Chapter 4

Clinical Effectiveness of Continuous Ambulatory Peritoneal Dialysis and Hemodialysis

Chapter 4

Clinical Effectiveness of Continuous Ambulatory Peritoneal Dialysis and Hemodialysis

Comparison of the effectiveness of chronic dialysis modalities requires information from controlled trials that involve patients with similar clinical characteristics. To date no such trials have been performed. In their absence, this case study takes information from reported clinical observations to draw qualitative conclusions on the relative effectiveness of continuous ambulatory peritoneal dialysis (CAPD), home hemodialysis (HD), and center HD. Further, the influence of case-mix differences on clinical outcomes is assessed from those few studies that have retrospectively examined the influence of patient characteristics on medical outcomes.

Patient survival is undeniably the central measure of treatment effectiveness in end-stage renal disease (ESRD). Chronic dialysis techniques (and renal transplantation) have markedly enhanced survival in patients with ESRD. Survival alone is an inadequate yardstick, however, and factors that relate to quality of life on dialysis also need to be considered. To this end, the following factors are examined in addition to survival: the ability of the patient to tolerate and remain on a dialysis modality (referred to as "procedure survival"), morbidity as measured by complication rates and the need for hospitalization, and proxies for the "quality of life" such as physical activity levels and ability to return to work. The "burden of treatment" as perceived by the patient and his or her family is also important, especially for a chronic illness such as ESRD. Information on this point is extremely limited, however.

PATIENT SURVIVAL

Tables 4-1, 4-2, and **4-3** present survival data for patients receiving CAPD or HD. Where possible, the differences between center HD and home HD are distinguished. All results are unadjusted for differences in the duration of ESRD, age, or other risk factors. Furthermore, these results do not account for the effects of varying actuarial methods. Overall, l-year survival on CAPD ranges from 74 percent in the Registry of the European Dialysis and Transplant Association (EDTA) (28) to 86 percent in the most recent results from the National Institutes of Health (NIH) CAPD Registry **(46)** (table 4-l). Single institution studies give higher figures, perhaps due to special local expertise or patient selection factors. Two-year survival on CAPD in the EDTA registry is *60* percent, while **2** year data had not been reported by the NIH CAPD Registry by *1983*.

Survival estimates for HD are from ESRD program enrollees **(27),** the Michigan Kidney Registry *(50),* and the EDTA Registry **(51)** (table **4-2).** In the ESRD program, survival on chronic dialysis was reported as 81 percent at 1 year and 56 percent at 3 years, but this report did not break results down by dialysis modality. It can be assumed that, in the period 1977-80 to which the results apply, the overwhelmingly dominant modality was HD and that the ratio of center HD to home HD was about **9** to 1. The Michigan Kidney Registry survival rates of **78** percent at 1 year and 61 percent at **2** years are for center HD alone,

98-824 0 - 85 - 3 : QL 3

Table 4-1.— Patient Survival and the Ability of Patients to Continue CAPD

Source[a] and population	Calendar year(s)	Number of patients	Patient-years	Patient survival 0.5 yr	Patient survival 1 yr	Patient survival 2 yr	Continued on CAPD[b] 0.5 yr	Continued on CAPD[b] 1 yr	Continued on CAPD[b] 2 yr
Nolph, et al., 1983 (NIH CAPD Registry). .	1981	567	320	930/0	900/0	—	79%0	600/0	—
NIH CAPD Registry, 1982	1981-82	4,858	—	93	86	–	76	62	56 (18 mo)
							88	82	76 (18 mo)[c]
Kramer, et al., 1982 (EDTA Registry)	1979-81	2,905	—	80	74	60	53	41	28
							62	53	46[c]
Oliver, 1983 (Churchill Hospital, Oxford) .	1978-82	126	124	91	86	80	72	57	38
Rubin, 1983	1979-81	56	—	—	—		80	50	35
Amair, 1982[d]	1978-81	20	24	—	92	81	—	87	76
Baum, 1983[e]	1979-82	20	—	95	95	95	78	78	53

[a] Full citations found in the References.
[b] Refers t. th, percent of the initial cohort who remain on CAPD. Hence, the denominator includes deaths and patients undergoing transplantation, as well as patients who change from one dialysis modality to another.
[c] Percent of patients still on chronic dialysis who remain in CAPD. Excludes deaths and transplants.
[d] All patients were diabetics.
[e] Patients were children with a mean age of 11.9 years. The mean period of observation was 0.95 years.

SOURCE: Office of Technology Assessment

Table 4-2.—Patient Survival on HD

Source[a] and population	Calendar years	Dialysis modality	Number of patients	Survival 1 yr	2 yr	3 yr	Comment
Krakauer, et al., 1983. .	1977-80	Predominantly HD	65,270	81 0/0	—	56°/0	ESRD program enrollees beginning dialysis in 1977-80. Results overestimate survival in ESRD, because they exclude deaths during the 3-month period following diagnosis before the patient becomes eligible for enrollment in the ESRD program. The vast majority (98+ %) of patients would have been on home or center HD in these years in an approximate ratio of 10:90
Weller, et al., 1982 (Michigan Kidney Registry)	1974-78	Center HD only All center HD	1,560 2,396	70.80/o 78.1	53,20/o 61.2	—	Actuarial survival curves were calculated separately for patients on center HD only and all patients on center HD including those subsequently transplanted or changed to another dialysis modality

[a]Full citations found in the References.

SOURCE' Office of Technology Assessment

Table 4.3.—Comparisons of Patient Survival on CAPD and HD

Source[a] and population	Calendar years	Dialysis modality	Number of patients	Survival 1 yr	Comments
Wing, et al., 1983 (EDTA Registry)	1979-81	HD CAPD	– –	840/o 78	Results apply to a low-risk "standard population" ages 20 to 60. Reference does not specify whether HD was in the home or in a center
Bovbjerg, et al., 1983 (ESRD program)	1981	Home HD Center HD CAPD	109 2,929 174	91 86 87	ESRD program enrollees who began dialysis between 1/1/81 and 3/31/81. The reference does not state whether survival rates are annualized or merely refer to survival in calendar year 1981 following enrollment

[a]Full citations found in the References.

SOURCE' Office of Technology Assessment.

and the EDTA Registry reported an 84 percent 1-year survival on HD in a low-risk "standard population."

First-year survival after the 3-month preenrollment period required by the ESRD program is greater in patients on home HD (91 percent) than for those on CAPD or center HD (87 and 86 percent, respectively) (8) (table 4-3). The better result in the home HD group is consistent with other reports and has been attributed to the selection of younger and healthier patients for home HD.

On balance, these results suggest that early survival on CAPD is equivalent to that on HD. This conclusion must be considered tentative, however, because studies of HD generally apply to earlier time periods, and because none of these studies takes into account the characteristics of the populations being dialyzed.

ABILITY TO CONTINUE ON A DIALYSIS MODALITY

The ability of a patient to remain on a dialysis modality over a prolonged period of time is important both because failures usually reflect treatment-related morbidity and because the cost of treating complications or changing modalities may be considerable.

For this study, systematic information on abandonment rates for HD was unobtainable. For example, no recent reports from sizable patient populations or registries could be found that described the frequency of transfer from HD to peritoneal dialysis or to cadaveric renal transplantation because of vascular access or other complications of dialysis. That failure rates of HD may be appreciable, however, can be inferred from the NIH CAPD Registry results that indicate that, among patients beginning CAPD between January 1, 1981, and March 31, 1982, 48.3 percent had previously received HD (table 4-4). Presumably, these patients either had vascular access problems, or for some other reason, preferred to change to CAPD.

Abandonment rates of patients on CAPD, on the other hand, have been well documented (table 4-1), and in fact, constitute the main argument against its proliferation. Patients still on CAPD after 1 year range from **41** percent in the European experience *(28)* to *62* percent in the 1983 report from the NIH CAPD Registry (46). The corresponding 2-year rate is **28** percent in Europe, and the 18-month rate is *56* percent in this country (28).

Calculation of abandonment rates depends importantly on whether elective transfers, deaths not directly related to procedure complications, transplanted patients, and patients who spontaneously recover renal function are counted in the population at risk. Hence, results must be examined closely. The above figures include in the denominator all patients starting on CAPD regardless of the reason for departure. Therefore, they significantly overestimate departures for reasons of procedure-related morbidity alone. When deaths and transplanted patients are removed, 1-year continuation rates for CAPD become *53* and 82 percent for the European and U.S. experiences, respectively.

Excessive peritonitis or noncompliance was the reason given for discontinuing CAPD in **27** percent of patients in the NIH CAPD Registry, and peritonitis alone was the reason in *50* percent of those in EDTA (see table 4-5). Inability to control "fluid/chemistry" or inadequate dialysis was the reason given for 12 and 10 percent of patients in these two registries, respectively.

Table 4-4.—Prior Treatment Modalities in Patients Entering the NIH CAPD Registry

Prior treatment	Number of patients	Percent
Hemodialysis	1,225	48.30/o
None	749	29.5
Intermittent peritoneal dialysis	483	19.0
Transplant	61	2.4
Continuous cycling peritoneal dialysis	20	0.8
Totals	2,538	100.0%

SOURCE: U.S. Department of Health and Human Services, National Institutes of Health, "CAPD Patient Registry Patient Population Demographics and Selected Outcome Measures, " Report No. 82-83, July 1, 1983.

Table 4-5.—Reasons for Leaving CAPD Other Than Transplantation or Return of Renal Function

Reason	Number of patients	Percent
NIH CAPD Registry:[a]		
Medical (not lack of fluid or chemical control)	257	39%0
Noncompliance or excessive peritonitis	176	27
Patient or family choice	101	16
CAPD not able to control fluid/chemistry	80	12
Other	30	5
Socioeconomic	8	1
Totals	652	100%
European Dialysis and Transplant Association (EDTA):[b]		
Peritonitis	153	50%
Other abdominal	43	14
Inadequate dialysis	31	10
Inability to cope	28	9
Other	28	9
Patient's request	22	7
Family's request	3	1
Totals	308	100%0

[a] U.S. Department of Health and Human Services, National Institutes of Health, "CAPD Patient Registry Patient Population Demographics and Selected Outcome Measures," Report No. 82-83, July 1, 1983.

bp. Kramer, M. Broyer, F. P, Brunner, et al., "Combined Report on Regular Dialysis and Transplantation in Europe, XII, 1981 ," presented at the XIXth Congress of the European Dialysis and Transplantation Association, Madrid, Spain, September 1982.

Better information on failures of HD will be required to permit valid comparisons with CAPD. Nonetheless, the high failure rates on CAPD give rise to justifiable concern that needs to be addressed through a combination of better patient selection, better patient training, and improved sterile techniques.

PATIENT MORBIDITY

Hospitalization Rates

Comparison of hospitalization rates indicates that patients receiving CAPD are hospitalized about 20 days per patient-year (range 19.7 to 23.2 days); those on center HD about the same or somewhat less (19.3 and 13.4 days in two studies); and patients on home HD about 9 days per patient-year (tables 4-6 and 4-7). About half of hospital stays in patients on CAPD were for complications of treatment, especially peritonitis, and the rest were for a variety of medical problems (33,51). No population-based data comparable to those in the NIH CAPD Registry are available for HD in the United States.

Although they are useful benchmarks, these crude hospitalization rates provide only a tentative basis for comparing morbidity among dialysis modalities. Most important, they do not account for differences among the treated populations that may influence the need for hospitali-

Table 4-6.—Hospitaiization Rates by Dialysis Modality

Source[a] and population	Calendar year	Number of patient-years	Days of hospitalization per patient-year			
			Center HD	Home HD	CAPD	Home IPD
Blagg and Wahl, 1983[b] (Northwest Kidney Center) . .	1982	430	19.3	9.2	19.7	26.3
Evans, 1983 (National Kidney Dialysis and Kidney Transplantation Study).	1981	859	13.4	8.2	20.6	—

[a]Full citations found in the References.
[b]Updated hospitalization rates areas follows: CAPD—16.2 days/pt-yr; center HD—9.1days/pt-yr; home HD—9.1days/pt-yr; and IPD—28.1days/pt-yr. (C. Blagg, Personal communication, 1983).

SOURCE: Office of Technology Assessment.

Table 4-7.—Hospitalization and Complication Rates in Patients on CAPD

Source[a] and population	Calendar year(s)	Hospitalizations per patient-year			Complications per patient-year			
		Number	Admissions	Days	Peritonitis		Exit or tunnel infections	Catheter replacement
Nolph, 1983, (NIH CAPD Registry)	1981	567	2.5	25.9	2.0		0.7	0.4
NIH CAPD Registry, 1982	1981-82	4,858	—	23.2	1.8		0.7	0.3
Kramer, 1982	1981	895	—	—	0	41.80/o	—	—
					1-3	49.7		
					4-6	7.0		
					>6	1.5		
Wing, et al., 1983[b] (EDTA)	1981	1,504	—	20	Males	1.4	—	—
					Females	1.6		
Oliver, 1983 (Churchill Hospital, Oxford).	1981-82	126	—	—	1.6		—	—
Amair, et al., 1982[c].	1978-81	20	–	–	0.6		—	—

[a]Full citations found in the References.
[b]Figures are for a "standard population" that includes only patients 20 to 60 years of age, without diabetes, malignancy, or other severe systemic illness, Or a primary diagnosis of ESRD having systemic disease implications (e.g., collagen disease).
[c]All patients were diabetics.

SOURCE: Office of Technology Assessment.

zation. The shorter periods of hospitalization experienced by patients on home HD, in particular, have been attributed to favorable patient selection factors. Age is one such factor, and the existence of comorbid conditions is another.

Furthermore, interpretation of hospitalization rates requires consideration of the length of time patients have been on a dialysis modality. For example, annualized hospitalization rates are considerably higher during the first 3 months of CAPD than in subsequent months. These higher rates reflect the hospital days required to initiate dialysis, the fact that patients starting out on dialysis are usually ill and require time to stabilize prior to discharge, and the days for treatment of complications that occur early in the course of dialysis. The same considerations apply to HD. A comparison of annualized days of hospitalization between two groups of patients which differ only in the proportion of patients beginning on dialysis would indicate a deceptive differential.

Finally, interpretation of reported hospitalization rates is complicated by methodological problems, including differences in the criteria used for including a patient in the study and differences in the method for dating the onset of dialysis. For example, a criterion that requires a patient to be on a dialysis modality for *30* days to qualify for entry into a study will result in a different case-mix from one that counts all patients started on a dialysis modality regardless of the duration of treatment.

Complications of Dialysis

Many patients on chronic renal dialysis have underlying medical problems such as hypertension, diabetes, and cardiovascular disease. Some treatment complications, therefore, may be more accurately regarded as part of a preexisting disease process than as a consequence of the treatment itself. Patients with ESRD due to diabetic nephropathy, for example, are at a higher than normal risk of developing cerebrovascular disease and suffering strokes. A high incidence of such a complication should be attributed at least in part to the diabetic disease process rather than to the specific technique of dialysis. Treatment complications, as other health outcomes, therefore, must be examined in the context of the population treated.

Complications of Hemodialysis

Complications of HD can be broadly classified into those occurring during dialysis, complications related to vascular access, and late complications seen in chronically treated patients. Although all are well known to occur, systematic data describing their frequencies could not be found for this case study.

The intermittent nature of HD and its efficiency as a method of dialysis can cause fluctuations in vascular-volume and serum chemistries that may lead to hypotension or cardiac arrhythmias or make hypertension more difficult to control. Associated shifts in central nervous system fluid balance have been alleged to contribute to some of the neurological symptoms that have been observed.

Extracorporeal circulation of the patient's blood through the dialyzer traumatizes and causes some destruction of red blood cells. Although' usually not serious, this red cell destruction, coupled with the loss of residual blood left in the dialyzer, blood loss due to numerous laboratory tests, and occasional blood leakage through the dialysis membrane, may aggravate the anemic state in ESRD. Blood transfusions occasionally are needed, and they increase the risk of serum hepatitis.

Patients are usually given the drug heparin during center HD to prevent coagulation of blood as it circulates extracorporeally. Careful medical supervision is required to restore normal coagulation as the blood returns to the body to minimize the risk of internal hemorrhage. This appears to be particularly important in diabetic patients who may be prone to ocular hemorrhages when repeatedly given anticoagulant drugs. Patients on home HD rarely receive heparin, because of the meticulous monitoring that is required.

There have been several deaths reported to have resulted from failures of the temperature regulating devices in the dialysis equipment. Clearly, equipment failures represent another potential complication of HD.

Vascular access is an absolute requirement of HD. The subcutaneous arteriovenous fistulae that are created for this purpose are subject to thrombosis and, rarely, to septic complications from repeated needle punctures. Replacement or transfer of the fistula to another site maybe required, and eventual depletion of convenient anatomical sites may necessitate change to another dialysis modality or renal transplantation. Access difficulties are only rarely encountered in young adults but are more likely in older patients with arteriosclerotic vessels and in diabetics. Children are also at higher risk of this complication because of the smaller sizes of their blood vessels.

The development of cardiovascular morbidity including myocardial infarctions, cerebrovascular accidents, and advanced peripheral vascular disease in patients on HD may result from the progression of preexisting disease, but at least circumstantial evidence suggests that the pace of these disorders may be accelerated by HD. Similarly, some reports attribute the occurrence of dementia to the presence of excessive amounts of aluminum in the dialysate. The possible importance of aluminum in antacid preparations taken by patients with ESRD also needs to be further evaluated.

Finally, the patient's dependence on a machine and reliance on the services of others when on HD, together with his/her awareness of social, parental, and conjugal inadequacies have been implicated as causes of severe depression and occasional suicides reported in patients on chronic HD.

Complications of CAPD

Peritonitis, or infection of the abdominal cavity, is far and away the most important complication of CAPD. The average patient in the NIH CAPD Registry suffered 1.8 episodes of peritonitis per patient-year (table 4-7), even though one-third of patients had no episodes during their first year of treatment **(46).** Peritonitis led to an average of slightly more than 10 days of hospitalization per patient-year and to occasional deaths. If detected and treated early, in some cases, peritonitis may be treated at home and cause minimal morbidity.

Peritonitis often results from a failure of the patient to adhere strictly to sterile procedures in effecting dialysate exchanges. Inadequate understanding of what is required, impaired manual dexterity, poor vision, and poor or inconsistent motivation all may be contributing factors.

A variety of approaches have been tried to improve CAPD techniques and to reduce the risk of peritonitis *(10,21,35,44).* To date, there is no evidence that the rates of the disease have been materially affected.

Reported peritonitis rates must be interpreted with caution because of widely varying definitions of what constitutes an episode. The presence of symptoms and signs such as fever and abdominal pain, cloudy dialysate effluent, a white cell count greater than 100 per cubic millimeter in the effluent, or a positive culture for bacteria, fungi, or other infectious agents all have been used individually or collectively. Causative organisms include a wide variety of bacteria and fungi **(3,25, 36,41,46).**

A second complication of CAPD has been infection of the subcutaneous tunnel in which the peritoneal catheter lies. Treatment with antibiotics or replacement of the catheter may be required. The NIH CAPD Registry indicates that these "exit or tunnel infections" occur an average of *0.7* times per patient-year (table 4-7).

Leakage of fluid around peritoneal catheter, obstruction to flow of dialysate in or out of the abdomen due to adherent organs or fibrous adhesions, inadequate circulation of the dialysate throughout the peritoneal cavity, adhesions, deep pelvic pain, intestinal obstruction, and perforation of neighboring abdominal viscera are additional reported complications of CAPD *(23,40).* For one reason or another, catheter replacement is required *0.3* to *0.4* times per patient-year (table 4-7).

In some patients, the peritoneum may undergo chronic changes during CAPD that reduces its effectiveness as a dialyzing membrane *(48).* These changes are incompletely understood at the present time, but many cases have been reported in which dialysis efficiency decreased over a period

of months (19). Moreover, during acute peritonitis, changes in the vascularity and dialyzing characteristics of the peritoneum may require alteration in the dialysis regimen or temporary discontinuation of CAPD. Usually this is required only if the infection is severe or resistant to antibiotic treatment.

Several metabolic effects of CAPD require mention even though they do not necessarily constitute complications. CAPD results in the loss of *8* to 10 grams of protein per day into the dialysate, more than half of which is albumin (6,7, 18,26). Hence, protein depletion can become a clinically important problem unless dietary intake compensates for this loss. Daily diets of 1.2 to 1.5 grams of protein per kilogram of body weight have been recommended (18) and generally can be achieved. A second metabolic effect of CAPD is weight gain due to absorption of glucose from the dialysate. This high carbohydrate intake also may induce elevation of serum triglycerides in susceptible patients, and potentially, accelerate atherogenesis. These metabolic effects require further study.

A variety of abdominal hernias have developed in patients on CAPD due to increased pressure created in the abdominal cavity by the dialysate. Preexisting weakness of the abdominal wall and poor muscle tone are predisposing causes, and women and older men seem especially prone to this complication. In one report involving 51 patients, 12 hernias were observed, but only 7 of these developed after the start of CAPD (40a). Other studies have reported up to an 11 percent incidence of abdominal hernias, many of which developed at the site of the peritoneal catheter insertion (17). Rarely, a hiatus hernia has been noted to develop or increase in size during CAPD.

Pleural effusions may occur even in the absence of any obvious opening in the diaphragm, presumably due to fluid transfer through transdiaphragmatic lymphatic and other pathways (31, **42,43).**

Other rare complications include: the development of ascites, dialysate draining from the vagina, uterine prolapse, rectocystocoeles, hemorrhoids, and chronic low back pain.

QUALITY OF LIFE ON DIALYSIS

Enthusiasm for the benefits of chronic renal dialysis in terms of improved survival must be tempered by the imperfect ability of treatment to free the patient from the symptoms of uremia, to ensure full participation in desired physical and social activities, and to maintain normal economic productivity. Even individuals who have undergone successful renal transplants do not lead normal lives, and patients on chronic dialysis are even more restricted. An important consideration is whether patients with ESRD may place less value on future years of life than healthy persons do and much greater value on the near-term balance between life's satisfactions and the frustrations of chronic illness and its treatment. Stated in economic terms, the pragmatic discount rate the patient intuitively applies to a life dominated by ESRD maybe so large that differences in survival may be given little weight in decisions about therapeutic choices. Although difficult to quantify, this tradeoff between future years of life and the present quality of life is a very real one that must be faced in any realistic evaluation of treatments for ESRD.

Available information does not definitively support one or another dialysis modality as being superior in terms of the ensuing quality of the patient's life on dialysis. Individuals' values vary widely, and it is probable that selection factors play a decisive role. Several studies do provide some useful insights, however (13,14,20,24).

These studies all focus on relatively objective measures of the quality of life, including the degree of functional impairment the patient experiences and his or her employment status. More subjective phenomena such as satisfaction with life, the sense of well-being, the relative value of different activities, and the perceived burden of treatment (physician visits, machine dependency, ritualism) on the patient and the family have received less attention.

Gutman (20) evaluated 2,481 patients on chronic HD in selected facilities and found that only *60* percent of nondiabetics and only *23* percent of diabetics were "normally active, " while 21 and 51 percent, respectively, were severely debilitated or moribund. Of the nondiabetics, only 34 percent were employed full-or part-time, and 14 percent worked at home. Return to full- or part-time employment depended importantly on pretreatment employment status, and while 55 percent of patients with a previous skilled job returned to work, only **27** percent of those with an unskilled job and 16 percent of those who were previously unemployed did so.

Johnson's study *(24)* provides complementary information by comparing quality of life measures of patients on chronic HD with those patients who either were awaiting a first transplant, had had a successful transplant, or had a failed transplant. Patients on chronic dialysis were more likely to feel tired, engaged in fewer physical activities, were less sexually active, and felt more tied down by their treatment than did patients with successful transplants. They were also less likely to be employed full-time or do full-time housework.

A summary of studies reporting employment status in ESRD patients compiled by Evans (13) is presented in table 4-8. Results vary widely. Differences no doubt reflect variations in case-mix, prior employment status, definitions of what constitutes full- or part-time employment, dialysis modality, and quality of ESRD treatment.

The National Kidney Dialysis and Kidney Transplantation Study is the first attempt to directly compare quality of life measures among different dialysis modalities and transplantation. Information is currently available only for functional impairment and current employment status, although future publications will evaluate differences on subjective and psychological measures as well. Table 4-9, which is adapted from a report of this study, indicates that fewer patients on center HD and CAPD were "able to carry on normal activities and to work" *(67* and 71 percent, respectively) than home HD patients (83 percent) or successful transplant (88 percent). Patients on CAPD were less likely to be employed (16 percent) than those on center HD **(24** percent), home HD **(40** percent), or those who had had a successful renal transplant (54 percent). These differences are impressive until they are adjusted by multiple regression analysis for differences among populations in age, sex, education, and perceived health status. After adjustment, the employment rate of patients on CAPD was still lower than on

Table 4-8.—Summary of Studies of the Employment Status of ESRD Patients

Study reference	Year	Number of patients	Place of Dialysis	Employment status		
				Full-time	Part-time	Not employed
Baillod, et al.	1969	60	Mostly at home	920/o		
Cameron, et al.	1970	24	Facility	77%		
		25	Home	920/o		
Pendras and Pollard	1970	110	Home	73%	240/o	3%
Strauch, et al.	1971	178	Facility	28.90/o		71.1%
Freyberger.	1973	48	Facility	550/0	240/o	21"!0
Reichsman and Levy	1972	25	Facility	560/o		44%
Malmquist	1973	17	Facility	47 "/0		53%
Foster, et al.	1973	21	Facility	47 "/0		53%
Cadnapaphornchoi, et al.	1974	41	Home	31 .9 "/0	31 .60/0	36.50/o
Kaplan DeNour and Czaczkes	1976	95	Facility	28.40/o	36.80/o	34.70/0
Disney and Row	1974	300	Facility	51 .2 "/0	31.4%	17.4"!0
		123	Home	81 .30/0	10.40/0	8.30/o
Brunner, et al.	1976	9,000	Facility	36.80/o	30.80/o	32.40/o
		2,500	Home	68.00/0	16.8 "/0	15.20/.
Bryan, et al.	1978	3,462	Facility	5.7%	7.1 "/0	87.20/o
		1,198	Home	20.8%	10.3 "/0	68.9%
Tews, et al.	1980	227	Hospital	23.00/o	27.00/o	50.0 "/0
		65	Limited care	40.00/0	20.0%	40.0%
		190	Home	56.00/o	19.0"/0	25.00/o

SOURCE: The full citations of the studies can be found in R. W. Evans, "Health Services Utilization and Disability Days: Indicators of the Quality of Patient Care Among ESRD Patients," *Battelle Human Affairs Research Centers Update No 18,* Jan. 6, 1983,

98-824 0 - 85 - 4 : QL 3

Table 4-9.—National Kidney Dialysis and Kidney Transplantation Study: Functional Impairment and Current Employment Status by Type of Dialysis (unadjusted for differences in case-mix)

Condition	Percent in category			
	Home HD	Center HD	CAPD	Transplant
Functional impairment (Karnofsky Index)[a]:				
Able to carry on normal activity and to work. No special care is needed	83%	67%	71%	88%
Unable to work. Able to live at home and care for most personal needs. A varying degree of assistance is needed	16	26	26	12
Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly	2	7	3	0
Totals	101%	100%	100%	100%
Work disability—current employment status[b]:				
Employed full-time or part-time or seeking employment	40%	24%	16%	54%
Unemployed or unable to work because of health (disabled)	37	49	55	28
Homemaker	12	10	11	13
Retired	8	16	16	1
Student full-time	4	1	1	5
Totals	99%	100%	99%	101%

[a]Adapted from: R.W. Evans, "Functional Impairment, Work Disability, and the Availability and Use of Rehabilitation Services by Patients With Chronic Renal Failure," *Battelle Human Affairs Research Centers Update* No. 16, December 20, 1982.
[b]Adapted from: R. W. Evans, "Health Services Utilization and Disability Days: Indicators of the Quality of Patient Care Among ESRD Patients," *Battelle Human Affairs Research Centers* Update No. 18, Jan. 8, 1983.

center HD but only marginally so. Inclusion of previous employment status might have affected comparisons even more.

The National Kidney Dialysis and Kidney Transplantation Study is an important one. It is cross-sectional, however, and relies primarily on self-reported information. A prospective, longitudinal study will be required to confirm and extend its findings.

Burden of Treatment

Some argue that the quality of life maybe better on CAPD than on HD because of the freedom it permits from chronic symbiosis with a machine and its relatively flexible schedule of treatments. On CAPD, dialysate exchanges can be performed at the convenience of the patient, while HD sessions must be scheduled in advance with the dialysis center. CAPD, however, imposes the burden of performing four or five daily exchanges, each of which requires meticulous attention to sterile technique. Center HD, on the other hand, frees the patient from responsibility for successful dialysis and places this responsibility on the professional staff. Home HD lies between CAPD and center HD by permitting more flexibility in scheduling dialysis sessions. It encourages self-responsibility, but at the cost of machine dependency and the need for considerable support by family of home health aides. Clearly, tradeoffs exist, and different value judgments on the part of the patients will favor one method of treatment or the other. The physician often plays an important role in clarifying these choices and helping the patient through a perplexing and unfamiliar decision process.

EFFECTS OF CASE= MIX DIFFERENCES ON THE OUTCOMES OF CHRONIC DIALYSIS

Whether patient survival, hospitalization or complication rates, the quality of life, or some combination is used as the outcome measure of interest, patient characteristics may have a profound influence on results. Some characteristics, such as age and the presence of diabetes, will affeet several of these outcomes regardless of the modality of treatment. Other patient characteristics, however, may be treatment specific in the sense that they adversely affect outcomes on one

type of treatment but not on another. Socioeconomic and psychological characteristics of the patient also may be critical determinants of success. Differences in patient characteristics *must* be taken into account if valid comparisons between treatment modalities are to be achieved.

All studies cited thus far in this case study were uncontrolled. They were performed in populations that differed widely in age, sex, race, comorbidity, and prior treatment for ESRD. Also, the calendar years of treatment varied, and undoubtable, so did the techniques and quality of treatment. Only the NIH CAPD and EDTA Registries report annual results from broadly representative populations of patients and providers. Other studies are either series of patients from single institutions or from selected multiple institutions and involve potential biases in patient selection and in the selection of "better" institutions and providers.

A randomized clinical trial would be the most definitive approach to resolving controversy over the relative merits of different treatment modalities for ESRD. In the absence of such a study, the best that can be done is to examine available information critically in an attempt to make the comparisons among studies more valid. '

Characteristics of ESRD Populations

Tables 4-10, 4-11, and 4-12 summarize the characteristics of patients in three distinct but overlapping ESRD populations: those enrolled in the NIH CAPD Registry, those who enrolled in the ESRD program early in 1981, and those sampled in the National Kidney Dialysis and Kidney Transplantation Study. All three studies include patients on CAPD. The age, sex, and race distributions of patients on CAPD in the three reports are very similar. Information on primary ESRD diagnosis and comorbidity is variable, however.

The two studies that compare CAPD to home HD and center HD reveal several important differences in the characteristics of populations treated (tables 4-11 and 4-12):

- Patients on center HD are, on average, slightly older than those on CAPD and definitely older than those on home HD.

Table 4-10.—NIH CAPD Registry: Characteristics of CAPD Population Enrolled in the NIH CAPD Registry in 1981 and 1982

Size of population	4,858
Demographics:	
Age:	
<20 yr.	5%
20-39	25
40-49	15
50-59	25
60-69	22
70+	9
	101%
Race:	
White	77 "/0
Black	16
Other	7
	100 "/0
Sex:	
Male	57 "/0
Female	43 "/0
	100 "/0
Primary diagnosis:	
Diagnosis available in	66 "/0
When diagnosis available:	
Glomerulonephritis	23
Diabetic nephropathy	19
Hypertensive renal disease	17
Polycystic kidney disease	8
Chronic pyelonephritis	4
Systemic immunologic diseases	3
Interstitial nephritis	3
Obstructive uropathy	3
Rapidly progressive GN	2
Miscellaneous	12
Unknown	6
	100 "/0

SOURCE: U.S. Department of Health and Human Services, National Institutes of Health, "CAPD Patient Registry Patient Population Demographic and Selected Outcome Measures," Report No. 82-83, July 1, 19S3.

- Patients on CAPD or home HD are much less likely than center HD patients to be black.
- The proportion of patients on home HD who are male is much higher than that on the other types of dialysis.
- The proportion of patients with diabetes is higher in the CAPD population than in the center HD or home HD populations.

Implications of Differences in Patient Characteristics for Health Outcomes

If the population differences noted above were generally applicable to patients on dialysis, what would be their impact on the outcomes of treatment? Several recent studies address this question by examining the individual effects of age, sex,

Table 4.11.—Patients Beginning Chronic Dialysis in 1981 Under the ESRD Program

	CAPD	Home HD	Center HD
Size of population	174	109	*2,929*
General demographics:			
Mean age (yr)	51	47	55
Race (o/o):			
Black	17	13	27
White	78	84	67
Other	3	2	3
Sex (0/0):			
Female	49	29	*42*
Male	51	71	*58*
Medical diagnosis recorded (Al")	69	72	67
When diagnosis available (o/o):			
Diabetes (10 or 2°)	36	14	24
Hypertension (10 or 2°)	72	70	71
Malignant disease, past or present.	2	1	6
Number of associated diseases present:			
1	25	35	25
2-4	39	43	46
5+	30	18	24
First year outcomes:			
Died (o/o)	13	9	14
Hospitalization:			
Hospitalized (o/o).	71	55	*56*
Hospital days	22	15	*16*
Hospital stays	1.7	1.3	*1.2*

SOURCE: R. R. Bovbjerg, L. H. Kiamond, P. J. Held, and M. V. Pauly, "Continuous Ambulatory Peritoneal Dialysis: Preliminary Evidence in the Debate Over Efficacy and Cost," *Health Affairs* 96-102, summer 1983, Includes only patients whose "first dialysis was in the period from January-March 19S1." The paper did not state whether the 3-month waiting period prior to eligibility for the ESRD program was taken into account. Nor did it state whether first year outcomes were annualized or limited to calendar year, 1981.

race, primary diagnosis of ESRD, or comorbidity on patient survival (5,11,22,27):

- *Age:* Patient survival unequivocally and importantly is influenced by age. The magnitude of the age effect is exemplified by the survival statistics from the ESRD program *(27):*

	Survival	
Age (years)	l-year	3-year
11-20	95%	88%
21-30	91%	78%
31-40	89%	71%
41-50	88%	68%
over *50*	*77%*	*48%*

  Older patients also have markedly higher rates of hospitalization even in the absence of renal disease (45).
- Cause of *ESRD:* Patients with ESRD due to diagnoses of diabetic nephropathy or primary hypertensive disease experience poorer survival than patients with glomerulonephritis.
- Comorbidity: Survival is adversely influenced by the number of coexisting serious diseases such as ischemic heart disease, prior myocardial infarction, hypertension, congestive heart failure, or complications of diabetes.
- Sex and *Race:* The effects of race and sex appear to be small and inconsistent. The finding that black individuals with primary hypertension seem to survive better than their white counterparts is interesting, but may be explained by age or comorbidity differences.

The above results describe only the relationship between a single patient characteristic and survival. Determination of the relative importance of various characteristics in combination, however, is obviously critical if case-mix differences are to be removed from outcome measures in order to permit valid retrospective comparisons between treatment modalities.

A limited number of published studies address this issue in multivariate analyses. In one, Vollmer found striking independent effects on survival of age and the number of associated diseases at the inception of treatment (49). In another, Hutchinson demonstrated significant effects of age, duration of diabetes, and presence of left-sided heart failure on survival (22). These studies offer some important insights and, hopefully, will stimulate further similar efforts.

Finally, "time to treatment bias" or "time-dependence" *(50)* may exert important effects on comparisons among dialysis modalities or between dialysis and transplantation over and beyond those created by differences in patient characteristics. ESRD treatment begins at the time of diagnosis and often involves several sequential treatment modalities. A patient must survive a period of dialysis, for example, before he or she can receive a transplant or may have survived a period of HD before being transferred to CAPD. In either case, survival experience on the prior treatment must be taken into account when evaluating outcomes on the second treatment. When adjustments are made for time to treatment, differences in survival between home HD and cen-

Table 4-12.—National Kidney Dialysis and Kidney Transplantation Study: Population Characteristics of Random Samples of Prevalent Patients Undergoing Chronic Dialysis in Eleven Selected Dialysis Facilities, in 1981

	Dialysis type and location		
	CAPD/CCPD[a]	Home HD	Center HD
Sample size	61(CAPD) 20(CCPD)	287	347
General demographics:			
Mean age (yr)	52	49	54
Race(%)			
Black	10	8	42
White	84	87	54
Other	6	5	4
Sex (O/0)			
Male	46	61	50
Female	54	39	50
Education	12	13	11
Primary renal diagnosis (%)			
Interstitial nephritis	13	11	7
Polycystic kidney disease	10	17	8
Disease involving glomerular structures	30	44	34
Hypertensive renal disease	10	5	19
Nephrosclerosis	7	4	1
Diabetes	16	8	12
Other	13	11	10
Morbidity (%)[b]:			
Angina or myocardial infarction	20	15	25
Other cardiovascular problem	19	25	35
Respiratory disease	7	6	17
Gastrointestinal problems	12	9	25
Neurological problems, including stroke	7	10	14
Musculoskeletal disorders including bone disease	21	21	30
Other	7	13	31
Average number of comorbid conditions	0.94	0.98	1.77

[a]CAPD is continuous ambulatory peritoneal dialysis; CCPD is continuous cycling peritoneal dialysis.
[b]Totals may be greater than 100 percent because patients may have more than one comorbid condition.

SOURCE: R. W. Evans, "Health Services Utilization and Disability Days: indicators of the Quality of PatientCareAmong ESRD Patients/" *Battelle Human Affairs Research* Centers Update No. 18, Jan. 6, 1963.

ter HD and between center HD and cadaveric transplantation are markedly narrowed, especially if age is simultaneously controlled. Thus, the time to initiation of a treatment following the diagnosis of ESRD, as well as the demographic and medical characteristics of patients, are critical considerations.

Use of a "Standard Population" to Report Outcomes

The only systematic attempt to take case-mix considerations into account was reported at a symposium conducted by the American Society for Artificial Internal Organs at its meeting in April 1983. At this meeting, several dialysis program directors presented their results for a ''standard population" of patients 20 to 60 years of age at the onset of treatment. This standard population excluded patients who were "high risk, " either by virtue of having primary ESRD diagnoses with systematic implications such as primary hypertension, diabetic nephropathy and collagen diseases, or by having severe comorbidity such as cardiovascular disease or malignancy. The goal of the presentations was to minimize population differences and obtain comparable results for CAPD and HD.

The results of available reports' from these presentations are summarized in table 4-13. Both patient survival and the ability of patients to re-

'As of May 1984, when this case study was received for final editing.

Table 4-13.—Patient Survival and Ability to Continue on a Dialysis Modality in "Standard Population" of ESRD Patients[a]

Modality of dialysis	Source[b]	Calendar year(s)	Number of patients	Patient survival				Continued on modality[c]		
				0.5 yr	1 yr	2 yr	5 yr	0.5 yr	1 yr	2 yr
CAPD	Nolph, et al., 1983[d]	1981-82	2,137	97 "/0	94%	—	—	88 "/0	830/o	—
CAPD	Wing, et al., 1983[e]	1976-81	1,504	—	78	—	—	—	63	—
HD	Wing, et al., 1983[e]			—	84	—	—	—	64	—
HD	Blagg and Wahl, 1983	1976-82	367	—	96	88	73	—	—	—

				Interval mortality—3-mo intervals[f]				Interval procedures failure—3-mo intervals			
				3 mo	6 mo	12 mo	24 mo	3 mo	6 mo	1 yr	2 yr
CAPD	Wing, et al., 1983	1976-82	1,504	7.80/o	4.9 "/0	5.30/0	10.0 "/0	25.30/o	11.4%	11 .2 "/0	13.4 "/0
HD	Wing, et al., 1983	1976-82	35,532	5.3	3.9	3.6	3.3	15.1	11.4	6.8	5.2

[a]The "standard population" is defined as one 20 to 60 years of age at the date of first treatment; which does not have diabetes, malignancy, or other severe systemic illness; excludes primary diagnoses for ESRD such as collagen disease, primary hypertension, oxalosis, and/or myloidosis; and excludes high risk patients with cardiovascular disease.
[b]Full citations found in the References,
Calculations reflect both deaths and treatment failures resulting in transfers to other forms of chronic dialysis. Transplants are excluded and hence, are not considered to repreSent failures Of dialysis.
[d]Deaths are ascribed to CAPD if they occurred within 2 weeks of change to any other treatment modality.
[e]In survival calculations patients were censored on the day of change in treatment modality.
[f]Three-month interval rates are estimated from bar graphs and, therefore, are approximate. Populations at risk at each interval were not specified, but presumably excluded those removed at previous intervals.

SOURCE: Office of Technology Assessment.

main on CAPD after 1 year of treatment appears to be better in the United States than in Europe. One possible explanation for these differences is that the European Registry did not permit the exclusion of patients at high risk of cardiovascular events. Patient survival at 1 year on HD in a single U.S. center (5) appeared to be similar to that for CAPD in the NIH CAPD Registry *(33)*.

Examination of survival within discrete intervals of followup in the European registry provides some interesting contrasts between CAPD and HD (table 4-13). The mortality rate on HD was highest in the first 3 months of treatment and then quickly plateaued, while mortality on CAPD fluctuated at higher levels than HD over the entire period of observation. Procedure failure was higher in the first *3* to *6* months of treatment for both modalities, but remained higher for CAPD than for HD during subsequent time periods.

This effort to "compare" outcomes of dialysis in a standard population, though commendable, falls far short of what is needed to establish credible comparisons among dialysis modalities. For example, important residual differences in age were found between patients on CAPD and HD in the EDTA Registry (51). Furthermore, there is a possible deception in limiting comparisons to a low risk population. Subtle differences between dialysis techniques, if they exist, are more likely to become manifest in patients at a higher risk of mortality or morbidity. An analysis confined to low risk patients may obscure these differences.