tivariate analysis has the missing data bias due to absence of data on comorbidity and dialysis dose.

The modality selection bias appears unlikely to be a factor in the three studies (1–3) which showed no difference in patient survival between modalities; 34-56% of patients were prescribed PD compared to only 14% in the report from the USA (4) indicating worse survival on PD.

The censoring bias is present and favors PD in 2 of 3 studies reporting PD as equivalent to HD (1–3). It is less evident in the Bloembergen et al. (4) study as an intention to treat analysis ignores transfers and this would decrease the bias favoring PD. On the other hand, the censoring of transplantation would favor the modality with the lower transplant rate.

The most important bias is the missing data bias. In no study was residual renal function or adequacy of dialysis included as an independent variable in the multivariate analysis. The importance of dialysis dose in patient survival in HD and PD has been well established (5, 6).

Using data from the RKDP Minneapolis database for HD and from the Canada-USA Peritoneal Dialysis Study (6), incident patients were matched by age, diabetic status and by Kt/V according to the peak urea concentration hypothesis (7, 8). For a PD weekly Kt/V of 1.7–2.1; the HD equivalent thrice weekly Kt/V was 1.0–1.5. For a PD weekly Kt/V > 2.1, the HD equivalent was >1.5. Within each of these Kt/V ranges, patients matched for age and diabetic status had equivalent survival. While these data are also subject to selection bias (perhaps confounded by a country effect), censoring bias and missing data bias, the potential impact of adequacy of dialysis is clear.

Until a randomized clinical trial with random allocation to HD and PD is performed, the question of effectiveness will remain unanswered. I believe that such a trial, while difficult, is feasible. Random allocation would remove selection bias. Randomization could be stratified for major comorbidity and residual renal function. The target dialysis dose should be equivalent, perhaps according to the peak urea concentration hypothesis (7). Differential transfer and transplantation rates would occur with an intention to treat analysis being a reasonable approach. Interactions between modality and other important variables [e.g., diabetes, age, compliance] are amenable to analysis in this research design.

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The majority of ESRD patients are faced with choosing between treatment with hemodialysis (HD) or peritoneal dialysis (PD) as initial renal replacement therapy or after a failed transplant. To make an informed decision, in addition to consideration of their social circumstances, medical history, level of function and modality availability, some knowledge of the relative clinical outcomes of treatment with PD and HD is of paramount importance for the patient. This question of comparative outcomes of PD and HD is planned to be the subject of a large, multinational, randomized controlled trial, the pilot study of which has now been initiated. If the full-scale study is deemed feasible and proceeds, it should provide nephrologists and patients with the most definitive answer to this question. However, these results cannot be expected for a number of years. In the interim, we must consider the data which are currently available in decisions regarding modality choice.

Most comparative studies of HD and PD published prior to the 1990s (previously reviewed (1)) showed no consistent difference in mortality and perhaps a better quality of life with PD leading to the assumption that "*Peritoneal Dialysis can be Equivalent to (or better than) Optimal Hemodialysis.*" Thus the choice of modality has been made largely on the basis of factors other than clinical

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Seminars in Dialysis—Vol 9, No 3 (May–Jun) 1996 pp 241–243

outcomes. However, these studies have a number of limitations. Small sample sizes and short follow-up times are likely to have precluded the possibility of detecting clinically important differences in mortality even if they existed. Most lacked statistical adjustment for baseline variables. Many of the studies were of single or a few selected centers, begging the question whether results can be generalized to other centers. And lastly, these studies were done at a time when the mortality rate on HD was higher than it is today, perhaps due in part to the lower average dose of hemodialysis delivered at the time.

More recent studies challenge the premise that PD is equivalent to HD in terms of outcomes, at least in the U.S. These studies do not necessarily reflect the *potential* of PD but are a description of outcomes given the practice patterns before and during the years of study. In 1994, the USRDS published a study comparing mortality of randomly selected patients starting PD (n = 681) and HD (n = 3,376) during 1986 and 1987 (2). After adjusting for a large number of demographic variables and comorbid conditions, no difference in mortality was found among nondiabetics. However, among diabetics, PD treated patients had a higher risk of mortality than did HD treated patients, particularly in the older age groups. Although large, this study may also have had inadequate power to detect a clinically important difference in mortality that may have been present in nondiabetics as well. For example, in order to detect a 4 percentage point difference (i.e., 20 versus 24 deaths/100 patient years or 20% difference) in 1 year survival between PD and HD (RR = 1.2) with 90% power, a sample size of at least 1,400 patients per group would be required. Only two recently published studies are of this magnitude.

One of these was a study by Lowrie and colleagues (3) who compared 1,522 PD and 16,404 HD treated patients who were either prevalent on Jan. 1, 1992 or incident during 1992. Patients treated with PD had a 32% higher risk of mortality than those treated with HD after adjustment for cause of ESRD, demographic and laboratory values. The second study, using national data from the USRDS, compared mortality among all prevalent Medicare treated patients receiving HD or PD (CCPD or CAPD) in the U.S. on January 1 of 1987, 1988 or 1989 (1). Over 40,000 deaths occurred during 170,000 patient years of follow-up. Adjusting for differences in demographics, prevalent patients treated with PD had, on average, a 19% higher mortality risk than did those treated with HD. This risk was increasingly large and significant for ages >55 years and was accentuated in diabetics and females although it was also present in nondiabetics and males. An evaluation of cause of death found that the risk of death was increased among PD patients for all major cause of death categories except malignancy (4).

The most recent USRDS Annual Data Report (5) has, for the first time, presented a similar comparison of demographic adjusted death rates of prevalent patients for more recent years (1991–1992) and has also found an 18% higher risk of all-cause mortality among PD compared to HD treated patients. Comparing morbidity of PD and HD treated patients, another study of national data (1988–1990) also found PD to be associated with higher admission rates and more days in hospital than HD patients (6). These differences may decrease with time as fewer hospitalizations may be expected with recent advances in connection technology.

This phenomenon of higher risk associated with PD may be isolated to the U.S. For example, in direct contrast to the recent U.S. studies, the 1993 Report of the Canadian Organ Replacement Register (7) reports better survival among PD treated patients. The publication of a formal scientific paper describing these results, as well as the details of the analysis methodology used, would allow further evaluation of these data.

A limitation of the three recent U.S. studies evaluating mortality and morbidity (3, 4, 6) is that possible differences in comorbidity were not adjusted for, as these data were not available. However it should be mentioned that the largest and most rigorously designed evaluation of comorbidity differences between HD and PD found very few significant differences in the presence of comorbid conditions between new patients treated with these modalities (8). Nevertheless, the severity of the comorbid conditions may be greater among PD treated patients. Thus differential comorbidity remains one of the potential explanations for the higher mortality for PD observed in these studies. There may also be other unmeasured baseline differences in patients treated with these modalities which have not been accounted for.

Other potential explanations for the higher mortality observed among PD treated patents that have been put forth (1) include differences in patient compliance, medical quality of care, dose of dialysis or a true adverse treatment effect. There is now accumulating evidence that dose of dialysis may be a major contributing factor to the higher mortality rate observed among PD treated patients. Because of the differences in solute clearance of PD and HD it is difficult to directly compare dialysis dose. A number of years ago, the dose of hemodialysis was reported to be substantially lower than recommended by the National Cooperative Dialysis Study, and this, together with unacceptable mortality rates among HD treated patients, resulted in a gradual increase in dose of hemodialysis on a national level. Only recently has more attention been paid to the issue of adequacy of peritoneal dialysis and its relationship with more subtle and long term outcomes rather than uremic symptoms alone. The CANUSA study, a large prospective cohort study of 698 new PD patients, has recently found that higher total weekly clearances of urea and creatinine are associated with lower mortality (9). The results of this study also suggest that higher doses

than are currently delivered are necessary to achieve acceptable mortality rates.

A study by Keshaviah et al. (10) also supports the notion that the difference in mortality observed between PD and HD may be related to dose of dialysis. This study used the "peak concentration hypothesis" in order to directly compare dose of dialysis among PD and HD treated patients (e.g., Kt/V of 2.0 weekly for PD is "equivalent" to Kt/V of 1.3 per treatment for thrice weekly HD). This study, published in abstract form, found comparable survival rates for PD and HD treated patients treated with "equivalent" doses of dialysis. Assuming that it is appropriate to compare dose in this way, these results would suggest that by increasing dose of PD, yes, "*Peritoneal Dialysis (may) Be Equivalent to Optimal Hemodialysis*".

The practical concern, of course, is whether the dose of PD can be increased to be "equivalent" to the dose of HD. The dose of HD can be relatively easily increased with a change to a dialyzer with better clearance, an increase in blood flow or an increase in dialysis time. For patients using standard CAPD, increasing the number or volume of exchanges may be less acceptable. Furthermore, in patients with decreasing or absent residual renal function, large body mass, or low membrane permeability characteristics, it may be impossible to deliver adequate clearance using standard CAPD. However, the use of automated techniques hold the promise to meet these needs. There is hope that future technological advances in PD delivery techniques will allow the provision of optimal therapy at a cost that is not prohibitive, either from an economic perspective or in terms of the patient's lifestyle.

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There are now several comparisons (1, 2, 3, 4, 5) of the survival achievable with hemodialysis (HD) and peritoneal dialysis (PD). However, rather than shedding light on the subject, these comparisons have created confusion because of conflicting results.

In the study of Maiorca et al. (1), after adjusting for other risk factors, no significant differences in patient survival were seen between continuous ambulatory peritoneal dialysis (CAPD) and HD. However, elderly patients over the age of 53.5 were shown to have a lower risk of death on CAPD than on HD. Contradicting this, in the study of Held et al. (2), while nondiabetic patients had comparable survival on CAPD and HD, elderly diabetics (age 58.7 years) had a higher relative risk of death on CAPD (RR = 1.26) compared to HD. In the study of Wolfe et al. (3), diabetic CAPD patients in the 50-59 age group had a relative risk of 0.70 compared to HD. The lower mortality rate on CAPD was significant up to the age of 52 years. The recent data of the Canadian Registry (4) suggest a better survival on CAPD than on HD in all age groups for both diabetic and nondiabetic patients (Table 1). The Bloembergen study (5), on the other hand, suggests a 19% higher mortality risk for CAPD relative to HD, this risk being insignificant for ages <55 and increasingly large and significant for ages >55, especially in diabetic patients.

TABLE 1. Relative risk of death by treatment [Canadian Registry, 1981–1993 (5)]

	HD	Age 0–64 CAPD/CCPD	Age 65+ CAPD/CCPD
Diabetic	1.0	0.84*	0.92
Non-diabetic	1.0	0.90*	0.82

*$p < 0.05$

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Seminars in Dialysis—Vol 9, No 3 (May–Jun) 1996 pp 243–245