Cost-Effectiveness of Frequent In-Center Hemodialysis

Chris P. Lee,* Stefanos A. Zenios,† and Glenn M. Chertow‡

*The Wharton School, University of Pennsylvania, Philadelphia, Pennsylvania; and †Department of Operations, Information and Technology, Graduate School of Business, and ‡Division of Nephrology, Department of Medicine, Stanford University, Stanford, California

ABSTRACT

Published evidence suggests that frequent hemodialysis (more than three times per week) for patients with ESRD may improve health-related quality of life and has the potential to increase longevity and reduce hospitalization and other complications. Here, a Monte Carlo simulation model was used to compare varying combinations of in-center hemodialysis frequency (three to six treatments per week) and session length (2 to 4.5 h per session) with regard to unadjusted and quality-adjusted life-years and total lifetime costs for a cohort of 200,000 patients, representing the prevalent ESRD population. The incremental cost-effectiveness ratio was calculated for the various regimens relative to a conventional hemodialysis regimen (three treatments per week, 3.5 h per session). Using conservative assumptions of the potential effects of more frequent hemodialysis on outcomes, most strategies achieved a cost-effectiveness ratio of <$125,000, although all had a cost-effectiveness ratio of >$75,000. The cost-effectiveness ratio increased with the frequency of hemodialysis. More frequent in-center hemodialysis strategies could become cost-neutral if the cost per hemodialysis session could be reduced by 32 to 43%. No other change in model assumptions achieved cost neutrality. In conclusion, given the extraordinarily high costs of the ESRD program, the viability of more frequent hemodialysis strategies depends on significant improvements in the economic model underlying the delivery of hemodialysis.

J Am Soc Nephrol 19: 1792–1797, 2008. doi: 10.1681/ASN.2008010001

ESRD affects approximately 400,000 people in the United States, with the majority on hemodialysis, typically prescribed three times weekly for between 3.0 and 4.0 h per session. The rationale for frequency (three rather than one or two or four or more sessions per week) was initially based on effects of hemodialysis on neurocognitive function[1] as well as logistic issues (*e.g.*, machine availability, payment strategies) and the perceived burden of care relative to the burden of disease. The usual hemodialysis session length has varied over time, influenced by technological advances (*e.g.*, larger surface area dialyzers) and informed by evidence from observational databases and, to a lesser extent, randomized clinical trials. Despite improvements in dialysis technology and efforts to enhance therapy through evidence-based practice, mortality rates have remained extremely high (generally >20% per year in the United States).[2] Although dialysis has been reasonably effective at sustaining life in the majority of patients with ESRD, dialysis has failed to restore their health. Hospitalization is frequent and often prolonged, and studies examining functional capacity and health-related quality of life have suggested that patients on dialysis experience unacceptable degrees of morbidity associated with their disease.[2–4]

In recent years, several hemodialysis centers in the United States, Canada, and Europe have explored strategies of more frequent hemodialysis in selected patients. Published reports on frequent he-

Received January 1, 2008. Accepted May 8, 2008.

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Glenn M. Chertow, Stanford University School of Medicine, 780 Welch Road, Suite 106, Palo Alto, CA 94034. Phone: 650-725-4738; Fax: 650-721-1443; E-mail: gchertow@stanford.edu

Copyright © 2008 by the American Society of Nephrology

modialysis (five or six times per week with variable session lengths) have suggested improvements in health-related quality of life,[5–7] along with other benefits that might be expected to enhance survival, including a reduction in left ventricular hypertrophy[8,9]; correction of sleep apnea[10]; and improved control of hypertension, mineral metabolism, endocrine abnormalities, and anemia.[11,12] These observations have been criticized on the basis of the selection of study subjects and the unblinded assessment of outcomes, some of which are highly subjective, although published (and unpublished) reports were compelling enough to prompt the National Institutes of Health and the Centers for Medicare and Medicaid Services to sponsor two randomized clinical trials comparing frequent (in-center and home nocturnal) and conventional hemodialysis (http://www.clinicaltrials.gov/ct/show/NCT00271999). Because of feasibility concerns and fiscal limitations, the planned sample sizes of the randomized clinical trials were fixed at 250 per study with an on-treatment study duration of 12 mo; calculated statistical power was insufficient to infer estimates of the effects of changes in hemodialysis frequency on life expectancy.

To address the potential effects of hemodialysis frequency and session length on life expectancy, costs, and cost-effectiveness, we conducted a Monte Carlo simulation altering hemodialysis frequency from three to six times per week while altering session length between 2.0 and 4.5 h. We provided base case assumptions of the effects of session length on mortality on the basis of integrated evidence from the published literature[13–16] and imputed estimates of the effects of frequency on mortality derived from expert opinion, using conservative estimates and sensitivity analysis to bracket a range of potential effects. Our goal was to examine whether under very conservative estimates of the effects of frequency on mortality, any frequent in-center hemodialysis strategies that would enhance longevity at a reasonable cost could be identified. A complementary objective was the identification of the key factors that could enhance the cost-effectiveness of such strategies.

RESULTS

On the basis of reasonable assumptions of the potential effects of more frequent hemodialysis on mortality and hospitalization, we determined that a change from conventional in-center hemodialysis (three times per week, 3.5 h per session) to a more frequent hemodialysis strategy would be expected to increase life expectancy by between 2 and 24 mo (depending on the frequency—four, five, or six times per week), across a range of session lengths (2.0 to 4.5 h per session). More frequent in-center hemodialysis would be considerably more expensive, but cost-effectiveness ratios were generally estimated in the range of $100,000 per quality-adjusted life-year (QALY).

Figure 1 demonstrates the incremental costs on the vertical axis and the incremental life expectancy on the horizontal axis relative to current practice under the baseline assumption for all frequency and session length combinations tested. The dotted lines indicate the "lines of identity" at $75,000 per life-year and $125,000 per life-year saved. Table 1 provides simulation output data for three of the strategies—(3, 3.5) (conventional therapy), (4, 3.0), and (5, 2.5)—showing data on the average life expectancy, total lifetime costs, the probability of survival at 1 and 5 yr, hospital admissions per patient per year, and the incremental cost-effectiveness ratios.

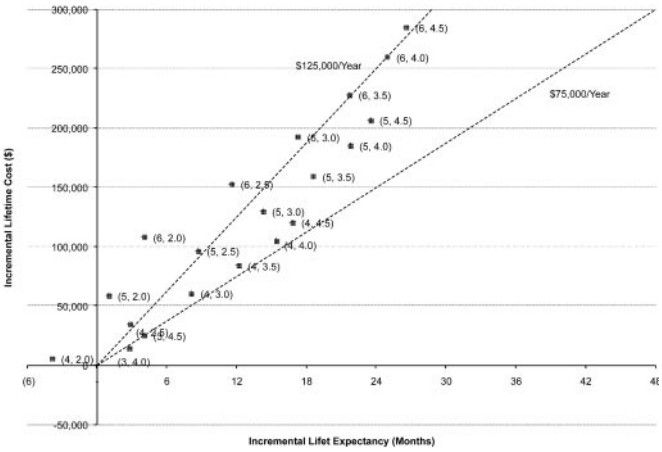

Figure 1. Incremental cost and incremental life expectancy relative to current practice under baseline assumptions. The dotted lines indicate "lines of identity" at $75,000 per life-year and $125,000 per life-year saved.

Results for break-even analyses and are shown in Tables 2 and 3. Our analysis indicated that it was not possible for (4, 3.0) and (5, 2.5) to break even with (3, 3.5) in terms of total lifetime cost just by reducing the relative risk for hospitalization; however, it was possible to break even in average annual cost, and the break-even points are shown in Table 2: (4, 3.0) required the relative risk to decrease to 0.46, whereas (5, 2.5) required a complete elimination of hospitalization to break even with (3, 3.5). Also shown in Table 3, it was possible to break even in total lifetime cost by reducing the cost rate for dialysis: For (4, 3.0), the reduction needed was 32%; for (5, 2.5), a reduction of 43% was required.

When the analysis was repeated using the more conservative assumptions, all cost-effectiveness ratios increased and break-even assumptions changed as expected: Under the reduced effect of time assumptions, (4, 3.0) and (5, 2.5) required dialysis costs to be reduced by 34 and 46%, respectively, whereas under reduced effect of frequency assumptions, the corresponding required cost reductions were 23 and 33%.

DISCUSSION

Clinical trials provide the gold standard for guiding changes in dialysis practice; however, large-scale clinical trials on frequent *versus* conventional hemodialysis may never be conducted. Culleton *et al.*[17] recently reported results from a randomized clinical trial in which 52 patients were recruited from 10 dialysis units at two universities in Alberta and treated on protocol with either five to six nights per week for 6 h per session or conventional thrice-

Table 1. Simulation output for three dialysis strategies under three scenarios[a]

Parameter	Dialysis Strategies		
	(3, 3.5)	(4, 3.0)	(5, 2.5)
Total lifetime Medicare costs ($000)			
baseline	307 (0.3)	368 (0.3)	404 (0.4)
reduced effect of time	307 (0.3)	372 (0.3)	413 (0.4)
reduced effect of frequency	307 (0.3)	348 (0.3)	376 (0.4)
First-year cost ($000)			
baseline	64 (0.0)	72 (0.0)	78 (0.0)
reduced effect of time	63 (0.0)	71 (0.0)	78 (0.0)
reduced effect of frequency	63 (0.0)	72 (0.0)	79 (0.0)
Life expectancy			
baseline	74 (0.1)	82 (0.1)	83 (0.1)
reduced effect of time	74 (0.1)	84 (0.1)	86 (0.1)
reduced effect of frequency	74 (0.1)	76 (0.1)	75 (0.1)
1-Yr patient survival (%)			
baseline	78 (0.0)	79 (0.0)	80 (0.0)
reduced effect of time	78 (0.0)	80 (0.0)	80 (0.0)
reduced effect of frequency	78 (0.0)	78 (0.0)	78 (0.0)
5-Yr patient survival (%)			
baseline	34 (0.0)	38 (0.0)	38 (0.0)
reduced effect of time	34 (0.0)	38 (0.0)	39 (0.0)
reduced effect of frequency	34 (0.0)	35 (0.0)	35 (0.0)
Hospital admissions per patient per year			
baseline	1.20 (0.00)	1.07 (0.00)	1.06 (0.00)
reduced effect of time	1.20 (0.00)	1.05 (0.00)	1.03 (0.00)
reduced effect of frequency	1.20 (0.00)	1.17 (0.00)	1.19 (0.00)
Incremental cost-effectiveness ratio ($000/yr)			
baseline		89	133
reduced effect of time		83	112
reduced effect of frequency		291	1491

[a]Simulation output data for three of the strategies: (3, 3.5), (4, 3.0), and (5, 2.5). These strategies were chosen as benchmarks for simplicity of presentation. "Baseline" refers to the optimistic assumptions in Tables 5 and 6, whereas "reduced effect of time" ("reduced effect of frequency") refers to the combination of the optimistic assumptions in Table 5 (5) and the conservative assumptions in Table 6 (4). "First-year cost" refers to the total cost within the first year of initiating dialysis. SE are shown in parentheses.

Table 2. Break-even analyses

Strategy	"Break Even" Relative Risk for Hospitalization	Lifetime Medicare Cost ($000)	Life Expectancy (Mo)	Cost ($000) per Year
(3, 3.5)	1.00	307	74	50
(4, 3.0)	0.46	347	83	50
(5, 2.5)	0.00	374	89	51

Table 3. Break-even analyses

Strategy	Total Lifetime Cost ($000)	Cost Over 3.0 × 3.5	Lifetime Dialysis Cost	Break-Even Cost Reduction
(3, 3.5)	307	–	135	0.00
(4, 3.0)	368	60	188	0.32
(5, 2.5)	404	96	224	0.43

weekly hemodialysis over a 6-mo study period. The primary outcome was change in left ventricular mass. Prespecified secondary outcomes included change in health-related quality of life, change in predialysis systolic BP, change in erythropoietin-to-hematocrit ratio, and change in calcium-phosphate product.

Using an intention-to-treat approach (assuming no change among patients with no follow-up cardiac imaging), there was a relative difference in left ventricular mass of 15.3 g between the groups; the difference was of marginal statistical significance. Among the secondary outcomes explored, nocturnal hemodialysis resulted in the use of fewer antihypertensive medications and trends toward lower systolic and diastolic BP.

Predialysis serum phosphorus was significantly reduced by nocturnal hemodialysis despite reduced use of phosphate binders. Nocturnal hemodialysis did not result in a change in health-related quality of life as assessed by the EuroQol EQ-5D index score, although it did yield improvements in the perceived "effects" and "burden" of kidney disease, from the Kidney Disease Quality of Life Short Form (KDQOL-SF) questionnaire. There was no difference in the frequency or duration of hospitalizations or in complications, including those associated with vascular access.

Gaps in the current evidence base regarding the efficacy of more frequent hemodialysis may be filled by the ongoing National Institutes of Health– and Centers for Medicare and Medicaid Services–sponsored trials; however, neither the Canadian trial nor the ongoing US trials had sufficient power to detect measurable differences in mortality or event rates. At best, these trials can determine the effects of frequent hemodialysis on selected intermediate outcomes, some of which are self-reported and subject to bias. They will not provide reliable estimates on the effects of frequent hemodialysis on survival or cost-effectiveness.

The aim of this study was to determine the cost-effectiveness of a variety of frequent in-center hemodialysis strategies, assuming that there are favorable effects of increased frequency on patient outcomes (if there are not favorable effects, then frequent in-center hemodialysis would be "strictly dominated" as a more costly but not more effective alternative). Figure 1 demonstrates that the incremental cost-effectiveness ratio for any new policies relative to current practice will be at least $75,000 per life-year gained under a set of conservative assumptions about the efficacy of frequent in-center hemodialysis. None of the strategies using six-times a week hemodialysis achieved a cost-effectiveness ratio of <$125,000. Using the conventional benchmark of $50,000 per life-year gained, these results suggest that frequent in-center hemodialysis strategies are unlikely to be considered cost-effective unless increasing the frequency of in-center hemodialysis exerts much more favorable effects on outcomes and associated costs than assumed here.

This in turn raised the question on which of the assumptions made in the analysis could potentially lead to a better (lower) cost-effectiveness ratio. We focused on assumptions about hospital admission rates and in-center hemodialysis session costs. We have found that for more frequent in-center hemodialysis strategies to be "cost-effective" by conventional metrics, they should be accompanied with a dramatic reduction in hospital admission rates (in some cases, complete reduction of hospital admissions). On the basis of current evidence, such reduction seems ambitious and unlikely. We have also discovered that a reduction in the per-session cost of in-center hemodialysis could considerably improve the cost-effectiveness of more frequent in-center hemodialysis strategies. If the per-session costs were reduced by between 32 and 43% relative to current costs, then strategies involving more frequent in-center hemodialysis could be budget-neutral.

The major implication from this analysis is that more frequent in-center hemodialysis strategies are unlikely to be considered cost-effective unless they involve four or five times per week (rather than six or seven) and are accompanied by a commensurate reduction in the cost of each session. Given that our model already assumed what many would consider a generous benefit of increased frequency on outcomes (a 32% reduction in mortality with 6 compared with 3 d/wk), costs of more frequent in-center hemodialysis may be prohibitive unless the benefits are overwhelming and/or the costs of delivering hemodialysis could be significantly reduced.

The analyses presented here have several important strengths. The input data were derived from a national registry highly representative of the US hemodialysis population. We used sophisticated, previously validated modeling methods to generate stable estimates of life expectancy, costs, and incremental cost-effectiveness. We provided multiple alternatives of frequency and session length and conservative estimates of the effects of these interventions. There are also several important limitations. Although we integrated extensive data on the associations between session length and mortality, there were no available data on the association between frequency and mortality and the available data on frequency and hospitalization were so heavily confounded by indication that they were not used; therefore, we imputed hazard ratios for the estimated effects of frequency on mortality and hospitalization. We believe that these estimates were conservative and reasonable, on the basis of the effects of frequent hemodialysis on intermediate outcomes in the published literature. For instance, left ventricular hypertrophy[17–19] and hyperphosphatemia[17,20,21] have been consistently associated with large (20 to >50%) increases in the relative risk for death in multiple observational studies. Finally, the precise measures of longevity, costs, and cost-effectiveness derived from the simulation depend on factors other than frequency and session length, including the covariates included in Table 4; however, the simulation model was validated previously and shown to replicate closely observed outcomes across all major patient subgroups. Moreover, the goals of this endeavor were to provide ballpark estimates rather than precise ones, particularly in light of the absence of data on the relation between hemodialysis frequency and outcomes.

In summary, using Monte Carlo simulation, we have provided estimates of longevity, costs, and cost-effectiveness for a variety of potential alterations in in-center hemodialysis frequency and session length. These results should not be considered definitive but may provide a framework on which to consider how changes in the provision of hemodialysis care might affect patient outcomes and ESRD program costs. Although modest improvements related to more frequent in-center hemodialysis might enhance longevity and potentially enhance health-related quality of life, strategies using more frequent in-center hemodialysis would likely increase ESRD program costs considerably, unless the effects of frequent hemodialysis on hospitalization are dramatically more beneficial than we have assumed; therefore, major changes in dialysis delivery systems (*e.g.*, a transition to home-based therapies) will be required to derive any benefits that might be present without incurring excessive costs.

Table 4. Model attributes and possible values in Monte Carlo simulation[a]

Attribute	Possible Values
Demographics	
age	<50, 50 to 59, 60 to 69, 70 to 79, ≥80
gender	Female, Male
race	White, African American, Asian, Native American
Hispanic ethnicity	Hispanic, non-Hispanic
blood type	O, A, B, AB
Comorbid conditions	
Diabetes	Present, absent
atherosclerotic cardiovascular disease	Present, absent
congestive heart failure	Present, absent
cancer	Present, absent
Disease markers	
eGFR (ml/min per 1.73 m^2)	<6, 6 to <9, 9 to <12, 12 to <15, 15 to 29
serum albumin (g/dl)	≥3.6, <3.6
Clinical flags	
"previously hospitalized"	Present, absent
"currently on a transplant"	Present, absent

[a]eGFR, estimated GFR.

CONCISE METHODS

A computer simulation model simulated costs and outcomes for various choices of hemodialysis frequency and session length. The simulation model has been previously described.[22] Briefly, the model had two components. The patient generation component created representative patient cohorts by sampling with replacement from the prevalent patient population in the US Renal Data System (USRDS). The patient simulation component generated a sequence of simulated transitions among health states for all patients in the patient cohorts. Transitions among health states were governed by probabilities estimated empirically using data from the USRDS and Kaiser Permanente Northern California, an integrated health care delivery system. Approximately one quarter of a million possible health states were included in the model to capture the demographic, comorbid, laboratory, and modality factors described in Table 4. Transitions among states captured common clinical events in ESRD: Hospital admissions, decline in kidney function, transplantation, graft failure, and death. We previously demonstrated that the simulation model realistically replicated long-term outcomes and treatment costs for all patient cohorts simulated.[22]

Patient Cohorts

For this study, we simulated a cohort of 200,000 patients representing a random sample from the USRDS. The large sample size was chosen to ensure high confidence in the average quantities obtained from the simulation. The simulation was replicated five times for each cohort for calculating SE for the simulation-generated averages.

Dialysis Strategies

Patients were slated to start dialysis when their estimated GFR fell below 9 ml/min per 1.73 m^2. Dialysis would occur at a fixed frequency and session length until the patient received a transplant (when an organ became available) or died. The following combinations of frequency (N) and session length (T) were considered (denoted as paired values in the form of (N, T): (3, 3.5), (3, 4.0), (3, 4.5), (4, 2.0), (4, 2.5), (4, 3.0), (4, 3.5), (4, 4.0), (4, 4.5), (5, 2.0), (5, 2.5), (5, 3.0), (5, 3.5), (5, 4.0), (5, 4.5), (6, 2.0), (6, 2.5), (6, 3.0), (6, 3.5), (6, 4.0), and (6, 4.5).

Dosage-Response Representation

An important component of the simulation model was the representation capturing the relation between hemodialysis "dosage" [represented here by paired values (N, T)] and transition rates between health states. Ordinarily, to develop such a representation, one would need data from actual patients receiving hemodialysis differing from the standard (3, 3.5) average dosage, but no such data were available; therefore, we took a different approach in which we first estimated hazard rates at the standard dosage; assumptions were then made about the effect on hazard rates as a result of each incremental deviation from the standard dosage. For example, compared with a session length of T = 3.5, we assumed a certain percentage reduction in hazard when T was increased to T = 4.0 and a further incremental reduction when T was increased to T = 4.5; the overall (cumulative) reduction in hazard when time was increased from 3.5 to 4.5 would be the product of the two percentages. A similar scheme was assumed for hemodialysis frequency. When both frequency and time differed from the standard average values of (3, 3.5), the resulting hazard reduction was assumed to be the product of the independent reductions for frequency and time.

This dosage-response model was used to describe how changes in hemodialysis might attenuate hospital admissions and mortality in the simulation. Two sets of assumptions, one optimistic and the other conservative, were used for each dosage parameter. Tables 5 and 6 summarize these assumptions in terms of incremental and cumulative reductions (the latter in parentheses). Optimistic assumptions reflect larger effects of frequency and time; the conservative assumptions reflect smaller effects. In other words, where estimating the effects of alterations in time, the "optimistic" assumptions yielded lower relative risks for session lengths longer than 3.5 h and higher relative risks for session lengths shorter than 3.5 h compared with the "conservative" assumptions.

Pairing assumptions in Tables 5 and 6 led to three "dosage response" scenarios: "Baseline" (optimistic assumptions for both frequency and time), "reduced effect of frequency" (conservative assumptions for frequency and optimistic assumptions for time), and "reduced effect of time" (optimistic assumptions for frequency and conservative assumptions for time).

The simulation was replicated for each of the three scenarios. In total, the simulation was replicated 315 times: 315 = 21 (strategies) × 3 (dose

Table 5. Underlying assumptions for the dosage-response model: Impact of frequency on mortality hazard ratios[a]

Frequency (N)	3	4	5	6
Optimistic	1.000	0.800	0.900	0.950
	(1.000)	(0.800)	(0.720)	(0.680)
Conservative	1.000	0.900	0.925	0.950
	(1.000)	(0.900)	(0.830)	(0.790)

[a]Frequency expressed in sessions per week.

Table 6. Underlying assumptions for the dosage response model: Impact of time on mortality hazard ratios

Time (T)	2.0	2.5	3.0	3.5	4.0	4.5
Optimistic	1.150	1.100	1.075	1.000	0.950	0.975
	(1.360)	(1.180)	(1.075)	(1.000)	(0.950)	(0.930)
Conservative	1.100	1.075	1.050	1.000	0.975	0.9875
	(1.240)	(1.130)	(1.050)	(1.000)	(0.975)	(0.960)

[a]Time expressed in hours per session.

response scenarios) × 5 (for SE calculations). Each time, the simulation evolved 200,000 patients from the onset of ESRD through death.

Outcomes

The outcomes from the simulation included costs, life expectancy, and QALY. Life expectancy measured the total survival time from the beginning of the simulation; QALY was similar to life expectancy but adjusted each period of survival by the health utility of the patient during that period, with discounting. Discounting was used in calculating both costs and QALY to reflect intertemporal tradeoff. A standard discount rate of 3% was used. Costs included all treatment-related expenses over the simulated lifetime of each patient: Dialysis (fixed and variable components), erythropoietin and other drugs, transplantation (initial event and each subsequent year), transplant failure, inpatient hospital admissions, and outpatient checkups. Cost rates were estimated using data of actual Medicare payments from the USRDS and included both Part A (institutional) and Part B (institutional and physician/supplier) claims. Details regarding the estimation or sources of health utilities and cost rates have been previously published.[4]

Break-Even Analyses

To examine the factors that affect the cost-effectiveness of frequent hemodialysis strategies, we performed "break-even analysis" as follows. For simplicity of presentation, we took (4, 3.0) and (5, 2.5) as benchmarks for increased frequency (shown in Table 1). For each of the benchmark strategies, we determined the necessary reduction in hospital admission rates and dialysis cost rates that would make the total lifetime costs equal to the cost of the current strategy (3, 3.5).

DISCLOSURES

None.

REFERENCES

1. Teschan PE, Ginn HE, Walker PJ, Bourne JR, Ward JW, Fristoe MW, McLain LW: Assessing adequacy of dialysis using measures of neurological function. *Proc Clin Dial Transplant Forum* 4: 160–165, 1974
2. US Renal Data System: *USRDS 2005 Annual Report*, Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2005
3. Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang H, Lazarus JM: Quality-of-life evaluation using Short Form 36: Comparison in hemodialysis and peritoneal dialysis patients. *Am J Kidney Dis* 35: 293–300, 2000
4. Gorodetskaya I, Zenios SA, McCulloch CE, Bostrom A, Hsu CY, Bindman AB, Go AS, Chertow GM: Health-related quality of life and estimates of utility in chronic kidney disease. *Kidney Int* 68: 2801–2808, 2005
5. Heidenheim AP, Muirhead N, Moist L, Lindsay RM: Patient quality of life on quotidian hemodialysis. *Am J Kidney Dis* 42: 36–41, 2003
6. 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* 42: 1020–1035, 2003
7. Traeget J, Galland R, Delawari E, Arkouche W, Hadden R: Six years' experience with short daily hemodialysis: Do the early improvements persist in the mid and long term? *Hemodial Int* 8: 151–158, 2004
8. Chan CT, Floras JS, Miller JA, Richardson RM, Pierratos A: Regression of left ventricular hypertrophy after conversion to nocturnal hemodialysis. *Kidney Int* 61: 2235–2239, 2002
9. Ayus JC, Mizani MR, Achinger SG, Thadhani RT, Go AS, Lee S: Effects of short daily versus conventional hemodialysis on left ventricular hypertrophy and inflammatory markers: A prospective, controlled study. *J Am Soc Nephrol* 16: 2778–2788, 2005
10. Hanly PJ, Pierratos A: Improvement of sleep apnea in patients with chronic renal failure who undergo nocturnal hemodialysis. *N Engl J Med* 344: 102–107, 2001
11. 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* 67: 1500–1508, 2005
12. Suri RS, Nesrallah GR, Mainra R, Garg AX, Lindsay RM, Greene T, Daugirdas J Daily hemodialysis: A systematic review. *Clin J Am Soc Nephrol* 1: 33–42, 2006
13. Held PJ, Levin NW, Bovbjerg RR, Pauly MV, Diamond LH: Mortality and duration of hemodialysis treatment. *JAMA* 265: 871–875, 1991
14. Eknoyan G, Beck GJ, Cheung AK, Daugirda JT, Greene T, Kusek JW, Allon M, Bailey J, Delmez JA, Depner TA, Dwyere JT, Levey AS, Levin NW, Milford E, Ornt DB, Rocco MV, Schulman G, Schwab SJ, Teehan BP, Toto R, Hemodialysis (HEMO) Study Group; Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med* 347: 2010–2019, 2002
15. 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* 69: 1229–1236, 2006
16. Saran R, Bragg-Greshem JL, Levin NW, Twardowski ZJ, Wizemann V, Saito A, Kimata N, Gillespie BW, Combe C, Bommer J, Akiba T, Mapes DL, Young EW, Port FK: Longer treatment time and slower ultrafiltration in hemodialysis: Associations with reduced mortality in the DOPPS. *Kidney Int* 69: 1222–1228, 2006
17. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE: The prognostic importance of left ventricular geometry in uremic cardiomyopathy. *J Am Soc Nephrol* 5: 2024–2031, 1995
18. London GM, Pannier B, Guerin AP, Blacher J, Marchais SJ, Darne B, Metivier F, Adda H, Safar ME: Alterations in left ventricular hypertrophy in and survival of patients receiving hemodialysis: Follow-up of an interventional study. *J Am Soc Nephrol* 12: 2759–2767, 2001
19. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM: Mineral metabolism, mortality and morbidity in maintenance hemodialysis. *J Am Soc Nephrol* 15: 2208–2218, 2004
20. Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, Akizawa T, Kurokawa K, Bommer J, Piera L, Port FK: Predictors and consequences of altered mineral metabolism: The Dialysis Outcomes and Practice Patterns Study. *Kidney Int* 67: 1179–1187, 2005
21. Culleton BF, Walsh M, Klarenbach SW, Scott-Douglas N, Quinn RR, Tonelli M, Donnely S, Freidrich MG, Kumar A, Mahallati H, Hemmelgarn B, Manns BJ: Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: A randomized controlled trial. *JAMA* 298: 1291–1299, 2007
22. Lee CP, Zenios SA, Chertow GM: A simulation model to estimate the cost and effectiveness of alternative dialysis strategies. *Med Decis Making* 26: 535–549, 2006