9 Prescriptions for Home Hemodialysis

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Implementing Hemodialysis in the Home
A Global Perspective

ISHD
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Prescriptions for Home HD

Abstract

Prescribing a regimen that provides "optimal dialysis" to patients who wish to dialyze at home is of major importance, yet there is substantial variation in how home hemodialysis (HD) is prescribed. Geographic location, patient health status and clinical goals, and patient lifestyle and preferences all influence the selection of a prescription for a particular patient—there is no single prescription that provides optimal therapy for all patients, and careful weighing of potential benefit and burden is required for long-term success. This module describes how home HD prescribing patterns have changed over time and provides examples of commonly used home HD prescriptions. In addition, associated clinical outcomes and adequacy parameters as well as criteria for identifying which patients may benefit most from these diverse prescriptions are also presented.

Introduction

Throughout the world, there is significant variation in the percentage of prevalent dialysis patients performing hemodialysis (HD) in their homes (Figure 1).[1] Not only is there a difference in the percentages of home HD patients between countries, but there is also a difference in the number of patients doing home HD within each country.

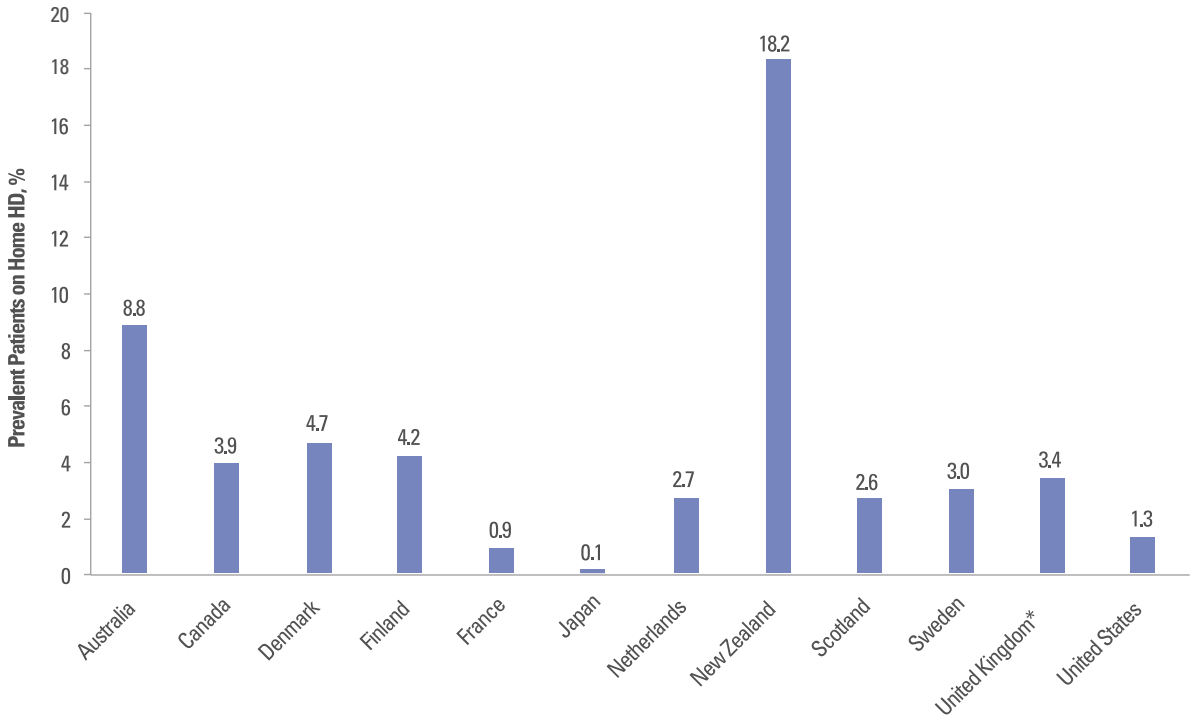

Figure 1. Proportion of prevalent dialysis patients on home hemodialysis

*United Kingdom includes England, Wales, and Northern Ireland. Scotland data reported separately.

Prescriptions for Home HD

Similarly, there is considerable variation in how home HD treatment is prescribed. Most home HD patients throughout the world use traditional machines designed for in-center or self-care HD. In the United States, the large majority of home HD patients are treated with short daily HD using a non-traditional, low-flow dialysate rate machine.[2]

In the early years of dialysis therapy, practitioners recognized that clinical well-being formed an important part of the assessment of dialysis adequacy. Modern thinking has again embraced this concept. Instead of providing adequate dialysis, we should strive for "optimal dialysis", defined in terms of excellence in quality of life, control of symptoms, and normalization of risk factors, including blood pressure, cardiac structure and function, mineral balance, nutrition, hormonal status, and survival.[3] If we, as clinicians, define optimal dialysis in these terms, it is unlikely that any single dialysis prescription will be optimal for all patients, but rather that we should strive to offer a range of HD prescriptions for patients that best address their individual needs.

There are 4 fundamental principles of home HD prescriptions that have emerged from international studies (Table 1).[4–16] The benefits of these principles must be weighed with the goals of the patient, as well as the burden to the patient and patient care partner.

This module will describe the most commonly used home HD prescriptions, focusing on outcome data and descriptions of patients who may benefit from the particular prescriptions.

Table 1. Fundamental Principles of Home HD Prescription

Minimum adequate HD can be defined as urea reduction ratio > 65% and a single-pool Kt/V of 1.2 per treatment for 3 times per week HD[4]
Increased total hours of HD per week is associated with improved survival[5-12]
Avoidance of high interdialytic weight gains (> 3–4 kg) and chronic fluid overload is associated with improved survival[12-14]
Avoidance of a long 3-day interdialytic break is associated with improved survival[15, 16]

HD = hemodialysis.

Rationale for Home HD Prescriptions

Throughout the world, HD is currently most commonly prescribed as 3 sessions per week (Mondays, Wednesdays, and Fridays or Tuesdays, Thursdays, and Saturdays), with each session lasting 3 to 5 hours.[16,17] This regimen has emerged as the most popular as a result of multiple logistic and patient factors. In the very early years of dialysis, treatment was prescribed as 2 to 3 sessions weekly, 8 hours per session. Over time, HD session durations have shortened to 3 to 5 hours, primarily on the basis that with the improving technologies, small-molecule clearance appeared to be adequate using this dialysis dose,[18] and it was logistically and financially easier to deliver therapy to the growing patient population. Regular dialysis every second or third day adequately controls accumulations of minerals (eg, potassium) and water that are known to have negative short-term effects, while also offering reasonable control of more long-term concerns, such as uremic symptoms and general well-being, for the majority of patients. It is possible for patients to sit attached to the dialysis machine for these 3- to 5-hour durations while still allowing some time for other activities that enhance quality of life. Dialyzing on the same days each week makes it easier for patients to schedule work and other important life commitments around dialysis. This scheduling is also easy for dialysis units and allows up to 6 shifts to be accommodated each week while avoiding excessive overnight and weekend overtime pay rates, as well as the associated life disruption for patients and staff.

Patients always desire the lowest possible dialysis treatment durations and frequency to avoid unnecessary intrusion of chronic disease on their lives.[19,20] From the late 1970s, HD treatment grew in numbers; technical advances in dialysis equipment allowed more efficient clearance of a broader range of toxins and potentially shorter treatment sessions, and financial constraints created an interest in defining clinical efficacy in a mathematical way (ie, identifying the lowest dialysis dose that would produce satisfactory clinical outcomes).[18,21] This resulted in the birth of the concept Kt/V as a measure of dialysis adequacy, where K is clearance of a molecule, t is the time on dialysis, and V is the volume of distribution for the molecule.[4] Clearance on dialysis of any substance can be defined in terms of Kt/V. Urea was one of the first identified and best understood uremic toxins and its quantification was easy and readily available. Therefore, Kt/V urea became the central focus of efforts to define a minimal dialysis requirement.[19]

In the modern era, there is a divergence of opinion and practice between clinicians from different countries in terms of the use of urea kinetic modeling for home HD patients. In the United States, urea kinetic modeling is deeply embedded in customary practices and clinician belief systems, and this extends to home HD. In fact, there are regulatory and reimbursement requirements that demand regular reporting and monitoring of Kt/V urea for all dialysis patients, including those on home HD. This situation is unique and contrasts with the policies in most other countries. In Australia and New Zealand, for instance, only about half of home HD patients have either a urea reduction ratio or Kt/V urea measured, and it is usually only calculated for those patients undergoing thrice-weekly schedules.[17] Many clinicians believe there are insufficient data to correlate Kt/V with clinical outcomes in home HD patients because frequency of dialysis and session length are markedly different from facility HD norms. Notwithstanding, Kt/V urea is a fundamental determinant of home HD prescription in some countries such as the United States, and it is important that the clinicians from those countries understand the underlying principles of Kt/V urea as applied to home HD.

The minimum adequate HD dose for patients being treated with standard thrice-weekly HD regimens has been defined as a single-pool Kt/V urea of 1.2 per dialysis session.[4] This target is primarily based on the results of 2 sentinel multicenter randomized controlled trials. The National Dialysis Cooperative Study examined outcomes in 151 patients undergoing HD for 3 sessions weekly.[22] Patients were randomized to either short (2.5 to 3.5 hours) or long (4.5 to 5.0 hours) session duration and within these groups, to either high-efficiency (time averaged blood concentration of urea [TAC urea] 50 mg/dL) or low-efficiency

(TAC urea 100 mg/dL) dialysis. Participants in the high TAC urea groups experienced more hospitalizations ($P < .001$) and withdrawals from dialysis ($P < .001$). In both the high and low TAC urea groups, those patients dialyzed for the shorter therapy duration experienced more hospitalizations than did those patients undergoing long therapy duration (P = 0.06).[22] Subsequent analyses of these data in a mechanistic study by Gotch and Sargent[23] and of the final data set by Keshaviah[24] found that Kt/V urea < 0.8 was associated with increased patient failure rates,[23] and that there were similar failure rates for patients with single-pool Kt/V values of 0.9 to 1.5.[21,24]

In the HEMO Study, 1846 patients were randomized to either standard (Kt/V goal of 1.05) or high-dose HD (Kt/V goal of 1.45), and to either low- or high-flux dialysis membranes.[25] The mean single-pool Kt/V urea was 1.32±.09 for the standard dose and 1.71±.11 for the high-dose group; however, no improvement in survival was observed with either intervention, although in subgroup analysis, there were some associations of mortality benefit in female participants.[25]

It should be noted that Kt/V has only been established as a surrogate marker of dialysis outcomes for short-hours, thrice-weekly dialysis regimens. Although there have been studies examining the effect of quotidian HD regimens on urea reduction estimated by various equations, its role for predicting patient outcomes in long-hour regimens has not been determined.[4,26] However, The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) has suggested a standardized weekly Kt/V of 2.0 for more frequent and longer HD treatments as well as for continuous ambulatory peritoneal dialysis (CAPD) and continuous cycling peritoneal dialysis (CCPD) as a minimal adequacy standard.[4]

The ultimate objective of any prescription is to provide the best long-term clinical outcomes possible for any given patient. This contrasts with the early days of HD, where dialysis was exclusively used short-term for treatment of acute kidney injury and subsequently, as a bridge to kidney transplantation for those who did not recover kidney function.[18] Over time, HD has evolved into a long-term therapy for patients with end-stage renal disease (ESRD) who for whatever reason cannot receive a kidney transplant. Lengthy transplant waiting lists in some regions also means that many patients require maintenance dialysis for substantial periods before a suitable organ becomes available. These changes have demanded a refocus of our attention to improving longer-term survival for dialysis-dependent patients with ESRD. The choice to dialyze at home relieves patients from many of the logistic influences on dialysis frequency and duration that have shaped our in-center HD regimens. Further, previous studies have shown that quality of life is higher in patients who are provided with a choice of dialysis modality,[27] and it is therefore possible that providing home HD patients with the autonomy of alternating between different HD modalities may further increase quality of life. The best renal replacement therapy will always be kidney transplantation; however, only a minority of ESRD patients will receive one. For the rest, the flexibility of home HD prescriptions—which can be modified based on preferred frequency, duration, personal schedule, and on clinical needs—can provide patients with improved clinical and quality-of-life outcomes while they are on dialysis, which are the closest outcomes to those achieved with transplant, had these patients been fortunate enough to receive one.

Traditional Standard-Hours Home HD Using Standard Dialysate Flow Machines

Outcome Data

Standard-hours home HD 3.0 to 3.5 times per week is a suitable prescription for use in the home (Table 2). For those dialysis units that are new to offering patients home HD, it can be easiest to begin providing this familiar regimen while unit personnel gain experience supervising HD at home.

Survival of patients with HD-dependent ESRD managed with the conventional thrice-weekly regimen is markedly lower than that of the age-matched general population.[17] Overall mortality rates for ESRD patients managed with standard chronic HD regimens in developed countries range from 5% to 27%, and the mortality in these patients is primarily related to cardiovascular disease, infection, and voluntary withdrawal from treatment.[17,28,29]

In addition to reduced quantity of life, ESRD patients also experience reduced quality of life as a consequence of symptoms of uremia that include fatigue, weakness, reduced sensation, impaired cognitive functions, dizziness, disturbed sleep, restless leg syndrome, neuropathy, anorexia, nausea, altered taste and smell, itching, cramps, sexual dysfunction, infertility, and depression and anxiety.[30] Currently available dialysis therapies

Table 2. Traditional Standard-Hours Home HD Prescription Using Standard Dialysate Flow Machines

Frequency	3.0-3.5 sessions per week
Session Duration	3.5-5.0 hours
Blood Flow Rate	300-400 mL/min
Dialysate Flow Rate	500-800 mL/min
Membrane	1.4-2.5 m^2 high flux
Dialysate Sodium	138 mmol/L (range, 134-140 mmol/L)
Dialysate Potassium	2 mmol/L (range, 2-3 mmol/L)
Dialysate Calcium	1.25 mmol/L (range, 1.0-1.5 mmol/L) 2.5 mEq/L (range, 2.0-2.5 mEq/L)
Dialysate Bicarbonate	34 mmol/L (range, 32-36 mmol/L)
Anticoagulation	• Standard heparin bolus (50 U/kg) • Low-molecular-weight heparin is also effective, but is used less commonly due to cost. Dose is typically administered as a bolus; it may be fixed or weight-based, depending on the patient and local policies
Assessment of Adequacy	Kt/V urea > 1.2 per session URR > 65% per session
Special Considerations	Excellent regimen for dialysis units that are new to home HD to use while experience is gained

HD = hemodialysis; URR = urea reduction ratio.

place a great burden on patients and their families as they require a substantial time commitment, adherence to intrusive dietary restrictions, and the use of multiple medications. In addition to the effects of uremia, the HD procedure itself has been associated with symptoms including fatigue, headache, nausea, restlessness, cramps, hypotension, and cognitive dysfunction. This has been termed the dialysis disequilibrium syndrome.[29]

The ability to teach patients to perform their own HD at home has been associated with improved survival and quality-of-life outcomes during traditional home HD.[31,32] Therefore it is still a worthwhile exercise to teach patients to dialyze at home even if they are only willing to use a standard HD prescription.

Patients Who May Benefit From this Prescription

We would recommend standard-hours dialysis for patients where minimizing time committed to HD therapy is of paramount importance, such as patients with palliative treatment goals or patients who, despite appropriate counseling about the benefits of increased frequency and extended-hours HD regimens, insist on performing a standard-hours HD regimen. Patients should be advised to avoid the standard prescription as it relates to the 3-day interdialytic break, as this long interdialytic interval is associated with increased cardiovascular events and mortality.[15,16]

There may also be a role for standard-hours regimens for patients who are newly commencing HD and who still have considerable residual renal function. These patients can usually achieve excellent control of fluid, serum parameters, and symptoms with fewer dialysis treatment hours for the first months, and dialysis dose can be gradually titrated upwards. This approach can assist patients in developing good habits with diet and fluid restrictions that will be compatible with excellent control of blood chemistry and fluid balance on an optimized dialysis regimen once residual renal function is lost. It can also be advantageous for patients starting dialysis at home to schedule their sessions during office hours, when maximum staff assistance is available; standard-hours regimens are particularly amenable to this. However, some patients may have difficulties adjusting to gradually increasing dialysis hours and may be better placed commencing a more intensive HD routine at the outset.

Alternate-Night Nocturnal Home HD Using Standard Dialysate Flow Machines

Outcome Data

There are no randomized, controlled data supporting the use of home alternate-night nocturnal HD (NHD) for the management of ESRD; however, there are data from observational and non-randomized, controlled studies that suggest benefits over conventional HD regimens. An example prescription is presented in Table 3.

Extended-hours HD, 3 sessions weekly has been practiced in-center in Tassin, France, for many years with reportedly excellent survival rates, control of hypertension, and higher clearance parameters.[18,33]

The Turkish Long Dialysis Study Group compared patients managed with a thrice-weekly (8 hours per session) in-center NHD regimen (n = 247) with matched control patients managed with a 4-hours-per-session conventional HD regimen (CHD; n = 247) in a prospective, controlled study over 12 months.[34] Use of an NHD regimen was associated with a 72% risk reduction for overall mortality ($P < 0.01$), a lower hospitalization rate, improved nutritional status, and improvement in echocardiographic parameters (eg, chamber diameters, left

Prescriptions for Home HD

Table 3. Alternate-Night Nocturnal Home HD Prescription Using Standard Dialysate Flow Machines

Frequency	3.5 sessions per week	**Anticoagulation**	• Minimum to prevent dialysis circuit thrombosis • Usually an extra 1000 U of unfractionated heparin bolus will be required above the standard regimen requirement. Thereafter, unfractionated heparin infusion at the same hourly rate used for standard HD regimens can be used and adjusted upwards if evidence of clotting is observed in the circuit • If fractionated heparin is used, an infusion following the initial bolus may be required to prevent clotting in patients prescribed longer session hours • Low-molecular-weight heparin is also effective, but is used less commonly due to cost. Dose is typically administered as a bolus; it may be fixed or weight-based, depending on the patient and local policies	**Special Considerations**	• Arguably, this is the easiest of the extended-hours HD regimens to maintain long term • Very little increase in consumable requirement that of above standard-hours HD (associated little increase in cost or stock storage requirements) • May reduce dialysis access complications compared with daily HD regimens • Addition of phosphate to the dialysate is rarely required. Addition of phosphate to the acid component of the dialysate in the form of Fleet® 5-40 mL may be required if serum phosphate predialysis is < 1 mmol/L and post-dialysis is lower than the recommended normal reference range when phosphate binders have been ceased and dietary phosphate intake is encouraged • Greater loss of water-soluble vitamins. Routine replacement of vitamins C, B group, and folic acid is recommended • Requires reliable monitoring for blood leak (eg, blood leak sensor and alarm system and/or remote monitoring) • Requires a large receptacle to hold 2 bottles of acid component of dialysis and a large size bicarbonate bag to ensure there are enough dialysate components to complete the treatment
Session Duration	6-10 hours				
Blood Flow Rate	250-350 mL/min				
Dialysate Flow Rate	300-500 mL/min				
Membrane	1.4-2.1 m^2 high flux				
Dialysate Sodium	138 mmol/L (range, 135-138 mmol/L)				
Dialysate Potassium	2 mmol/L (range, 2-3 mmol/L)				
Dialysate Calcium	1.5 mmo/L (range, 1.5-1.75 mmol/L) 3 mEq/L (range, 2.5-3 mEq/L)				
Dialysate Bicarbonate	32 mmol/L (range, 28-35 mmol/L)	**Assessment of Adequacy**	• Meets internationally accepted guidelines for electrolyte control and fluid balance • No or minimal requirement for antihypertensive medications and phosphate binders • Excellent reported quality of life		

HD = hemodialysis

ventricular hypertrophy) compared with CHD. NHD was associated with a significant reduction in serum phosphate level and accompanied by a reduction in phosphate binder use; similarly, hemoglobin levels increased and the use of erythropoietin was reduced. While there was no significant difference in blood pressure between groups, use of antihypertensive therapies was reduced with the NHD regimen ($P = .02$). Cognitive functions were improved with NHD but not CHD, and quality-of-life scores remained stable with NHD but deteriorated in the CHD group.[34]

Fresenius Medical Care in the United States compared 746 patients converted to 3 sessions weekly in-center NHD with 2062 matched control patients followed over a 2-year period.[8] This study reported a survival advantage of 25% with NHD ($P = .004$). While the interdialytic weight gain was higher with NHD, phosphate control was significantly improved and ultrafiltration rates were decreased owing to the longer session duration.[8]

A regimen of 3 to 4 NHD sessions weekly is the most commonly prescribed extended-hours HD regimen for HD patients in Australia.[35] Jun et al.[36] examined all-cause mortality, technique failure, and access complication rates in 286 Australian ESRD patients managed with extended-hours HD (> 24 hours per week). The majority of patients performed alternate-day, extended-hours HD. The overall survival rates (98%, 92%, and 83%) and technique survival rates (90%, 77%, and 68%) at 1, 3, and 5 years, respectively, were excellent. Increased frequency of HD was associated with an increased likelihood of developing an access event; however, access-related adverse event–free survival rates were 80%, 68%, and 61% at 1, 3, and 5 years, respectively.[36]

Reports from Brisbane, Australia, on patients who converted from home CHD (3 to 5 sessions weekly, 3 to 6 hours per session) to alternate-night home NHD (6 to 10 hours per session, 3 to 5 sessions weekly) describe improvements in blood pressure control with reduced antihypertensive requirement[37]; lower serum phosphate, calcium-phosphate product, and parathyroid hormone levels with reduced requirement for phosphate binding medications[37-39]; reduced vascular and ectopic calcification[38]; lower prolactin and higher testosterone levels in male patients[40]; reduced erythropoietin requirement[39,40]; improvements in general health and overall health ratings, physical function, physical role, and energy and fatigue scores on the kidney disease quality of life (KDQOL) assessment tool[39,40]; longer distance covered during the 6-minute walk test[39]; and improved small and middle molecule clearances.[39] The risk of dialysis access infectious complications appeared to be increased, particularly when the buttonhole cannulation technique was used in conjunction with extended-hours HD.[40] In contrast to the cardiovascular benefits reported in previous studies, no improvements in cardiovascular structure and function or hospitalization rates were observed following conversion to alternate-night NHD in this study.[37,41] Notably, the majority of patients in these studies dialyzed 3.5 to 4.0 sessions weekly and avoided a 3-day-long interdialytic break both at baseline and follow-up. The allowance of an interdialytic break of > 2 days on a regular basis should be discouraged as this longer dialysis-free interval has been associated with increased cardiovascular events and mortality.[16]

Interdialytic weight gains remain higher with alternate-day, extended-hours HD regimens compared with daily HD regimens. High interdialytic weight gains may be an indicator of improved nutritional status, but also remain a source of ongoing cardiovascular stress that may counteract the effects of improved control of other uremic toxins.[14-16] Interdialytic weight gains greater than approximately 3 to 4 kg and ultrafiltration rates higher than 10 to 13 mL/kg/h have been associated with increased mortality in adult long-term HD patients. This is the result of extracellular fluid expansion, which promotes hypertension and congestive cardiac failure, and high ultrafiltration rates, which promote cardiovascular instability and organ ischemia during dialysis sessions.[14-16]

Patients Who May Benefit from this Prescription

Alternate-night NHD is best suited to patients who desire their waking hours to be largely free of dialysis and are able to sleep while undergoing dialysis treatment, and those who do not have

reason to frequently get up at night and do not wish or are unable to sustain a daily HD regimen.

The 2-day break may lead to large, problematic interdialytic weight gains. Thus, alternate-night NHD is ideal for patients who struggle to maintain reasonable interdialytic weight gains or who have significant cardiac dysfunction.

Arguably, this prescription is the easiest of the extended-hours HD regimens to maintain long term. There is very little increase in consumable requirements for this treatment above standard-hours HD, so the increase in cost and storage requirements is minimal. This prescription may be associated with fewer vascular access-related complications compared with daily HD regimens.

Traditional Short Daily Home HD Using Standard Dialysate Flow Machines

Outcome Data

The short daily HD regimen (Table 4) is supported by results from many cohort and non-randomized studies that have suggested survival, cardiovascular, and quality-of-life benefits.[42-44] Short daily HD is also the regimen with the most robust randomized, controlled evidence for associated meaningful health benefits when compared with standard HD regimens. The Frequent Hemodialysis Network (FHN) conducted a randomized, controlled trial in which 125 patients managed with 6 sessions weekly, 1.5 to 2.75 hours per session, were compared with 120 patients managed with 3 sessions weekly, 2.5 to 4.0 hours per session HD, over 12-months.[45-47] The short daily HD regimen was associated with significantly better outcomes, including composite outcome of death or change in left ventricular mass, composite outcome of death and physical health composite score, decreased left ventricular mass, and improved hypertension and serum phosphate control. There was no difference between the 2 groups in cognitive performance, depression scores, albumin, erythropoietin sensitivity, the composite measure of death and hospitalization rates, serum calcium, parathyroid hormone, or rate of loss of residual renal function. Short daily HD was associated with an increased need for vascular access interventions in this group compared with the interventions experienced in the standard HD frequency group.[45-47] It should be noted that the FHN trial included a relatively small number of highly selected participants and the mortality outcomes were composite measures, so results of this trial may not apply to all patients or patient populations.

Patients Who May Benefit from this Prescription

Any patient who is willing and able to sustain dialyzing on a daily basis may benefit from a short daily regimen. Patients who are unable to tolerate increased hours per session, particularly when sleeping during dialysis or when sitting for long periods is not possible, may benefit the most. Short daily schedules may be the preferred option that fits best around some patients' other daily commitments such as employment or education, particularly if these patients do not tolerate or are not willing to perform nocturnal HD regimens.

Prescriptions for Home HD

Table 4. Traditional Short Daily Home HD Prescription Using Standard Dialysate Flow Machines	
Frequency	5-6 sessions per week
Session Duration	2.5-3.5 hours
Blood Flow Rate	350-450 mL/min
Dialysate Flow Rate	350-600 mL/min
Membrane	1.4-2.1 m^2 high flux
Dialysate Sodium	138 mmol/L
Dialysate Potassium	2 mmol/L
Dialysate Calcium	1.25 mmo/L (range, 2.5 mEq/L)
Dialysate Bicarbonate	32-36 mmol/L
Anticoagulation	• Standard heparin bolus (50 U/kg) • Low-molecular-weight heparin is also effective, but is used less commonly due to cost. Dose is typically administered as a bolus; it may be fixed or weight-based, depending on the patient and local policies
Assessment of Adequacy	• Achieve a single pool Kt/V of 1.2 per treatment and/or a standardized weekly Kt/V of 3.0 • Maximize fluid control resulting in less blood pressure medications with optimal blood pressure control • Liberalize dietary intake • Provide > 12 hours of RRT per week
Special Considerations	To receive adequate therapy, patients must perform at least 5-6 treatments per week, which results in increased supplies, increased storage requirements, and increased cost for the provider. Fluid gain between treatments is less; however, with shorter treatment time, the amount of fluid required to remove per hour may exceed a safe ultrafiltration rate

Although fluid gains between treatments are usually reduced, high ultrafiltration rates may remain a problem with substantially shortened session durations. Also, daily HD regimens consume increased amounts of disposable supplies per week compared with thrice-weekly HD, which generates increased cost and a need for increased storage space in the home. Patients with cannulation phobias or vascular access that is difficult to cannulate or those prone to complications may be less suited to daily HD regimens (see "The Care and Keeping of Vascular Access in Home Hemodialysis Patients" module).

HD = hemodialysis; RRT = renal replacement therapy.

Traditional Nocturnal Home HD Using Standard Dialysate Flow Machines

Outcome Data

There are two randomized, controlled trials that examine patient outcomes with traditional daily NHD regimens (Table 5) compared with standard-hours HD regimens. Culleton et al.[48] conducted a randomized, controlled trial comparing outcomes in 27 patients receiving daily NHD with 25 patients receiving CHD over a 6-month period. Daily NHD was associated with improved left ventricular mass measured by cardiac magnetic resonance imaging, effect of kidney disease and burden of kidney disease domains of the KDQOL Scale, blood pressure with associated reduction in antihypertensive use, and serum phosphate with reduction in phosphate binder requirement. There was no benefit detected in overall quality of life or anemia management parameters.[48] The FHN Group[49] conducted a randomized, controlled trial comparing outcomes in 45 patients managed with daily NHD with 42 patients managed with CHD regimens. Daily NHD was not associated with improvement in the study's primary composite outcomes: death or change in left ventricular mass, and death or physical health composite score. Nocturnal HD was associated with improved serum phosphate and hypertension control. No improvement was seen in cognitive performance, depression scores, nutrition, anemia management, or hospitalization rates. The FHN Nocturnal Trial patient enrollment goal was 250 patients in the original study design, but this goal was reduced to 125 due to enrollment difficulties, and only 87 patients were randomized. This makes drawing firm conclusions from the trial problematic.[49]

Other non-randomized studies have consistently reported improvements in blood pressure control, when assessed, but variable changes in left ventricular hypertrophy, anemia, bone mineral metabolism, and quality-of-life measures.[50] Longer and more frequent dialysis sessions allow ultrafiltration to occur at a lower rate, which has been associated with less intradialytic hypotension and consequently less myocardial stunning and inflammation.[51] Pauly et al.[52] compared outcomes in a cohort of 177 NHD patients with 531 renal transplant recipients over 5 years and found survival rates were comparable between the 2 groups; however, in the most recent retrospective cohort study of intensive home HD patients and kidney transplant recipients, kidney transplantation was associated with superior treatment and patient survival.[53] Small cohort studies have demonstrated improvement in sleep apnea syndrome, sleep patterns, and restless leg syndrome with short daily HD and NHD.[54,55]

There are a few small cohort studies describing the potential for improved fertility and successful pregnancy outcomes using frequent NHD.[56-58] Hladunewich et al.[59] compared cohorts of female patients undergoing home daily NHD and CHD patients in Toronto, Canada, and the United States, respectively, over a 13-year period and found a dose-response relationship between the intensity of dialysis and pregnancy outcomes, including live birth rate, gestational age, and birth weight. If home NHD is not an option for a pregnant patient, an intensive, in-center NHD-like regimen (ie, 35 to 45 hours per week on dialysis) should be offered.[60]

Patients Who May Benefit from this Prescription

Daily home NHD is ideal for patients who are employed or have daytime commitments. Dialyzing during sleep allows patients to receive maximum renal replacement therapy with minimal burden, helps prevent patient and care partner burnout, and provides free time during waking hours for work or leisure activities. Patients with multiple medical problems—including those who have failed PD or transplant, or are on a transplant waiting list and are > 60 years of age—benefit from increased time and frequency of HD sessions, which maximizes stability during their treatment; this increases their quality of life and decreases comorbid events while they are on dialysis. Patients who are pregnant or planning to become pregnant should

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Table 5. Traditional Nocturnal Home HD Prescription Using Standard Dialysate Flow Machines

Frequency	4-6 sessions per week	**Anticoagulation**	• Standard heparin bolus (50 U/kg) with heparin pump, providing 500-1500 U/hr. Heparin should be stopped 1 hour before end of treatment if the patient has an AVF or AVG, and at the end of treatment if the patient has a CVC • Low-molecular-weight heparin is also effective, but is used less commonly due to cost. Dose is typically administered as a bolus; it may be fixed or weight-based, depending on the patient and local policies	**Special Considerations**	• The majority of patients will dialyze 4-5 times per week, which is a minimal increase in supply cost compared with typical alternate-day home HD • Most patients who dialyze using NHD an average of 5 days per week can maintain their phosphate levels in adequate range by increasing phosphate intake. Only 20-30% of patients will need to add additional phosphate to their dialysate. Addition of phosphate to the acid component of the dialysate in the form of Fleet® 5-40 mL may be required if serum phosphate predialysis is < 1 mmol/L and post-dialysis is lower than the recommended normal reference range, and when phosphate binders have been ceased and dietary phosphate intake has been encouraged • A standard renal replacement vitamin and vitamin C 500 U daily provides adequate water-soluble vitamin replacement • Requires reliable monitoring for blood leak. Blood leak sensor and alarm system are recommended. There appears to be no advantage in remote monitoring • Because the dialysate flow is 200-300 mL/min, there is no need for additional acid or bicarbonate jugs to provide adequate dialysate for a 6- to 8-hour treatment • Starting with a calcium bath of 1.5 mmol/L with the ability to increase to 1.75 mmol/L is standard of care and critical in the management of traditional NHD
Session Duration	6-8 hours				
Blood Flow Rate	250-350 mL/min				
Dialysate Flow Rate	200-300 mL/min				
Membrane	1.4-2.1 m^2 high flux				
Dialysate Sodium	138 mmol/L				
Dialysate Potassium	3 mmol/L				
Dialysate Total Calcium	1.5-1.75 mmol/L (3.0-3.5 mEq/L)				
Dialysate Bicarbonate	28-35 mmol/L	**Assessment of Adequacy**	• Provide a standardized weekly Kt/V ≥ 4.0 • Control phosphorus without the use of binders • Control blood pressure without the use of antihypertensive medication • Provide ≥ 24 hours of RRT per week		

HD = hemodialysis; AVF = arteriovenous fistula; AVG = arteriovenous graft; CVC = central venous catheter; NHD = nocturnal hemodialysis; RRT = renal replacement therapy.

have their dialysis hours per week increased, and this can be conveniently offered by a home NHD prescription. Daily home NHD also suits patients who value maximized dietary freedom while maintaining optimized blood chemistry. A standard renal replacement multivitamin and vitamin C 500 U daily provides adequate water-soluble vitamin replacement.

The majority of NHD patients will dialyze 5 times per week, which generates a moderate increase in cost and the need for increased storage space in the home compared with alternate-day home HD. Patients with cannulation phobias or vascular access that is difficult to cannulate or those prone to complications may be less suited to NHD regimens (see "The Care and Keeping of Vascular Access in Home Hemodialysis Patients" module).

Low-Flow Dialysate Short Daily Home HD

Low-Flow Dialysate HD Machine

Specifically designed low-flow dialysate HD machines are typically used only in the United States. Dialysate volume for the low-flow dialysate HD machine is 15 to 60 L per short daily treatment, or 90 to 360 L per week.[61] In comparison, the typical dialysate volume for traditional CHD machines is 90 to 200 L per treatment (270 to 600 L per week).

While uncommon in most areas of the world, in the United States more than 85% of the > 6000 patients on home HD use a low-flow dialysate machine to perform short daily home HD.[2,62] This machine was approved by the US Food and Drug Administration (FDA) and Health Canada in July 2003[63] for HD, hemofiltration, and/or ultrafiltration for treatment of renal failure or fluid overload in the in-center dialysis and acute-care settings, and was evaluated[64] and approved for home HD by the FDA in June 2005.

Short daily home HD prescriptions using a low-flow dialysate HD machine (Table 6) are not based on time per treatment, but rather on a flow fraction of 30% to 35% (a ratio of blood flow rate to dialysate flow rate of 3 to 1) to maximize urea saturation of dialysate used, shorten dialysis time per treatment, meet the minimal adequacy KDOQI standards, and decrease the amount of sterile fluid used per treatment.[64,65]

A web-based HD dose calculator is available to help physicians prescribe low-flow dialysate HD and to better meet prescription goals and needs of their patients (see https://dosingcalculator.nxstage.com/Account/Login.aspx). This calculator allows the physician to suggest a weekly standardized Kt/V goal, blood flow rate, weekly ultrafiltration rate, maximum ultrafiltration rate per hour, minimal hours per week, and frequency of treatments per week. Once the physician completes the required fields, the calculator will provide varied prescriptions that meet the physician's specified goals. This approach moves away from flow fraction–based prescribing and providing minimally adequate dialysis, and toward frequency and time per week of HD for more optimal dialysis.

It should be noted that clearances with low-flow dialysate systems are reduced in efficiency compared with other currently available HD systems. Thus, most patients will require an increased intensity HD prescription to maintain optimal health. Great care is needed to ensure adequate dialysis is maintained as residual renal function wanes and patients gradually modify their HD schedules at home.

Outcome Data

There are no randomized, controlled studies supporting the use of low-flow dialysate short daily HD for the management of ESRD; however, there are several observational studies that support the efficacy and safety of this prescription.

Table 6. Low-flow dialysate short daily home HD prescription

Frequency	5-6 sessions per week	**Anticoagulation**	Standard heparin bolus (50 U/kg)	**Special Considerations**	• This machine has built-in moisture detectors in the pan under the machine to detect any type of leak related to the machine and artificial kidney • It is important to note that because this machine uses a lower dialysate flow rate, the clearance of small molecules is reduced compared with traditional machines • Frequency of treatment, simple set up and take down procedures, and portability make the low-flow machine unique for short daily dialysis • Low-flow machine only provides a calcium bath of 1.5 mmol/L
Session Duration	2.5-4 hours	**Assessment of Adequacy**	• Provide a standardized weekly Kt/V ≥ 2.1 (meeting specified KDOQI guidelines) • Control blood pressure without the use of antihypertensive medications • Liberalize dietary intake • Provide > 12 hours of RRT weekly Note: In the United States the Center for Medicaid and Medicare Services regulates meeting specified KDOQI guideline requirements and minimizing the cost of supplies. A more optimal prescription would include five treatments per week, use of > 30 L of dialysate per treatment, and > 15 hours RRT per week		
Blood Flow Rate	300-400 mL/min				
Dialysate Flow Rate	83-300 mL/min (20-60 L of dialysate per treatment)				
Membrane	1.8 m² high flux				
Dialysate Sodium	138 mmol/L				
Dialysate Potassium	2.0 mmol/L				
Dialysate Total Calcium	1.5 mmol/L (3.0 mEq/L)				
Dialysate Bicarbonate	40-45 mmol/L				

HD = hemodialysis; KDOQI = Kidney Disease Outcomes Quality Initiative; RRT = renal replacement therapy.
Note: This machine is typically used only in the United States.

Prescriptions for Home HD

In a study of 5 patients, the rate of removal of solutes (β_2 microglobulin, phosphorus, potassium, and urea nitrogen) from the serum per dialysis session was demonstrated to be lower with low-flow dialysate short daily HD than with thrice-weekly HD using higher dialysate flow rates.[61] While the solute removal rates were lower per session using lower flow rates, the increased frequency of sessions with short daily HD (17.5 hours per week) compared with CHD resulted in an overall increase in solute removal.[61]

Clinical outcomes, including improvements in prevalence and severity of symptoms of restless leg syndrome and sleep disturbances, have been reported with low-flow, short daily HD.[55] An observational study by Finkelstein et al.[66] enrolled 291 participants and used the SF-36 health survey to evaluate health-related quality of life (HRQOL) in home HD patients. Results indicated long-term improvements from baseline in HRQOL over the course of 12 months, including physical and mental components, when patients were initiated on low-flow daily home HD.[66] A prospective, open-label study comparing the safety of in-center and home HD using this low-flow dialysate HD machine was conducted by Kraus et al.[64]They reported lower rates of adverse events during home HD compared with in-center HD ($P = .007$). Despite a lower rate of adverse events, only a modest improvement in survival has been observed with low-flow, short daily HD compared with in-center CHD, with the cumulative incidence of death of 19.2% and 21.7%, resepctively.[67]

The FHN Daily Trial was a randomized, controlled study that compared outcomes in patients managed with 6 or 3 HD sessions weekly using traditional in-center machines with higher dialysate flow rates.[45] Findings revealed a reduction in left ventricular mass and improvement in quality-of-life indicators with more frequent dialysis. While this trial included a frequent HD prescription with a similar number of dialysis hours per week to that used in a low-flow, short daily HD prescription, the improved outcomes achieved with the higher dialysate flow rate cannot be extrapolated to a low-flow dialysate system without performing a similar study using a low-flow machine.

Previous studies have elicited concern associated with low-flow dialysate HD machines and why there appears to be significant technique failure at 1 year. The FREEDOM study, which reported improvements in HRQOL with short daily HD, also reported a high study discontinuation rate.[66] A total of 291 participants completed the SF-36 health survey, of which 154 completed the 12-month follow up (47% discontinuation rate). The majority (54%) of patients who withdrew from the study did so within the first 4 months. Participants withdrew from the study for the following reasons: modality change or return to in-center dialysis (63 patients), kidney transplantation (14 patients), death (13 patients), off short daily HD for > 6 weeks (12 patients), transfer out of a participating dialysis center (7 patients), non-compliance (3 patients), recovery of kidney function (2 patients), and other reasons (23 patients). Considering only those patients who changed modalities, died, or were off short daily HD for > 6 weeks, the rate of discontinuation over a 1-year period for this low-flow dialysate machine was 30%. Additional studies are required to explain why technique failure rates appear to be higher for this prescription than for home NHD.[66]

Patients Who May Benefit from this Prescription

Patients who may benefit from low-flow short daily HD regimens are the same as those who benefit from traditional short daily regimens (refer to discussion in "Traditional Short Daily Home HD Using Standard Dialysate Flow Machines" section).

In addition, the low-flow dialysate HD machine used in the United States is particularly suited to patients who wish to use short daily HD regimens because the machine has been designed to minimize time spent setting up, cleaning, and maintaining the system. The machine allows patients to dialyze at home with limited quantity and/or poor quality water supply, and is also useful for those who are unable to significantly modify their residence (eg, temporary accommodation or apartment dwelling). Dialysate can be easily prepared from drinking-quality tap water using the disposable water purification system and built-in water quality testing, which requires no regular maintenance by the patient or routine water testing by the supervising dialysis unit. Alternatively, dialysate is available in premade sterile bags (for more information, see "Infrastructure, Water, and Machines in the Home" module).

Patients who need or wish to travel and have experienced difficulties organizing in-center HD at their desired destinations may particularly benefit from this machine, which is relatively compact and portable. Patients who intend to travel with this machine should seek information regarding associated costs, baggage restrictions, and requirements for local medical supervision at the destination (see "Psychosocial Aspects in Home Hemodialysis" and "Infrastructure, Water, and Machines in the Home" modules).

Low-Flow Dialysate Nocturnal Home HD

Outcome Data

Low-flow dialysate machines are typically used only in the United States and for short daily home HD. As such, there are no randomized studies evaluating low-flow dialysate NHD, but its use is supported by published observational studies. Pierratos et al.[68] presented the Toronto 3-year experience with nocturnal dialysis in 1998. It is important to note that this dialysis prescription for the first 3 years was a low surface area (0.7 m^2, Fresenius F40) dialyzer, blood flow rate of 250 to 300 mL/min, and a dialysis flow rate of 100 mL/min.[68] This would be considered low-flow dialysate HD, which would suggest that nocturnal dialysis could be performed utilizing the low-flow dialysate HD machine presently used in the United States. An example prescription is presented in Table 7.

Lockridge et al.[69] presented data on 15 patients over a 3-year period who were trained on the low-flow dialysate HD machine to perform NHD. The HD machine was reprogrammed to convert it from a flow fraction–to a time-based machine using the following settings:

- Flow fraction: 100% (setting 1)
- Dialysate flow rate: Liter dialysate per treatment ÷ hours per session (setting 2)
- Dialysate volume: Liter dialysate per treatment ÷ hours per session (setting 5)
- Access pod: "Off" (setting 53)
- Cartridge: 171-B
- Heparin pump: External

Low-flow NHD was performed successfully in this diverse group of patients with a mean treatment time of 6.8 (6.0 to 7.0) hours per treatment, 4.8 (4.0 to 5.0) treatments per week, and 56 L of dialysate per treatment. After patients had been on the NHD therapy for 3 months or longer, the mean Kt/V for this dialysis prescription was 3.8 (3.10 to 4.56), and few patients required antihypertensive medications (1 of 15 patients) or phosphate binders (4 of 15 patients).[69] Reprogramming a low-flow dialysate system with the addition of an external heparin pump allowed for the convenience of NHD with optimized dialysate adequacy.

Patients Who May Benefit from this Prescription

Patients who may benefit from low-flow NHD regimens are the same as those who benefit from traditional NHD. Please (refer to discussion in "Traditional Nocturnal Home HD Using Standard Dialysate Flow Machines" section).

Table 7. Low-flow dialysate home NHD

Frequency	4-6 sessions per week	**Anticoagulation**	• Standard heparin bolus (50 U/kg) with heparin pump, providing 500-1500 U/hr. Heparin should be stopped 1 hour before end of treatment if the patient has an AVF or AVG, and at the end of treatment if the patient has a CVC • Low molecular weight heparin is also effective, but is used less commonly due to cost. Dose is typically administered as a bolus; it may be fixed or weight-based, depending on the patient and local policies	**Special Considerations**	• Most low-flow dialysate nocturnal patients dialyzing 5 days per week can maintain their phosphate levels in an adequate range. This low-flow dialysate machine does not offer the ability to add phosphorus to the dialyses bath • A standard renal replacement vitamin and vitamin C 500 U daily provides adequate water soluble vitamin replacement • This machine has built-in moisture detectors in the pan under the machine to detect any type of leak related to the machine and artificial kidney. Because this machine uses a lower dialysate flow rate, the clearance of small molecules is reduced compared with traditional machines. Large-molecule clearance that is time-based is the same rate as that achieved with traditional machines • The only low-flow dialysate machine available at present can only provide a calcium bath of 1.5 mmol/L, which could be problematic if there is calcium depletion associated with ultrafiltration
Session Duration	6-8 hours				
Blood Flow Rate	300-350 mL/min				
Dialysate Flow Rate	62.5-166.6 L/min (30-60 L of dialysate/treatment)				
Membrane	1.8 m^2 high flux				
Dialysate Sodium	138 mmol/L	**Assessment of Adequacy**	• Provide a standardized weekly Kt/V ≥ 3.0-4.5 (optimal RRT) • Control of phosphorus without the use of binders • Control blood pressure without the use of antihypertensive medications • Provide ≥ 24 hours of RRT per week		
Dialysate Potassium	2.0 mmol/L				
Dialysate Total Calcium	1.5 mmol/L (3.0 mEq/L)				
Dialysate Lactate	Lactate baths 40-45 mmol/L				

NHD = nocturnal hemodialysis; AVG = arteriovenous graft; AVF = arteriovenous fistula; CVC = central venous catheter; RRT = renal replacement therapy.

Note: This machine is typically used only in the United States.

Summary

There are numerous prescriptions available for ESRD patients who wish to perform HD in the home, and no single prescription can provide optimum dialysis for all patients. Comparisons of commonly used prescriptions from around the world can be found in Tables 8 and 9. Providers must weigh clinical goals against patient preferences and overall patient and care partner burden to ensure successful home HD therapy.

Table 8. Home HD Modality Prescriptions

Modality	Sessions per Week	Session Duration, hours	QB mL/min	QD mL/min	Base, mmol/L	K^+, mmol/L	Ca^{2+}, mmol/L	PO_4 added
Traditional (standard hours)	3-3.5	3-5	300-400	500-800	HCO_3, 32-36	2	1.25	none
Alternate-Night Nocturnal	3.5	6-8	250-350	300-500	HCO_3, 28-35	2	1.25	rare
Traditional Short Daily	5-6	2.5-3.5	350-400	350-600	HCO_3, 32-36	2	1.25	none
Traditional Nocturnal	4-6	6-8	250-350	300	HCO_3, 28-35	3	1.5-1.75	20-30% of time
Low-flow Dialysate Short Daily	5-6	2.5-4	300-400	90-300	Lactate, 40-45	2	1.5	none
Low-flow Dialysate Nocturnal	4-6	6-8	300-350	83-166	Lactate, 40-45	2	1.75	none

QD = dialysis fluid flow rate; QB = blood flow rate; K^+ = potassium; Ca^{2+} = calcium; PO_4 = phosphate; HCO_3 = bicarbonate.

Prescriptions for Home HD

Table 9. Comparative Efficacy Across Prescriptions Relative to Renal Transplant

	Regimen Intensity		Efficacy Relative to Transplant (5 = Transplant, 0 = No Treatment)			
Renal Replacement Therapy	**Sessions per Week**	**Session Duration, hours**	**Controls Volume**	**Controls PO_4**	**Minimum Adequacy[a]**	**Optimal Adequacy[b]**
Transplant	–	–	5	5	4	5
CAPD and CCPD Without Residual Renal Function	–	–	1	1	4	0
Traditional HD (Standard Hours)	3	3-5	2	1	4	1
	3.5	3-5	3	2	4	2
Traditional Short Daily HD	5-6	2.5-3.5	5	3	4	3
Traditional Nocturnal HD	3.5	6-8	4	4	4	4
	5-6	6-8	5	5	4	5
Low-flow Dialysate Short Daily HD	5-6	2.5-4.0	5	2	4	3
Low-flow Dialysate Nocturnal HD	5-6	6-8	5	4	4	4

Note: Outcomes data available to make direct comparisons between dialysis regimens and renal transplant are limited. Relative efficacy values are largely opinion-based and provided only as estimates.

[a]Minimal adequacy is the minimally adequate dialysis dose defined in the KDOQI Clinical Practice Guidelines and Recommendations 2006 Update on Hemodialysis Adequacy.[4]

[b]Optimal adequacy is the dialysis dose provided by longer and more frequent dialysis sessions.

HD = hemodialysis; PO_4 = phosphate; CAPD = continuous ambulatory peritoneal dialysis; CCPD = continuous cycling peritoneal dialysis.

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