CORE CURRICULUM IN NEPHROLOGY

Home Hemodialysis, Daily Hemodialysis, and Nocturnal Hemodialysis: Core Curriculum 2009

Jeffrey Perl, MD, FRCP(C), and Christopher T. Chan, MD, FRCP(C)

INTRODUCTION

Given the recent results of the Hemodialysis (HEMO) and Adequacy of Peritoneal Dialysis in Mexico (ADEMEX) studies, historical concepts of dialysis adequacy were challenged after increasing small-solute clearance failed to impact on the survival of patients with end-stage renal disease (ESRD). As a result, increasing interest has shifted to augmentation of both the frequency and duration of hemodialysis (HD). Intensification of HD is achieved by increasing the frequency of therapy (in the case of short daily HD [SDHD]), duration of treatment, or both (in the case of home nocturnal HD [NHD]). Intensive HD may be performed either in-center or in the patient's home. Cardiovascular benefits of intensive HD have included improvements in blood pressure (BP) control, endothelial function, and left ventricular geometry. Other clinical benefits of intensive HD include enhanced clearance of middle-molecular uremic toxins, superior anemia and phosphate control, and improvements in sleep disorders, fertility, and quality of life. Although observational data suggest that intensification of dialysis has translated into improved clinical outcomes, confirmation through randomized controlled trials is necessary and ongoing. Few absolute contraindications to SDHD or NHD exist. These are based largely on patient motivation and support, suitability of vascular access, and, if applicable, appropriateness of the home environment. When possible, dialysis in the home should be encouraged; however, significant system and social barriers may limit the widespread use of home HD. Early patient referral, appropriate patient selection, education, and home preparation are integral components of a successful home dialysis program.

Terminology

I. No universal nomenclature exists to describe alternative dialysis schedules[1]
II. Conventional HD (CHD) is intermittent HD performed in-center for 4-hour sessions thrice weekly
III. Intensive HD describes collectively all methods that offer either longer duration or higher frequency of HD compared with CHD, including (Fig 1):
   A. Quotidian HD (daily HD [5-7 sessions/wk]), which may be:
      1. NHD, or long nightly dialysis (during sleep)
      2. SDHD, or daily dialysis of shortened duration
   B. Long intermittent HD (intermittent HD [3 sessions/wk]) of increased duration:
      1. Nocturnal intermittent HD (NIHD)
      2. Hemeral (daytime) long intermittent HD
IV. Many of these techniques can be performed at home (particularly NHD)

History of Intensive HD and Home HD

I. 1960s: Very long and infrequent HD sessions (12-18 hours) every 10-15 days out of necessity[3]
II. 1960s: Shaldon first to offer long intermittent HD at night at home to patients dialyzing 2-3 nights/wk[4,5]
III. 1960s: DePalma et al[6,7] published the first study of the use of daily HD in 7 patients dialyzed 5 times/wk for 4-5 h/session
IV. 1970s: use of more efficient plate and later hollow-fiber dialyzers allow for shortening the length of dialysis sessions to 3.5-5 hours
V. 1970s: Tassin Center in France started and continues long intermittent HD for $>$ 800 patients during 40 years (8 hours, thrice

From the Division of Nephrology, University Health Network, Toronto, Ontario, Canada.

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Address correspondence to Christopher T. Chan, MD, FRCP(C), Toronto General Hospital, 200 Elizabeth St-8N-842, Toronto, Ontario, Canada, M5G 2C4. E-mail: christopher.chan@uhn.on.ca

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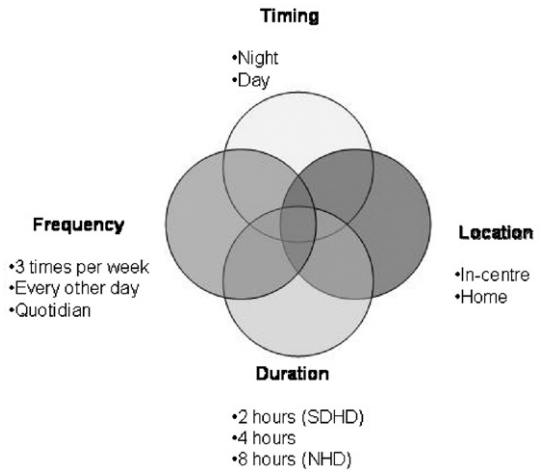

Figure 1. Methods of dialysis intensification. Abbreviations: NHD, nocturnal hemodialysis; SDHD, short daily hemodialysis. Adapted from Pereira, Sayegh, and Blake[2] with permission of Elsevier.

weekly) and reports excellent BP control and 10-year survival[8,9]

VI. 1980s: several groups, including Buoncristiani and Ting, establish SDHD programs in which SDHD is used as rescue therapy for patients for whom CHD failed[10-12]
VII. 1990s: Uldall created the first home NHD program in Toronto, Canada, funded by the Ministry of Health of Ontario. The first patient was treated in 1994.[13] A permanent indwelling internal jugular catheter is designed for use during dialysis at night[14]
VIII. 2000: large NHD programs established worldwide with variable government funding. Lockridge[15] leads the largest home NHD program in the United States
IX. 2007: first randomized controlled trial of NHD versus CHD published[16]

Quantification of Solute Removal

I. Weekly small-solute clearance is lower on peritoneal dialysis (PD) therapy compared with HD (weekly Kt/V, 2.0 vs 3.2)
II. Equivalent patient survival between PD and HD despite lower weekly small-solute clearance on PD therapy is suggestive that daily or continuous renal replacement therapy may provide improved outcomes at similar degrees of small-solute clearance[17]
III. No universal method exists to quantify dialysis dose across different HD schedules and various dialysis modalities (Table 1). Current measures include:

A. Standard Kt/V (stdKt/V):
   1. Introduced by Gotch[18]
   2. Calculated based on the midweek predialysis urea level
   3. Assumption: mean predialysis urea level portends equivalent uremic toxicity to steady-state urea concentrations of continuous therapies (ie, continuous ambulatory PD)
   4. Dialysis regimens with the same midweek predialysis blood urea nitrogen (BUN; also known as steady-state BUN) level have the same weekly stdKt/V (including native kidney function)
   5. stdK = urea generation divided by mean peak predialysis urea concentration
   6. Urea generation and V are calculated based on traditional urea kinetic modeling
   7. stdK then multiplied by dialysis time and divided by V
   8. Formula for mean peak predialysis urea concentration takes into account duration and number of treatments per week and degree of urea rebound (for intermittent therapies)

B. Normalized Kt/V:
   1. Proposed by Depner[19]
   2. Based on a hypothetical solute that has slower diffusion across the dialysis membrane than urea

Table 1. Comparison of Treatment Parameters Across Intensive HD Schedules

	CHD	SDHD	NHD	NxStage HD
Treatments/wk	3	6	5-6	6
Treatment time (h)	4	2-3	6-8	2.5-3.5
Blood flow rate (mL/min)	400	400	200	400
Dialysate flow rate (mL/min)	500	800	300	130
Single-pool Kt/V/ treatment	1.2	0.5	1.8	0.5[a]

Abbreviations: CHD, conventional hemodialysis; HD, hemodialysis; NHD, nocturnal hemodialysis; SDHD, short daily hemodialysis.

[a]Using Nxstage short daily prescription.

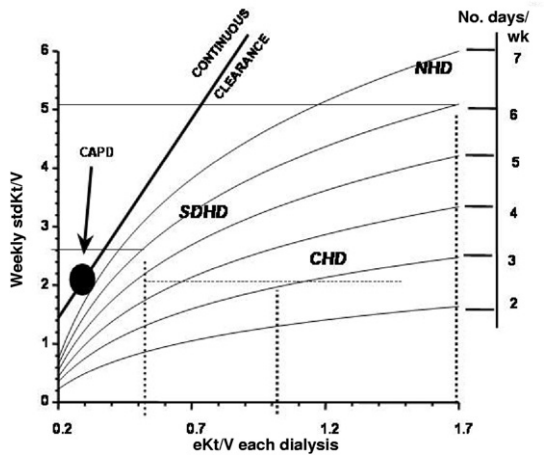

Figure 2. Relationship between weekly standardized Kt/V (stdKt/V) and equilibrated Kt/V (eKt/V) across dialysis modalities and schedules. With increasing frequency of therapy, lower eKt/V is required per dialysis session to achieve a similar stdKt/V. Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; CHD, conventional hemodialysis; NHD, nocturnal hemodialysis; SDHD, short daily hemodialysis. Adapted from Gotch[18] with permission of Oxford University Press.

3. Favors intensive dialysis because solute removal increases with time and duration

C. Equivalent renal urea clearance:
1. Proposed by Casino and Lopez[20]
2. Equal to amount of urea clearance provided by native kidney function (ie, amount required to produce a BUN concentration equal to the time-averaged concentration of urea [achieved on dialysis])

IV. Comparison of stdKt/V across dialysis modalities and schedules[18] (Fig 2):
A. In PD, stdKt/V of 2.0 corresponds to a weekly Kt/V of 2.0 for PD[18]
B. In CHD, stdKt/V of 2.0 corresponds to a single-pool Kt/V (spKt/V) of 1.2 per treatment (minimally adequate dialysis as advocated by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative [KDOQI] guidelines)[21,22]
C. In NHD, daily dialysis is associated with a lower predialysis BUN level; therefore, stdKt/V of 4-5/wk (based on daily dialysis) is achieved with a spKt/V of ~1.8-2.5/treatment[23]; this is achieved even when using lower blood and dialysate flows compared with CHD[18]
D. In SDHD, targeting an stdKt/V of 2.0, the corresponding spKt/V typically is 0.53-0.56/treatment and equilibrated Kt/V (eKt/V) of 0.38/treatment; this is approximately half that achieved in a single CHD treatment

V. Daily HD allows for increased clearance of middle molecules because of less rebound
A. NHD increases middle-molecule removal as a result of higher frequency and duration of HD.[24-26] Greater convective removal also is seen as a result of higher weekly ultrafiltration
B. In 1 study, weekly dialysate β_2-microglobulin mass removal increased from 127 to 585 mg after conversion from CHD to NHD, whereas serum β_2-microglobulin levels decreased from 27.2 to 13.7 mg/dL after 9 months.[27] In another study, after conversion from 4 to 8 hours of HD, the relative increase in total solute removal was greatest for middle molecules, such as phosphorus and β_2-microglobulin, compared with small solutes, such as urea and creatinine (Fig 3)[28]

VI. Removal of protein-bound molecules, such as indole-3-acetic acid indoxyl sulfate, has been greater on SDHD compared with CHD[29]

HOME HD

Epidemiology of Home HD

I. Prevalence of home HD in the United States has decreased in the last 30 years
A. In 1970s, use in 40% of the US dialysis patient population[30]
B. In 2005, according to the US Renal Data System (USRDS), home HD constitutes 0.4% and 0.62% of all incident and prevalent dialysis patients, respectively[31]

II. Home HD almost exclusively available in high-income countries. Canada, Australia, New Zealand, and several European countries are among the countries with the highest prevalence of home HD[32]

III. Global home HD use correlated with higher prevalence of other forms of home dialysis (ie, PD)[32]

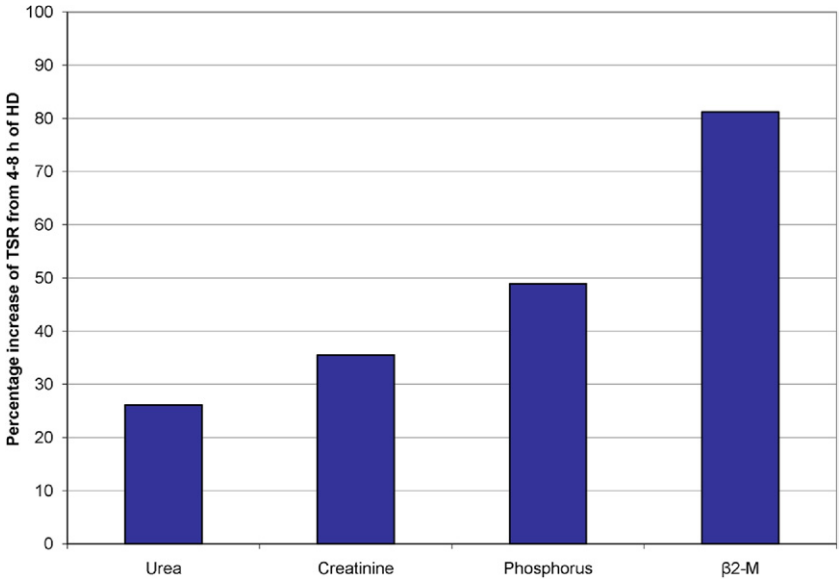

Figure 3. Relative increase in total solute removal (TSR) associated with a change from 4 to 8 hours of hemodialysis (HD): middle molecules versus small solutes. The impact of changes in TSR on conversion from 4 to 8 hours of HD is greater for middle molecules, such as phosphorus and β_2-microglobulin (β_2-M), compared with small solutes, such as urea and creatinine. Source: Eloot et al.[28]

Patient Evaluation for Home HD

I. Considerations for intensive HD:
   A. To improve kidney disease–associated quality of life (ie, work during the day, liberalize diet)
   B. To lessen intra-/interdialytic complications associated with CHD:
      1. Unstable hemodynamics during CHD
      2. Uncontrolled hypertension[33,34]
      3. Impaired left ventricular function and/or congestive heart failure[35]
      4. Uncontrolled ascites[36]
      5. Persistent hyperphosphatemia, metastatic calcification[37-39]
   C. Severe sleep apnea[40]
   D. Maintenance of home dialysis: NHD has been used successfully in patients in whom PD failed[41]
   E. When kidney transplant is not possible or is contraindicated
   F. Inadequate control of uremia (ie, large patient, poor access flow)

II. Absolute contraindications:
   A. Unsuitable access for HD or access unsuitable for self-cannulation
   B. Patient and/or partner unable to make appropriate decisions or follow instructions:
      1. Uncontrolled psychiatric disease
      2. Current drug abuse
      3. Adherence issues
      4. Severe dementia or encephalopathy

III. A relative contraindication is if anticoagulation is not possible:
   A. For heparin-induced thrombocytopenia, may be able to use alternative anticoagulation (ie, argatroban, danaparoid, citrate-based dialysate); however, cost may limit long-term use[42]
   B. May be able to perform saline flushes, particularly if using SDHD at home

Barriers to Use of Home HD

I. System related:
   A. Lack of experience with home HD in nephrologists and nephrology training programs
   B. Small number of programs are able to offer home HD
   C. Unfavorable financial reimbursement structure
   D. Late referral of patients with chronic kidney disease and limited predialysis modality education

II. Patient related:
   A. Patient/partner willingness to learn
   B. Patient-perceived barriers[43,44]: in a cross-sectional survey of 66 prevalent NHD and 153 CHD patients using validated instruments, study-specific questions, and

ethnographic interviews,[43] despite similar levels of education and perceived support, patient-perceived barriers in CHD patients converting to NHD were:
1) Primarily fears of self-cannulation, inability to perform dialysis at home, and a catastrophic event
2) Concerns about burden on family

C. Lack of social support
D. Medical contraindications (see previous section)
E. Poor manual dexterity
F. Poor visual acuity

III. Treatment related: lack of functional vascular access and/or fears of self cannulation[43]
IV. Home related: lack of appropriate home environment for HD (ie, space, telephone, lighting, plumbing, waste management).[45,46] May be overcome in part with use of novel home dialytic technologies

Vascular Access

I. An arteriovenous fistula (AVF) is the preferred vascular access for intensive and home HD
II. Arteriovenous grafts (AVGs) and tunneled central venous catheters (CVCs) are used successfully for home HD[47]
III. Single-needle cannulation of AVFs and AVGs:
A. Reduces dose of dialysis by decreasing effective dialysis time and potentially increasing the degree of access recirculation (may compromise dose of SDHD)
B. May increase safety in case of accidental needle dislodgement
C. Theoretically may increase access survival because of fewer cannulation events than with 2-needle cannulation
IV. Floor moisture sensors may aid in the detection of blood or dialysate leaks and should be used[48,49]
V. AVFs:
A. "Buttonhole technique" of AVF cannulation[50]
1. A subcutaneous tract (composed of scar tissue between the skin and the access) is created, allowing for repeated cannulation at the same arterial and venous sites
2. One of several methods of AVF cannulation in large home HD centers and self-care HD patients[51]
3. Reports of greater patient comfort and greater ease of self-cannulation than
the traditional "rope ladder" technique[51]
4. Allows use of noncutting needles, which are guided into the fistula through a tract and may be associated with a lower incidence of blood leak
5. Meticulous attention to scab removal and aseptic technique necessary to limit risk of local and systemic infection

B. Taping of a moisture sensor (such as an enuresis alarm or newly developed sensor patch) close to the fistula needle sites may allow the patient to recognize early needle dislodgement[48,49,52]
C. Observational studies suggest no increase in risk of AVF complications for NHD and SDHD compared with CHD[53,54]

VI. CVCs:
A. Use of preperforated nonremovable CVC caps (ie, Interlink [Becton Dickinson, NJ, USA], Tego [ICU Medical Inc, San Clemente, CA]) may minimize the risk of air embolism by obviating the need for cap removal for HD
B. Nondisposable locking box may prevent accidental separation of blood tubing and catheter
C. Prospective observational study suggests that the incidence of catheter-related bacteremia is similar between CHD and NHD patients[55]
D. Review of sterile technique should be encouraged after an episode of catheter-related bacteremia. Self administration of antibiotics during treatment is possible
E. Potential for longer catheter survival with NHD, which may be caused by greater cumulative exposure to anticoagulation[55]
F. Initiation of NHD with a CVC may be followed successfully by creation of an AVF, but will require retraining for self-cannulation

VII. AVGs:
   A. Buttonhole technique is not possible with AVGs, and self-cannulation of access may be more challenging than with AVFs
   B. No increased risk of AVG complications or reduced survival when used for SDHD compared with CHD[53,54]
   C. Single-needle cannulation may be particularly useful with AVGs to allow self-cannulation

Remote Monitoring and Home HD

I. Remote monitoring may be achieved using telephone or Internet connection
II. Practiced by several dialysis centers; in absence of a partner, some centers/jurisdictions mandate remote monitoring[56,57]
III. Centralized monitoring of large numbers of patients improves cost-effectiveness
IV. Observer may respond to alarms unattended by the patient, help with patient troubleshooting after hours, or mobilize emergency services as needed
V. May aid in documenting adherence to treatment regimens
VI. May provide patient reassurance, particularly during the first several months of home HD
VII. May allow for data collection to study physiological effects of NHD
VIII. Incremental safety of remote monitoring requires further prospective study

Advances in Home Hemodialytic Technologies

I. Standard HD machine may be used for all forms of intensive HD
II. Attempts to modify standard HD machines for use at home may aid in the adoption of home HD[58-61]
III. Emerging design of HD machines specifically for use at home is engineered to obviate the needs for home electrical and/or plumbing modifications
   A. Aksys Personal Hemodialysis System[62]:
      1. Online ultrapure dialysate (which may be used for intravenous infusion, obviating the need for saline bags)
      2. Hot water disinfection allows dialyzer reuse and tubing (reduces storage requirements and waste)
      3. No longer available
   B. NxStage System One (NxStage, Lawrence, MA)[63]:
      1. Smaller than traditional HD machines (70 lb)
      2. Uses 4-6-L preformed bags of ultrapure dialysate
         a) Obviates need for electrical connections, plumbing, or modifications
         b) Can perform dialysis away from home
      3. Licensed for daily HD at home
      4. Online dialysate production possible for patients who need increased clearance (Nxstage PureFlow SL)
      5. Dialysate flow rates determined to achieve a target flow-fraction of 35% (range, 25%-40%), in which flow fraction is defined by dialysate flow rate + ultrafiltration rate divided by blood flow rate
   C. Renal Solutions Allient Sorbent Hemodialysis System (Allient, Warendale, PA)[64]
      1. Sorbent cartridge-based system designed for 3-8-hour sessions
      2. Requires electrical source and 6 L of drinking water
      3. Water is mixed with small packets of dry chemical and converted to dialysate by the sorbent cartridge
      4. Continuous dialysate regeneration by sorbent cartridge
      5. Possibility for smaller travel-friendly sorbent device in the future
      6. Not widely available at present

CLINICAL BENEFITS OF INTENSIVE HD

A summary of the clinical benefits of intensive HD is listed in Table 2.

Cardiovascular

I. BP
   A. Superior control of BP with fewer or no medications with both SDHD and NHD shown by multiple observational studies and 1 randomized controlled trial[16,48,49,65-67]

Table 2. Clinical Benefits of Intensive Hemodialysis

	Nocturnal Hemodialysis	Short Daily Hemodialysis
Blood pressure control	+++ (↓ total peripheral resistance)	++ (↓ extracellular fluid volume)
Left ventricular hypertrophy	+++ (↓ afterload)	++ (↓ preload)
Left ventricular systolic function	+++	Not shown
Arterial compliance	+++	Not shown
Sleep apnea	Correction	Not shown
Cardiac autonomic nervous system abnormalities	Restoration	Not shown
Phosphate control	+++	Depends on duration
Anemia	++ (↓ erythropoietin resistance)	+ (↓ erythropoietin resistance)
Malnutrition	++	++
Inflammation	↓ C-reactive protein, interleukin 6	↓ C-reactive protein
Cognition	+	Not shown
Fertility	++	Not shown
Quality of life	++[a]	++

[a]Improvement in kidney-specific domains of quality of life.

   B. Restoration of normal BP in 28 patients followed up for 3 years after conversion to NHD from CHD. Mechanisms of improvements in BP between SDHD and NHD may differ[66]:
      1. SDHD: decrease in extracellular fluid volume[68]
      2. NHD: decrease in peripheral vascular resistance and lower levels of circulating catecholamines[69]

II. Left ventricular geometry
   A. Reduction in left ventricular mass index using 2-dimensional echocardiography in several prospective observational studies of patients converted from CHD to SDHD or NHD[16,65,66,70]
   B. In a recent randomized controlled trial, 52 CHD patients at 2 Canadian centers were randomly assigned to CHD versus 6-times-weekly NHD.[16] The primary outcome, left ventricular mass index (assessed using cardiac magnetic resonance imaging), was significantly decreased in the NHD group (mean difference, 15.3 g; 95% confidence interval, 1.0-29.6)
   C. Improvement in left ventricular systolic function in patients converted to NHD from CHD in those with pre-existing impaired left ventricular ejection fraction[35]
   D. Restoration of endothelial progenitor cell number and function in patients converted from CHD to NHD.[71] Improved endothelial progenitor cell number and function were directly related to intensity of dialysis and inversely proportional to left ventricular mass index

III. Endothelial function: improvements in endothelial-dependent (postischemic vasodilatation) and -independent vasodilatation (response to nitroglycerin) were noted after conversion from CHD to NHD[69]

IV. Coronary calcification: in 1 prospective observational study, 38 patients had coronary artery calcification scores (using multislice computed tomography) measured before and after conversion to NHD.[72] No change in coronary artery calcification scores was noted in patients with low baseline scores (<10). In patients with scores > 10, a nonsignificant increase was seen at 1 year

V. Autonomic nervous system
   A. Partial restoration of heart rate variability during sleep with NHD[73]
   B. Improvement in baroreceptor sensitivity and decreased circulating levels of catecholamines with NHD[69]
   C. Decrease in sympathetic activity upon conversion to SDHD[74]

Anemia and Erythropoietin Responsiveness

I. Conflicting reports of the impact of intensification of HD on the management of anemia
   A. SDHD:

1. Woods et al[75]: increase in hematocrit by 3% on conversion to SDHD in 72 patients
2. Ting et al[12]: conversion to SDHD from CHD associated with a decrease in recombinant human erythropoietin (rHuEPO) requirements by 45% and increase in hemoglobin (Hb) concentration

B. NHD:
1. Compared with 32 self-care CHD control patients, conversion to NHD in 63 patients was associated with an increase in Hb concentration and concomitant decrease in rHuEPO requirements[76]
2. Conversion to NHD from CHD is associated with improvement in hematopoietic progenitor cell growth (in vitro) and upregulation of genes relevant to hematopoietic progenitor cell growth mobilization and red blood cell production[77]
3. rHuEPO dose or change in Hb level was not different in the control and treatment groups in a randomized controlled trial by Culleton et al[16] (may be underpowered because this was not the primary outcome)

Phosphate Control and Mineral Metabolism

I. SDHD:
A. Increased phosphate removal by SDHD compared with CHD[78]
B. Improvement in serum phosphate level shown if duration of SDHD $>$ 2 h per session[12,78,79]

II. NHD:
A. Phosphate removal during NHD ~2 times greater than CHD
B. Patients no longer require phosphate binders on NHD therapy[16,38]
C. Removal of dietary phosphate restrictions[38]
D. Normalization of calcium-phosphate product[39]
E. Intradialytic phosphate supplementation may be required in some NHD patients to avoid hypophosphatemia.[38,49] Requirements may increase in:
1. Pregnancy[80]
2. Bone repair states

F. Phosphate supplementation:
1. Achieved by the addition of sodium phosphate (in the form of Fleet enema or Fleet Phosphosoda [Fleet, Lynchburg, VA]) to the acid concentrate
2. Typical dose is 60-90 mL/treatment
3. 120 mL of Fleet added to acid dialysate concentrate yields a final dialysate phosphate concentration of ~1.0 mmol/L
4. Calcium and phosphate do not precipitate in the presence of the acidic pH of the "acid concentrate"[81]
5. Titrate dose to maintain pre- and postdialysis phosphate levels within normal range

G. Risk of negative calcium balance due to minimal use of calcium-based phosphate binders. Risk increases with higher rates of ultrafiltration, in which calcium loss may be greater[82]
H. NHD may be a therapeutic option for patients with tumoral calcinosis or calcific uremic arteriolopathy, particularly if calcium-phosphate product is high at time of diagnosis[37]
I. Dialysate calcium must be titrated high enough to increase serum calcium levels during dialysis[82]
1. Postdialysis hypercalcemia is required to titrate appropriate dialysate calcium
2. Mean dialysate calcium concentration, −6.41 mg/dL (−1.6 mmol/L)
3. Bone densitometry may be a useful tool to guide dialysate calcium supplementation[39]
4. Normalization of alkaline phosphatase and maintenance of parathyroid hormone levels within recommended range
5. Calcium addition to the dialysate can be achieved by adding calcium chloride powder to dialysate (addition of 7 mL to 4 L of acid dialysate concentrate increases dialysate calcium by 1 mg/dL [0.25 mmol/L])[82]

J. Use of vitamin D analogues may be beneficial to maintain calcium balance and normalize serum phosphate level

III. Conversion to NHD from CHD is associated with increases in 1,25-dihydroxyvitamin D and 25-hydroxyvitamin D levels independent of exogenous supplementation[83]

Malnutrition and Inflammation

I. Patients converted to daily HD therapy experience improved appetite, weight gain, and muscle mass increase,[84,85] which may be caused by liberalization of the diet (ie, sodium, potassium, phosphate) and superior control of uremia[84,86,87]
II. Despite daily amino acid losses of 10 g into dialysate, total-body nitrogen measured using in vivo neutron-activation analysis did not show a decrease in 24 patients followed up on NHD for 15.7 months[88]
III. Several studies have reported increases in serum albumin levels after conversion to SDHD and NHD, whereas others have not.[12,48,79,85] This may be the result of varying patient selection criteria and length of follow-up
IV. Chazot et al[89] have shown stability of nutritional parameters at 5 years' follow-up in patients treated with long intermittent HD
V. Reports of decreased levels of inflammatory markers on conversion to daily HD (ie, C reactive protein [CRP] and interleukin 6 [IL-6])[90]
VI. Because of increased loss of water-soluble vitamins, the dose of daily multivitamin preparation is increased to 2 tablets/d.[48] No conclusive evidence of vitamin deficiency has been reported

Sleep Disorders

I. Sleep disorders, including sleep apnea syndrome (SAS), restless legs syndrome, and periodic limb movement disorder, are seen with increased frequency in patients with ESRD[91]
II. The prevalence of SAS is as high as 50%-70% in patients with ESRD[91]
III. SAS is associated with daytime sleepiness, heightened cardiovascular morbidity, and mortality[92]
IV. Conversion to NHD from CHD is associated with improvements in SAS[40,73]
V. No improvement in daytime sleepiness or periodic limb movement disorder of sleep after conversion to NHD from CHD[93]
VI. No published data regarding the effects of SDHD on sleep disorders

Fertility

I. It is recommended that dialysis be intensified for pregnant patients on CHD therapy or patients with stage 5 chronic kidney disease intending to become pregnant
II. Decreased fertility and increased maternal-fetal morbidity and mortality for patients on CHD therapy[94]
III. NHD may allow for improved fertility[80]
IV. Delivering a live infant at a mature gestational age is feasible for patients on NHD therapy[80,95]
V. In a single-center cohort study of 7 pregnancies in 5 patients while on NHD therapy, fewer maternal and fetal complications were noted compared with historical CHD controls[80]
VI. In a large registry study performed in the United States, there was a nonsignificant trend toward improved maternal survival and decreased preterm delivery in patients who received $>$ 20 h/wk of dialysis[96]

Cognition

Conversion to NHD from CHD is associated with improved psychomotor efficiency and increased attention and working memory.[97]

QUALITY OF LIFE

I. Quality of life and vocational abilities are traditionally poor in patients with ESRD[98]
II. Use of a variety of self assessment questionnaires (such as the 36-Item Short Form Health Survey [SF-36], Sickness Impact Profile, and Beck Depression Inventory) has shown improvements in most parameters after a switch to NHD from CHD in prospective observational studies[84,99]
III. In a randomized controlled trial, NHD was associated with significant improvements in selected kidney-specific domains of quality of life (effects of kidney disease and burden of kidney disease) compared with CHD.[16,100] No difference in overall quality of life

(assessed using the EuroQol-5D index) was seen between the 2 groups

IV. In a cross-sectional study of comparison of quality of life and illness intrusiveness in patients treated with home dialysis (either NHD or PD), NHD was not perceived as a more intrusive treatment compared with PD.[101] Similar perceived symptomatic control of kidney disease was seen between the 2 groups

V. Using utility scores (which measure overall quality of life by assessing a patient's preference between health states), McFarlane et al[102] and Heidenheim et al[103] showed higher utility scores with NHD compared with CHD

COST-EFFECTIVENESS

I. Because of the increased frequency of NHD and SDHD, the cost of consumables is higher compared with CHD

II. Personnel cost of NHD is lower than that of CHD and SDHD in North America[104]

III. In developed countries, cost of personnel is greater than the cost of consumables. Depending on the ratio of cost of personnel to cost of consumables, NHD may be less or more expensive than in-center HD

IV. Lower rate of medication use (rHuEPO, antihypertensives, phosphate binders) may decrease total costs of NHD[16]

V. Decreased hospitalization rates reported with NHD compared with CHD[12,105]

VI. In 2 prospective randomized studies comparing the costs of CHD versus NHD in Canada, treatment costs for NHD patients were 20% lower than those for CHD[106,107]; similar findings in 1 US study[99]

VII. Improved cost and quality of life have translated into higher cost-utility scores for NHD compared with CHD[102]

VIII. Limited studies regarding the cost-effectiveness of SDHD alone compared with CHD and NHD; 1 retrospective study using cost data obtained from the USRDS, Centers for Disease Control and Prevention (CDC), and Medicare Payment Advisory Commission showed that a decrease of at least 8% in hospital days are required for daily dialysis to be cost saving[99]

FUTURE DIRECTIONS

I. Despite several reported clinical benefits, the impact of intensive HD on survival is unclear

II. Observational studies suggest that both SDHD and NHD are associated with improved survival compared with CHD.[75,108-110] These studies need to be interpreted in the context of the study design, in which patient selection for intensive HD may be limiting adequate adjustment of residual confounding

   A. SDHD: in 1 series, 5-year survival of 80% reported.[75] In a second series, 5-year survival of 68%, which was 2-3 times better than the survival of matched (age, sex, primary diagnosis) 3-times-weekly HD patients, was reported by the USRDS[111]

   B. NHD: 5-year survival of 81%[108]

III. According to USRDS data, use of any form of home HD was associated with a 44% decreased risk of death after adjustment for age and comorbidities compared with in-center HD[112]

IV. Equivalent survival shown between 177 Canadian NHD patients and 513 deceased donor kidney transplant recipients matched on the basis of race and cause of ESRD and after adjustment for age, sex, and comorbid conditions[113]

V. The development of an intensive HD registry and prospective randomized studies sponsored by the National Institutes of Health (NIH) and Centers for Medicare & Medicaid Services (CMS) will shed further light on the impact of intensive HD on important clinical end points[114-117]

VI. The Frequent Hemodialyis Network (FHN), sponsored by the NIH and the CMS, currently is sponsoring 2 randomized clinical trials:

   A. The first will randomly assign patients to an in-center daily (6 times weekly) versus a conventional in-center (3 times weekly) HD regimen. Anticipated differences in weekly median treatment time and stdKt/V_{urea} between the control and treatment groups are 29% and 52%, respectively[118]

B. The second trial will compare a regimen consisting of 6 weekly 8-hour nocturnal treatments versus three 4-hour conventional treatments. Anticipated differences in weekly median treatment time and stdKt/V_{urea} between the control and treatment groups in the second trial are 234% and 133%, respectively.[118] This is a substantially greater difference than that achieved in the HEMO Study, in which only a 17%-18% difference in median treatment time and stdKt/V_{urea} was achieved between the treatment and control groups.[119] This may explain in part the inability of the HEMO Study to show a survival benefit to an increase in delivered dialysis dose

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REFERENCES

1. Agar JW, Macgregor MS, Blagg CR. Chronic maintenance hemodialysis: making sense of the terminology. *Hemodial Int.* 2007;11:252-262.

2. Pereira BJG, Sayegh MH, Blake PG. Chronic kidney disease, dialysis, and transplantation. In: Pereira BJG, Sayegh MH, Blake PG, eds. *A Companion to Brenner and Rector's The Kidney.* Philadelphia, PA: Saunders; 2005:472-480.

3. Scribner BH, Buri R, Caner JE, Hegstrom R, Burnell JM. The treatment of chronic uremia by means of intermittent hemodialysis: a preliminary report. *Trans Am Soc Artif Intern Organs.* 1960;6:114-122.

4. Shaldon S. Independence in maintenance haemodialysis. *Lancet*. 1968;1:520.

5. Baillod RCC, Shaldon S. Over-night unattended haemodialysis in the home. *Proc EDTA*. 1965;2:99-109.

6. Depalma JR, Pecker EA, Maxwell MH. A new automatic coil dialyzer system for 'daily' dialysis. *Hemodial Int.* 2004;8:19-23.

7. DePalma JR, Pecker EA, Maxwell MH. A new automatic coil dialyzer system for daily dialysis. *Proc Eur Dial Transplant Assoc.* 1967;6:26-34.

8. Charra B, Calemard E, Ruffet M, et al. Survival as an index of adequacy of dialysis. *Kidney Int.* 1992;41:1286-1291.

9. Laurent G, Charra B. The results of an 8 h thrice weekly haemodialysis schedule. *Nephrol Dial Transplant*. 1998;13(suppl 6):S125-131.

10. Buoncristiani U, Quintaliani G, Cozzari M, Giombini L, Ragaiolo M. Daily dialysis: long-term clinical metabolic results. *Kidney Int Suppl.* 1988;24:S137-140.

11. Buoncristiani U. Fifteen years of clinical experience with daily haemodialysis. *Nephrol Dial Transplant.* 1998; 13(suppl 6):S148-151.

12. 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*. 2003;42:1020-1035.

13. Uldall R, Ouwendyk M, Francoeur R, et al. Slow nocturnal home hemodialysis at the Wellesley Hospital. *Adv Ren Replace Ther.* 1996;3:133-136.

14. Uldall R, DeBruyne M, Besley M, McMillan J, Simons M, Francoeur R. A new vascular access catheter for hemodialysis. *Am J Kidney Dis.* 1993;21:270-277.

15. Lockridge RS Jr. Daily dialysis and long-term outcomes—the Lynchburg Nephrology NHHD experience. *Nephrol News Issues.* 1999;13:16-23.

16. 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;298:1291-1299.

17. Vonesh EF, Snyder JJ, Foley RN, Collins AJ. Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us? *Kidney Int Suppl*. 2006;103:S3-11.

18. Gotch FA. The current place of urea kinetic modelling with respect to different dialysis modalities. *Nephrol Dial Transplan*t. 1998;13(suppl 6):S10-14.

19. Depner TA. Daily hemodialysis efficiency: an analysis of solute kinetics. *Adv Ren Replace Ther.* 2001;8:227-235.

20. Casino FG, Lopez T. The equivalent renal urea clearance: a new parameter to assess dialysis dose. *Nephrol Dial Transplant.* 1996;11:1574-1581.

21. National Kidney Foundation. Guideline I. NKF-K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy: update 2000. In: K/DOQI Clinical Practice Guidelines: update 2000. *Am J Kidney Dis.* 2001;37(suppl 1): S7-64.

22. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Hemodialysis Adequacy, update 2006. In: KDOQI Clinical Practice Guidelines for Hemodialysis Adequacy, update 2006. *Am J Kidney Dis.* 2006;48(suppl 1):S2-90.

23. Suri R, Depner TA, Blake PG, Heidenheim AP, Lindsay RM. Adequacy of quotidian hemodialysis. *Am J Kidney Dis.* 2003;42:42-48.

24. Clark WR, Leypoldt JK, Henderson LW, Mueller BA, Scott MK, Vonesh EF. Quantifying the effect of changes in the hemodialysis prescription on effective solute removal with a mathematical model. *J Am Soc Nephrol.* 1999;10:601-609.

25. Goldfarb-Rumyantzev AS, Cheung AK, Leypoldt JK. Computer simulation of small-solute and middle-molecule removal during short daily and long thrice-weekly hemodialysis. *Am J Kidney Dis.* 2002;40:1211-1218.

26. Pierratos A. Effect of therapy time and frequency on effective solute removal. *Semin Dial.* 2001;14:284-288.

27. Raj DS, Ouwendyk M, Francoeur R, Pierratos A. Beta(2)-microglobulin kinetics in nocturnal haemodialysis. *Nephrol Dial Transplant.* 2000;15:58-64.

28. Eloot S, Van Biesen W, Dhondt A, et al. Impact of hemodialysis duration on the removal of uremic retention solutes. *Kidney Int.* 2008;73:765-770.

29. Fagugli RM, Vanholder R, De Smet R, et al. Advanced glycation end products: specific fluorescence changes of pentosidine-like compounds during short daily hemodialysis. *Int J Artif Organs*. 2001;24:256-262.

30. Blagg CR. A brief history of home hemodialysis. *Adv Ren Replace Ther.* 1996;3:99-105.

31. US Renal Data System. USRDS 2008 Annual Data Report. Bethesda MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2008:98.

32. MacGregor MS, Agar JW, Blagg CR. Home haemodialysis—international trends and variation. *Nephrol Dial Transplant.* 2006;21:1934-1945.

33. Chan CT, Jain V, Picton P, Pierratos A, Floras JS. Nocturnal hemodialysis increases arterial baroreflex sensitivity and compliance and normalizes blood pressure of hypertensive patients with end-stage renal disease. *Kidney Int.* 2005;68:338-344.

34. McCormick BB, Chan CT. Improved blood pressure control with nocturnal hemodialysis: review of clinical observations and physiologic mechanisms. *Curr Hypertens Rep.* 2004;6:140-144.

35. Chan C, Floras JS, Miller JA, Pierratos A. Improvement in ejection fraction by nocturnal haemodialysis in end-stage renal failure patients with coexisting heart failure. *Nephrol Dial Transplant.* 2002;17:1518-1521.

36. Pauly RP, Sood MM, Chan CT. Management of refractory ascites using nocturnal home hemodialysis. *Semin Dial.* 2008;21:367-370.

37. Kim SJ, Goldstein M, Szabo T, Pierratos A. Resolution of massive uremic tumoral calcinosis with daily nocturnal home hemodialysis. *Am J Kidney Dis.* 2003;41:E12.

38. Mucsi I, Hercz G, Uldall R, Ouwendyk M, Francoeur R, Pierratos A. Control of serum phosphate without any phosphate binders in patients treated with nocturnal hemodialysis. *Kidney Int.* 1998;53:1399-1404.

39. Toussaint N, Boddington J, Simmonds R, Waldron C, Somerville C, Agar J. Calcium phosphate metabolism and bone mineral density with nocturnal hemodialysis. *Hemodial Int*. 2006;10:280-286.

40. Hanly PJ, Pierratos A. Improvement of sleep apnea in patients with chronic renal failure who undergo nocturnal hemodialysis. *N Engl J Med.* 2001;344:102-107.

41. Wong JH, Pierratos A, Oreopoulos DG, Mohammad R, Benjamin-Wong F, Chan CT. The use of nocturnal home hemodialysis as salvage therapy for patients experiencing peritoneal dialysis failure. *Perit Dial Int.* 2007;27:669-674.

42. Faratro R, D'Gama C, Chan C. The use of alternative anti-coagulation strategies for a nocturnal home hemodialysis patient with heparin-induced thrombocytopenia. *CANNT J*. 2008;18:32-35.

43. Cafazzo JA, Leonard K, Easty AC, Rossos PG, Chan CT. Patient-perceived barriers to the adoption of nocturnal home hemodialysis. *Clin J Am Soc Nephrol.* 2009;4:784-789.

44. McLaughlin K, Manns B, Mortis G, Hons R, Taub K. Why patients with ESRD do not select self-care dialysis as a treatment option. *Am J Kidney Dis.* 2003;41:380-385.

45. Mehrabian S, Morgan D, Schlaeper C, Kortas C, Lindsay RM. Equipment and water treatment considerations for the provision of quotidian home hemodialysis. *Am J Kidney Dis.* 2003;42:66-70.

46. Piccoli GB, Jeantet A, Gai M, et al. Home dialysis, garbage, and privacy: nothing is trivial in home hemodialysis [letter]. *Kidney Int.* 2005;67:1190.

47. Piccoli GB, Bermond F, Mezza E, et al. Vascular access survival and morbidity on daily dialysis: a comparative analysis of home and limited care haemodialysis. *Nephrol Dial Transplant.* 2004;19:2084-2094.

48. Pierratos A, Ouwendyk M, Francoeur R, et al. Nocturnal hemodialysis: three-year experience. *J Am Soc Nephrol*. 1998;9:859-868.

49. Pierratos A. Nocturnal home haemodialysis: an update on a 5-year experience. *Nephrol Dial Transplant*. 1999; 14:2835-2840.

50. Twardowski Z, Kubara H. Different sites versus constant sites of needle insertion into arteriovenous fistulas for treatment by repeated dialysis. *Dial Transplant.* 1979;8:978-980.

51. Verhallen AM, Kooistra MP, van Jaarsveld BC. Cannulating in haemodialysis: rope-ladder or buttonhole technique? *Nephrol Dial Transplant.* 2007;22:2601-2604.

52. Ahlmen J, Gydell KH, Hadimeri H, Hernandez I, Rogland B, Strombom U. A new safety device for hemodialysis. *Hemodial Int.* 2008;12:264-267.

53. Suri RS, Nesrallah GE, Mainra R, et al. Daily hemodialysis: a systematic review. *Clin J Am Soc Nephrol.* 2006; 1:33-42.

54. Lindsay RM. The London, Ontario, Daily/Nocturnal Hemodialysis Study. *Semin Dial.* 2004;17:85-91.

55. Perl J, Lok CE, Chan CT. Central venous catheter outcomes in nocturnal hemodialysis. *Kidney Int.* 2006;70: 1348-1354.

56. Hoy C. Remote monitoring in nocturnal home hemodialysis 2003. *Hemodial Int*. 2004;8:144-150.

57. Heidenheim AP, Leitch R, Kortas C, Lindsay RM. Patient monitoring in the London Daily/Nocturnal Hemodialysis Study. *Am J Kidney Dis*. 2003;42:61-65.

58. Ledebo I, Fredin R. The Gambro system for home daily dialysis. *Semin Dial.* 2004;17:162-163.

59. Schlaeper C, Diaz-Buxo JA. The Fresenius Medical Care home hemodialysis system. *Semin Dial.* 2004;17:159-161.

60. Kelly TD. Baxter Aurora dialysis system. *Semin Dial.* 2004;17:154-155.

61. Trewin E. Bellco Formula Domus Home Care System. *Semin Dial.* 2004;17:156-158.

62. Kjellstrand CM, Blagg CR, Bower J, Twardowski ZJ. The Aksys personal hemodialysis system. *Semin Dial.* 2004; 17:151-153.

63. Clark WR, Turk JE Jr. The NxStage System One. *Semin Dial.* 2004;17:167-170.

64. Ash SR. The Allient dialysis system. *Semin Dial*. 2004;17:164-166.

65. Fagugli RM, Reboldi G, Quintaliani G, et al. Short daily hemodialysis: blood pressure control and left ventricular mass reduction in hypertensive hemodialysis patients. *Am J Kidney Dis.* 2001;38:371-376.

66. Chan CT, Floras JS, Miller JA, Richardson RM, Pierratos A. Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. *Kidney Int*. 2002;61: 2235-2239.

67. Nesrallah G, Suri R, Moist L, Kortas C, Lindsay RM. Volume control and blood pressure management in patients undergoing quotidian hemodialysis. *Am J Kidney Dis.* 2003; 42:13-17.

68. Fagugli RM, Pasini P, Pasticci F, Ciao G, Cicconi B, Buoncristiani U. Effects of short daily hemodialysis and extended standard hemodialysis on blood pressure and cardiac hypertrophy: a comparative study. *J Nephrol.* 2006;19: 77-83.

69. Chan CT, Harvey PJ, Picton P, Pierratos A, Miller JA, Floras JS. Short-term blood pressure, noradrenergic, and vascular effects of nocturnal home hemodialysis. *Hypertension*. 2003;42:925-931.

70. Walsh M, Culleton B, Tonelli M, Manns B. A systematic review of the effect of nocturnal hemodialysis on blood pressure, left ventricular hypertrophy, anemia, mineral metabolism, and health-related quality of life. *Kidney Int.* 2005;67:1500-1508.

71. Chan CT, Li SH, Verma S. Nocturnal hemodialysis is associated with restoration of impaired endothelial progenitor cell biology in end-stage renal disease. *Am J Physiol Renal Physiol.* 2005;289:F679-684.

72. Yuen D, Pierratos A, Richardson RM, Chan CT. The natural history of coronary calcification progression in a cohort of nocturnal haemodialysis patients. *Nephrol Dial Transplant.* 2006;21:1407-1412.

73. Chan CT, Hanly P, Gabor J, Picton P, Pierratos A, Floras JS. Impact of nocturnal hemodialysis on the variability of heart rate and duration of hypoxemia during sleep. *Kidney Int.* 2004;65:661-665.

74. Zilch O, Vos PF, Oey PL, et al. Sympathetic hyperactivity in haemodialysis patients is reduced by short daily haemodialysis. *J Hypertens.* 2007;25:1285-1289.

75. Woods JD, Port FK, Orzol S, et al. Clinical and biochemical correlates of starting "daily" hemodialysis. *Kidney Int*. 1999;55:2467-2476.

76. Schwartz DI, Pierratos A, Richardson RM, Fenton SS, Chan CT. Impact of nocturnal home hemodialysis on anemia management in patients with end-stage renal disease. *Clin Nephrol.* 2005;63:202-208.

77. Chan CT, Liu PP, Arab S, Jamal N, Messner HA. Nocturnal hemodialysis improves erythropoietin responsiveness and growth of hematopoietic stem cells. *J Am Soc Nephrol*. 2009;20:665-671.

78. Yuen D, Richardson RM, Chan CT. Improvements in phosphate control with short daily in-center hemodialysis. *Clin Nephrol.* 2005;64:364-370.

79. Kooistra MP, Vos J, Koomans HA, Vos PF. Daily home haemodialysis in The Netherlands: effects on metabolic control, haemodynamics, and quality of life. *Nephrol Dial Transplant.* 1998;13:2853-2860.

80. Barua M, Hladunewich M, Keunen J, et al. Successful pregnancies on nocturnal home hemodialysis. *Clin J Am Soc Nephrol.* 2008;3:392-396.

81. Ing TS, Yu AW, Agrawal B, et al. Increasing plasma phosphorus values by enriching with phosphorus the "acid concentrate" of a bicarbonate-buffered dialysate delivery system. *Int J Artif Organs.* 1992;15:701-703.

82. Al-Hejaili F, Kortas C, Leitch R, et al. Nocturnal but not short hours quotidian hemodialysis requires an elevated dialysate calcium concentration. *J Am Soc Nephrol.* 2003;14: 2322-2328.

83. Nessim SJ, Jassal SV, Fung SV, Chan CT. Conversion from conventional to nocturnal hemodialysis improves vitamin D levels. *Kidney Int.* 2007;71:1172-1176.

84. McPhatter LL, Lockridge RS Jr, Albert J, et al. Nightly home hemodialysis: improvement in nutrition and quality of life. *Adv Ren Replace Ther.* 1999;6:358-365.

85. Spanner E, Suri R, Heidenheim AP, Lindsay RM. The impact of quotidian hemodialysis on nutrition. *Am J Kidney Dis.* 2003;42:30-35.

86. Galland R, Traeger J, Arkouche W, Cleaud C, Delawari E, Fouque D. Short daily hemodialysis rapidly improves nutritional status in hemodialysis patients. *Kidney Int.* 2001;60:1555-1560.

87. Galland R, Traeger J, Arkouche W, Delawari E, Fouque D. Short daily hemodialysis and nutritional status. *Am J Kidney Dis*. 2001;37(suppl):S95-98.

88. Raj DS, Ouwendyk M, Francoeur R, Pierratos A: Plasma amino acid profile on nocturnal hemodialysis. *Blood Purif.* 2000;18:97-102.

89. Chazot C, Vo VC, Blanc C, et al. Stability of nutritional parameters during a 5-year follow-up in patients treated with sequential long-hour hemodialysis. *Hemodial Int.* 2006;10:389-393.

90. Yuen D, Richardson RM, Fenton SS, McGrath-Chong ME, Chan CT. Quotidian nocturnal hemodialysis improves cytokine profile and enhances erythropoietin responsiveness. *ASAIO J.* 2005;51:236-241.

91. Perl J, Unruh ML, Chan CT. Sleep disorders in end-stage renal disease: 'markers of inadequate dialysis'? *Kidney Int.* 2006;70:1687-1693.

92. Lavie P, Lavie L. Cardiovascular morbidity and mortality in obstructive sleep apnea. *Curr Pharm Des.* 2008;14: 3466-3473.

93. Hanly PJ, Gabor JY, Chan C, Pierratos A. Daytime sleepiness in patients with CRF: impact of nocturnal hemodialysis. *Am J Kidney Dis.* 2003;41:403-410.

94. Bagon JA, Vernaeve H, De Muylder X, Lafontaine JJ, Martens J, Van Roost G. Pregnancy and dialysis. *Am J Kidney Dis.* 1998;31:756-765.

95. Bamberg C, Diekmann F, Haase M, et al. Pregnancy on intensified hemodialysis: fetal surveillance and perinatal outcome. *Fetal Diagn Ther.* 2007;22:289-293.

96. Okundaye I, Abrinko P, Hou S. Registry of pregnancy in dialysis patients. *Am J Kidney Dis.* 1998;31:766-773.

97. Jassal SV, Devins GM, Chan CT, Bozanovic R, Rourke S. Improvements in cognition in patients converting from thrice weekly hemodialysis to nocturnal hemodialysis: a longitudinal pilot study. *Kidney Int.* 2006;70:956-962.

98. Bell CM, Chapman RH, Stone PW, Sandberg EA, Neumann PJ. An off-the-shelf help list: a comprehensive catalog of preference scores from published cost-utility analyses. *Med Decis Making*. 2001;21:288-294.

99. Mohr PE, Neumann PJ, Franco SJ, Marainen J, Lockridge R, Ting G. The case for daily dialysis: its impact on

costs and quality of life. *Am J Kidney Dis.* 2001;37:777-789.

100. 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;75:542-549.

101. Fong E, Bargman JM, Chan CT. Cross-sectional comparison of quality of life and illness intrusiveness in patients who are treated with nocturnal home hemodialysis versus peritoneal dialysis. *Clin J Am Soc Nephrol.* 2007;2: 1195-1200.

102. McFarlane PA, Bayoumi AM, Pierratos A, Redelmeier DA. The quality of life and cost utility of home nocturnal and conventional in-center hemodialysis. *Kidney Int.* 2003;64:1004-1011.

103. Heidenheim AP, Muirhead N, Moist L, Lindsay RM. Patient quality of life on quotidian hemodialysis. *Am J Kidney Dis.* 2003;42:36-41.

104. McFarlane PA. Reducing hemodialysis costs: conventional and quotidian home hemodialysis in Canada. *Semin Dial.* 2004;17:118-124.

105. Bergman A, Fenton SS, Richardson RM, Chan CT. Reduction in cardiovascular related hospitalization with nocturnal home hemodialysis. *Clin Nephrol.* 2008;69:33-39.

106. McFarlane PA, Pierratos A, Redelmeier DA. Cost savings of home nocturnal versus conventional in-center hemodialysis. *Kidney Int.* 2002;62:2216-2222.

107. Kroeker A, Clark WF, Heidenheim AP, et al. An operating cost comparison between conventional and home quotidian hemodialysis. *Am J Kidney Dis.* 2003;42:49-55.

108. Pierratos A. Daily nocturnal home hemodialysis. *Kidney Int.* 2004;65:1975-1986.

109. Charra B, Terrat JC, Vanel T, et al. Long thrice weekly hemodialysis: the Tassin experience. *Int J Artif Organs.* 2004;27:265-283.

110. Marshall MR, Byrne BG, Kerr PG, McDonald SP. Associations of hemodialysis dose and session length with mortality risk in Australian and New Zealand patients. *Kidney Int.* 2006;69:1229-1236.

111. Kjellstrand CM, Buoncristiani U, Ting G, et al. Short daily haemodialysis: survival in 415 patients treated for 1006 patient-years. *Nephrol Dial Transplant.* 2008;23: 3283-3289.

112. Woods JD, Port FK, Stannard D, Blagg CR, Held PJ. Comparison of mortality with home hemodialysis and center hemodialysis: a national study. *Kidney Int.* 1996;49:1464-1470.

113. Pauly RP. Nocturnal home hemodialysis and short daily hemodialysis compared with kidney transplantation: emerging data in a new era. *Adv Chronic Kidney Dis.* 2009;16:169-172.

114. Nesrallah GE, Suri RS, Carter ST, et al. The International Quotidian Dialysis Registry: annual report 2007. *Hemodial Int.* 2007;11:271-277.

115. Nesrallah GE, Moist LM, Awaraji C, Lindsay RM. An international registry to compare quotidian dialysis regimens with conventional thrice-weekly hemodialysis: why, how, and potential pitfalls. *Semin Dial.* 2004;17:131-135.

116. Pauly RP, Boivin JF, Chan CT. Methodological considerations for research in nocturnal home hemodialysis. *J Nephrol*. 2007;20:381-387.

117. Kliger AS. High-frequency hemodialysis: rationale for randomized clinical trials. *Clin J Am Soc Nephrol.* 2007;2:390-392.

118. Greene T, Daugirdas JT, Depner TA, Gotch F, Kuhlman M. Solute clearances and fluid removal in the frequent hemodialysis network trials. *Am J Kidney Dis*. 2009;53:835-844.

119. Eknoyan G, Beck GJ, Cheung AK, et al. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med.* 2002;347:2010-2019.