor nutritional status, unmanaged anemia, and inadequate dialysis.

~~Repeated need~~Need for additional dialysis sessions as noted by 90999-KX is expected to be ~~subsequently~~ addressed in the ~~monthly~~ POC and medical documentation. (See medical documentation requirements below.)

Analysis of Evidence
(Rationale for Determination)

KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 Update Guidelines 4.1.1 states to 'Consider additional hemodialysis sessions or longer hemodialysis treatment times for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor metabolic control (such as hyperphosphatemia, metabolic acidosis, and/or hyperkalemia).'

This specific recommendation was 'Not Graded' in the Guidelines but based on expert opinions. However, these guidelines are determined by a panel of experts and are felt to have a STRONG level of evidence to follow.

National experts were also contacted for input during development of this policy.

Based on KDOQI Practice Guidelines as well as Kidney Disease: Improving Clinical Outcomes (KDIGO) Guidelines, the listed conditions in the LCD may be considered reasonable and necessary to have created medical justification for additional payments.

Based on local collaborative data, Medicare contractors expect the list of diagnoses in this LCD would represent the great majority of claims for which additional payment might be medically justified.

Facilities with sites in multiple states should be able to submit claims in a unified approach.

However, this LCD would not be the appropriate approach to change the payment methodology by CMS and reconsiderations to this LCD to potentially try to change the CMS payment process will be denied as invalid reconsideration to this LCD.

Synopsis of Changes

Commented [A5]: KDOQI Adequacy Guideline: 2015 Update, Guideline 3.1

Commented [A6]: K-DOQI HD Adequacy Guideline: 2015 Update, Guideline 3.3

Commented [A7]: Medicare payment policy has been consistent for decades. CMS pays for medically justified hemodialysis session in excess of three per week, irrespective of whether these sessions are ordered under a POC. CMS payment policy is clearly articulated in Medicare Manuals. See e.g., Chapter 11, Section 50.A of the Medicare Benefit Policy Manual.

Commented [A8]: Revisions made to clarify that the prescription of additional dialysis sessions are not limited to acute clinical conditions.

Commented [A9]: Revision made to clarify that all patients receiving medically appropriate more frequent hemodialysis sessions are not unstable, and monthly POC updates may not be necessary in order to comply with the POC requirements of the ESRD Conditions for Coverage.

CHANGES	FIELDS CHANGED
Not Applicable	N/A

Associated Information

Documentation Requirements

1. All documentation must be maintained in the patient's medical record and made available to the contractor upon request.
2. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The documentation must include the legible signature of the physician or non-physician practitioner responsible for and providing the care to the patient.
3. The submitted medical record must support the use of the selected ICD-10-CM code(s). The submitted CPT/HCPCS code must describe the service performed.
4. The medical record documentation must support the medical necessity of the services as directed in this policy.
5. The medical records documentation should include the order from the prescribing physician for the additional sessions. This should be available for ~~each and every~~ all additional ~~session~~sessions outside the usual 13/14 treatments per month with the CG modifier appended as well as those described in this LCD with the KX modifier appended. Should the records not show the order and evaluation leading to additional ~~session~~sessions, denials will occur.
6. POC should be available upon request and should be the annual update or monthly depending on the guidelines above and the stability of the patients. Should a patient require consistent additional dialysis sessions, the POC should ~~show changes in~~note the ~~dialysis prescription or other parameters~~medical justification to address the repeated need for additional sessions and be updated on at least a quarterly basis, for stable patients, or at least monthly for unstable patients. Lack of this documentation will lead to denials.

Utilization Guidelines

In accordance with CMS Ruling 95-1 (V), utilization of these services should be consistent with locally acceptable standards of practice.

With continued utilization of additional sessions by a specific provider generally, or for a given beneficiary, providers should expect medical review of medical records by contractors.

Sources of Information

Contractor is not responsible for the continued viability of websites listed.

Bibliography

KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1-150.
National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. *Am J Kidney Dis*. 2012;60(5):850-886.
National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. *Am J Kidney Dis*. 2015;66(5):884-930.

Other Contractor's Policies:
Palmetto GBA, L34575 - Frequency of Dialysis
Novitas Solutions, Inc., L35014 - Frequency of Dialysis
Contractor Medical Director ESRD Workgroup

Open Meetings/Part B MAC Contractor Advisory Committee (CAC) Meetings

MEETING DATE	MEETING TYPE	MEETING STATE(S)	MEETING INFORMATION
11/07/2017	Carrier Advisory Committee (CAC) Meeting	Kentucky	This policy will be presented at the Kentucky CAC meeting on November 7, 2017.
11/08/2017	Carrier Advisory Committee (CAC) Meeting	Ohio	This policy will be presented at the Ohio CAC meeting November 8, 2017.

Comment Period Start Date

11/09/2017

Commented [A10]: Revision made to clarify that the physician does not need to write a new prescription each time a patient receives an additional session of hemodialysis per week. Physicians may write prescriptions for medically appropriate more frequent hemodialysis on a chronic basis. As long as progress notes, medical records and POC reviews support the ongoing prescription, there should be no need for the physician to rewrite a prescription every week and for each additional treatment.

Commented [A11]: Even though patients receiving more frequent HD as part of their plan of care may be stable, we appreciate that the MAC may desire confirming documentation of medical necessity more regularly, but the provision of such support should not be overly inefficient or burdensome.

Commented [A12]: This LCD references three publications, and none of these support restricting coverage to "occasion[al] "acute conditions", as suggested by the POC-related restrictions. Rather, the KDOQI guidelines discuss patient conditions in which more frequent dialysis may be indicated on a routine basis, and provide adequacy guidelines for more frequent HD. The proposed LCD notes that the Guidelines, although 'Not Graded' "are determined by a panel of experts and are felt to have a STRONG level of evidence to follow." The MAC then "follows" this evidence and indicates that "the listed conditions in the LCD may be considered reasonable and necessary to have created medical justification for additional payments." Unfortunately, the POC restrictions completely eviscerate the clinical integrity of the coverage proposed and render these conditions, most of which are chronic in nature, uncovered, creating a nonsensical interpretation of the strong, but limited, evidence cited. As articulated in the Medicare Program Integrity Manual, and in case law, jurisdiction-wide coverage restrictions established by LCDs must be "based on the strongest evidence available. . . . LCDs should be based on: . . . [p]ublished authoritative evidence[] and . . . [g]eneral acceptance by the medical community (standards of practice), as supported by sound medical evidence. (See Medicare Program Integrity Manual, Chapter 13, §13.7.1 and *see generally In Re CMS LCD Complaint*, No. A-09-123 at 14 (DAB May 3, 2010), *available at* https://www.hhs.gov/sites/default/files/static/dab/decisions/board-decisions/2010/dab2315.pdf (noting the applicable "reasonableness" standard that must be satisfied in order to conclude that a contractor's LCD is not reasonably based on the "strongest available evidence")).

Comment Period End Date
12/24/2017

Released to Final LCD Date
Please Note: This is not the LCD Effective Date.
N/A

Reason for Proposed LCD
- Provider Education/Guidance

Proposed Contact
Earl Berman, MD
Attn Medical Review
Two Vantage Way
Nashville, TN 37228-
Attn Medical Review
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cmd.inquiry@cgsadmin.com

Bill Type Codes:
Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

072x	Clinic - Hospital Based or Independent Renal Dialysis Center

Revenue Codes:
Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.
Note: The contractor has identified the Bill Type and Revenue Codes applicable for use with the CPT/HCPCS codes included in this LCD. Providers are reminded that not all CPT/HCPCS codes listed can be billed with all Bill Type and/or Revenue Codes listed. CPT/HCPCS codes are required to be billed with specific Bill Type and Revenue Codes. Providers are encouraged to refer to the CMS *Internet-Only Manual* (IOM) Pub. 100-04, *Claims Processing Manual,* for further guidance.

0821	Hemodialysis - Outpatient or Home - Hemodialysis Composite or Other Rate
0881	Miscellaneous Dialysis - Ultrafiltration

CPT/HCPCS Codes

Group 1 Paragraph:
Note: Providers are reminded to refer to the long descriptors of the CPT codes in their CPT book.

Group 1 Codes:

90999	Dialysis procedure

ICD-10 Codes that Support Medical Necessity

Group 1 Paragraph:
It is the provider's responsibility to select codes carried out to the highest level of specificity and selected from the ICD-10-CM code book appropriate to the year in which the service is rendered for the claim(s) submitted.
Medicare is establishing the following limited coverage for CPT/HCPCS code: **90999**

Group 1 Codes:

ICD-10 CODES	DESCRIPTION
E83.30	Disorder of phosphorus metabolism, unspecified
E83.39	Other disorders of phosphorus metabolism
E87.2	Acidosis
E87.5	Hyperkalemia
E87.70	Fluid overload, unspecified
E87.71	Transfusion associated circulatory overload
E87.79	Other fluid overload
I30.0	Acute nonspecific idiopathic pericarditis
I30.1	Infective pericarditis
I30.8	Other forms of acute pericarditis
I30.9	Acute pericarditis, unspecified
I32	Pericarditis in diseases classified elsewhere
I50.1	Left ventricular failure, unspecified
I50.20	Unspecified systolic (congestive) heart failure
I50.21	Acute systolic (congestive) heart failure
I50.22	Chronic systolic (congestive) heart failure
I50.23	Acute on chronic systolic (congestive) heart failure
I50.30	Unspecified diastolic (congestive) heart failure
I50.31	Acute diastolic (congestive) heart failure
I50.32	Chronic diastolic (congestive) heart failure
I50.33	Acute on chronic diastolic (congestive) heart failure
I50.40	Unspecified combined systolic (congestive) and diastolic (congestive) heart failure
I50.41	Acute combined systolic (congestive) and diastolic (congestive) heart failure
I50.42	Chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.43	Acute on chronic combined systolic (congestive) and diastolic (congestive) heart failure
I50.810	Right heart failure, unspecified
I50.811	Acute right heart failure
I50.812	Chronic right heart failure

I50.813	Acute on chronic right heart failure
I50.814	Right heart failure due to left heart failure
I50.82	Biventricular heart failure
I50.83	High output heart failure
I50.84	End stage heart failure
I50.89	Other heart failure
I50.9	Heart failure, unspecified
I77.0	Arteriovenous fistula, acquired
I95.3	Hypotension of hemodialysis
J81.0	Acute pulmonary edema
M32.12	Pericarditis in systemic lupus erythematosus
N25.81	Secondary hyperparathyroidism of renal origin
O09.211	Supervision of pregnancy with history of pre-term labor, first trimester
O09.212	Supervision of pregnancy with history of pre-term labor, second trimester
O09.213	Supervision of pregnancy with history of pre-term labor, third trimester
O09.219	Supervision of pregnancy with history of pre-term labor, unspecified trimester
O09.891	Supervision of other high risk pregnancies, first trimester
O09.892	Supervision of other high risk pregnancies, second trimester
O09.893	Supervision of other high risk pregnancies, third trimester
O09.899	Supervision of other high risk pregnancies, unspecified trimester
R60.1	Generalized edema
R63.5	Abnormal weight gain
T82.898A - T82.898S	Other specified complication of vascular prosthetic devices, implants and grafts, initial encounter - Other specified complication of vascular prosthetic devices, implants and grafts, sequela

ICD-10 Codes that DO NOT Support Medical Necessity

Group 1 Paragraph:
~~All those~~N/A. Diagnoses with a KX modifier which are not listed under the "ICD-10 Codes that Support Medical Necessity" section of this policy will be considered as supporting payment on a case by case basis.

Commented [A13]: Revision made to indicate that the ICD-10 code list is not exclusive, allowing for the use of other diagnoses codes, on a case by case basis, based upon the individualized documentation of medical justification submitted.

Group 1 Codes: N/A

ICD-10 Additional Information

Attachments
N/A
Related Local Coverage Documents
N/A
Related National Coverage Documents

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SUMMARY OF RELEVANCE OF REFERENCES IN PROPOSED LCD REGARDING MEDICAL NECESSITY OF MORE FREQUENT HD

SUMMARY OF RELEVANCE OF REFERENCES IN PROPOSED NORIDIAN LCD REGARDING MEDICAL NECESSITY OF MORE FREQUENT HD
(including implied references included in previous Palmetto L34575 and Novitas L35014 LCDs)

Summary: The currently proposed LCD directly references 3 published clinical practice guidelines, and through reference to other LCDs references an additional 10 manuscripts. Of these 13 in total, 4 are not clinically relevant and support neither medical necessity nor categorical restrictions of more frequent HD. The other 9 support or consider in proposed clinical practice guidelines the medical necessity of more frequent HD for selected patients. Importantly, not one of the referenced manuscripts supports any categorical restriction.

Referenced Manuscript	Why reference is relevant to more frequent HD?	Support of Medical Necessity	Support of Categorical Restrictions
KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.	Not relevant; the guideline focuses on management of non-dialysis-dependent chronic kidney disease and addresses dialysis to the extent that it offers suggestions about timing the initiation of renal replacement therapy	None	None
National Kidney Foundation. KDOQI Clinical Practice Guideline for Diabetes and CKD: 2012 update. *Am J Kidney Dis*. 2012;60(5):850-886.	Not relevant; the guideline focuses on the treatment of diabetes in patients with chronic kidney disease	None	None
National Kidney Foundation. KDOQI clinical practice guideline for hemodialysis adequacy: 2015 update. Am J Kidney Dis. 2015;66(5):884-930.	Multiple clinical practice guidelines regarding hemodialysis frequency	Suggests in-center short frequent hemodialysis as an alternative to conventional in-center thrice-weekly, after considering patient preferences, potential quality of life and physiological benefits, and risk of these therapies (including a possible increase in vascular access procedures, potential for hypotension during dialysis, potential for increased caregiver burden(in the home setting), and accelerated decline in residual kidney function); also suggests that physicians consider additional hemodialysis sessions or longer hemodialysis treatment times for patients with large weight gains, high ultrafiltration rates, poorly controlled blood pressure, difficulty achieving dry weight, or poor metabolic control	None

SUMMARY OF RELEVANCE OF REFERENCES IN PROPOSED NORIDIAN LCD REGARDING MEDICAL NECESSITY OF MORE FREQUENT HD - continued
(including implied references included in previous Palmetto L34575 and Novitas L35014 LCDs)

Referenced Manuscript	Why reference is relevant to more frequent HD?	Support of Medical Necessity	Support of Categorical Restrictions
Foley RN, Gilbertson DT, Murray T, Collins AJ. Long interdialytic interval and mortality among patients receiving hemodialysis. N Engl J Med. 2011;365(12):1099-107. *(L35014 reference)*	Evaluated risks of death and cardiovascular (CV) hospitalization after the long intradialytic interval; this interval is reduced with more frequent HD	In 32,065 patients, demonstrated increased risks of death and CV hospitalization and death after long intervals, thus supporting the rationale for more frequent HD	None
FHN Trial Group. In-center hemodialysis six times per week versus three times per week. N Engl J Med. 2010;363(24):2287-300. *(L35014 and L34575 reference)*	National Institutes of Health-funded randomized clinical trial comparing short daily HD to conventional HD for 1 year	Statistically significant, beneficial effects of short daily versus conventional HD on the co-primary endpoints of the composite of change in left ventricular mass or death and the composite of change in physical health-related quality of life or death	None (actually demonstrated clinical benefits of "short" frequent HD, contrary to the proposed categorical restriction)
Kalantar-Zadeh K, Regidor DL, Kovesdy CP, Van Wyck D, Bunnapradist S, Horwich TB, Fonarow GC. Fluid retention is associated with cardiovascular mortality in patients undergoing long-term hemodialysis. Circulation. 2009;119(5):671-9. *(L35014 reference)*	Evaluated risk of cardiovascular death as a function of 3-month averaged interdialytic weight gain (IDWG)	In 34,107 patients, demonstrated lower risk of cardiovascular death with IDWG <1.0 kg and higher risk of cardiovascular death with IDWG ≥4.0 kg, thus supporting the rationale for more frequent HD	None
Kumar VA, Ledezma ML, Rasgon SA. Daily home hemodialysis at a health maintenance organization: three-year experience. Hemodial Int. 2007;11(2):225-30. *(L35014 reference)*	Small study of more frequent HD in Kaiser health system	Demonstrated daily HD improved nutritional status and decreased hospital admissions	None
National Kidney Foundation. Guidelines and Commentaries. https://www.kidney.org/professionals/guidelines/guidelines_commentaries, date accessed: 8/5/13. *(L35014 reference)*	Electronic reference to KDOQI Guideline documents, presumably inclusive of the 2015, 2012, and 2006 documents referenced elsewhere	See other KDOQI references	None

SUMMARY OF RELEVANCE OF REFERENCES IN PROPOSED NORIDIAN LCD REGARDING MEDICAL NECESSITY OF MORE FREQUENT HD - continued

(including implied references included in previous Palmetto L34575 and Novitas L35014 LCDs)

Referenced Manuscript	Why reference is relevant to more frequent HD?	Support of Medical Necessity	Support of Categorical Restrictions
Weinhandl ED, Liu J, Gilbertson DT, Arneson TJ, Collins AJ. Survival in daily home hemodialysis and matched thrice-weekly in-center hemodialysis patients. J Am Soc Nephrol. 2012;23(5):895-904. *(L35014 reference)*	Comparison of mortality risk in 1,873 patients on more frequent home HD and 9,365 matched patients on conventional in-center HD	Demonstrated a 13% (intent-to-treat) to 18% (as-treated) reduction in all-cause mortality with more frequent home HD	None
Cooper BA, Branley P, Bulfone L, Collins JF, Craig JC, Fraenkel MB, Harris A, Johnson DW, Kesselhut J, Li JJ, Luxton G, Pilmore A, Tiller DJ, Harris DC, Pollock CA; IDEAL Study. A randomized, controlled trial of early versus late initiation of dialysis. N Engl J Med. 2010;363(7):609-19. *(L34575 reference)*	Not relevant (tested the effect of early vs. late initiation of dialysis)	None	None
Himmelfarb J et al. Hemodialysis. In Brenner BM, Rector FC, eds., *Brenner and Rector's The Kidney*. Vol. 2, 8th ed. Philadelphia: Saunders Elsevier, 2008: 1957-2006. *(L34575 reference)*	Not relevant (medical textbook with one chapter on HD)	None	None
Himmelfarb J. Success and challenge in dialysis therapy. N Engl J Med. 2002;347(25):2068-70. *(L34575 reference)*	Editorial concerning the National Institutes of Health-funded HEMO trial (assessing the effects of hemodialysis dose and dialyzer flux)	Suggested that the NIH should sponsor a study of more frequent HD (which it subsequently did)	None
Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis. 2006;48 Suppl 1:S2-90. *(L34575 reference)*	Guidelines for HD adequacy, including applications of more frequent HD	Suggested that patients who are malnourished or underweight, hyperphoshatemic, chronically fluid overloaded, or having sleep apnea might benefit from more frequent HD	None

EVIDENCE MATRIX – CLINICAL INDICATIONS BY PUBLISHED STUDY WITH STUDY TYPE, DURATION, PATIENT COUNT AND BINDER CONTAINING REFERENCES

Evidence Matrix – Clinical Indications by Published Study with Study Type, Duration, Patient Count and Binder Containing References

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Assimon MM, Wenger JB, Wang L, et al. Ultrafiltration Rate and Mortality in Maintenance Hemodialysis Patients. Am J Kidney Dis. 2016;68(6):911-922	Not applicable	Retrospective		Important background This study demonstrates a potent association of high ultrafiltration rate with risk of death among thrice-weekly hemodialysis patients in a large dialysis organization in the US.				
Ayus JC, Achinger SG, Mizani MR, et al. Phosphorus balance and mineral metabolism with 3 h daily hemodialysis. Kidney Int. 2007;71(4):336-342. doi:10.1038/sj.ki.5002044.	26	Prospective	12 months			X		
Ayus JC, Mizani MR, Achinger SG, Thadhani R, Go AS, Lee S. Effects of short daily versus conventional hemodialysis on left ventricular hypertrophy and inflammatory markers: a prospective, controlled study. J Am Soc Nephrol JASN. 2005;16(9):2778-2788. doi:10.1681/ASN.2005040392.	26	Prospective	12 months	X	X	X		
Bansal N, McCulloch CE, Lin F, et al. Blood Pressure and Risk of Cardiovascular Events in Patients on Chronic Hemodialysis: The CRIC Study (Chronic Renal Insufficiency Cohort). Hypertension 2017;70(2):435-443	Not applicable	Retrospective		Important background The study reveals that out-of-dialysis-unit systolic blood pressure is linearly associated with risk of cardiovascular events among hemodialysis patients in the Chronic Renal Insufficiency Cohort (CRIC) study.				
Banshodani M, Kawanishi H, Fukuma S, et al. The impact of hemodialysis schedules on the day of the week of hospitalization for cardiovascular and infectious diseases, over a period of 20 years. PLoS One 2017;12(7):e0180577	Not applicable	Retrospective		Important background The Japanese study confirms the finding of numerous other studies from around the world: risk of hospitalization is markedly higher after the two-day gap in the conventional hemodialysis schedule.				
Buoncristiani U, Fagugli R, Ciao G, et al. Left ventricular hypertrophy in daily dialysis. Miner Electrolyte Metab. 1999;25(1-2):90-94. doi:57427.	72	Suite of 4 studies: Retrospective (N = 2) Prospective (N = 2)	6-24 months		X			
Chan CT, Chertow GM, Daugirdas JT, et al. Effects of daily hemodialysis on heart rate variability: results from the Frequent Hemodialysis Network (FHN) Daily Trial. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc. 2014;29(1):168-178. doi:10.1093/ndt/gft212.	131	Prospective	12 months	X				

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Chan CT, Floras JS, Miller JA, Richardson RMA, Pierratos A. Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. Kidney Int. 2002;61(6):2235-2239. doi:10.1046/j.1523-1755.2002.00362.x.	28	Retrospective	24 months	X	X	X		
Chan CT, Greene T, Chertow GM, et al. Determinants of left ventricular mass in patients on hemodialysis: Frequent Hemodialysis Network (FHN) Trials. Circ Cardiovasc Imaging. 2012;5(2):251-261. doi:10.1161/CIRCIMAGING.111.969923.	170	Randomized trial	12 months	X				
Chazot C, Vo-Van C, Lorriaux C, et al. Even a Moderate Fluid Removal Rate during Individualised Haemodialysis Session Times Is Associated with Decreased Patient Survival. Blood Purif 2017;44(2):89-97	Not applicable	Retrospective		Important background This study extends the understanding of the association of ultrafiltration intensity and mortality: even ultrafiltration rates >6.8 mL/hour/kg are associated with increased risk of death.				
Culleton BF, Walsh M, Klarenbach SW, et al. Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. JAMA. 2007;298(11):1291-1299. doi:10.1001/jama.298.11.1291.	26	Randomized trial	6 months	X	X	X	X	
Daugirdas JT, Chertow GM, Larive B, et al. Effects of frequent hemodialysis on measures of CKD mineral and bone disorder. J Am Soc Nephrol JASN. 2012;23(4):727-738. doi:10.1681/ASN.2011070688.	170	Randomized trial	12 months			X		
Evangelidis N, Tong A, Manns B, et al. Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi Survey. Am J Kidney Dis. 2017;70(4):464-475	Not applicable	Survey		Important background The study shows that dialysis patients highly value outcomes regarding quality of life.				

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
FHN Trial Group, Chertow GM, Levin NW, et al. In-center hemodialysis six times per week versus three times per week. N Engl J Med. 2010;363(24):2287-2300. doi:10.1056/NEJMoa1001593.	125	Randomized trial	12 months	X	X		X	
Finkelstein FO, Schiller B, Daoui R, et al. At-home short daily hemodialysis improves the long-term health-related quality of life. Kidney Int. 2012;82(5):561-569. doi:10.1038/ki.2012.168.	291	Prospective	12 months				X	
Finkelstein FO, Tighiouart H, Wuerth D, Finkelstein S, Jaber BL. Self-reported experiences with short daily hemodialysis: interim results from the FREEDOM study. November 2014. https://www.asn-online.org/api/download/?file=/education/kidneyweek/archives/KW14Abstracts.pdf. Accessed May 20, 2015.	289	Prospective	12 months				X	
Flythe JE, Assimon MM, Overman RA. Target weight achievement and ultrafiltration rate thresholds: potential patient implications. BMC Nephrol 2017;18(1):185	Not applicable	Retrospective		Important background The association of ultrafiltration rate with risk of death is apparent in all body sizes.				
Garg AX, Suri RS, Eggers P, Finkelstein FO, Greene T, Kimmel PL, Kliger AS, Larive B, Lindsay RM, Pierratos A, Unruh M, Chertow GM; Frequent Hemodialysis Network Trial Investigators.. Patients receiving frequent hemodialysis have better health-related quality of life compared to patients receiving conventional hemodialysis. Kidney Int. 2017 Mar;91(3):746-754. doi:10.1016/j.kint.2016.10.033.	170	Randomized trial	12 months				x	X
Hall YN, Larive B, Painter P, et al. Effects of six versus three times per week hemodialysis on physical performance, health, and functioning: Frequent Hemodialysis Network (FHN) randomized trials. Clin J Am Soc Nephrol CJASN. 2012;7(5):782-794. doi:10.2215/CJN.10601011.	170	Randomized trial	12 months				X	

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Hanly PJ, Pierratos A. Improvement of sleep apnea in patients with chronic renal failure who undergo nocturnal hemodialysis. N Engl J Med. 2001;344(2):102-107. doi:10.1056/NEJM200101113440204.	14	Prospective	15 months				X	
Heidenheim AP, Muirhead N, Moist L, Lindsay RM. Patient quality of life on quotidian hemodialysis. Am J Kidney Dis Off J Natl Kidney Found. 2003;42(1 Suppl):36-41.	23	Prospective	18 months				X	
Hussein WF, Arramreddy R, Sun SJ, et al. Higher Ultrafiltration Rate Is Associated with Longer Dialysis Recovery Time in Patients Undergoing Conventional Hemodialysis. Am J Nephrol 2017;46(1):3-10	Not applicable	Retrospective		Important background Among thrice-weekly hemodialysis patients, higher ultrafiltration rate is significantly associated with longer post-dialysis recovery time.				
Jaber BL, Collins AJ, Finkelstein FO, et al. Daily hemodialysis reduces the need for anti-hypertensive medications. October 2009. https://www.asn-online.org/api/download/?file=/education/kidneyweek/archives/RW09Abstracts.pdf. Accessed May 20, 2015.	57	Prospective	12 months		X			
Jaber BL, Lee Y, Collins AJ, et al. Effect of daily hemodialysis on depressive symptoms and postdialysis recovery time: interim report from the FREEDOM (Following Rehabilitation, Economics and Everyday-Dialysis Outcome Measurements) Study. Am J Kidney Dis Off J Natl Kidney Found. 2010;56(3):531-539. doi:10.1053/j.ajkd.2010.04.019.	239	Prospective	12 months				X	X
Jaber BL, Schiller B, Burkart JM, et al. Impact of short daily hemodialysis on restless legs symptoms and sleep disturbances. Clin J Am Soc Nephrol CJASN. 2011;6(5):1049-1056. doi:10.2215/CJN.10451110.	235	Prospective	12 months				X	

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Jefferies HJ, Virk B, Schiller B, Moran J, McIntyre CW. Frequent Hemodialysis Schedules Are Associated with Reduced Levels of Dialysis-induced Cardiac Injury (Myocardial Stunning). Clin J Am Soc Nephrol CJASN. 2011;6(6):1326-1332. doi:10.2215/CJN.05200610.	34	Cross-sectional	Not applicable					X
Karpetas A, Loutradis C, Bikos A, et al. Blood pressure variability is increasing from the first to the second day of the interdialytic interval in hemodialysis patients. J Hypertens. 2017 Aug 12. doi:10.1097/HJH.0000000000001478	Not applicable	Retrospective		Important background Blood pressure variability, which is a cardiovascular risk factor, increases during the two-day gap at the end of the conventional hemodialysis schedule.				
Kennedy C, Ryan SA, Kane T, et al. The impact of change of renal replacement therapy modality on sleep quality in patients with end-stage renal disease: a systematic review and meta-analysis. J Nephrol. 2017 Jun 1. doi:10.1007/s40620-017-0409-7	Not applicable	Systematic review		Important background Sleep disturbance, sleep apnea, and restless legs syndrome all tend to improve when a switch is made to intensive dialysis or transplant.				
Kotanko P, Garg AX, Depner T, et al. Effects of frequent hemodialysis on blood pressure: Results from the randomized frequent hemodialysis network trials. Hemodial Int Int Symp Home Hemodial. 2015;19(3):386-401. doi:10.1111/hdi.12255.	170	Randomized trial	12 months		X			X
Kraus M, Burkart J, Hegeman R, Solomon R, Coplon N, Moran J. A comparison of center-based vs. home-based daily hemodialysis for patients with end-stage renal disease. Hemodial Int Int Symp Home Hemodial. 2007;11(4):468-477. doi:10.1111/j.1542-4758.2007.00229.x.	32	Prospective	18 weeks		X			
Laskin BL, Huang G, King E, et al. Short, frequent, 5-days-per-week, in-center hemodialysis versus 3-days-per week treatment: a randomized crossover pilot trial through the Midwest Pediatric Nephrology Consortium. Pediatr Nephrol 2017;32(8):1423-1432	8	Randomized trial	6 months		X			

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Lindsay RM, Heidenheim PA, Nesrallah G, Garg AX, Suri R, Daily Hemodialysis Study Group London Health Sciences Centre. Minutes to recovery after a hemodialysis session: a simple health-related quality of life question that is reliable, valid, and sensitive to change. Clin J Am Soc Nephrol CJASN. 2006;1(5):952-959. doi:10.2215/CJN.00040106.	22	Prospective	18 months					X
Lockridge RS, Spencer M, Craft V, et al. Nightly home hemodialysis: five and one-half years of experience in Lynchburg, Virginia. Hemodial Int Int Symp Home Hemodial. 2004;8(1):61-69. doi:10.1111/j.1492-7535.2004.00076.x.	40	Retrospective	60 months		X	X	X	
Manns BJ, Walsh MW, Culleton BF, et al. Nocturnal hemodialysis does not improve overall measures of quality of life compared to conventional hemodialysis. Kidney Int. 2009;75(5):542-549. doi:10.1038/ki.2008.639.	26	Randomized trial	6 months				X	
Murashima M, Kumar D, Doyle AM, Glickman JD. Comparison of intradialytic blood pressure variability between conventional thrice-weekly hemodialysis and short daily hemodialysis. Hemodial Int Int Symp Home Hemodial. 2010;14(3):270-277. doi:10.1111/j.1542-4758.2010.00438.x.	12	Retrospective	6 months					X
Painter P, Krasnoff JB, Kuskowski M, Frassetto L, Johansen K. Effects of modality change on health-related quality of life. Hemodial Int Int Symp Home Hemodial. 2012;16(3):377-386. doi:10.1111/j.1542-4758.2012.00676.x.	10	Prospective	6 months				X	
Raimann JG, Chan CT, Daugirdas JT, et al. The Effect of Increased Frequency of Hemodialysis on Volume-Related Outcomes: A Secondary Analysis of the Frequent Hemodialysis Network Trials. Blood Purif. 2016;41(4):277-286. doi:10.1159/000441966.	170	Randomized trial	12 months	X				

Evidence Matrix – More Frequent Hemodialysis

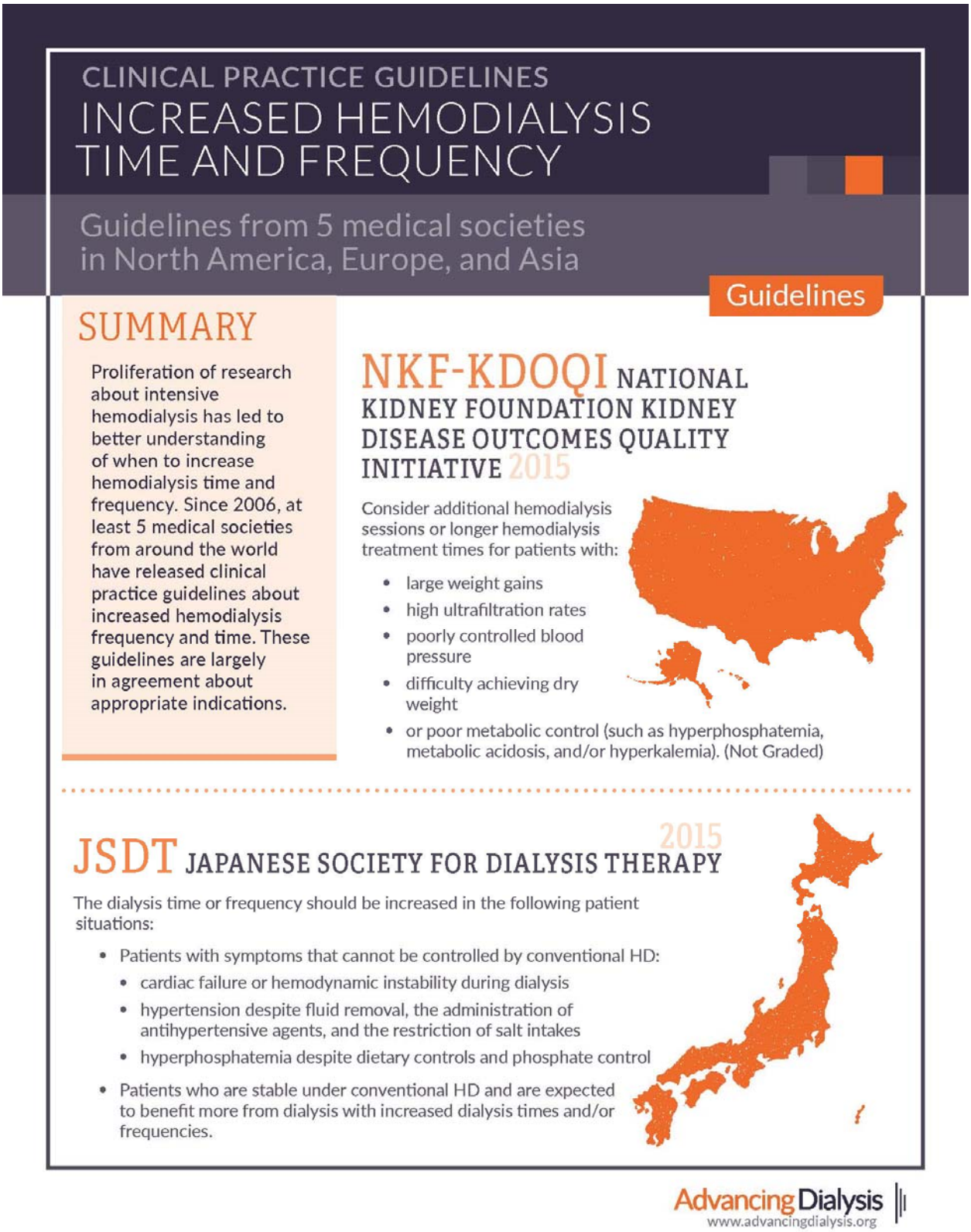
Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Rocco MV, Lockridge RS, Beck GJ, et al. The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial. Kidney Int. 2011;80(10):1080-1091. doi:10.1038/ki.2011.213.	45	Randomized trial	12 months	X	X		X	
Sarafidis PA, Persu A, Agarwal R, et al. Hypertension in dialysis patients: a consensus document by the European Renal and Cardiovascular Medicine (EURECA-m) working group of the European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) and the Hypertension and the Kidney working group of the European Society of Hypertension (ESH). J Hypertens 2017;35(4):657-676	Not applicable	Systematic review		Important background Sodium and volume excess is the prominent mechanism of hypertension in dialysis patients. Nonpharmacologic interventions targeting sodium and volume excess are fundamental for hypertension control in this population. Increasing hemodialysis treatment time and frequency may be efficacious.				
Silverstein DM. Frequent hemodialysis: history of the modality and assessment of outcomes. Pediatr Nephrol 2017;32(8):1293-1300	Not applicable	Systematic review		Important background There seems to be evidence that for some patients the advantages of frequent hemodialysis may outweigh the risks, caution is necessary to identify patients most suitable for frequent and/or home hemodialysis.				
Sirich TL, Fong K, Larive B, et al. Limited reduction in uremic solute concentrations with increased dialysis frequency and time in the Frequent Hemodialysis Network Daily Trial. Kidney Int 2017;91(5):1186-1192	30	Randomized trial	12 months	Important background The beneficial effects of more frequent hemodialysis that were observed in the Frequent Hemodialysis Network Daily Trial were not mediated by significant changes in uremic solute concentrations.				
Suri RS, Li L, Nesrallah GE. The risk of hospitalization and modality failure with home dialysis. Kidney Int. 2015;88(2):360-368. doi:10.1038/ki.2015.68.	1116	Retrospective	1.6 years (mean)	X				
Thomson BKA, Huang S-HS, Chan C, Urquhart B, Skanes A, Lindsay RM. Nocturnal home hemodialysis associates with improvement of electrocardiographic features linked to sudden cardiac death. ASAIO J Am Soc Artif Intern Organs 1992. 2014;60(1):99-105. doi:10.1097/MAT.0000000000000023.	50	Retrospective	>12 months	X				

Evidence Matrix – More Frequent Hemodialysis

Article	Number of Patients on Frequent HD	Type of Study	Duration of Study	Clinical Indication				
				Cardiovascular Disease	Hyper-tension	Hyper-phosphatemia	Quality of Life	Hemodialysis Tolerability
Ting GO, Kjellstrand C, Freitas T, Carrie BJ, Zarghamee S. Long-term study of high-comorbidity ESRD patients converted from conventional to short daily hemodialysis. Am J Kidney Dis Off J Natl Kidney Found. 2003;42(5):1020-1035.	42	Prospective	72 months				X	
Unruh ML, Larive B, Chertow GM, et al. Effects of 6-times-weekly versus 3-times-weekly hemodialysis on depressive symptoms and self-reported mental health: Frequent Hemodialysis Network (FHN) Trials. Am J Kidney Dis Off J Natl Kidney Found. 2013;61(5):748-758. doi:10.1053/j.ajkd.2012.11.047.	170	Randomized trial	12 months				X	
Weinhandl ED, Gilbertson DT, Collins AJ. Mortality, Hospitalization, and Technique Failure in Daily Home Hemodialysis and Matched Peritoneal Dialysis Patients: A Matched Cohort Study. Am J Kidney Dis Off J Natl Kidney Found. 2016;67(1):98-110. doi:10.1053/j.ajkd.2015.07.014.	4201	Retrospective	1.8 years (mean)	X				
Weinhandl ED, Liu J, Gilbertson DT, Arneson TJ, Collins AJ. Survival in daily home hemodialysis and matched thrice-weekly in-center hemodialysis patients. J Am Soc Nephrol JASN. 2012;23(5):895-904. doi:10.1681/ASN.2011080761.	1873	Retrospective	1.8 years (mean)	X				
Weinhandl ED, Nieman KM, Gilbertson DT, Collins AJ. Hospitalization in daily home hemodialysis and matched thrice-weekly in-center hemodialysis patients. Am J Kidney Dis Off J Natl Kidney Found. 2015;65(1):98-108. doi:10.1053/j.ajkd.2014.06.015.	3480	Retrospective	1.5-2.1 years (mean)	X				
Zoccali C, Moissl U, Chazot C, et al. Chronic Fluid Overload and Mortality in ESRD. J Am Soc Nephrol 2017;28(8):2491-2497	Not applicable	Retrospective		Important background Regardless of pre-dialysis systolic blood pressure, chronic fluid overload, as measured by bioimpedance spectroscopy, is a strong risk factor for death among thrice-weekly hemodialysis patients.				

INCREASED HEMODIALYSIS TIME AND FREQUENCY: GUIDELINES FROM 5 MEDICAL SOCIETIES IN NORTH AMERICA, EUROPE, AND ASIA

INCREASED HEMODIALYSIS TIME AND FREQUENCY: Guidelines from 5 Medical Societies in North America, Europe, and Asia



INCREASED HEMODIALYSIS TIME AND FREQUENCY
CLINICAL PRACTICE GUIDELINES

UK RA UNITED KINGDOM RENAL ASSOCIATION 2011

We suggest that an increase in treatment and/or frequency of HD should be considered in patients with:

- refractory fluid overload
- uncontrolled hypertension
- hyperphosphataemia
- malnutrition
- cardiovascular disease (2C)

EBPG 2007 EUROPEAN BEST PRACTICE GUIDELINES

An increase in treatment time and/or frequency should be considered in:

- patients with haemodynamic or cardiovascular instability (Evidence level II)
- patients who remain hypertensive despite maximum possible fluid removal (Evidence level III)
- patients with impaired phosphate control (Evidence level III)
- malnourished patients (Opinion)

CSN CANADIAN SOCIETY OF NEPHROLOGY 2006

- In patients with poorly controlled BP, consider the use of frequent hemodialysis (Grade D) or sustained hemodialysis. (Grade C)
- In patients with significant left ventricular hypertrophy or impaired left ventricular systolic function, consider the use of frequent hemodialysis as adjunctive therapy. (Grade D)
- In patients who exhibit hemodynamic instability with conventional hemodialysis, the use of frequent hemodialysis should be considered. (Grade D, opinion)
- In patients with refractory hyperphosphatemia and/or secondary hyperparathyroidism, consider the use of NHD as adjunctive therapy. (Grade D, opinion)
- In patients with refractory peripheral vascular disease and ectopic calcification, consider the use of NHD as salvage therapy. (Grade D, opinion)
- In patients who exhibit chronic malnutrition, consider the use of frequent hemodialysis as salvage therapy. (Grade D, opinion)