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### Title

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### Permalink

<https://escholarship.org/uc/item/92h1779f>

### Journal

Archives of internal medicine, 171(2)

### ISSN

0003-9926

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### Publication Date

2011

### DOI

10.1001/archinternmed.2010.352

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## ONLINE FIRST

# Similar Outcomes With Hemodialysis and Peritoneal Dialysis in Patients With End-Stage Renal Disease

Rajnish Mehrotra, MD; Yi-Wen Chiu, MD; Kamyar Kalantar-Zadeh, MD; Joanne Bargman, MD; Edward Vonesh, PhD

**Background:** The annual payer costs for patients treated with peritoneal dialysis (PD) are lower than with hemodialysis (HD), but in 2007, only 7% of dialysis patients in the United States were treated with PD. Since 1996, there has been no change in the first-year mortality of HD patients, but both short- and long-term outcomes of PD patients have improved.

**Methods:** Data from the US Renal Data System were examined for secular trends in survival among patients treated with HD and PD on day 90 of end-stage renal disease (HD, 620 020 patients; PD, 64 406 patients) in three 3-year cohorts (1996-1998, 1999-2001, and 2002-2004) for up to 5 years of follow-up using a nonproportional hazards marginal structural model with inverse probability of treatment and censoring weighting.

**Results:** There was a progressive attenuation in the higher risk for death seen in patients treated with PD in earlier cohorts; for the 2002-2004 cohort, there was no significant difference in the risk of death for HD and PD patients through 5 years of follow-up. The median life expectancy of HD and PD patients was 38.4 and 36.6 months, respectively. Analyses in 8 subgroups based on age (<65 and ≥65 years), diabetic status, and baseline comorbidity (none and ≥1) showed greater improvement in survival among patients treated with PD relative to HD at all follow-up periods.

**Conclusion:** In the most recent cohorts, patients who began treatment with HD or PD have similar outcomes.

*Arch Intern Med.* 2011;171(2):110-118.

Published online September 27, 2010.

doi:10.1001/archinternmed.2010.352


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**A**T THE END OF 2008, THERE were over 500 000 Americans living with end-stage renal disease (ESRD).<sup>1</sup> Even though patients with ESRD constitute less than 1% of the Medicare population, they account for 5.8% of the expenses for the program (excluding the costs for the prescription benefit).<sup>1</sup> For eligible subjects, renal transplant is associated with a higher life expectancy, better quality of life, and substantially lower long-term expenses compared with continued treatment with dialysis.<sup>1,2</sup> However, limited

fer to HD for PD patients.<sup>1,3</sup> Recognizing the potential for cost savings, the Centers for Medicare & Medicaid Services has continued to provide financial incentives to promote greater use of PD. However, the relative use of PD for the treatment of ESRD has continued to decline, and in 2008, only 7% of dialysis patients were treated with this dialysis modality.<sup>1</sup>

*See also pages 107 and 119*

Even though the determinants of the use of dialysis modality are largely nonmedical, there has been considerable interest in understanding if there is any difference in the mortality outcomes of HD and PD patients.<sup>4,5</sup> A randomized controlled trial is probably the best way to determine if the differences in outcomes between HD and PD patients are attributable to the dialysis therapy. However, given the disparate effects of the 2 dialysis modalities on patients' lifestyles, attempts to date at randomizing patients to the different dialysis modalities have been unsuccessful.<sup>6</sup> Numerous observational studies have been undertaken, including those from various national registries from different parts of the

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availability of organ donors means that most patients with ESRD are treated with dialysis for prolonged periods; in-center hemodialysis (HD) and home peritoneal dialysis (PD) are the 2 most common forms of dialysis therapy. In 2007, the annual, per-person costs for PD patients were almost \$20 000 lower than that of HD patients; the substantial cost advantage for PD is robust even when data are adjusted for better health and higher rates of trans-

world.<sup>4</sup> These comparisons have highlighted the difficulties in comparing dialysis modalities when the allocation to therapy is not random. To exemplify the complexity of these comparisons, at least 4 clinically important statistical interactions have been identified that affect the comparison of risk between HD and PD—change in relative risk over time and different relative risks based on age, diabetic status, and coexisting diseases.<sup>4</sup> Thus, patients treated with PD have a lower risk for death in the first few years of dialysis therapy, and this is greatest in young, nondiabetic individuals with no coexisting illnesses.

We have recently demonstrated that over the last 8 years, there has been a consistent and substantial reduction in mortality rates for new patients starting PD in the United States.<sup>7</sup> In contrast, no such improvements were observed for HD patients.<sup>7</sup> This differential change in outcomes mandates a re-examination of outcomes of HD and PD using contemporary cohorts. We undertook this study to test the hypothesis that initial dialysis modality has no effect on the life expectancy of patients with ESRD in the United States using marginal structural models.

## METHODS

### DATA SOURCE

The study protocol was reviewed and approved as exempt by the institutional review board at the Los Angeles Biomedical Research Center, Los Angeles, California. The data for all patients with incident ESRD in the United States over a 9-year period (1996-2004) were obtained from the patient and MEDVID files of the US Renal Data System (USRDS), the national registry for all patients with ESRD. The MEDVID file contains data from the Medical Evidence Form 2728, a form required to be filed for every new patient with ESRD in the United States and contains demographic and clinical information at the start time of renal replacement therapy. The data were linked to the RXHIST60 file, which uses information from claims data and other sources to provide start and end dates for each treatment modality and to assign dialysis modality, and to the Facility File for dialysis unit characteristics.

### DEFINITIONS

For individuals eligible but not receiving Medicare benefits prior to the first dialysis treatment, coverage for in-center hemodialysis begins on day 90; thus, complete information is available from that point onward. Hence, as per convention, the dialysis modality 90 days after the first service date and continuous treatment for at least 60 days (“60-d rule”), was considered to be the initial modality. Presence or absence of various coexisting illnesses and the initial laboratory results were obtained from the Medical Evidence Form 2728. The unit affiliation was defined as the dialysis facility where the patient was being treated on day 90 of ESRD. Data for each patient were linked with the facility data from the same year as the one in which the patient first started renal replacement therapy. For this analysis, only patients whose initial modality on day 90 was either in-center HD, continuous ambulatory PD, or automated PD were included; home HD or “other” PD patients were excluded.

### COVARIATES

For all statistical analyses, the models were adjusted for demographics (age, sex, race, and current employment status), fa-

cility characteristics (period-prevalent patient census, and for-profit or not-for-profit status), cause of ESRD, 10 different comorbid conditions (cardiac arrest or dysrhythmia, cerebrovascular disease, congestive heart failure, ischemic heart disease or myocardial infarction, peripheral vascular disease, limited activities of daily living, chronic obstructive pulmonary disease, current smokers, diabetes primary or contributing, and malignant neoplasm), baseline estimated glomerular filtration rate, body mass index, and selected laboratory variables (serum albumin, blood urea nitrogen, and hemoglobin).

## STATISTICAL ANALYSES

Baseline characteristics of HD and PD patients were compared using Pearson  $\chi^2$  tests for categorical variables and the unpaired *t* test for continuous variables. Patients were followed up until death, transplant, or transfer to home HD or “other PD” treatment, whichever happened first, or last follow-up examination (September 30, 2007). Patients who switched modality after 90 days were treated in survival analysis according to their modality on day 90. A detailed description of the statistical methods is presented in the eAppendix (<http://www.archinternmed.com>). Supplemental data are presented in eTables 1 and 2 and eFigures 1 through 7.

Nonproportional hazards models using a piecewise exponential survival model were used to compare case mix-adjusted survival of HD and PD patients.<sup>8,9</sup> Outcomes were compared using a marginal structural model with inverse probability of treatment and censoring weighting (IPTCW).<sup>10,11</sup> As a first step, propensity scores (PSs) were calculated as a single summary measure of confounding. The PS is the estimated probability of being treated initially with PD, given a patient’s set of baseline demographic, clinical, and laboratory characteristics; adjustment for PS is sufficient to remove bias due to these measured confounding variables.<sup>12</sup> Proportional and nonproportional hazards marginal structural models use weighted regression with weights equal to 1/PS (ie, inverse probability of treatment weighting) to provide hazard ratio (HR) estimates that are unbiased estimates of a causal treatment effect under the unverifiable assumption that there are no unmeasured confounding variables.<sup>10-12</sup> While this assumption is likely not to hold in observational studies like ours, the use of proportional and nonproportional hazards marginal structural models will tend to minimize the bias associated with each and every measured confounding variable in our study. By further weighting on the inverse probability of remaining uncensored, marginal structural models using IPTCW provide further protection against any differential selection bias resulting from transplant and other censoring mechanisms.<sup>10,11</sup> The transplant rates, adjusted for all measured baseline characteristics, in the United States are 30% to 60% higher for PD patients than for HD patients with incident ESRD (eFigure 5). Robust standard errors based on an empirical sandwich estimator of the variance-covariance matrix of regression estimates were used to calculate confidence intervals. Additional details about the methods including model assessment and sensitivity analyses are provided in the eAppendix.

Results were summarized through up to 5 years of follow-up and are presented in terms of adjusted HRs and adjusted population survival curves. Adjusted population survival curves were obtained by exponentiation of the adjusted cumulative hazard functions for PD and HD. Based on these survival curve estimates, median life expectancies were computed using life table methodology.<sup>13</sup> Hazard ratios were computed under a proportional hazards marginal structural model as a means for summarizing the overall relative risk of death between PD and HD over the course of a 5-year follow-up. Absolute risks are presented in terms of the 1-, 2-, 3-, 4-, and 5-year adjusted survival estimates for PD and HD. All *P* values for comparing survival

**Table 1. Selected Characteristics of HD and PD Patients With Incident ESRD in the United States (1996-2004) at the Start of Renal Replacement Therapy**

| Characteristic  | HD Patients<br>(n=620 020) | PD Patients<br>(n=64 406) |
|---|----------------------------|---------------------------|
| Cohort period, No. (%)  |                            |                           |
| 1996-1998   | 175 361 (28)               | 23 580 (37)               |
| 1999-2001   | 211 577 (34)               | 20 947 (33)               |
| 2002-2004   | 233 082 (38)               | 19 879 (31)               |
| Age group, %  |                            |                           |
| 18-44   | 14                         | 22                        |
| 45-64   | 36                         | 43                        |
| ≥65   | 50                         | 35                        |
| Male sex, %   | 53                         | 53                        |
| Race, %   |                            |                           |
| White   | 62                         | 73                        |
| Black   | 31                         | 20                        |
| Asian   | 4                          | 4                         |
| Other   | 3                          | 3                         |
| Cause of ESRD, %  |                            |                           |
| Diabetes  | 47                         | 46                        |
| Hypertension  | 28                         | 22                        |
| Glomerulonephritis  | 9                          | 15                        |
| Others  | 17                         | 17                        |
| Cardiac arrest or dysrhythmia, %  | 6                          | 5                         |
| Cerebrovascular disease, %  | 9                          | 7                         |
| Congestive heart failure, %   | 33                         | 22                        |
| Ischemic heart disease or myocardial infarction, %                          | 27                         | 22                        |
| Peripheral vascular disease, %  | 14                         | 11                        |
| Limited activities of daily living, %                                       | 4                          | 1                         |
| Chronic obstructive pulmonary disease, %                                    | 7                          | 4                         |
| Current smokers, %  | 5                          | 6                         |
| Diabetes, primary or secondary, %   | 50                         | 47                        |
| Malignant neoplasm, %   | 5                          | 4                         |
| ≥1 Comorbidity, %   | 60                         | 48                        |
| BMI, mean (SD)  | 27 (7)                     | 27 (6)                    |
| Hemoglobin, mean (SD), g/dL   | 9.7 (1.8)                  | 10.3 (1.8)                |
| Serum albumin, mean (SD), g/dL  | 3.1 (0.7)                  | 3.5 (0.7)                 |
| Serum urea nitrogen, mean (SD), mg/dL                                       | 88 (34)                    | 83 (29)                   |
| Estimated glomerular filtration rate, mean (SD), mL/min/1.73 m <sup>2</sup> | 8.9 (4.3)                  | 8.8 (4.0)                 |
| Center Census, period-prevalent patient numbers                             |                            |                           |
| Hemodialysis patients, No. (SD)   | 91 (55)                    | 95 (61)                   |
| Peritoneal dialysis patients, No. (SD)                                      | 11 (18)                    | 38 (29)                   |
| All dialysis, No. (SD)  | 103 (66)                   | 134 (74)                  |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ESRD, end-stage renal disease.

SI conversion factors: To convert hemoglobin and albumin to grams per liter, multiply by 10; and serum urea nitrogen to millimoles per liter, multiply by 0.357.

between PD and HD were adjusted to reflect simultaneous inference over a 5-year follow-up using the Sidak method.<sup>14</sup>

Finally, consistent with previous findings, we performed a set of a priori subgroup analyses in which the impact of treatment modality on outcome was examined within 8 subgroups of patients defined by age, diabetes, and presence or absence of comorbid conditions.<sup>15</sup> All analyses were performed using the SAS statistical software package version 9.2 (SAS Institute Inc, Cary, North Carolina).

## RESULTS

### PATIENT CHARACTERISTICS

Over the 9-year study period, 684 426 patients started dialysis therapy in the United States, survived at least 90 days, and had a Medical Evidence Form 2728 submitted (HD patients, 620 020; PD patients, 64 406). Given the large sample size, the differences in all patient characteristics between HD and PD patients (except sex distribution) were statistically significant (**Table 1**). The PD patients with incident ESRD were younger, more likely to be white, and less likely to have other comorbidities. Even though the differences in the baseline laboratory variables were statistically significant, they were not clinically meaningful (Table 1).

Preliminary analyses revealed that the concordance index for the logistic regression model used to compute PSs was 0.766, indicating a reasonably good prediction of modality selection. Moreover, there was excellent balance with

**Table 3. Adjusted Hazard Ratios (HRs) for Mortality, Stratified by Cohort Periods, Using Marginal Structural Models With Inverse Probability of Treatment and Censoring Weighting<sup>a</sup>**

| Cohort    | HR (95% CI) <sup>b</sup> | P Value |
|-----------|--------------------------|---------|
| 1996-1998 | 1.07 (1.04-1.11)         | <.001   |
| 1999-2001 | 1.08 (1.06-1.11)         | <.001   |
| 2002-2004 | 1.03 (0.99-1.06)         | .10     |

Abbreviations: CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis.

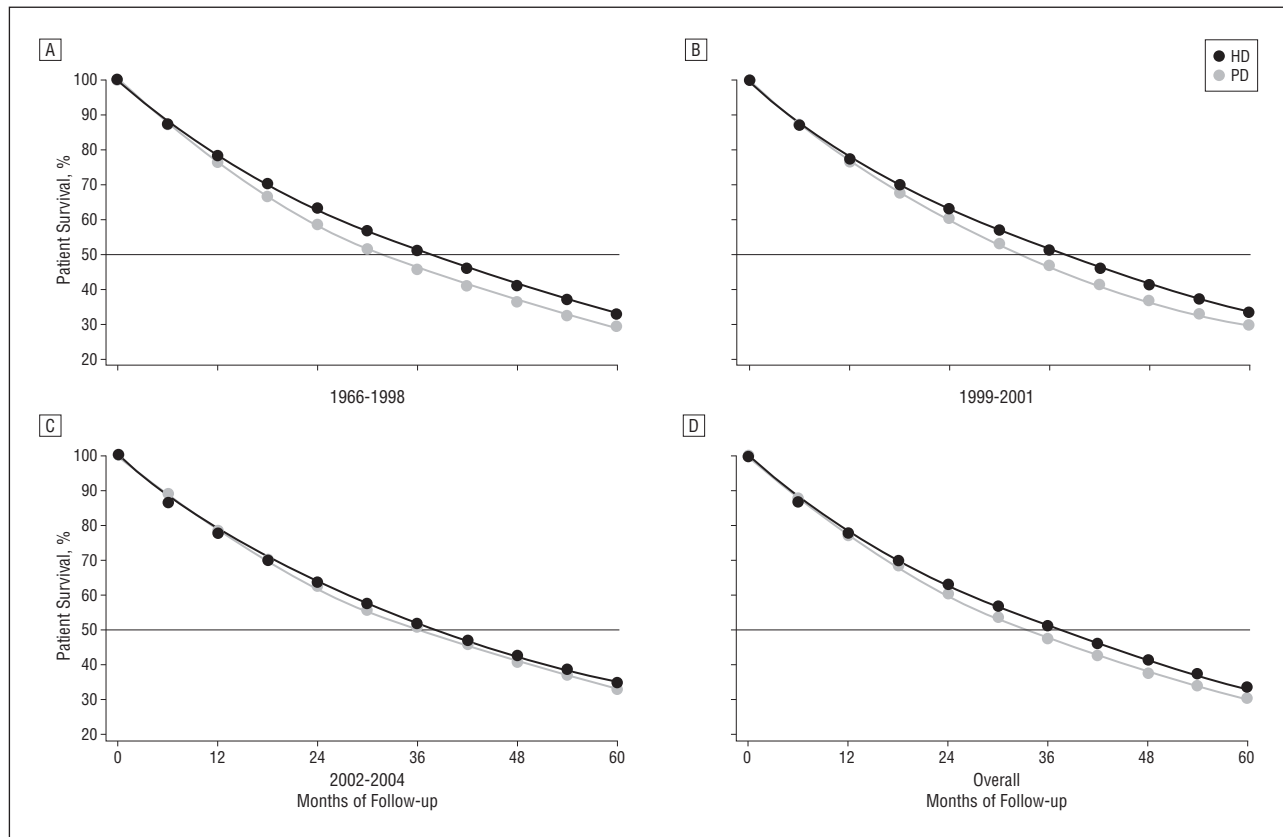
<sup>a</sup>Median follow-up time for HD patients with incident ESRD: 1996-1998, 29.1 mo; 1999-2001, 29.5 mo; and 2002-2004, 30.0 mo. Median follow-up time for PD patients with incident ESRD: 1996-1998, 24.9 mo; 1999-2001, 27.0 mo; and 2002-2004, 28.8 mo.

<sup>b</sup>Overall relative risk of death between PD and HD over the course of a 5-year follow-up.

**Table 2. Adjusted Survival of Patients Treated With HD and PD for Up to 5 Years in Each of 3 Cohort Periods**

| Year of Follow-up | Cohort Period |       |         |           |       |         |           |       |         |
|-------------------|---------------|-------|---------|-----------|-------|---------|-----------|-------|---------|
|                   | 1996-1998     |       |         | 1999-2001 |       |         | 2002-2004 |       |         |
|                   | HD, %         | PD, % | P Value | HD, %     | PD, % | P Value | HD, %     | PD, % | P Value |
| 1                 | 78            | 76    | <.001   | 78        | 77    | NS      | 78        | 79    | NS      |
| 2                 | 63            | 59    | <.001   | 63        | 60    | <.001   | 63        | 62    | NS      |
| 3                 | 51            | 46    | <.001   | 51        | 47    | <.001   | 52        | 51    | NS      |
| 4                 | 41            | 36    | <.001   | 41        | 37    | <.001   | 43        | 41    | .05     |
| 5                 | 33            | 29    | <.001   | 33        | 30    | <.001   | 35        | 33    | NS      |

Abbreviations: HD, hemodialysis; NS, not significant; PD, peritoneal dialysis.



**Figure 1.** Adjusted population survival curves comparing the outcome of peritoneal dialysis (PD) and hemodialysis (HD) patients with incident end-stage renal disease in the United States stratified by cohort period. A, 1966-1998 Cohort: adjusted median life expectancy, 37.2 months for HD patients and 31.7 months for PD patients; B, 1999-2001 cohort: adjusted median life expectancy, 37.3 months for HD patients and 33.0 months for PD patients; C, 2002-2004 cohort: adjusted median life expectancy, 38.4 months for HD patients and 36.6 months for PD patients; and D, overall: adjusted median life expectancy, 37.6 months for HD patients and 33.7 months for PD patients.

respect to all measured covariates between PD and HD patients having similar PSs (eFigures 1-3), suggesting that PS adjustment via a marginal structural model using IPTCW was sufficient in removing the majority of confounding due to all measured baseline covariates.

#### OVERALL COMPARISON OF OUTCOMES OF HD AND PD PATIENTS WITH INCIDENT ESRD BY COHORT PERIOD

Adjusted survival of HD and PD patients at 1 year-intervals for up to 5 years of follow-up for each of the 3 cohort periods are summarized in **Table 2**. Adjusted HRs comparing the relative risk of death for PD and HD patients with incident ESRD over 5 years of follow-up for each of the 3 cohort periods (1966-1998, 1999-2001, and 2002-2004) are summarized in **Table 3**. For the 2002-2004 patients with incident ESRD, there was no significant difference in the risk for death between those treated with HD or PD through 5 years (HR, 1.03; 95% confidence interval [CI], 0.99-1.06 [ $P = .10$ ]). The adjusted median life expectancy increased for both HD and PD patients with incident ESRD and was very similar for the 2002-2004 cohort (HD and PD, 38.4 vs 36.6 months, respectively). Improvement in outcomes over time—with no difference in outcomes among the 2002-2004 cohort of patients treated with the 2 dialysis modalities—was observed in the adjusted population survival curves (**Figure 1**).

#### OUTCOME OF HD AND PD PATIENTS WITH INCIDENT ESRD STRATIFIED BY AGE, DIABETIC STATUS, AND COMORBIDITY FOR 3 COHORT PERIODS

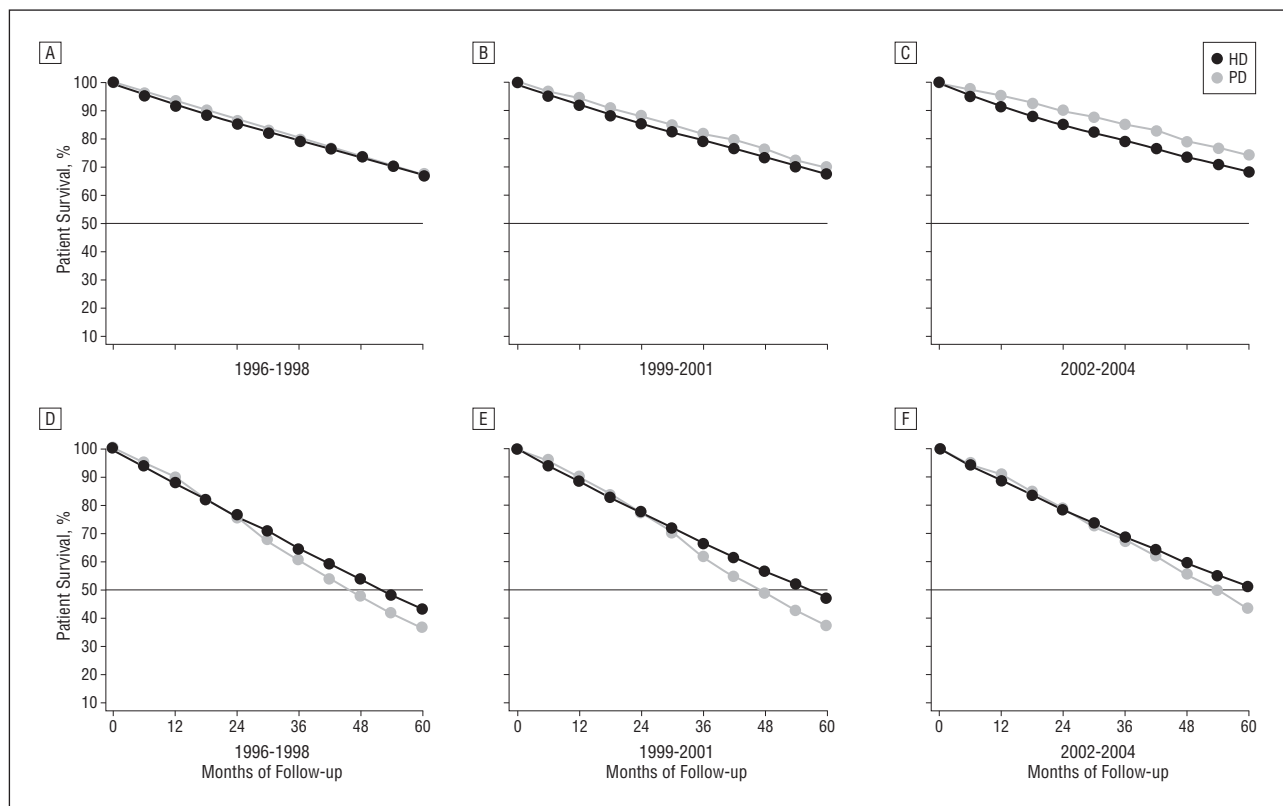
Results of the comparisons of patients treated with HD and PD in 8 subgroups for each of the 3 cohort periods are summarized in **Table 4**, and the adjusted population survival curves are presented in **Figures 2, 3, 4, and 5**. Among younger nondiabetic patients with no additional comorbidity, the relative risk for death for patients treated with PD progressively decreased; from 1999 onwards, patients treated with PD had a significantly lower risk for death compared with those treated with HD. Furthermore, the higher risk for death among older patients with additional comorbidity who were treated with PD dissipated over time, such that for the 2002-2004 incident cohort, there was no significant difference in risk for death in patients treated with HD or PD.

Diabetic patients who started dialysis between 1996 and 2001 and were treated with PD had a significantly higher risk for death irrespective of age or additional comorbidity. The relative risk for death of diabetic patients treated with PD, who started dialysis during 2002-2004, was lower than that seen in previous years for each of the 4 subgroups. During this period, there was no significant difference in the risk for death for younger diabetic patients with no additional comorbidity who were

**Table 4. Hazard Ratios (HRs) for Mortality in 3 Different Cohort Periods in 8 Subgroups, Based on Age, Diabetic Status, and Level of Baseline Comorbidity Adjusted Using IPTCW**

| Diabetic Status,<br>Age, y | ≥1 Comorbidity | HR (95% CI) <sup>a</sup>      |                               |                               |
|----------------------------|----------------|-------------------------------|-------------------------------|-------------------------------|
|                            |                | 1996-1998                     | 1999-2001                     | 2002-2004                     |
| Nondiabetic                |                |                               |                               |                               |
| 18-64                      | Absent         | 0.94 (0.84-1.05)              | 0.89 (0.82-0.97) <sup>b</sup> | 0.72 (0.63-0.81) <sup>b</sup> |
|                            | Present        | 1.08 (0.996-1.17)             | 0.97 (0.89-1.06)              | 1.00 (0.90-1.11)              |
| ≥65                        | Absent         | 1.03 (0.96-1.11)              | 1.02 (0.93-1.11)              | 0.92 (0.84-1.01)              |
|                            | Present        | 1.13 (1.07-1.20) <sup>b</sup> | 1.18 (1.11-1.25) <sup>b</sup> | 1.06 (0.99-1.13)              |
| Diabetic                   |                |                               |                               |                               |
| 18-64                      | Absent         | 1.16 (1.10-1.23) <sup>b</sup> | 1.21 (1.13-1.29) <sup>b</sup> | 1.08 (0.99-1.18)              |
|                            | Present        | 1.30 (1.23-1.37) <sup>b</sup> | 1.19 (1.12-1.27) <sup>b</sup> | 1.13 (1.04-1.22) <sup>b</sup> |
| ≥65                        | Absent         | 1.29 (1.18-1.41) <sup>b</sup> | 1.33 (1.23-1.44) <sup>b</sup> | 1.16 (1.05-1.29) <sup>b</sup> |
|                            | Present        | 1.38 (1.29-1.47) <sup>b</sup> | 1.26 (1.18-1.35) <sup>b</sup> | 1.21 (1.11-1.31) <sup>b</sup> |

Abbreviations: CI, confidence interval; IPTCW, inverse probability of treatment and censoring weighting.  
<sup>a</sup>Overall relative risk of death between peritoneal dialysis and hemodialysis over the course of a 5-year follow-up.  
<sup>b</sup>P < .01.



**Figure 2.** Adjusted population survival curves comparing the outcomes of PD and HD patients with incident ESRD who were younger than 65 years with no additional comorbidity, stratified by DM status and cohort period. A-C, ESRD + non-DM cohort. D-F, ESRD + DM cohort. DM indicates diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; and PD, peritoneal dialysis.

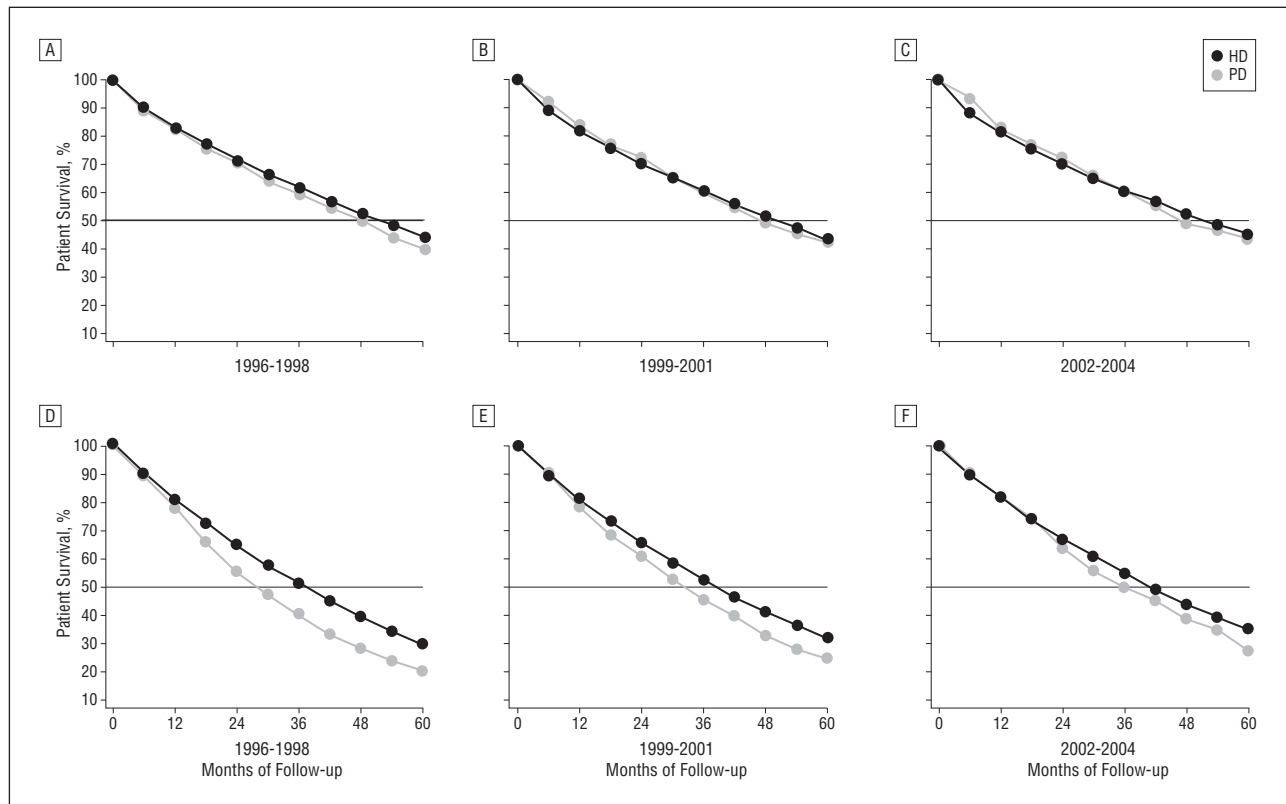
treated with HD or PD. The higher risk of death for PD patients was seen in the other 3 subgroups of diabetic patients; the HRs were lower than that seen in the previous years.

**COMMENT**

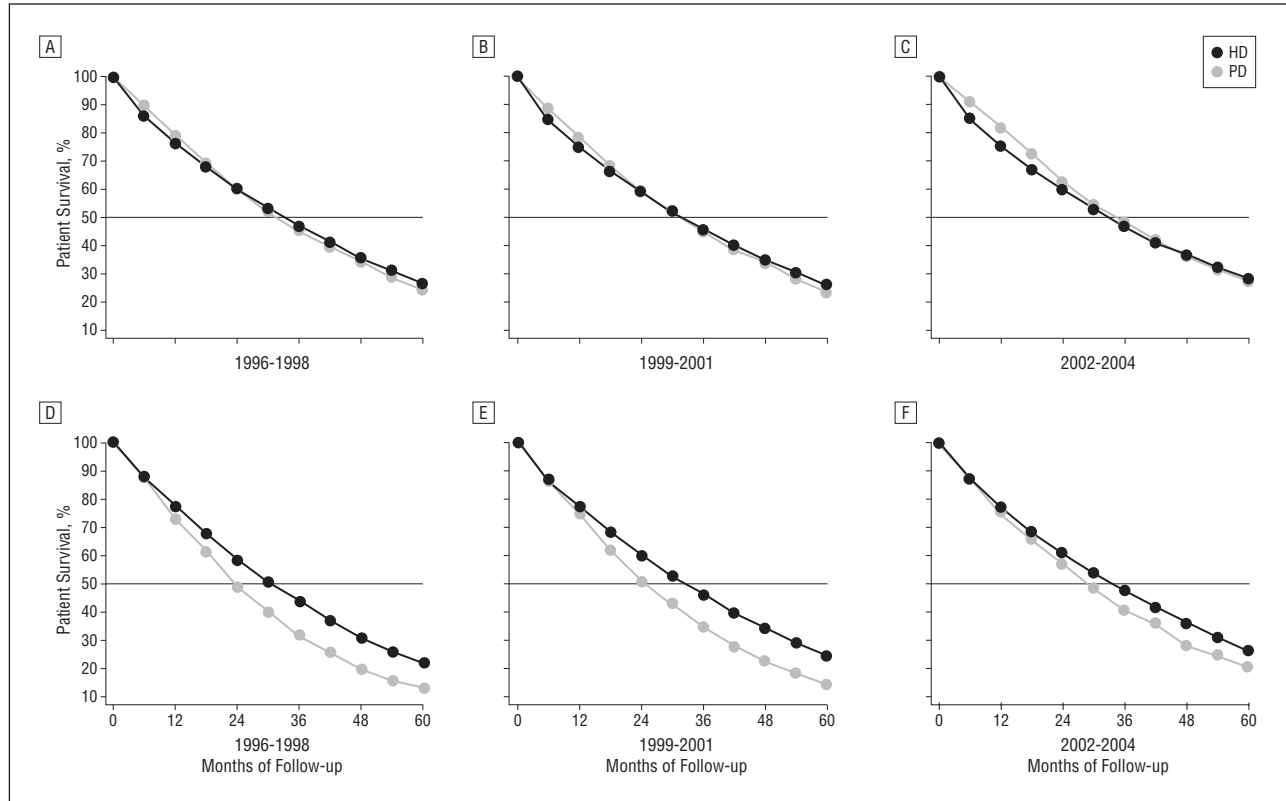
In the largest study to our knowledge to date, we were unable to demonstrate any significant overall difference in outcomes of patients with ESRD who began treat-

ment with either HD or PD in 2002-2004—the most contemporary cohort for which data are available. Furthermore, progressive improvements in outcomes of PD patients (relative to HD patients) were seen in virtually all of the 8 subgroups examined.

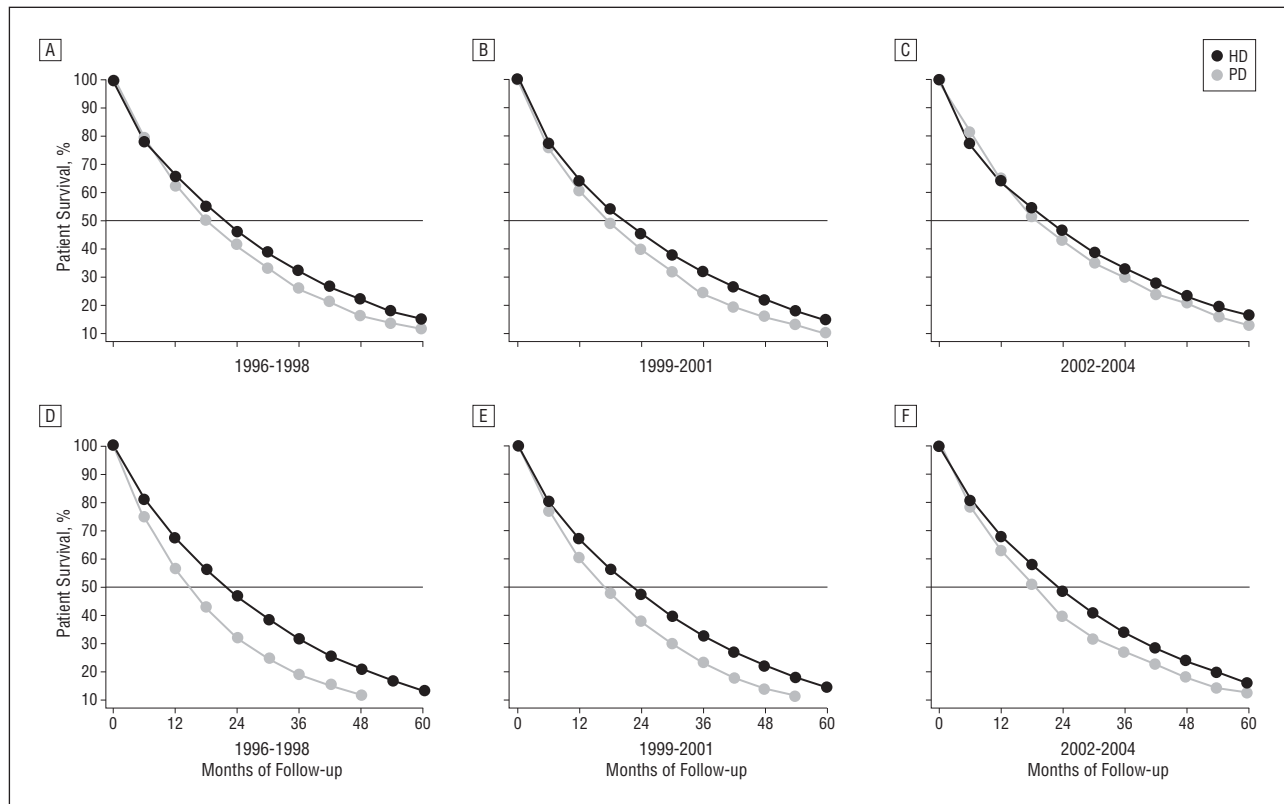
Studies from different parts of the world have compared the outcomes of patients with ESRD treated with HD vs PD.<sup>15-27</sup> Even though there is heterogeneity in the results of these comparisons, there are some consistent themes. Patients treated with PD have been shown to have



**Figure 3.** Adjusted population survival curves comparing the outcomes of PD and HD patients with incident ESRD who were younger than 65 years and had 1 or more comorbidity, stratified by DM status and cohort period. A-C, ESRD + non-DM cohort. D-F, ESRD + DM cohort. DM indicates diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; and PD, peritoneal dialysis.



**Figure 4.** Adjusted population survival curves comparing the outcomes of PD and HD patients with incident ESRD who were 65 years or older with no additional comorbidity, stratified by DM status and cohort period. A-C, ESRD + non-DM cohort. D-F, ESRD + DM cohort. DM indicates diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; and PD, peritoneal dialysis.



**Figure 5.** Adjusted population survival curves comparing the outcomes of PD and HD patients with incident ESRD who were 65 years or older and had 1 or more comorbidity, stratified by DM status and cohort period. A-C, ESRD + non-DM cohort. D-F, ESRD + DM cohort. DM indicates diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; and PD, peritoneal dialysis.

a lower risk for death early during the course of ESRD—the magnitude and length of time over which this lower risk for death is evident depends on age, diabetes status, and the presence of associated comorbidity. After the first few years of treatment, many studies have also shown a higher risk of death for patients treated with PD. However, virtually all the studies to date have enrolled patients with incident ESRD from the 1990s. Recent data have shown a differential improvement in outcomes of HD and PD patients, and thus it is probably inappropriate to use the results of studies of older cohorts when making therapeutic decisions in the present era.<sup>7,25</sup> It is this differential change in outcomes of HD and PD patients that formed the rationale for us to study the secular trends in relative outcomes of patients treated with the 2 dialysis modalities. To our knowledge, only 4 published studies that have compared the outcomes of HD and PD patients with incident ESRD have included subjects who started dialysis treatment after 2000<sup>23-25,28</sup>; however, secular trends between PD and HD were not examined in 3 of the 4 studies (from the Netherlands, Taiwan, and the United States).<sup>23,24,28</sup> Data from the Australia and New Zealand registry are consistent with our findings, and in that study the adjusted relative risk for death of PD patients also decreased over time such that no significant difference in outcomes of HD and PD patients were seen among those who commenced dialysis therapy in 2005.<sup>25</sup> Consistent with the findings from Australia and New Zealand, no significant difference in the risk of death is demonstrable among patients with incident ESRD in

2002-2004 treated with either HD or PD in the United States for up to 5 years. Improvements in relative outcomes were observed in each of the 8 subgroups analyzed. Thus, a higher risk of death seen particularly in diabetic patients with additional comorbidity, though still present in the most recent cohorts, was progressively attenuated over time. In contrast, the lower risk of death among younger nondiabetic patients with no additional comorbidity persisted with progressively lower HRs in the most recent cohorts.

In addition to examining secular trends, our study has significant additional strengths. First, to our knowledge, it is the largest study done in this field to date. Our findings are relevant because we also examined secular trends of outcomes in 8 subgroups of patients. Furthermore, because our study includes data from all centers in the United States, our findings have considerable external validity.

Second, marginal structural models such as those used in this study provide robust estimates in observational studies, at least to the extent to which the measured baseline characteristics capture information relevant to all known and unknown confounders. This approach has not been used in either registry or cohort studies that have compared outcomes of HD and PD in the United States.

Third, to our knowledge, this is the first study from the United States that has adjusted for the probability of censoring. In survival studies of dialysis patients, renal transplant is one of the most common reasons for censoring participants. However, this has the risk of introducing substantial bias when considering the outcomes



of maintenance dialysis patients. The unadjusted transplant rate for PD patients with incident ESRD is more than 2-fold higher than for HD patients.<sup>7</sup> In this study, the adjusted transplant rate for incident PD patients was still 30% to 60% higher. This differential transplant rate between PD and HD suggests that some degree of selection bias due to censoring for transplant does exist and that perhaps healthier patients are removed at a faster rate over time from the PD cohorts when compared with HD cohorts. It is conceivable that a higher transplant rate may have accounted for some of the apparent increase in risk of death in patients treated with PD with increasing dialysis vintage. Furthermore, the transplant waiting times have become longer in many parts of the country. The prolongation in transplant waiting times would lead to inclusion of a larger number of healthier PD patients for longer periods in the later cohorts than HD patients (since PD patients have a higher transplant rate). This may have explained the differential improvement in outcomes of HD and PD patients.<sup>7</sup> In the marginal structural models used in this study, we weighted the analysis by the inverse probability of censoring, and this allowed us to adjust for selection bias from unmeasured confounders associated with censoring. This is a considerable strength of the present study and further reduces bias.

Fourth, rather than focusing on time-dependent HRs, we focused on the accumulated effects of the initial choice of dialysis modality by performing an “intent-to-treat” survival analysis based on the dialysis modality on day 90. The rate of transfer of PD patients to HD is higher than that of HD patients to PD.<sup>7</sup> An analysis that does not consider these transfers, as performed herein, allows us to consider the effect of initial stable treatment modality on day 90 and encompasses the higher risk associated with the transfer of patients from one modality to the other. Moreover, it effectively preserves the conditional randomization property that PSs impart on PD vs HD comparisons. Specifically, the set of all measured baseline characteristics will be conditionally independent of modality selection given the PS. This means that PD and HD patients with similar PSs will be similar with respect to all measured baseline characteristics as well as any unmeasured confounders that are strongly associated with those characteristics.

Our study does not allow us to determine the causes of the differential improvement in outcomes of HD and PD patients. A greater reduction in risk for infectious complications, greater improvements in prescription management of PD patients, and a more selective assignment of patients to the therapy are possible explanations for our findings. The important question to consider is if the overall equivalency of outcomes will persist if a larger proportion of patients with incident ESRD begin treatment with PD. The use of PSs and the marginal structural model with IPTCW reduces the possibility of confounding; however, in observational studies the possibility of residual confounding remains. However, a larger proportion of patients with incident ESRD are treated with PD in Canada (18%) and Australia and New Zealand (42%), and similar outcomes have been reported with the 2 dialysis therapies in the most recent data.<sup>25</sup> Nevertheless, the effect of expanding PD use on outcomes of patients remains speculative.

Our study is not without limitations. The assignment of patients to the 2 therapies was not random, and thus one has to be cautious before inferring causality. However, randomization of patients to 2 therapies with disparate effects on lifestyle is challenging, and previous attempts at conducting a randomized controlled comparison of HD and PD have been unsuccessful.<sup>6</sup> It is unlikely that a randomized, controlled comparison of the 2 dialysis therapies will be undertaken in the industrialized world. Furthermore, information on additional diseases was obtained from the Medical Evidence Form 2728, a source that has been shown to lead to underestimation of the comorbidity.<sup>29</sup> In addition, data on only baseline comorbidity were available. As a result of these reasons, we cannot exclude residual confounding. The 2002-2004 cohort has limited 5-year follow-up in that only those patients with incident ESRD from January-September of 2002 would have a maximum follow-up of 5 years. Finally, we did not consider transfers from one dialysis modality to the other. Thus, the equivalency of outcomes pertains only to the dialysis modality on day 90, and no conclusions can be made regarding the direct effects of the modality.

In conclusion, in this study we demonstrate a reduction in the adjusted relative risk of death of PD patients in the United States compared with those beginning treatment with HD. In the most recent cohorts, the life expectancy of patients treated with either HD or PD on day 90 of ESRD was remarkably similar. The lower costs of peritoneal dialysis and equivalent outcomes with the 2 therapies provide support for a larger use of PD for the treatment of ESRD in the United States, particularly in subgroups in which the patients treated with PD have similar or lower risk for death when compared with HD (nondiabetic and younger diabetic patients with no additional comorbidity; almost two-thirds of patients with incident ESRD). However, the improvement in PD outcomes may have been a result of more selective assignment of patients to the therapy over the last decade. Thus, should such an expansion of PD use be undertaken, close monitoring of outcomes of patients treated with different dialysis modalities should continue.

**Accepted for Publication:** April 27, 2010.

**Published Online:** September 27, 2010. doi:10.1001/archinternmed.2010.352

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**Financial Disclosure:** Dr Mehrotra has received grant support, honoraria, and served as an ad hoc consultant for Baxter Health Care. Dr Bargman has received honoraria

from Baxter Health Care. Dr Vonesh is a consultant for Baxter Healthcare.

**Funding/Support:** This work was supported by research grants from Baxter Health Care and National Institutes of Health (grant R21 DK077341). Dr Mehrotra is also supported by grant RR18298 from the National Institutes of Health and by the American Heart Association. Drs Mehrotra and Kalantar-Sadeh are supported by a grant from DaVita Inc.

**Disclaimer:** These data were supplied by the USRDS and the findings do not represent the opinion of the US government or the USRDS.

**Online-Only Material:** The eAppendix, eTables 1 and 2, and eFigures 1 through 7 are available at <http://www.archinternmed.com>.

**Additional Contributions:** Eileen Eriksen managed the data obtained from the USRDS.

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