**Variation in Peritoneal Dialysis Time on Therapy by Country: Results from The Peritoneal Dialysis Outcomes and Practice Patterns Study**

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**Running Title:** Global Variation in PD Time on Therapy

**Word counts:** Abstract: 232 Body: 3327 Figures: 4 Tables: 1

**ABSTRACT**

**Background and Objectives:** Quantifying contemporary peritoneal dialysis (PD) time on therapy is important for patients and providers. We describe time on PD in the context of outcomes of hemodialysis (HD) transfer, death, and kidney transplantation based on the multinational observational PDOPPS from 2014-2017.

**Design, setting, participants and measurements:** Among 218 randomly selected PD facilities (7121 patients) in PDOPPS from Australia/New Zealand, Canada, Japan, Thailand, UK, and US, we calculated the cumulative incidence from PD start to HD transfer, death, or kidney transplantation over 5 years, and adjusted hazard ratios for patient and facility factors associated with death and hemodialysis transfer.

**Results:** Median time on PD ranged from 1.7 [IQR 0.8-2.9] (UK) to 3.2 [IQR 1.5-6.0] (Japan) years and was longer with lower kidney transplantation rates [range: 32% (UK) to 2% (Japan, Thailand) over 3 years]. Adjusted HD transfer risk was lowest in Thailand, but death risk was higher in Thailand and the US compared to most countries. Infection was the leading cause of HD transfer, with higher HD transfer risks seen in patients having psychiatric disorder history or elevated BMI. The proportion of patients with total weekly Kt/V ≥1.7 at a facility was not associated with death or HD transfer.

**Conclusions:** Variation in time on PD across PDOPPS countries should be interpreted considering differential death and kidney transplantation rates. Identification of infection as a leading cause of HD transfer and patient and facility factors associated with risk of HD transfer can facilitate interventions to reduce these events.

**Keywords:** Hemodialysis Transfer, Peritoneal Dialysis, Patient Survival, Technique Survival, Kidney Transplantation

**INTRODUCTION**

Worldwide, among those receiving dialysis, only 11% receive treatment with peritoneal dialysis (PD) with the majority treated with facility-based hemodialysis (HD)1-2. PD is associated with similar survival compared to facility-based HD 3-6. Compared to HD patients, patients receiving PD experience superior treatment satisfaction, longer preservation of residual kidney function, and often lower annualized treatment costs 7-11. As a result, PD increase in low and middle-income countries may contain growing kidney failure-associated costs with countries, such as Thailand, employing a PD-first policy 12. Changes in dialysis reimbursement have led to recent PD utilization increases in the United States 13.

Efforts to increase PD utilization are limited by the shortened treatment time on PD as compared to facility-based HD. A transition from PD to hemodialysis (HD) is costly, is a period of high morbidity, and has worsened quality of life 14-15. The Standardized Outcomes in Nephrology-Peritoneal Dialysis (SONG-PD) study established PD treatment failure as one of the core outcomes of importance to stakeholders 16. In collaboration with the International Society for Peritoneal Dialysis (ISPD), The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) is a multicenter, international observational cohort study designed to identify modifiable practices associated with patient and technique survival among PD patients 17. The primary objective of this investigation was to quantify PD time on therapy across countries employing a standard definition of transition to HD. Secondary objectives were to explore differences by country in causes of HD transfer identifying patient and facility factors associated with lower risks of death and HD transfer.

# METHODS

## ***Study Design and Data Source***

Maintenance PD patients ≥18 years were enrolled randomly from national samples of randomly selected PD facilities treating at least 20 PD patients at selection, and stratified by geographic region and center size within countries. We included 2014-2017 data from Australia/New Zealand, Canada, Japan, Thailand, the United Kingdom (UK), and the United States (US). Study details are provided at <https://www.dopps.org/OurStudies/PeritonealDialysisPDOPPS.aspx>.

Patient demographics, comorbidities, and laboratory data were captured at study enrollment (Table 1A). Data from US patients receiving care at large dialysis organization (LDO) facilities were imported from electronic health records. All other data were obtained by abstraction of medical charts and entered into a web-based data collection tool. PDOPPS obtained IRB study approval and patient consent was obtained to meet national and local ethics regulations.

***Clinical Outcomes***

Follow-up started at study enrollment, and ended with first of either: death, 7 days after permanent change in dialysis modality, loss to follow-up, kidney transplantation, end of study phase, or the most recent date of available data. Permanent HD transfer was defined as either a modality switch to HD identified as permanent, or temporary transfers from PD to HD lasting at least 12 weeks (84 days). In primary analyses, hybrid therapy switches (addition of any HD to continued PD therapy) were counted as HD transfer event. Deaths, including within seven days of permanent transfer to HD, were not included as HD transfer events.

The Fine and Gray competing risks model was used to generate cumulative incidence curves for death, HD transfer, and kidney transplantation, separately for each country 18,and to determine median time on PD by country and outcome proportions at 3 years.

Cox regressions were used to investigate the association between country and HD transfer, all-cause mortality, the composite of both, and kidney transplantation. Models were left truncated to account for PD vintage at study enrollment. All models accounted for patient clustering within facilities using robust sandwich-type covariance estimators, and where appropriate stratified by country. Analyses were conducted on death, HD transfer, and transplant using cause-specific models, as recommended for etiological analyses 19. The composite outcome was included.

The crude event rates within each PD vintage time period were estimated as the number of events per 100 patient-years at risk within that time period. In this analysis, each patient who had follow-up in PDOPPS during the corresponding period (e.g., <6 months on dialysis) contributed time at risk to that period and, potentially, an event during that period.

***Patient and facility factors as predictors of clinical outcomes***

Patient factors evaluated included age, sex, cardiovascular disease, diabetes, prior HD experience, caregiver involvement, psychiatric disorder, body mass index (BMI), black race, urine volume, serum albumin, and transplant waiting list status.

Facility factors evaluated included facility size, PD facility age (years since facility first started caring for PD patients), patient/nurse ratio, routine multidisciplinary review, and whether PD nurses were routinely retrained, as well as facility proportion of patients using 4.25% PD solution (Table 1B) or with a KT/V of above 1.7 per week. Given variability in median facility size across countries, facilities within the lowest quartile for their country were defined as small, facilities in the upper quartile were defined as large, and the remaining facilities were defined as medium. Facility size was also evaluated as a continuous variable.

Cox models including patient and facility factors were used to calculate the adjusted hazard ratios for death, HD transfers and the combined outcome and stratified by country and large dialysis organization in the US. Models on transplantation adjusted for all factors except kidney transplant waiting list status. Each facility factor was assessed one at a time in models that controlled for the patient characteristics.

***Sensitivity analysis***

In a sensitivity analysis, hybrid transfer (defined as the addition of HD but continuation of PD) events were censored, not counted as HD transfer. In another sensitivity analysis testing the impact of our choice of threshold for temporary vs. permanent transfers, temporary HD and hybrid transfers were counted as HD transfer.

***Treatment of Missing Data***

Missing values were multiply imputed using the Sequential Regression Multiple Imputation Method by IVEware 20. Results from 20 imputed data sets were combined for the final analysis using Rubin’s formula 21. Missing data was <25% for all imputed covariates, except PD facility age (27% missing), caregiver involvement (41% missing), urine volume (36% missing), transplant waiting list (40% missing), and prior HD (59% missing). Analyses used SAS software, version 9.4 (SAS institute Inc., Cary, NC).

# RESULTS

## ***Patient and facility characteristics by country***

Table 1A presents patient characteristics. Mean patient age ranged from 56 years in Thailand to 64 years in Japan. The proportion of male patients in Thailand (51%) and US (56%) was lower compared to other countries (62%-67%). Patients in Japan (15%) and Thailand (24%) were less likely to be on a kidney transplant waiting list (vs. 48%-62% elsewhere).

The median numbers of patients treated in Japanese and US PD facilities were 29 and 32, respectively. Other countries had median facility sizes of 50-53 PD patients, except Thailand with a median number of 102 patients. Routine multidisciplinary review was more common in the UK (79%) and the US (81%) than in other countries (40%-69%). US facilities had a higher proportion of facilities with a KT/V of 1.7 or greater (69%) and Japan and Thailand the highest proportion with KT/V 1.7 or lower (58%-75%). Hypertonic (4.25%) PD solution was rarely used in Japan and UK, but was used in at least 20% of patients in 80% of US facilities (Table 1B).

## ***Absolute time on therapy and relative hazard by country***

Overall, median time on PD was 2.3 (interquartile range 1.1-4.4) years (Supplemental Table 1). Japan had the longest median time on PD of 3.2 years, followed by 2.8 years in Thailand, 2.1-2.3 years in A/NZ, Canada, and US, and 1.7 years in UK (Figure 1).

Overall, 19% (N=1379) of the PD patients transferred to HD/hybrid, 13% (N=907) died, and 7% (N=514) received a transplant during follow-up (median 1.1 years, IQR 0.6-1.7), but these outcomes varied by country. Less than 1% (N = 8) died within seven days of HD transfer. By 3 years on PD, 36% of patients in Thailand died, compared to 11%-18% of patients in other countries. HD transfer was common, with 24%-35% of patients having HD transfer by 3 years on PD, except Thailand, where only 16% of patients transferred to HD. In Japan, 11% of patients switched to hybrid therapy by 3 years on PD, while this was <1% in other countries. Only 2% had received a kidney transplant by 3 years on PD in Japan and Thailand while in other countries, 10%-32% had a transplant by 3 years on PD. Similar results were seen when we included any HD/hybrid transfer (including any temporary transfer) as an event (Supplemental Figure 1).

When compared to the US, the adjusted hazard ratio (HR) for the composite outcome, HD transfer or death, was lowest for patients in Japan (HR=0.75, 95% confidence interval [CI] 0.61-0.91)], followed by Thailand (0.77, 0.61-0.97) and A/NZ (0.85, 0.69-1.04). Adjusted HRs in Canada and the UK were similar to that of US patients (Figure 2). Adjusted hazard ratios of HD transfer were lowest in Thailand and similar elsewhere (Figure 2). Adjusted hazard ratios for death were lowest for patients in A/NZ and Japan (Figure 2). When not counting patients transferred to hybrid therapy as HD transfer, Japan had a hazard ratio (compared to the US) of 0.84 (0.67-1.05) for HD transfer and 0.56 (0.46-0.68) for the combined outcome of death or HD transfer (Supplemental Figure 2). Japan and Thailand had a lower incidence of transplantation, while A/NZ, Canada, and UK had higher incidence, compared to the US (Figure 2).

In the model on mortality adjusted only for demographics and comorbidities, Thailand had a hazard ratio of 1.79 (1.35-2.36) compared to the US, but this dropped to 0.99 (0.73-1.33) after adjustment for serum albumin, urine volume, and caregiver involvement (Supplemental Table 2).

## ***Event rate by time on therapy and by country***

In general, rates of the combined outcome of HD transfer or death were higher with higher PD vintage. Yet Thailand, and to some degree the US, were exceptions, with rates largely constant over PD vintage (Supplemental Figure 3A). As PD vintage increased, the rate of HD transfer was slightly higher in A/NZ, Japan, Thailand, and the UK, but not in Canada and the US (Supplemental Figure 3B). Patients in Thailand had the lowest rate of HD transfer. Thailand had high death rates across all PD vintages (Supplemental Figure 3C).

## ***Reason for HD Transfer***

Infection was the most common reason PD patients permanently switched to HD (Figure 3A). Issues relating to solute clearance was also a common reason, especially in Canada (13%) and Japan (16%). Among the causes of inadequate solute clearance leading to HD transfer, those characterized by low Kt/V or low creatinine clearance represented 60% of these (Supplemental Table 3). Water removal problems were common in Japan (29%), but not in other countries (4%-10%). Switching for psychosocial/medical reasons did not occur in Thailand, but was 8%-20% in other countries. Catheter-related problems accounted for 17% of HD transfer in Thailand, and <6% elsewhere. As PD vintage increased, there were more infections, solute/water clearance problems, and psychosocial/medical problems, but fewer peritoneal leaks/hernia and catheter-related problems (Figure 3B).

***Patient characteristics as predictors of clinical outcomes***

As shown in Figure 4A (and Supplemental Table 4A), male sex, diabetes, or psychiatric disorders were associated with higher risk of death or HD transfer. Patients who needed caregiver help with PD exchanges had a higher risk of death (1.57, 1.30-1.91), but not HD transfer (0.86, 0.70-1.06). Patients on a kidney transplant waiting list had a lower risk of death (0.62, 0.49-0.78), while not being associated with HD transfer. Patients with BMI values less than 20 kg/m2 had a higher mortality risk (1.38, 1.06-1.78), while patients with BMI values greater than 30 kg/m2 had a higher risk of HD transfer (1.28, 1.11-1.14). Black race was associated with lower risk of death (0.75, 0.59-0.94).

***Facility factors as predictors of clinical outcomes***

Compared to medium-size facilities, patients in smaller facilities had lower risk of death (overall HR 0.81, 0.68-0.97, Figure 4B, Supplemental Table 4B), largely driven by low mortality risk in small facilities in Canada (Supplemental Table 5C). Overall, there was little association between facility size and HD transfer. Smaller facility size was associated with an adjusted hazard ratio of HD transfer in the UK of 1.78 (0.94-3.38) versus medium facility size, but the adjusted hazard ratio for HD transfer in the US was 0.81 (0.66-1.01) (Supplemental Table 5B).

Patients in facilities with routine multidisciplinary review had a hazard ratio for the combined outcome of death or HD transfer of 0.92 (0.83-1.03), and for HD transfer alone of 0.88 (0.77-1.01) (Figure 4B, Supplemental Table 4B). Facilities using any 3.86% PD solution in more than 20% of their patients had a HR of mortality of 1.24 (0.93-1.65). We found no relationship between the proportion of patients at a facility achieving a total Kt/V of 1.7 or higher on the risk of death or HD transfer. We did not observe strong associations between other facility factors and clinical outcomes.

**Discussion**

In the first large-scale comparison of key clinical outcomes for patients on PD across countries, we quantified an overall median time on PD of 2.3 years with wide observed variability across countries, mostly driven by differences in kidney transplantation (Figures 1A-1F). Modest differences in mortality were evident, particularly after adjusting for patient case mix, with smaller differences in HD transfer.

The cumulative incidence curves of time on PD demonstrate the difficulties in making meaningful international comparisons regarding what time on PD means. For example, the observed time on PD was longer in Japan (3.5 years) than in the UK (1.7 years). However, this ignores that a larger fraction of UK PD patients received a kidney transplant in the first 3.5 years than in Japan (34% vs. 2%), which is important from a patient outcomes perspective.

In Thailand, the median time on PD of 2.8 years was longer than that seen for the UK, but most Thai patients no longer receiving PD 3.5 years after PD start had died. One can expect that the same issues in making meaningful international comparisons regarding time on PD can also exist across facilities within a country. Thus, consideration of a time on PD quality metric(s) for making comparisons across countries or facilities should account for both transplantation and death. Patients considering PD as a dialysis modality may appreciate a metric that considers the likelihood of either remaining on PD or receiving a kidney transplant as a meaningful positive outcome measure.

Adjusting for patient case-mix highlights apparent differences in mortality between countries. The effect estimates for all countries relative to the US become smaller, with Thailand moving from a higher to an equivalent death rate, and other countries moving from an equivalent to a lower death rate. Transplantation may cause informative censoring due to removal of healthier patients from the PD population, such that the effect estimate for countries with a high transplant rate could be biased upwards. As the US had a lower adjusted transplant incidence compared to Australia/ New Zealand, Canada, and the UK, the apparent difference in survival could be larger, although the change for Thailand and Japan could be reduced (Figure 2).

Studies from thirty years ago demonstrated higher mortality in US compared to Canadian PD patients.22 This discrepancy, not explained then nor now by measurable differences in patient case-mix, was evident and persisted despite improvements in death rates in the US PD population.23,24. An analysis of time on therapy in the US using 2008-2011 USRDS data demonstrated a median survival on PD of 1.9 years25 compared to our finding of 2.3 years. The difference may be reconciled by our restriction of facilities with greater than 20 patients, all insurance types included, and inclusion of a more contemporary cohort.

Despite younger age and lower comorbidities, individuals in Thailand had higher caregiver involvement and lower serum albumin and residual kidney function compared to US patients (Table 1A), all of which may have been indications of patient frailty and suboptimal pre-dialysis CKD care, and potentially explaining the worse unadjusted mortality. Unique socioeconomic, healthcare, and educational factors in Thailand may also explain this mortality difference, 26 including possible reluctance for HD transfer in moribund individuals. Adjusting for measured patient case-mix differences, Thailand did not have a higher adjusted death rate compared to the US (Supplemental Table 2) providing encouraging results to a country with a “PD first” policy 27.

Adjusting for patient case-mix had little impact on the overall rate of HD transfer, other than explaining a small difference in risks of HD transfer in Australia/New Zealand. Age and comorbidities, including diabetes and cardiovascular disease, were more strongly associated with death than with HD transfer.

Similar to a previous report, we found an association between the reason for HD transfer and duration of therapy. Catheter problems, leaks, and hernia were important causes for HD transfer early in PD therapy and become proportionally less common, whereas poor water or solute clearance and psychosocial/medical reasons become more common with increasing PD vintage 28. The absence of psychosocial causes of HD transfer in Thailand may speak to resistance by patients to HD transfer due to logistical or transportation challenges, or consequences of a “PD first” policy resulting in many long-term patients persisting with PD despite struggling with burnout. External pressures could result in HD transfer for when absolutely medically indicated.

We found those with a history of psychiatric disorders faced higher risks of transfer to HD. Previous studies found that depression in PD patients carried higher peritonitis risks and may have been relatively underdiagnosed across HD and PD patients, particularly in Japan 29,30. Whether interventions targeting mental health may extend time on PD for these individuals requires evaluation.

Higher BMI was associated with a higher risk of HD transfer. Previous studies have yielded inconsistent findings, 31, 32, *33* but these differences across studies may reflect different BMI cutoffs used, populations studied, and definitions of HD transfer employed. It is also unclear if the risks associated with elevated BMI were driven by increased muscle, fat, or fluid, and whether already established mechanisms, such as the known association with peritonitis, or concerns regarding adequate small solute clearance or metabolic complications exacerbated by glucose absorption could explain this. The US had a greater proportion of high BMI individuals and greatest use of hypertonic (4.25%) PD solutions. Whether or not glucose minimization strategies may mitigate these risks requires further study.

We found that routine multidisciplinary review had a trend to lower risk of HD transfer. Patient review may facilitate identification of at-risk patients and earlier interventions which could mitigate HD transfer events but may be a proxy for other practices, such as the routine availability of allied health professionals such as pharmacists, dietitians, and social workers.

We found no consistent relationship between PD facility size and the risk of HD transfer. In countries such as the US, the majority of facilities treat fewer than 20 patients 24, but to ascribe practices at a facility to outcomes, the PDOPPS sample required a minimum number of 20 PD patients per facility for study participation. These results should be exercised with caution because it is possible that all PDOPPS clinic sizes may have been above a critical threshold whereby no relationship exists between size and outcomes. This is supported by a systematic review demonstrating small facility size adversely impacts outcomes predominantly with clinic sizes less than 20.34

The 2006 ISPD PD prescribing guidelines emphasized the need for a total (peritoneal and kidney) Kt/V of 1.7 based on limited evidence, 35 and many national quality metrics now focus on this 36. Recent ISPD guidelines and a KDOQI commentary have de-emphasized the role of small solute clearance in delivering high quality PD care, recommending that many other factors be considered 37, 38. We found no relationship between the proportion of patients at a facility at PDOPPS enrollment achieving a total Kt/V of 1.7 or higher on the risk of death or HD transfer. This needs to be interpreted in the context of the restricted number of facilities for which this was available. However, this finding reinforces the need to reevaluate facility-based Kt/V as a quality measure and a sole marker of the quality of dialysis delivery. Just over 50% of problems with solute clearance causing HD transfer were due to concerns over Kt/V (Supplementary Table 3). It is unclear if this was the sole indication to transfer to HD but if so it suggests that a significant minority of patients may experience HD transfer unnecessarily.

The strengths of this study include the large, diverse, multinational patient sample providing a unique opportunity to quantify and explore time on PD differences and mortality risks across countries. Furthermore, interpretation of the patient factors shown in Figures 4A and 4B should be understood to represent their independent contribution within the models used, outside of the treatment factors listed, and not an attempt to describe their overall causal impact, as per the ‘table 2 fallacy’ described by Westreich et al39. The PDOPPS sample relies on voluntary participation and, despite attempts to obtain national representative samples, differences may result from restriction of recruitment to clinics with more than 20 patients and other minor differences may exist in facility and patient characteristics compared with non-participating clinics and patients40,41. We explored a select set of patient and facility characteristics, but our findings may have been impacted by unmeasured confounding or informative censoring.

Notwithstanding these limitations, we have demonstrated differences in median time on PD across countries in PDOPPS and the important role that death and particularly kidney transplantation play in their interpretation. Infection continues to remain a leading cause of HD transfer across all countries. In all countries, opportunities exist to improve time on PD. PDOPPS will continue to focus on identifying important facility practices that will shed light on reducing premature HD transfer and improve survival and quality of life for patients receiving PD.

**Disclosures**

Simon J. Davies has received consulting fees from Baxter Healthcare and Ellen Medical. He has received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Fresenius Medical Care.

Hideki Kawanishi has no conflicts of interest to declare.

Mauricio Sanabria is an employee of Baxter Renal Care Services, a company of Baxter Health Care Corp.

Talerngsak Kanjanabuch has received consultancy fees from VISTERRA as a country investigator and current recipient of the National Research Council of Thailand and received speaking honoraria from Astra Zeneca and Baxter Healthcare.

Jenny I. Shen has received funding from the Canadian Institutes of Health Research and is supported by grant K23DK103972 from the NIH-NIIDDK.

Yong-Lim Kim received speaker honorarium from FibroGen.

James A. Sloand was employed by Baxter Healthcare Corporation at the time of conception/planning of work, employed by AstraZeneca at the time of development, and owner of Baxter and AstraZeneca Stock/Options.

Mark Lambie has received speakers honoraria from Baxter Healthcare and Fresenius Medical Care. He received a research grant from Baxter Healthcare in 2013.

David W. Johnson has received consultancy fees, research grants, speaker’s honoraria and travel sponsorships from Baxter Healthcare and Fresenius Medical Care, consultancy fees from Astra Zeneca, Bayer, and AWAK, speaker’s honoraria from ONO and BI & Lilly, and travel sponsorships from Ono and Amgen. He is a current recipient of an Australian National Health and Medical Research Council Leadership Investigator Grant.

Jeffrey Perl reports grants from AHRQ, during the conduct of the study; personal fees from Baxter Healthcare, Fresenius medical care, Davita Healthcare Partners, US Renal Care, Astra Zeneca Canada and is on the advisory board for Liberdi, outside of the submitted work.

Junhui Zhao, Keith McCullough, Ronald L. Pisoni, Bruce M. Robinson are employees of Arbor Research Collaborative for Health, which administers the DOPPS Programs. Global support for the ongoing DOPPS Program is provided without restriction on publications by a variety of funders. For details see https://www.dopps.org/AboutUs/Support.aspx. Bruce Robinson has received consultancy fees or travel reimbursement since 2018 from AstraZeneca, GlaxoSmithKline, and Kyowa Kirin Co., all paid directly to his institution of employment.

**Funding**

This manuscript was directly supported by Baxter International Inc. (USA). The Dialysis Outcomes and Practice Patterns Study (DOPPS) Program is funded by a consortium of private industry, public funders, and professional societies. More information on DOPPS funding can be found here: <https://www.dopps.org/AboutUs/Support.aspx>.

Funding for PDOPPS has been provided by: National Health and Medical Research Council (Australia); National Institute for Health Research (UK); National Institute of Diabetes and Digestive and Kidney Diseases, (USA); Patient-Centered Outcomes Research Institute, (USA); Japanese Society of Peritoneal Dialysis; Canadian Institute for Health Research (Canada); Baxter International Inc. (USA); The National Research Council of Thailand (2558-113); Rachadaphiseksompot Endorcement Fund (GCURS\_59\_12\_30\_03), Chulalongkorn University, Thailand; and the National Science and Technology Development Agency (NSTDA), Thailand.

# Author Contributions

1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data: JZ, BMR, ML, DWJ, JS, Y-LK, JP, KM, TK, RLP, SJD

2) drafting the article or revising it critically for important intellectual content: JZ, BMR, ML, DWJ, HK, JS, Y-LK, JIS, JP, KM, MS, TK, RLP, SJD

3) final approval of the version to be published: JZ, BMR, ML, DWJ, HK, JS, Y-LK, JIS, JP, KM, MS, TK, RLP SJD

4) agreement to be accountable for all aspects of the work: JZ, BMR, ML, DWJ, HK, JS, JIS, JP, KM, MS, TK, RLP, SJD

Jeffrey Perl confirms that he has had full access to the data in the study and final responsibility for the decision to submit for publication.

# Acknowledgments

*We acknowledge and thank the following individuals for their contributions.*

*PDOPPS Steering Committee members: David Johnson (Australia); Jeffrey Perl (Canada); Hideki Kawanishi (Japan); Yong-Lim Kim (South Korea); Talerngsak Kanjanabuch (Thailand); Simon Davies (United Kingdom); Angelito Bernardo, Ron Pisoni, Bruce Robinson, Jenny Shen (United States). Additional PDOPPS Research Group members: Sunil Badve, Neil Boudville, Fiona Brown, Josephine Chow, John Collins, Rachael Morton, Scott Wilson (Australia); Andreas Vychytil (Austria); Wim Van Biesen (Belgium); Ana Figueiredo, Thyago de Moraes (Brazil); Gillian Brunier, Arsh Jain, Vanita Jassal, Sharon Nessim, Matthew Oliver, Valerie Price, Rob Quinn (Canada); Wei Fang (China); CC Szeto, Angela Wang (Hong Kong); Mizuya Fukasawa, Yasuhiko Ito, Munekazu Ryuzaki, Tadashi Tomo (Japan); Alfonso Cueto Manzano (Mexico); Mark Marshall (New Zealand); Susanne Ljungman (Sweden); Sarinya Boongird, Chanchana Boonyakrai, Areewan Cheawchanwattana, Guttiga Halue, Suchai Sritippayawan, Sajja Tatiyanupanwong, Kriang Tungsanga (Thailand); Elaine Bowes, Edwina Brown, Richard Fluck, Bak Leong Goh, Helen Hurst, Martin Wilkie, Graham Woodrow (United Kingdom); Filitsa Bender, Judith Bernardini, Dinesh Chatoth, John Crabtree, Fred Finkelstein, Arshia Ghaffari, Rajnish Mehrotra, Beth Piraino, Martin Schreiber, Isaac Teitelbaum (United States).*

Jennifer McCready-Maynes, an employee of Arbor Research Collaborative for Health, provided editorial support for this paper.

**Supplemental Material ToC**

Supplement Figure 1A. Cumulative incidence curve of death, HD transfer, and transplant, in A/NZ, including all temporary transfer as HD transfer event.

Supplement Figure 1B. Cumulative incidence curve of death, HD transfer, and transplant, in Canada, including all temporary transfer as HD transfer event.

Supplement Figure 1C. Cumulative incidence curve of death, HD transfer, and transplant, in Japan, including all temporary transfer as HD transfer event.

Supplement Figure 1D. Cumulative incidence curve of death, HD transfer, and transplant, in Thailand, including all temporary transfer as HD transfer event

Supplement Figure 1E. Cumulative incidence curve of death, HD transfer and transplant, in UK, including all temporary transfer as HD transfer event.

Supplement Figure 1F. Cumulative incidence curve of death, HD transfer, and transplant, in US, including all temporary transfer as HD transfer event.

Supplement Figure 2. Hazard ratio of PD discontinuation by country, compare to US, not counting hybrid transfers as transfer to HD events. Hazard ratio was estimated using left truncated Cox model based on PD vintage. Model adjusted for patient age, sex, BMI, black race, heart disease, diabetes, psychiatric disorder, prior HD experience, urine volume, albumin, care giver involvement, transplant waitlist referred, and accounting for facility clustering. Separate models for each outcome.

Supplement Table 1. Distribution of time on therapy in years by country, based on cumulative incidence curve in Figure 1.

Supplemental Table 2. Hazard ratios for mortality with 95% confidence interval in comparison to the US, showing effects of sequential levels of adjustment.

Supplemental Table 3. Detailed reason among 111 patients with solute clearance as reason for HD transfer.

Supplemental Table 4A. Hazard ratio for patient characteristics.

Supplemental Table 4B. Adjusted hazard ratio of facility factors.

Supplemental Table 5. Adjusted hazard ratio for other facility factors, overall and by country, for outcomes of: A) death or HD transfer B) HD transfer, C) for death. Models were left truncated based on PD vintage, and accounting for facility clustering. Facility factors were evaluated one at a time, adjusted for patient factors including: age, sex, BMI, Black race, heart disease, diabetes, psychiatric disorder, prior HD experience, urine volume, albumin, care giver involvement, transplant waitlist referred.

Supplemental Figure 3. Crude event rates by country and by PD vintage, A) permanent transfer to HD or death, B) permanent transfer to HD, C) death. Number of patients at risk for each PD vintage group see table below.

References

Pecoits-Filho R, Okpechi IG, Donner JA, Harris DC, Aljubori HM, Bello AK, Bellorin-Font E, Caskey FJ, Collins A, Cueto-Manzano AM, Feehally J: Capturing and monitoring global differences in untreated and treated end-stage kidney disease, kidney replacement therapy modality, and outcomes. Kidney Int Suppl 10(1):e3-e9, 2020

Li PK, Chow KM, Van de Luijtgaarden MW, Johnson DW, Jager KJ, Mehrotra R, Naicker S, Pecoits-Filho R, Yu XQ, Lameire N: Changes in the worldwide epidemiology of peritoneal dialysis. Nat Rev Nephrol. 13: 90–103, 2017

Collins AJ, Hao W, Xia H, Ebben JP, Everson SE, Constantini EG, Ma JZ: Mortality risks of peritoneal dialysis and hemodialysis. Am J Kidney Dis. 34(6):1065-74, 1999

McDonald SP, Marshall MR, Johnson DW, Polkinghorne KR: Relationship between dialysis modality and mortality. J Am Soc Nephrol. 20(1):155-63, 2009

Weinhandl ED, Foley RN, Gilbertson DT, Arneson TJ, Snyder JJ, Collins AJ: Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. J Am Soc Nephrol 21(3):499-506, 2010

Trinh E, Chan CT, Perl J: Dialysis modality and survival: Done to death. In: Seminars in dialysis Vol. 31, No. 4, pp. 315-324, 2018

Karopadi AN, Mason G, Rettore E, Ronco C: Cost of peritoneal dialysis and haemodialysis across the world. Nephrol Dial Transplant. 28(10):2553-69, 2013

Rubin HR, Fink NE, Plantinga LC, Sadler JH, Kliger AS, Powe NR: Patient ratings of dialysis care with peritoneal dialysis vs hemodialysis. Jama. 291(6):697-703, 2004

Moist LM, Port FK, Orzol SM, Young EW, Ostbye T, Wolfe RA, Hulbert-Shearon T, Jones CA, Bloembergen WE: Predictors of loss of residual renal function among new dialysis patients. J Am Soc Nephrol. 11(3):556-64, 2000

Misra M, Vonesh E, Van Stone JC, Moore HL, Prowant B, Nolph KD: Effect of cause and time of dropout on the residual GFR: a comparative analysis of the decline of GFR on dialysis. Kidney Inter. 59(2):754-63, 2001

Jansen MA, Hart AA, Korevaar JC, Dekker FW, Boeschoten EW, Krediet RT: Predictors of the rate of decline of residual renal function in incident dialysis patients. Kidney inter. 62(3):1046-53, 2002

Chuengsaman P, Kasemsup V: PD first policy: Thailand’s response to the challenge of meeting the needs of patients with end-stage renal disease. In: Seminars in nephrology Vol. 37, No. 3, pp. 287-295, 2017

Mehrotra R, Kermah D, Fried L, Kalantar-Zadeh K, Khawar O, Norris K, Nissenson A: Chronic peritoneal dialysis in the United States: declining utilization despite improving outcomes. J Am Soc Nephrol. 18(10):2781-8, 2007

Imbeault B, Nadeau-Fredette AC: Optimization of dialysis modality transitions for improved patient care. Can J Kidney Health Dis. 2054358119882664, 2019

Chui BK, Manns B, Pannu N, Dong J, Wiebe N, Jindal K, Klarenbach SW: Health care costs of peritoneal dialysis technique failure and dialysis modality switching. Am J Kidney Dis. 61(1):104-11, 2013

Manera KE, Johnson DW, Craig JC, Shen JI, Gutman T, Cho Y, Wang AY, Brown EA, Brunier G, Dong J, Dunning T: Establishing a core outcome set for peritoneal dialysis: report of the SONG-PD (Standardized Outcomes in Nephrology–Peritoneal Dialysis) consensus workshop. Am J Kidney Dis. 75(3):404-12, 2020

Perl J, Davies SJ, Lambie M, Pisoni RL, McCullough K, Johnson DW, Sloand JA, Prichard S, Kawanishi H, Tentori F, Robinson BM: The Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS): unifying efforts to inform practice and improve global outcomes in peritoneal dialysis. Perit Dial Int. 36(3):297-307, 2016

Fine JP, Gray RJ: A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc 94(446):496-509, 1999

Austin PC, Lee DS, Fine JP: Introduction to the analysis of survival data in the presence of competing risks. Circulation. 133(6):601-9, 2016

Raghunathan T, Solenberger P, Van Hoewyk J: IVEware: Imputation and Variance Estimation Software User Guide. 2002

Little R, Rubin D: Statistical Analysis with Missing Data. J. Educ. Stat. 16: 150–155, 1991

Churchill DN, Thorpe KE, Vonesh EF, Keshaviah PR: Lower probability of patient survival with continuous peritoneal dialysis in the United States compared with Canada. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol. 8(6):965-71, 1997

United States Renal Data System. 2020 *USRDS Annual Data Report: Epidemiology of kidney disease in the United States.* National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2020.

Sukul N, Mukhopadhyay P, Schaubel DE, Pearson J, Turenne M, Saran R, Robinson BM, Pisoni RL: Peritoneal dialysis and mortality, kidney transplant, and transition to hemodialysis: trends from 1996-2015 in the United States. Kidney med. 2(5):610-9, 2020

1. McGill RL, Weiner DE, Ruthazer R, Miskulin DC, Meyer KB, Lacson E Jr. Transfers to Hemodialysis Among US Patients Initiating Renal Replacement Therapy With Peritoneal Dialysis. Am J Kidney Dis. 2019 Nov;74(5):620-628. doi: 10.1053/j.ajkd.2019.05.014. Epub 2019 Jul 10. PMID: 31301926; PMCID: PMC6815249.

Changsirikulchai S, Sriprach S, Thokanit NS, Janma J, Chuengsaman P, Sirivongs D: Survival analysis and associated factors in Thai patients on peritoneal dialysis under the PD-first policy. Perit Dial Int. 38(3):172-8, 2018

1. Kanjanabuch T, Takkavatakarn K: Global dialysis perspective: Thailand. Kidney360. 30;1(7):671-5, 2020

Kolesnyk I, Dekker FW, Boeschoten EW, Krediet RT.: Time-dependent reasons for peritoneal dialysis technique failure and mortality. Perit Dial Int. 30(2):170-7, 2010

Brown EA, Zhao J, McCullough K, Fuller DS, Figueiredo AE, Bieber B, Finkelstein FO, Shen J, Kanjanabuch T, Kawanishi H, Pisoni RL: Burden of kidney disease, health-related quality of life, and employment among patients receiving peritoneal dialysis and in-center hemodialysis: findings from the DOPPS Program. Am J Kidney Dis, 2021

Troidle L, Watnick S, Wuerth DB, Gorban-Brennan N, Kliger AS, Finkelstein FO: Depression and its association with peritonitis in long-term peritoneal dialysis patients. Am J Kidney Dis. 42(2):350-4, 2003

Perl J, Wald R, Bargman JM, Na Y, Jassal SV, Jain AK, Moist L, Nessim SJ: Changes in patient and technique survival over time among incident peritoneal dialysis patients in Canada. Clin J Am Soc Nephrol. 7(7):1145-54, 2012

Jegatheesan D, Johnson DW, Cho Y, Pascoe EM, Darssan D, Htay H, Hawley C, Clayton PA, Borlace M, Badve SV, Sud K: The relationship between body mass index and organism-specific peritonitis. Perit Dial Int. 38(3):206-14, 2018

McDonald SP, Collins JF, Rumpsfeld M, Johnson DW: Obesity is a risk factor for peritonitis in the Australian and New Zealand peritoneal dialysis patient populations. Perit Dial Int. 24(4):340-6, 2004

Pieper D, Mathes T, Marshall MR: A systematic review of the impact of center volume in dialysis. BMC research notes. 8(1):1-9, 2015

Lo WK, Bargman JM, Burkart J, Krediet RT, Pollock C, Kawanishi H: Guideline on targets for solute and fluid removal in adult patients on chronic peritoneal dialysis. Perit Dial Int. 26(5):520-2, 2006

1. Finalized PY 2018 Clinical Measure; Kt/V Dialysis Adequacy Measure Topic: Hemodialysis .https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/ESRDQIP/Downloads/ESRDQIPPY2018finaltechnicalmeasurespecifications-.pdf

Brown EA, Blake PG, Boudville N, Davies S, de Arteaga J, Dong J, Finkelstein F, Foo M, Hurst H, Johnson DW, Johnson M: International Society for Peritoneal Dialysis practice recommendations: Prescribing high-quality goal-directed peritoneal dialysis. Perit Dial Int. 40(3):244-53, 2020

Teitelbaum I, Glickman J, Neu A, Neumann J, Rivara MB, Shen J, Wallace E, Watnick S, Mehrotra R: KDOQI US commentary on the 2020 ISPD practice recommendations for prescribing high-quality goal-directed peritoneal dialysis. Am J Kidney Dis. 77(2):157-71, 2021

Westreich D, Greenland S. The table 2 fallacy: presenting and interpreting confounder and modifier coefficients. Am J Epidemiol. 2013 Feb 15;177(4):292-8. doi: 10.1093/aje/kws412. Epub 2013 Jan 30. PMID: 23371353; PMCID: PMC3626058.

Ethier I, Boudville N, McDonald S, et al. Representativeness of the PDOPPS cohort compared to the Australian PD population. Peritoneal Dialysis International. November 2021. doi:10.1177/08968608211056242

PDOPPS Practice Monitor. DPM-PD Sampling, Study Design, and Calculation Methods. https://www.dopps.org/DPM-PD/Data\_Sources\_Methods.pdf

Table 1A. Patient characteristics.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   | **A/NZ** | **Canada** | **Japan** | **Thailand** | **UK** | **US** |
|  |   |   |   |   |   |   |
| Number of patients | 549 | 907 | 795 | 830 | 354 | 3686 |
| Patient age, years | 63(14) | 61(15) | 64(13) | 56(14) | 60(15) | 58(15) |
| Male sex, % | 67% | 62% | 67% | 51% | 64% | 56% |
| Time on PD, years | 1.33(1.69) | 1.24(2.04) | 1.86(2.32) | 1.50(1.86) | 1.34(2.06) | 1.53(1.84) |
| Body mass index, kg/m2 |  |  |  |  |  |  |
|    < 20 | 3% | 6% | 19% | 26% | 6% | 4% |
|    20-29 | 68% | 65% | 77% | 68% | 69% | 56% |
|    30+ | 28% | 29% | 4% | 5% | 26% | 40% |
| Race, % |  |  |  |  |  |  |
|    Asian | 17% | 13% | 100% | 99% | 8% | 4% |
|    Black |  0% | 5% | 0% | 0% | 4% | 26% |
|    White | 70% | 70% | 0% | 0% | 86% | 68% |
|    Other | 13% | 12% | 0% | 1% | 2% | 2% |
| Heart disease, % | 50% | 49% | 42% | 24% | 44% | 37% |
| Diabetes, % | 44% | 48% | 40% | 49% | 27% | 52% |
| Psychiatric disorderⱡ, % | 10% | 14% | 3% | 1% | 7% | 19% |
| Prior HD\*, % | 20% | 24% | 17% | 39% | 15% | 36% |
| Urine volume, L/24 hr | 0.98(0.76) | 1.06(0.74) | 0.90(0.62) | 0.50(0.58) | 1.27(0.83) | 0.83(0.77) |
| Caregiver(s) involved in PD exchanges\*, % | 17% | 19% | 13% | 60% | 23% | 16% |
| Albumin, g/dL  | 3.25(0.48) | 3.44(0.51) | 3.32(0.52) | 3.27(0.60) | 3.42(0.55) | 3.51(0.46) |
| Transplant waitlist referred\*,% | 48% | 51% | 15% | 24% | 62% | 58% |

ⱡ Psychiatric disorders include depression, bipolar disorder, schizophrenia/psychotic disorder, alcohol abuse w/in past 12 months, or other substance abuse w/in past 12 months. \* Prior HD, caregiver(s) involved in PD exchanges, Transplant waitlist referred, and PD solution dextrose concentration were missing in US large dialysis organizations. Results shown as prevalence, mean (standard deviation), or median [interquartile range]

Table 1B Facility characteristics.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|   | **A/NZ** | **Canada** | **Japan** | **Thailand** | **UK** | **US** |
| Number of facilities | 20 | 20 | 31 | 22 | 19 | 106 |
| Facility size | 53[36,82] | 51[40,90] | 29[20,36] | 102[48,208] | 50[27,65] | 32[24,43] |
| Patient nurse ratio | 11[7,13] | 14[11,17] | 5.78[2.58,8.00] | 38[19,49] | 8.13[6.63,9.25] | 11[8,14] |
| Facility years experience treating PD patients |  |  |  |  |  |
|    <5 | 0% | 0% | 0% | 5% | 0% | 7% |
|    5-9 | 9% | 15% | 0% | 68% | 0% | 28% |
|    10+ | 91% | 85% | 100% | 27% | 100% | 65% |
| Facility % of patients total Kt/V urea < 1.7 |  |  |  |  |  |  |
|    <10% | 29% | 24% | 17% | 25% | 40% | 69% |
|    10-19% | 24% | 35% | 8% | 17% | 50% | 26% |
|    20%+ | 47% | 41% | 75% | 58% | 10% | 5% |
| Facility % of patients use 4.25% solution |  |  |  |  |  |
|    0% | 47% | 32% | 96% | 24% | 79% | 12% |
|    1-19% | 37% | 53% | 4% | 52% | 21% | 8% |
|    20%+ | 16% | 16% | 0% | 24% | 0% | 80% |
| Routine multidisciplinary review  | 50% | 40% | 69% | 46% | 79% | 81% |

Results shown as prevalence, or median [interquartile range]

**Figure Legends**

**Figure 1A. Cumulative incidence curve of death, HD TRANSFER, and transplant, in A/NZ.**

**Figure 1B. Cumulative incidence curve of death, HD TRANSFER, and transplant, in Canada.**

**Figure 1C. Cumulative incidence curve of death, HD TRANSFER, and transplant, in Japan.**

**Figure 1D. Cumulative incidence curve of death, HD TRANSFER, and transplant, in Thailand.**

**Figure 1E. Cumulative incidence curve of death, HD TRANSFER, and transplant, in UK.**

**Figure 1F. Cumulative incidence curve of death, HD TRANSFER, and transplant, in US.**

**Figure 2. Hazard ratio of PD discontinuation due to death/HD TRANSFER, death, HD TRANSFER, or transplant, by country, compared to the US. Hazard ratios were estimated separately for each outcome using Cox models left truncated based on PD vintage. Models were adjusted for patient age, sex, BMI, Black race, heart disease, diabetes, psychiatric disorder, prior HD experience, urine volume, albumin, care giver involvement, transplant waitlist referred, and accounting for facility clustering. Transplant waitlist referred was excluded as an adjustment from the model for transplant outcome.**

**Figure 3. Primary and secondary reasons patients switch to HD, A) by country, B) by PD vintage at time of modality switch. Excluding EHR data where no reason was reported, with 287 events. Another 196 events were excluded due to missing reason.**

**Figure 4A. Hazard ratio for patient characteristics. Hazard ratio was estimated using left truncated Cox model based on PD vintage. Model adjusted for patient age, sex, BMI, black race, heart disease, diabetes, psychiatric disorder, prior HD experience, urine volume, albumin, care giver involvement, transplant waitlist referred, and accounting for facility clustering. Separate models for each outcome.**

**Figure 4B. Adjusted hazard ratio of facility factors. Hazard ratio was estimated using left truncated Cox model based on PD vintage. Model adjusted for patient age, sex, BMI, black race, heart disease, diabetes, psychiatric disorder, prior HD experience, urine volume, albumin, care giver involvement, transplant waitlist referred, and accounting for facility clustering. Separate models for each outcome.** For facility size and patient nurse ratio, small<=q1, large>=q3, medium q1-q3, within country. Median IQR were listed in Table 1B.