

CONFLICT OF INTEREST STATEMENT

None declared.

(See related article by Otteman and Ishani. Comparing US and Chinese dialysis patients: an editorial on Cheng *et al.* Mortality rates among prevalent hemodialysis patients in Beijing: a comparison with USRDS data. *Nephrol Dial Transplant* 2013; 28: 495–497.)

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Underutilization of peritoneal dialysis: the role of the nephrologist's referral pattern

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ABSTRACT

Background. The incidence of end-stage renal disease is increasing, placing a tremendous burden on health care resources. Peritoneal dialysis (PD) is cheaper than hemodialysis and has many potential advantages and few contraindications as an initial modality selection. This study examined differences in patient PD attempt rates between nephrologists using technique survival and mortality as outcomes.

Methods. We performed a retrospective review of the Manitoba Renal Program databases from January 2004 to January 2010. Analysis of 630 patients who commenced dialysis and had demographic data available was performed. A genetic matching algorithm was used to balance potential differences between patient characteristics. Each nephrologist was then compared against their peers to calculate a PD attempt rate. The highest attempt rate group was compared with the lowest.

Results. When comparing PD attempt rates between groups, all the results were significant. PD technique survival at >90 days showed no significant differences ($P = 0.42$). Patient mortality at >90 days was also not significant when comparing groups ($P = 0.14$).

Conclusions. Our data suggest that when comparing the low- with high-attempt groups, the factors limiting PD utilization do not include on-site availability of PD, case mix, funding, patient location or reimbursement. Aggressive approaches of starting more patients on PD did not lead to lower technique survival or higher mortality rates. If the PD attempt rate was maximized, a significant amount of money and resources could be saved or directed toward helping a larger population without significant harm to patients.

INTRODUCTION

The global incidence of end-stage renal disease (ESRD) continues to climb. In 1990, just over 400 000 patients required maintenance dialysis. In 2010, over 2 million were on dialysis, placing a tremendous burden on health care resources around the world [1]. Peritoneal dialysis (PD) has been shown to be less costly than facility-based hemodialysis (HD) as an initial renal replacement modality choice in most countries [1–4]. PD has the added benefits of preserving a patients residual renal urine output, translating into better solute and volume clearance, providing similar or better patient quality of life and perhaps mortality in the first 12–24 months of therapy [5–12]. Few contraindications preclude the use of PD in patients [13]. Despite this, large variations of PD penetration patterns exist at international, national and even local levels, reflecting a possible complex interplay of patient, social, economic and political factors [14–22].

The primary intent of this study was to isolate the effect of individual nephrologist propensity for their patients to

attempt PD in a large, universal payer/provider, Canadian renal program. The data will be explored further to determine the effect of these differing practices on PD outcomes in the form of technique failure and mortality.

MATERIALS AND METHODS

The Manitoba Renal Program (MRP) nephrologists are responsible for all referred chronic kidney disease (CKD) patients in addition to managing the renal replacement therapy (RRT) services in the province of Manitoba, Canada (pop. 1.2 million). In 2010, the MRP cared for about 1200 prevalent dialysis patients, with ~20% of patients receiving PD and 2% of patients on home HD yielding about 936 facility-based HD patients. All the patients in the MRP database (including billing claims data) with entries between 3 January 2004 and 24 June 2010 were considered for inclusion in this study. The study focused on the 630 patients that began either HD or PD during the period, and whose first contact in the program corresponded to a dialysis clinic visit no earlier than March 2005. The purpose of the last constraint was to allow association of patients with a particular nephrologist, who could be identified as a first contact with the renal program and multidisciplinary CKD clinic participation prior to dialysis. If a patient was started on HD and then switched to PD, the first contact nephrologist would be ‘credited’ with the PD attempt as we assumed that the majority of modality education would have occurred in the clinic setting. Patients who were never followed in the clinic and began dialysis acutely were excluded from our analysis. This study received appropriate local research ethics board approval from the University of Manitoba.

The primary outcome of interest was whether a patient ever attempted PD or not. A PD attempt was defined as the presence of at least one instance of billing for PD, corresponding to an entry for that patient into the MRP PD database. The explanatory variables considered in the analysis included demographic variables (e.g. age, sex, race, rural location of residence), primary cause of ESRD (eg. acute tubular necrosis, cancer, congenital renal disease, diabetes mellitus type 1 or 2, failed transplant, glomerulonephritis, hypertension and polycystic kidney disease) and comorbid risk factors, including cerebrovascular disease, peripheral vascular disease, angina, chronic obstructive pulmonary disease, prior myocardial infarction, prior coronary artery bypass graft or percutaneous coronary intervention, smoking, diabetes, hypertension, congestive heart failure and malignancy. The MRP database that was interrogated for demographic variables, cause of ESRD and comorbid risk factors has been described elsewhere in terms of validation steps in place to ensure data quality and integrity [23]. In brief, all comorbidities and modality commencement and discontinuations were adjudicated at a formal interdisciplinary rounds session conducted on a weekly basis. Finally, health-system-related

factors were considered as explanatory variables such as availability of PD at initial site of referral and who the primary nephrologist was for pre-dialysis CKD clinic care.

Each explanatory variable of interest was first considered separately for association with the PD attempt variable by univariate analysis. All the variables considered were categorical and analyzed using Fisher's test. If a Fisher test showed a variable to be significantly (P -value < 0.05) associated with PD attempt, it was included in the model going forward. If the Fisher test showed that the variable was not significant, a genetic matching algorithm was applied to balance all other covariates, and the variable was then included in the model if the P -value (< 0.05) for a subsequent paired test showed significant association between the variable of interest and PD attempt [24]. This process allowed the inclusion of variables of interest whose association with PD attempt might be masked by interaction with other covariates. A similar process was applied to determine variables associated with technique survival and mortality at 90 days, where the Fisher and t -tests are replaced by log-rank tests for comparing survival curves with censored data. This process is depicted in Figure 1.

To assess the impact of nephrologist practice patterns on PD attempt rate, the odds ratio for attempting PD was calculated for each physician relative to all their peers. This allowed nephrologists to be divided into low- and high-attempt groups, using an odds ratio of 1 as a cutoff. PD attempt rates, technique survival and mortality at 90 days were then compared between the high-attempt and low-attempt groups. Each of the aforementioned variables included in the model in the tests of association with PD attempt was tested for balance across the high- and low-attempt group with Fisher tests. Any variable found to differ significantly (P -value < 0.05) between the two groups was balanced by the genetic matching algorithm [24].

This method constructs a list of matched pairs of patients, one from the control (low attempt) and one from the treatment (high attempt) group to make a virtual cohort. This virtual cohort is constructed such that there is no significant (P -value < 0.05) difference between the control and treatment

group with respect to univariate Fisher or t -test comparisons for any of the covariates included in the model (Figure 2). The genetic matching algorithm is a generalization of common matching methods such as those based on the Mahalanobis distance or a propensity score estimated by logistic regression. These methods have appealing theoretical properties when the distributions of covariates have certain properties, the true propensity score is known and the sample size is large; however, these constraints are difficult to satisfy in practice and, in their absence, matching will in general increase the bias of some of the covariates [25]. These methods, therefore, have the potential to increase the influence of some potential confounders and frequency do so in practice [26–28]. Genetic matching is a non-parametric method used by a variety of researchers in various fields [29–35], which employs a genetic algorithm to optimize the balance between covariates as much as possible and does not depend on the knowledge or estimation of the propensity score. In our study, genetic matching was employed to define two similar groups with balanced confounders and the technique survival and mortality at 90 days were compared between these two virtual cohorts.

RESULTS

Six hundred and thirty patients were included in the analysis. The baseline characteristics of these 630 patients are included in Table 1. The median time a patient spent in clinic before starting dialysis was 30 months. A plot of odds ratios for nephrologist PD 'attempt rate' with confidence intervals is depicted in Figure 3. Ten of the 19 nephrologists yielded an odds ratio of < 1.0 , with the remainder having an odds ratio for PD attempt > 1.0 relative to the set of their peers. For the purposes of comparison those nephrologists more likely to have patients attempt PD relative to their peers with those less likely, we separated them into two categories. Figure 4 depicts the relative influence of adding more nephrologists to the high and low PD attempt groups, affects the size of the

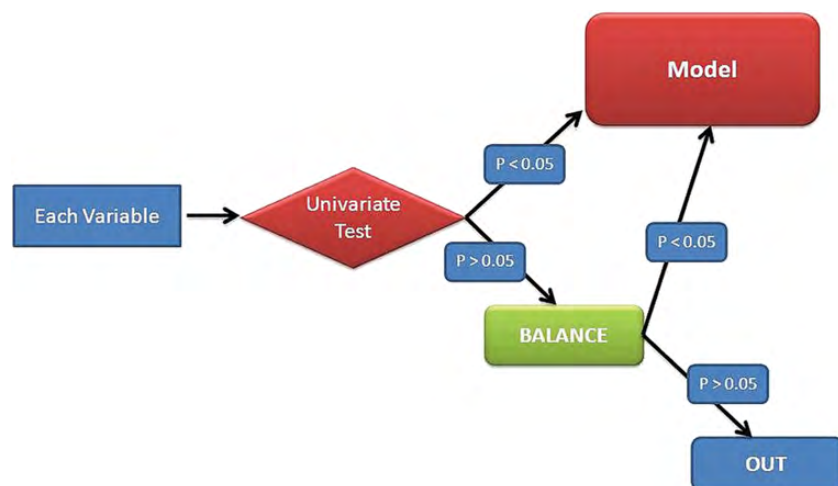


FIGURE 1: Variable analysis.

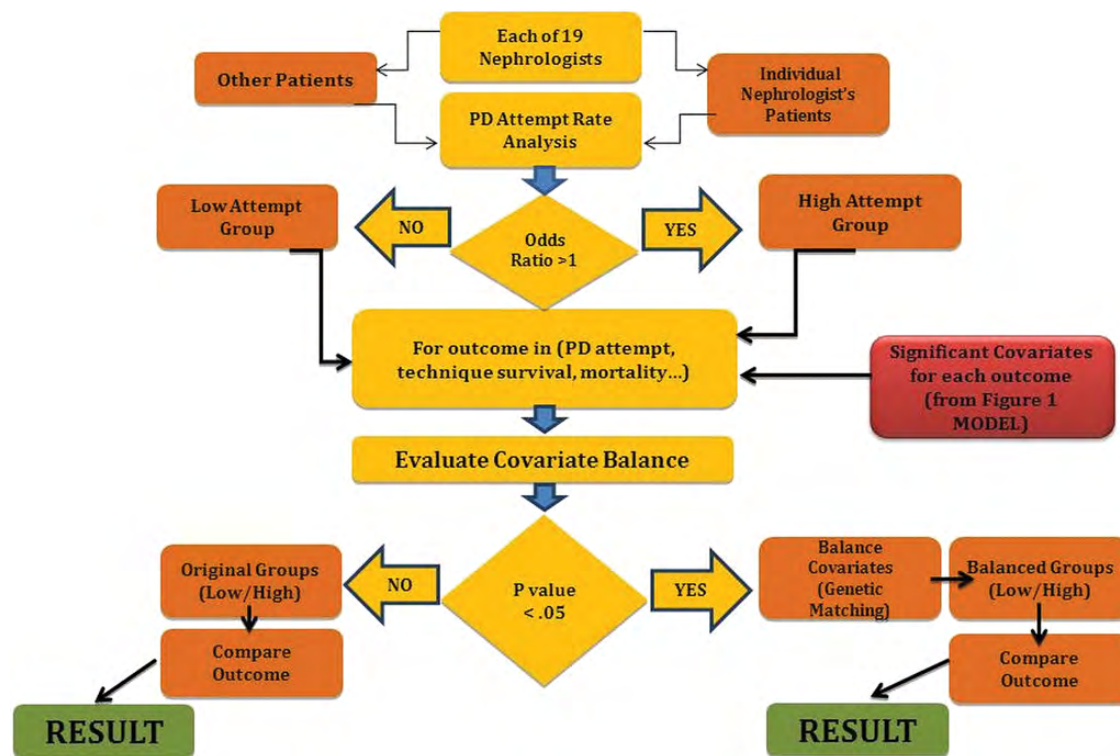


FIGURE 2: Nephrologist groupings.

effect between comparing groups and the confidence of the estimate. All nephrologists were included in the final model comparing high- and low- PD attempt groups.

When comparing survival outcomes between the high-attempt group (with 9 nephrologists) and the low-attempt group (with 10 nephrologists), the mortality at >90 days showed no significant difference (Figure 5, $P = 0.418$). The technique survival also found no significant difference between groups ($P = 0.142$) when compared. The comparisons of technique survival and mortality were performed on virtual cohorts, which were balanced so that there were no significant (P -value < 0.05) differences between groups in the variables determined in the manner described earlier to be associated with those two outcomes of interest.

DISCUSSION

This study demonstrates that there are significant differences between nephrologists as to whether or not their patients ever attempt PD out of the CKD clinic. We have shown that despite this variable attempt rate, patients of nephrologists with a more aggressive approach to PD do not suffer from an earlier technique survival or increased mortality. Therefore, a more aggressive PD approach does not appear to disadvantage patients as measured by these two important PD outcomes. To control for potential patient demographic and comorbidity differences and their effect on nephrologists' PD attempt rate, in addition to factors such as availability of on-site PD, we used a genetic matching algorithm with matched pairs to yield significant differences between groups. The

matched higher attempt group, or those who had more aggressive rates of PD compared with their peers, did not have a significant difference in either technique survival or mortality for patients lasting 90 days on treatment. In a provincial program with universally homogenous funding models, reimbursement schemes and clinic resources, this begs the question: 'Is individual nephrologist practice style a significant modifiable factor in increasing patient uptake of PD?'

The strengths of this study include the comprehensiveness of patient inclusion and follow-up in a defined geographic region, and the unique matching algorithm employed to isolate the effect of nephrologist attempt rate on PD. Manitoba, Canada, has a single-payer universal health care system, for which the MRP provides and tracks all renal services provided including pre-dialysis CKD care. In the MRP, once a patient begins PD, they are considered a patient of the 'PD service' which is rotated on by different PD nephrologists. Our largest site in Manitoba does not have PD services, meaning that the nephrologists at that site do not have extensive experience with PD, and yet site of referral was not a statistically significant predictor of whether or not a patient ever attempts PD. All nephrologists practice at one of four sites in the province, and there is no specific competition for referrals between or within sites. All CKD patients cared for by nephrologists have the same access to multidisciplinary teams, who typically work in more than one nephrologist clinic and are charged with extensive education of patients on dialysis modality choice. Despite this organizational structure designed to minimize biases in patient population followed by a nephrologist, and the standardized teaching on modalities patients receive, we employed very sophisticated

Table 1. Patient characteristics (<i>n</i> = 630)	
Primary ESRD diagnosis	Proportion
Renovascular/unknown	37.4%
Type 2 diabetes	28.6%
Glomerulonephritis	13.9%
Acute tubular necrosis	7.0%
Hypertension	6.6%
Type 1 diabetes	3.2%
Polycystic kidney disease	2.1%
Congenital	0.06%
Malignancy	0.05%
Failed transplant	0.01%
Comorbidities	Proportion
Hypertension (on medication)	84.8%
Type 2 diabetes	65.4%
Congestive heart failure	18.1%
Cardiovascular disease	15.5%
Peripheral arterial disease	14.5%
Smoker	14.1%
Ischemic heart disease	14.6%
Prior malignancy	9.1%
Coronary intervention (bypass, percutaneous)	8.9%
Angina	8.1%
Chronic obstructive pulmonary disease	6.3%
Type 1 diabetes	2.9%
Race	Proportion
Caucasian	53.2%
First nations	28.7%
Other	11.9%
Asian	6.2%
Sex	Proportion
Male	55.3%
Female	43.8%
Unknown	0.09%
Continuous variables	Mean \pm SD
Age	56.9 \pm 19.05
Body mass index	28.39 \pm 7.12
Km to nearest nursing station	195.54 \pm 72.20
Km to nearest HD center	42.13 \pm 35.24
Km to nearest health center	34.37 \pm 71.88
Km to nearest hospital	24.84 \pm 44.56

Odds Ratios for PD Attempt Rate by Nephrologist Relative to Set of Peers

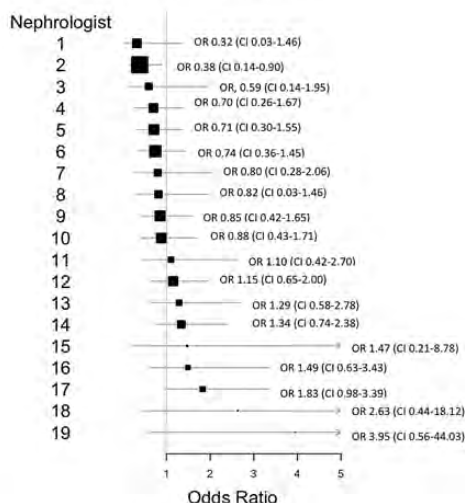


FIGURE 3: Odds ratio of PD attempt rates by individual nephrologists.

matching algorithms to isolate the effect that the attending nephrologist had on a patient's propensity to attempt PD. Our results indicate a strong signal in this area, which appears valid and confirms our hypothesis.

The cost of RRT poses a large financial and resource demand on health care systems throughout the world [1–4]. With growing numbers of ESRD patients, there is an urgent need to research and explore more cost-effective measures for RRT at a population level while optimizing patient quality of life, health outcomes and freedom of choice [4].

With few contraindications to PD [1, 13], this modality can fortunately be used for effective treatment in the majority of dialysis patients. By taking into account medical issues, the patients' social factors, cost effectiveness and overall benefit to the patients, an ideal modality option can be then determined [36]. With the consideration of all the potential advantages of PD, our project explores the effect of higher PD rates by an individual nephrologist, particularly, whether more aggressive rates of PD had a higher mortality or technique failures. Our study did not find any significant differences between the two groups for mortality at >90 days ($P = 0.418$) or with technique failure at >90 days ($P = 0.142$).

A possible explanation for our findings may be associated with the advantages that PD is purported to hold over conventional in-center HD. These benefits may balance out the potential downfalls of a more aggressive PD approach. The maintenance of residual renal function is hypothesized to contribute to the initial survival benefit for PD over conventional HD through augmented middle molecule clearance, improved nutrition through more liberal diet and fluid intake, increased endocrine function with higher hemoglobin levels, lower systolic blood pressures and fewer arrhythmias [1, 37, 38]. There appear to be no demonstrable differences in infectious complications between PD and HD [39, 40]. Episodes of potentially more severe bacteremia and fungemia

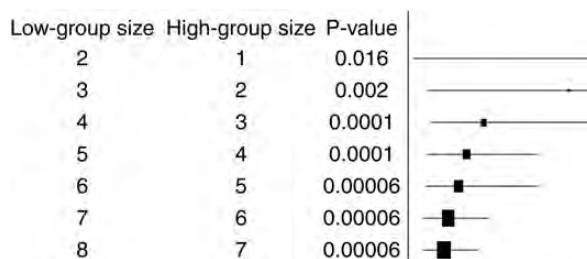


FIGURE 4: Odds ratio of PD attempt rates by groups. The first line depicts the two nephrologists least likely to have patients attempt PD (low group) compared with the one nephrologist most likely. As more nephrologists are added to each group, the odds ratio becomes less pronounced, but confidence intervals become narrower.

were found mainly in their HD population, whereas peritonitis was the main complication related to PD patients. The overall infection-related hospitalization rates were lower in PD patients [38]. Li and Chow [13] recently published a study stating that centers in Canada with >500 PD patients had a 29% relative risk reduction in mortality and lower technique failures compared with centers with <99 PD patients. Nephrologists at larger centers, similar to ours, may be better able to manage PD complications and may make more appropriate selections of patients for PD.

In addition to the aforementioned benefits, several studies have demonstrated an improved quality of life with PD [5, 6]. PD confers considerable cost savings compared with HD of at least \$20 000 USD per patient per year in Canada, the USA and Europe [1–5, 41–43]. The lower costs stem mainly from PD being a home-based therapy, requiring little overhead and nursing costs, as well as less medication, particularly erythropoietin therapy requirements [3, 21, 40].

The survival comparison outcomes from previous studies are controversial [7–12] with the majority of consensus agreeing that there is little difference in PD and HD mortality rates. The US Renal Data Systems 2008 annual report found no significant mortality difference at 60 months, and PD held a slight survival advantage in some population subsets. Canadian data found an initial 2-year survival benefit for PD [8]. Observational survival data comparing HD and PD are limited by the confounding of potential selection bias. We found only three other studies that have used propensity matching to compare survival between the two modalities [7–9]. The first study did not show any significant mortality difference at 90 days, while the second study used mortality after 90 days as an endpoint. The most recent study, published by Weinhandl *et al.* [9], showed a slight mortality benefit favoring PD, with a hazard ratio of 0.92 at 90 days ($P = 0.04$), with that benefit lost at 48 months. Hemmelgarn *et al.* [10] found that East Indian and Indo-Asian patients were 50% more likely than Caucasians to start PD.

Other studies have demonstrated that there are discordant opinions between nephrologists on whether or not PD is an optimal modality for most patients [44, 45]. Bouvier *et al.* were able to demonstrate a link between regional variations in PD prevalence to nephrologist opinion on the optimal mix

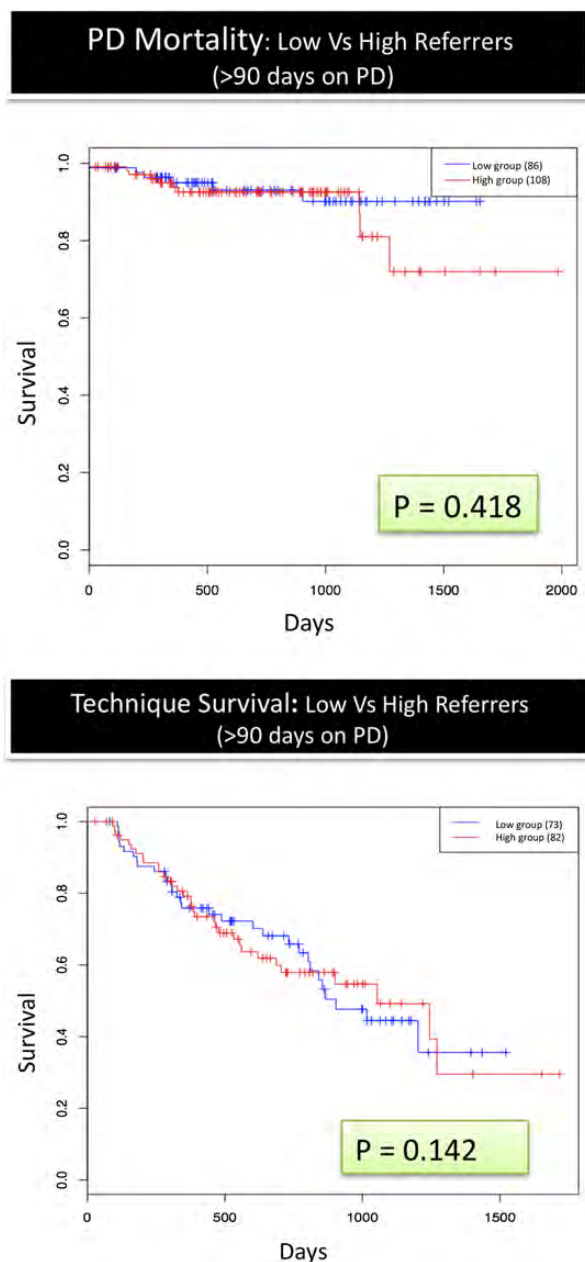


FIGURE 5: Mortality and technique survival comparisons between groups.

of HD: PD patients in the same region. Our study is the first, to our knowledge, that attempts to isolate the primary nephrologist for CKD care as a covariate in PD attempt rate. Variable uptake rates in other jurisdictions of PD would suggest that our results are likely generalizable to programs elsewhere. Over the course of this study, Manitoba had a PD prevalence ranging from 18 to 20%.

Our study has limitations. As it was a retrospective database review, we relied on the information entered into the database to be accurate. Further, as patients were not randomized and dialysis modalities were not randomly selected, causality cannot be confirmed. It is unlikely that a randomized trial will ever be conducted in this area because of the high value based on patient choice and motivation. Although

extensive matching algorithms were applied, our data were not able to account for socio-economic factors as a potential confounder. As mentioned, however, consults are for the most part distributed among nephrologists randomly within the three practicing centers located in Winnipeg. There were no univariate differences in patient characteristics by center.

In conclusion, PD as an initial modality choice has been shown to maintain or improve patient health-related quality of life, has similar mortality outcomes and is typically much less costly compared with HD. As per convention in health economics, when offering health technologies and interventions without significant differences in mortality or quality of life, the least expensive option should be promoted by health care payers and providers. While patient-related factors preventing the ability to perform PD are often non-modifiable (e.g. blindness, severe cognitive impairment), the majority of patients are still eligible to attempt PD as a renal replacement modality. Integrated renal care programs should therefore be organized to minimize the potential bias of clinicians in selecting modality choice ‘including standardized teaching algorithms and the assignment of patients to dedicated late-stage CKD interdisciplinary programs, not simply individual nephrologist practices’. We do, however, recognize that despite a PD first promotion strategy, patients may opt for facility-based HD and that the ability to choose still may be honored. Our study in a universally funded health care system is one of the first to show that clinician bias may be a significant modifiable factor in augmenting PD rates. We would suggest that this approach be taken in other health care regions to aid in appropriate policy recommendations specific to local practices.

CONFLICT OF INTEREST STATEMENT

The results presented in this paper have not been published previously in whole or part, except in abstract format.

(See related article by Woodrow. What are the factors underlying the variation in the use of peritoneal dialysis? *Nephrol Dial Transplant* 2013; 28: 501–504.)

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