

ORIGINAL RESEARCH

Comparing Treatment Modalities for End-Stage Renal Disease: A Meta-Analysis

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BACKGROUND: End-stage renal disease (ESRD) imposes significant economic and social burdens on patients and healthcare systems. In the United States alone, more than 600,000 Americans have ESRD, with an estimated annual cost of treatment of more than \$30 billion. Peritoneal dialysis and hemodialysis are competing renal replacement therapies in ESRD; however, data comparing quality-of-life outcomes between these 2 modalities are limited.

OBJECTIVES: To compare the effectiveness of peritoneal dialysis with the more common treatment modality of hemodialysis on the health-related quality of life (HRQoL) of patients with ESRD in the general, physical, and psychological domains; and to determine whether the time of publication and the origin of each study influenced its findings regarding the effectiveness of the 2 modalities.

METHODS: This meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines to collect the data. PubMed, MEDLINE, and PsycINFO were the primary databases searched. Only articles published in English were included in this meta-analysis. The measure of effect size was Cohen's standardized mean difference. A random-effects model was used to test the hypothesis of equality in the mean HRQoL.

RESULTS: A total of 15 studies with a combined sample size of 4318 patients met the study criteria and were included in the analysis. The pooled effect sizes based on the random-effects model were 0.24 (95% confidence interval [CI], -0.17-0.66) in the general domain; 0.10 (95% CI, -0.09-0.29) in the physical-functioning domain; and 0.29 (95% CI, -0.13-0.71) in the psychological-functioning domain. None of the summary effect sizes was statistically significant. Subgroup analyses favored peritoneal dialysis regarding the time and country of publication.

CONCLUSION: The majority of the studies included in this analysis favored peritoneal dialysis over hemodialysis in all 3 domains. However, the pooled effect sizes were not significant, resulting in the inability to conclude that peritoneal dialysis is the more effective of these 2 treatment modalities.

KEY WORDS: end-stage renal disease, health-related quality of life, hemodialysis, peritoneal dialysis, random-effects model, subgroup analysis

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End-stage renal disease (ESRD), also known as stage 5 kidney disease, is characterized by permanent kidney failure. At this stage, renal replacement therapies, such as dialysis or kidney transplantation, are mandatory.^{1,4} Currently, more than 678,000 Americans have ESRD, and projections indicate that the population of patients with this disease may exceed 2 million by 2030.^{1,2} ESRD places an enormous economic and social burden on patients and the healthcare system, with annual treatment costs in excess of \$32 billion.¹ Hemodialysis and peritoneal dialysis are 2 competing renal replacement therapies for ESRD, with hemodialysis being the most common treatment.¹ However, in recent years, a notable increase has been seen in the number of patients with

ESRD who start dialysis with peritoneal dialysis.¹

Technologic advances in dialysis therapy have contributed to the improved survival of patients with ESRD.^{1,3} Despite this, the day-to-day quality of life of patients with ESRD is still much lower than that of the overall population.^{1,3,4} With the projected rise in the incidence of ESRD, and the increasing healthcare costs, it is imperative that we identify robust interventions for patients with ESRD.¹⁻⁵

Health-related quality of life (HRQoL) reflects the welfare of patients based on their functional status in the physical, mental, and social domains, balanced with expectations and experiences in the face of a changing health status.⁶ Because of its importance as a critical measurement of the overall well-being of patients with ESRD, the Centers for Medicare & Medicaid Services has mandated that the HRQoL of patients on dialysis be evaluated on an annual basis.⁷

Today, medical research is increasingly focusing on

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HRQoL as an important variable for decision-making, and many randomized clinical trials now include HRQoL measures in assessing morbidity and mortality.⁸ Furthermore, it has become customary for clinicians and for public health officials to use HRQoL data to measure the effects of chronic diseases and treatments.

Quality of life is measured through the use of a wide variety of instruments, including the Short Form 12 (SF-12) and Short Form 36 (SF-36) outcome questionnaires,^{9,12} and other internationally recognized variants of these instruments, such as the World Health Organization (WHO) Quality of Life Survey (WHOQOL-100) and its modified version, the WHOQOL-BREF.¹³⁻¹⁶ According to the Centers for Disease Control and Prevention, HRQoL data can include aspects of patients' employment, personal wealth, environment, physical health, mental health, education, and recreation and leisure time.⁹

Published studies regarding the effect of dialysis modalities on the HRQoL of patients with ESRD have been conflicting. This may, in part, be caused by the wide variety of measures used to evaluate HRQoL, as well as the diversity among patients and populations used in HRQoL assessments.¹⁷ In general, research studies have agreed that patients who have had a transplant enjoy a better HRQoL than patients undergoing dialysis. By contrast, studies that compare the relative effectiveness of hemodialysis and peritoneal dialysis have been polarized in their findings regarding the dominance of one treatment versus the other.^{1,18} However, meta-analysis can provide a common metric for analyzing HRQoL data, regardless of the assessment used for measuring quality of life.^{17,19}

The main objective of this meta-analysis was to determine the relative effectiveness of peritoneal dialysis on the HRQoL of patients with ESRD versus hemodialysis, which is the predominant treatment modality in the United States. Our analysis also sought to determine whether 2 moderator variables—the time of publication and the origin of each study—influenced the findings of the studies on the relative effectiveness of hemodialysis and peritoneal dialysis.

Methods

This study used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines during data collection and management. **Figure 1** provides a flow chart illustrating the search process and the inclusion and exclusion criteria.

First, we conducted a review of the literature (studies in English only) on the effectiveness of dialysis modalities for patients with ESRD. The primary strategy used for finding published studies was a search of the PubMed, MEDLINE, and PsycINFO databases, which are among the most frequently used in healthcare research.

KEY POINTS

- ESRD places an economic and social burden on patients and healthcare, and its incidence is increasing.
- The main goal of this meta-analysis was to compare peritoneal dialysis and hemodialysis treatments in studies related to quality of life in patients with ESRD in 3 main domains.
- The second goal was to establish whether the study's year of publication and origin impacted the findings on the effectiveness of hemodialysis and peritoneal dialysis.
- Pooled effects based on the 15 studies that met the study criteria were 0.24 in the general domain, 0.10 in the physical-functioning domain, and 0.29 in the psychological-functioning domain.
- Most studies favored peritoneal dialysis over hemodialysis in all 3 domains.
- Although none of the pooled effect sizes was statistically significant, subgroup analyses favored peritoneal dialysis over hemodialysis in terms of year and country of origin.
- But the results could not confirm that peritoneal dialysis is more effective than hemodialysis.
- Future studies are needed to determine which of these 2 modalities improves the quality of life for patients with ESRD.

The next strategy was to contact a content expert to find studies that might have been missed in the primary search. All relevant studies between the years 2000 and 2017 were considered for inclusion. The key words used during the search phase included:

- “ESRD/ESKD,” “end-stage renal disease,” and “end-stage kidney disease” used as interchangeable terms
- “HD vs PD” and “hemodialysis vs peritoneal dialysis” used as interchangeable terms and refer to comparative studies of the 2 main treatment modalities investigated
- “Dialysis modalities compared” used to extract studies that compared modalities for ESRD
- “Quality of life” and “health-related quality of life” used to extract studies that covered topics on HRQoL of patients with ESRD.

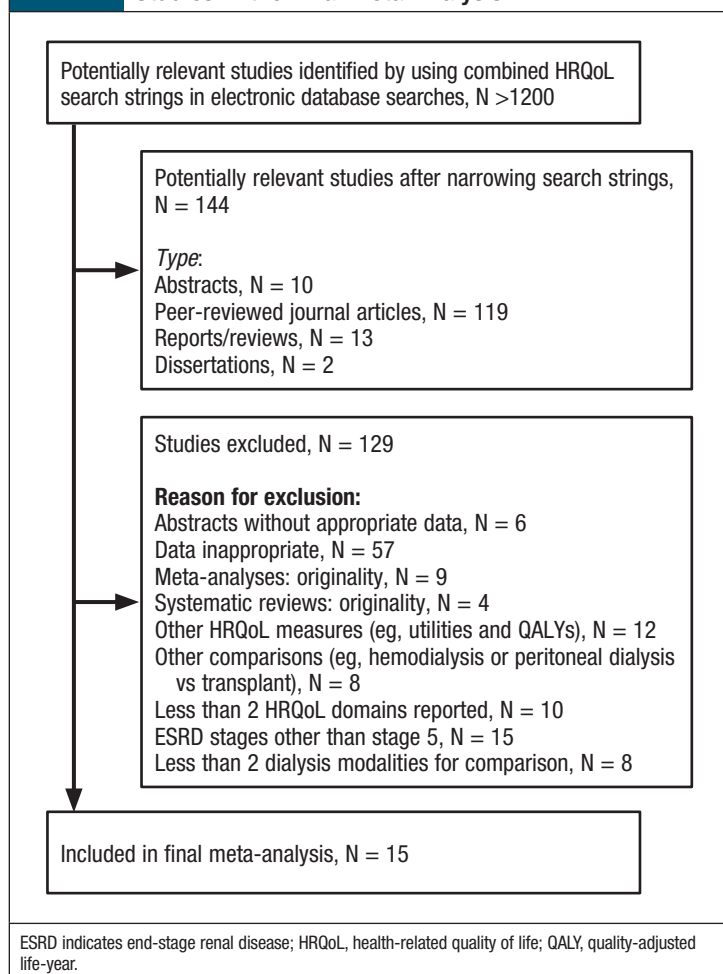
We also screened meta-analyses related to HRQoL for additional citations.

Inclusion and Exclusion Criteria

To be included in the analysis, studies had to meet the following criteria: have a publication date between the

Figure 1

Flow Chart Illustrating the Search Process, Reasons for Including or Excluding Studies, and Number of Studies in the Final Meta-Analysis



years 2000 and 2017; journal articles had to report the original data (ie, sample sizes, means, and standard deviations) to enable the calculation of the effect sizes; the instruments used for measuring HRQoL had to meet WHO standards; the studies were required to compare the 2 dialysis modalities (ie, hemodialysis and peritoneal dialysis); the patients' disease progression had to be stage 5 (end-stage), and patients had to be on dialysis for more than 1 year and at the time the study was done; the study data had to be reported for at least 2 of the 3 HRQoL domains addressed in our analysis.

All relevant journal articles that compared the effectiveness of peritoneal dialysis and hemodialysis were considered. These included abstracts, conference proceedings, case reports, dissertations, randomized controlled trials, and observational studies. By including small and large studies in the analysis, we enhanced our opportunities for reducing publication bias. Furthermore,

we increased the potential for capturing important effects that otherwise might not have been detected.^{20,21}

For example, researchers often omit small studies because of their perceived insignificance, which is not always a good practice. In many cases, small representative studies, particularly those representative of patients' comorbid conditions and health interventions being compared, can capture treatment effects that would have been lost if these studies were omitted. In addition, randomized controlled trials are the standard for making evidence-based decisions about the effectiveness of health interventions. A small clinical trial that is externally valid (ie, representative) can yield important findings about the interventions being compared. Therefore, evidence-based research should focus not only on large, but also on small studies, based on the assumption that they are representative studies.

The enlarged sample size afforded by including all relevant journal articles also facilitated subgroup analyses that could potentially reveal patterns of effectiveness related to the time and place of study. Finally, combining data from studies of different sizes, time frames, and country of origin can improve external validity.^{20,21} For studies with the same health outcome indicator, the interventions are comparable.²²

Therefore, all eligible studies reporting measures of HRQoL in the physical, psychological, and general domains in patients with ESRD who undergo peritoneal dialysis or hemodialysis were selected. Studies reporting the clinical and epidemiologic aspects of ESRD were not considered. Systematic reviews and meta-analyses with secondary data were not considered for inclusion.

Assessment of Study Quality

The primary function of coding assigned to each study was used to establish the criteria for assessing the quality of selected studies, and to identify the potential moderator variables. Two independent coders were used during the coding process. Whenever discrepancies were found, they were reconciled through discussion. Coders were not blinded to authors, affiliations, or journal names, because previous studies have shown this to be unnecessary.²³

Data Analysis

Test for homogeneity. The between-studies test of homogeneity for the outcome variable was achieved through the calculation of *Q*-statistics. These statistics provide descriptive information of within- and between-study variations. Tests for homogeneity have low power, and failure to reject the null hypothesis does not provide conclusive evidence of the absence of between-study variation.²³ Because of the wide variability in extracted studies (ie, sample sizes, time, and country

Table 1 Characteristics of Studies Included for Data Synthesis and Analysis

Study	Study title	Location	Sample size: hemodialysis vs peritoneal dialysis, N	Assessment method(s)	HRQoL domain(s) covered
Atapour et al, 2016 ²⁸	A comparison of the quality of life of the patients undergoing hemodialysis versus peritoneal dialysis and its correlation to the quality of dialysis	Iran	46:46	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Brown et al, 2010 ¹⁰	Broadening Options for Long-term Dialysis in the Elderly (BOLDE): differences in quality of life on peritoneal dialysis compared to haemodialysis for older patients	United Kingdom	70:70	Questionnaire (HRQOL SF-12) version 2	Physical functioning Psychological functioning
Zhang et al, 2007 ³⁰	Comparison of quality of life and causes of hospitalization between hemodialysis and peritoneal dialysis patients in China	China	408:654	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Theofilou, 2011 ¹³	Quality of life in patients undergoing hemodialysis or peritoneal dialysis treatment	Greece	84:60	Questionnaire (WHOQOL-BREF) ^a	General HRQoL Physical functioning Psychological functioning
Ginieri-Coccosis et al, 2008 ¹⁵	Quality of life, mental health and health beliefs in haemodialysis and peritoneal dialysis patients: investigating differences in early and later years of current treatment	Greece	38:17	Questionnaire (WHOQOL-BREF) ^a	General HRQoL Physical functioning Psychological functioning
Al Wakeel et al, 2012 ³¹	Quality of life in hemodialysis and peritoneal dialysis patients in Saudi Arabia	Saudi Arabia	151:41	Questionnaire (KDQOL-SF)	General HRQoL Physical functioning Psychological functioning
Ogutmen et al, 2006 ²⁶	Health-related quality of life after kidney transplantation in comparison intermittent hemodialysis, peritoneal dialysis, and normal controls	Turkey	302:207	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Wu et al, 2004 ¹¹	Changes in quality of life during hemodialysis and peritoneal dialysis treatment: generic and disease specific measures	United States	432:133	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Kutner et al, 2005 ¹²	Health status and quality of life reported by incident patients after 1 year on haemodialysis or peritoneal dialysis	United States	455:413	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Niu and Li, 2005 ³²	Quality of life of patients having renal replacement therapy	Taiwan	80:80	Questionnaire (WHOQOL-BREF TAIWAN) ^a	Physical functioning Psychological functioning
Sayin et al, 2007 ²⁵	Quality of life in hemodialysis, peritoneal dialysis, and transplantation patients	Turkey	75:20	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Mau et al, 2008 ³³	Health-related quality of life in Taiwanese dialysis patients: effects of dialysis modality	Taiwan	182:51	Questionnaire (KDQOL SF-36) Taiwanese version	General HRQoL Physical functioning Psychological functioning
Czyżewski et al, 2014 ²⁷	Assessment of health-related quality of life of patients after kidney transplantation in comparison with hemodialysis and peritoneal dialysis	Poland	40:30	Questionnaire (KDQOL-SF v.1.3)	General HRQoL Physical functioning Psychological functioning
Okpechi et al, 2013 ²⁹	Health-related quality of life in patients on hemodialysis and peritoneal dialysis	South Africa	56:26	Questionnaire (KDQOL SF-36)	General HRQoL Physical functioning Psychological functioning
Rodrigues Frutuoso et al, 2011 ³⁴	Quality of life in chronic kidney disease	Portugal	37:14	Questionnaire (KDQOL SF-36 v.1.3)	General HRQoL Physical functioning Psychological functioning

^aWHOQOL-BREF is a 28-item modified version of the WHOQOL-100 + questionnaire soliciting patient subjective assessment of HRQoL. HRQoL indicates health-related quality of life.

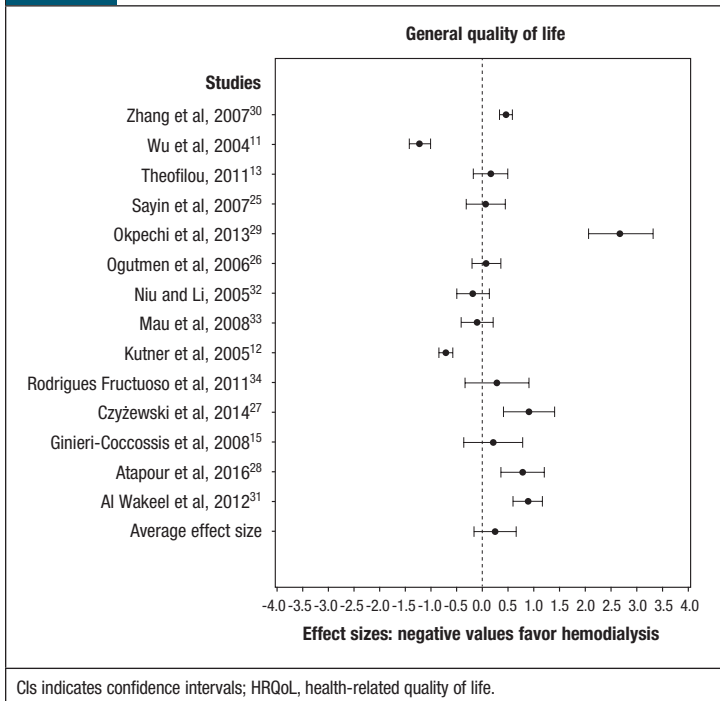
of publication), a random-effects model was used to calculate the overall (ie, average) effect sizes and 95% confidence intervals (CIs) for the outcome variable within each HRQoL domain.

To assess the effectiveness of interventions for ESRD, we evaluated the effectiveness of peritoneal dialysis using hemodialysis as the control. The decision to use hemodialysis as the control was a result of its popularity as the most frequently used dialysis modality.¹⁹ We used the

comprehensive meta-analysis software to fit random-effects models to the data to generate pooled effect sizes, their corresponding 95% CIs, standard errors, and P values. These estimates were used to identify significant peritoneal dialysis effects.

The statistical analysis system Base SAS version 9.3 (SAS Institute, Inc; Cary, NC) was used to generate forest plots using the effect sizes and 95% CIs obtained from each study.¹⁹ The direction of the effect size is in-

Figure 2 Effect Sizes and 95% CIs for Peritoneal Dialysis versus Hemodialysis in the General HRQoL Domain



indicative of which intervention was dominant, so negative effect sizes indicate hemodialysis as the dominant intervention.

Calculation of effect sizes. The effect sizes were computed based on a 1988 formula developed by Cohen to generate standardized mean differences.²⁴ The formula is:

$$d = \frac{\bar{X}^T - \bar{X}^C}{S_{Y_{pooled}}}$$

In this formula, *d* is the standardized mean difference from the treatment control comparison, \bar{X}^T is the average of the treatment or intervention group, \bar{X}^C is the average of the control group, and $S_{Y_{pooled}}$ is the pooled sample standard deviation.

According to Cohen, an effect size of 0.20 is considered a small effect; 0.50, a medium-sized effect; and 0.80, a large effect.²⁴

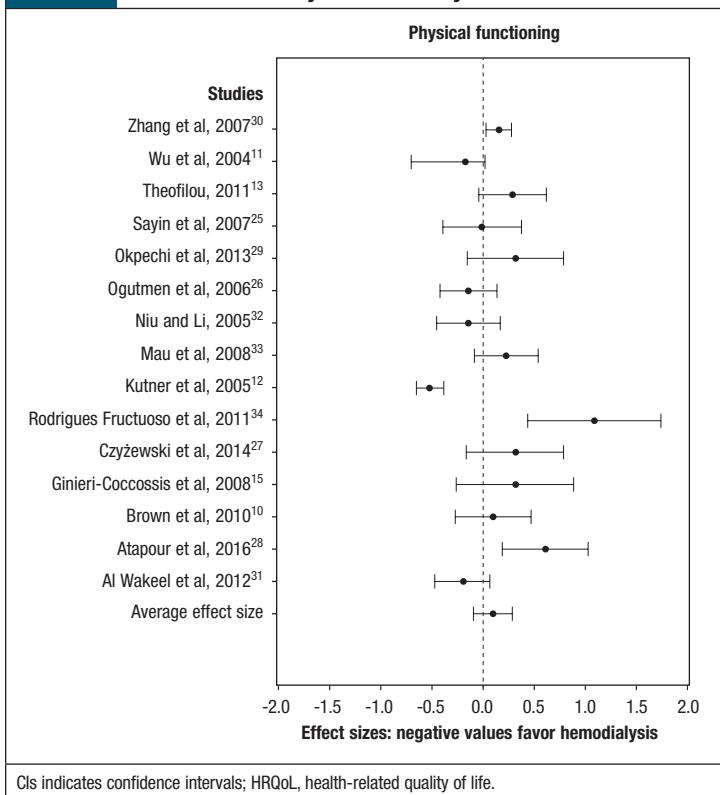
Assessment of moderator variables. The objectives of this meta-analysis included the determination of whether the year of publication and the country where the studies were done influenced the study findings. Two categorical variables representing the data collection year and the countries where the studies were conducted were identified during the coding process. The variable representing the year category was coded “new” for the newer studies (ie, after 2006) and “old” for the older studies (ie, 2000-2006). The other variable representing the country where the study was done was treated likewise, with “U.S.” representing studies conducted in the United States and “non-U.S.” for studies conducted in other countries.

We sought to determine whether these 2 variables were predictors of the reported effectiveness of peritoneal dialysis in the selected studies. The inclusion of these moderator variables was contingent on the belief that more recent studies (ie, after 2006) would find more significant intervention effects, because they were conducted when more advanced technology was available. With the United States being a developed country with high living standards, studies done in the United States may report better quality-of-life estimates than most studies done primarily in developing countries. However, the type of healthcare system adopted by the respective countries was not taken into consideration.

The subgroup analysis was confined to the effectiveness of peritoneal dialysis compared with hemodialysis, and, for convenience, we combined all 3 domains rather than performing 3 individual tests, which would be required for the pairwise comparisons across 3 domains.

Publication bias. As a precaution, we evaluated the studies to determine whether they were subjected to publication bias. The test for publication bias was achieved through the use of the Comprehensive Meta-

Figure 3 Effect Sizes and 95% CIs for Peritoneal Dialysis versus Hemodialysis in the Physical HRQoL Domain



Analysis version 2 software (Biostat; Englewood, NJ) by plotting the effect sizes against their standard errors to produce a funnel plot. The null hypothesis test of no publication bias was based on the classic fail-safe N test. A modified SAS code was used to assess the scores obtained from 2 independent coders across 15 items relating to study quality.

Results

The initial search strings returned more than 1200 related articles combined. However, narrower search strings requesting modality comparisons reduced the number to 144 potential studies that were retrieved for further review. After further screening, only 15 studies met the study criteria and were used in the comparison of the effectiveness of hemodialysis and peritoneal dialysis.^{10-13,15,25-34} An outline of the screening process and reasons for exclusion are illustrated in Figure 1.

Characteristics of extracted studies. Of the 15 studies extracted, 14 included all 3 quality-of-life domains (Table 1).^{10-13,15,25-34} The studies were characterized by considerable variation in sample sizes, the types of measurement instruments used, and the countries where they were done. The majority of studies were non-US (N = 13), were published after 2005 (N = 11), and used cross-sectional data obtained through questionnaires (N = 14) to measure HRQoL. The most common quality-of-life measurement instruments were the Kidney Disease Quality of Life (KDQOL) SF-36 survey, along with some of its adapted versions, and the WHO-QOL-100 with its variants.¹³⁻¹⁶ The sample size included in the meta-analysis was 4318 patients.

Statistical Analyses

The effectiveness of the interventions across the 3 quality-of-life domains, summarizing the effect sizes, as well as the effect sizes for individual studies, are illustrated in the respective forest plots in Figure 2, Figure 3, and Figure 4. Higher scores on quality-of-life scales indicate better quality of life; therefore, a negative effect size favors the control (ie, hemodialysis).

Peritoneal dialysis versus hemodialysis (general domain). In all, 14 studies were used in the comparison of the effectiveness of peritoneal dialysis relative to hemodialysis in the general HRQoL domain (Figure 2). A total of 5 studies indicated that peritoneal dialysis was more effective in improving HRQoL²⁷⁻³¹; 2 studies indicated that hemodialysis was more effective.^{11,12} The summary effect size was 0.28 (95% CI, -0.14-0.69; not significant).

Peritoneal dialysis versus hemodialysis (physical domain). A total of 15 studies were used in the comparison of the effectiveness of peritoneal dialysis relative to hemodialysis in the physical HRQoL domain (Figure 3). In all, 3

Figure 4 Effect Sizes and 95% CIs for Peritoneal Dialysis versus Hemodialysis in the Psychological HRQoL Domain

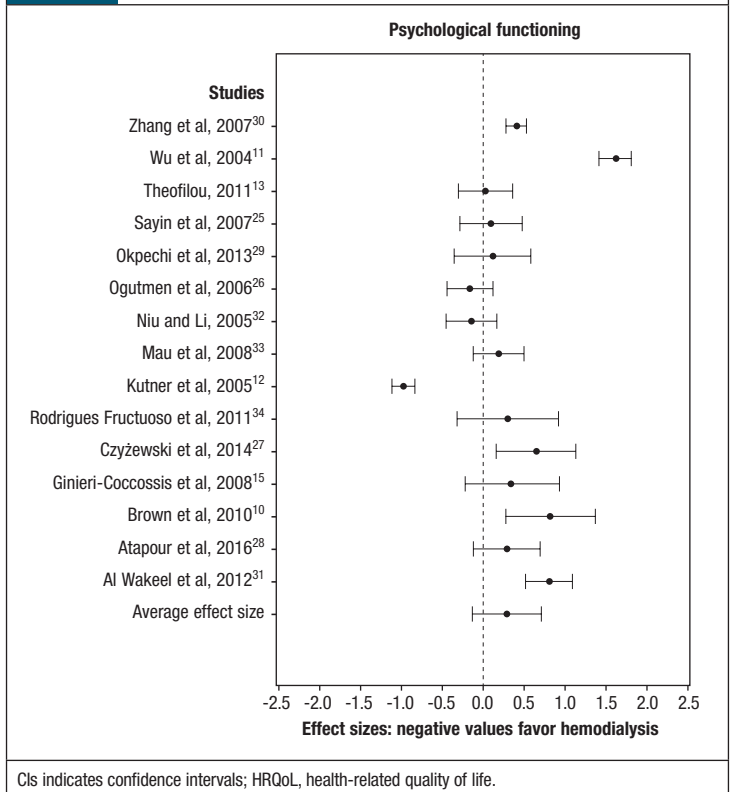


Table 2 Subgroup Analyses of Moderator Variables for the 3 HRQoL Domains Combined

Study grouping	Studies, N	Effect size	Z value	P value	Q _{df,p}
United States	2	-.033 (95% CI, -0.75-0.08)	-1.58	.110	12.85 _{1, 0.000}
Non-United States	13	0.30 (95% CI, 0.12-0.47)	3.33	.001	
Older (year 2000-2006)	4	-0.24 (95% CI, -0.05-0.03)	-1.64	.102	7.58 _{1, 0.006}
Newer (year 2006-2017)	11	0.39 (95% CI, 0.20-0.57)	4.06	.000	

studies indicated that peritoneal dialysis was more effective in improving HRQoL.^{25,27,29} Only 1 study indicated that hemodialysis was more effective.¹² The summary effect size was 0.10 (95% CI, -0.09-0.29; not significant).

Peritoneal dialysis versus hemodialysis (psychological domain). In all, 15 studies were included in the comparison of the effectiveness of peritoneal dialysis relative to hemodialysis in the psychological HRQoL domain (Figure 4). A total of 5 studies indicated that peritoneal dialysis was more effective in improving HRQoL,^{10,11,25,26} whereas 1 study indicated that hemodialysis was more effective.¹² The summary effect size was 0.29 (95% CI, -0.13-0.71; not significant).

Assessing the impact of moderator variables. Subgroup analyses were performed to determine whether 2 moderator variables, time of study, and country of study origin were important predictors of the effectiveness of the interventions. The results of the subgroup analyses are shown in **Table 2**.

Time of study. The majority of studies (N = 11) were published after 2006, and these studies tended to report larger effects than those published before 2006 (0.39 vs -0.24, respectively). For studies published after 2006, the standardized mean difference was 0.39 (95% CI, 0.20-0.57; Z = 4.06; P < .001).

The 11 newer studies tended to indicate peritoneal dialysis as the more effective modality. For the 4 older studies, the standardized mean difference was -0.24 (95% CI, -0.05-0.03; Z = -1.64; P = .10). Although the older studies advocated hemodialysis as the more effective modality, this finding was not statistically significant. The test of homogeneity indicated significant variation in effects between the studies ($Q_{\text{between}} = 12.85$; P < .001).

Country of study. The majority of studies (N = 13) used in this study were published outside of the United States. The standardized mean difference for the non-US studies was 0.30 (95% CI, 0.12-0.47; Z = 3.33; P = .001). The non-US studies indicated that peritoneal dialysis is the more effective modality. For US studies, the standardized mean difference was -0.33 (95% CI, -0.75-0.08; Z = -1.58; P = .11). Studies done within the United States reported numerically larger standardized mean differences in favor of hemodialysis; however, this finding was not statistically significant. The test of homogeneity indicated significant variation in effects between the US and non-US studies ($Q_{\text{between}} = 7.58$; P = .006).

Assessing publication bias. The results indicated evidence of publication bias. The Z-value for the classic fail-safe N test was 4.28 (P < .001), resulting in the rejection of the null hypothesis of no publication bias. The interrater reliability was 0.73, which is indicative of good interrater agreement and study quality.

Discussion

Despite HRQoL becoming an important rubric for determining the overall well-being of patients with ESRD in the United States, the vast majority of studies researching this topic are done in foreign countries. If healthcare officials in the United States continue to agree on the use of HRQoL as a rubric for determining the overall well-being of patients with ESRD, there is a need for more studies of this nature in the United States. The majority of studies in this analysis indicate that peritoneal dialysis is a more effective dialysis modality than hemodialysis, as was evident in all 3 HRQoL domains addressed in this study (Figures 2-4). However,

this finding is a function of moderating factors, particularly the time period in which the studies were done.

The more recent studies (ie, after 2006) tend to show peritoneal dialysis as the more effective of the 2 dialysis modalities. The inconsistency in the findings between the 2 time periods is supported by the tests for homogeneity indicating significant variation within and between time periods, as well as within and between studies. It is also possible that the respective study sizes and countries of origin could have influenced the results.

The older studies, which, in general, had larger sample sizes and were conducted within the United States, might have been more representative than the majority of non-US, smaller studies. However, when the summary effect sizes were taken into consideration, peritoneal dialysis was not a more effective dialysis modality in any of the 3 HRQoL domains; therefore, this review is unable to conclude that peritoneal dialysis is the more effective of the 2 modalities.

It is important to note that recent reports by the US Renal Data System indicate that patients with ESRD are starting dialysis with peritoneal dialysis more often than in previous years.¹ This trend is similar to what is already observed in non-US studies. If this trend continues in the future, studies such as our analysis may help to solidify whether patients undergoing peritoneal dialysis actually experience a better quality of life than patients undergoing hemodialysis.

Limitations

This study adhered to PRISMA protocols during the collection and management of data to compare the effectiveness of hemodialysis and peritoneal dialysis as they relate to the HRQoL of patients with ESRD. Throughout the process of identifying eligible studies, we sought to avoid publication bias by including any scholarly article that met the inclusion criteria. However, the avoidance of publication bias is often not realistically possible. Like reviews, meta-analyses are syntheses of existing data that are confined to previously selected study settings, interventions, populations, health outcomes, and designs. Thus, we are aware of the limitations of this study for not being able to fully account for variability resulting from these factors, as well as other factors, such as country-specific healthcare policies, racial, ethnic, and sex differences.

Another limitation is that our study did not address the effects of study size on the results. This is an important consideration, especially because the results showed that the larger studies tend to indicate statistically significant results. However, the inclusion of small studies is also justified, because small studies can often contain true intervention effects that would have been overlooked had they not been included.

Conclusion

Despite the noted limitations, the methodologies used in this study are conservative but efficient ways of examining the effects of dialysis modality choices, time, and country of origin on the study findings. Peritoneal dialysis and hemodialysis are 2 renal replacement therapies used for ESRD, but comparative data on quality-of-life outcomes between these modalities are limited.

Overall, the majority of studies included in this meta-analysis favored peritoneal dialysis over hemodialysis in all 3 HRQoL domains considered. Nevertheless, because the pooled effect sizes were not statistically significant, we were unable to conclude that peritoneal dialysis is more effective than hemodialysis. Additional studies are needed to determine which ESRD treatment modality is better in terms of patients' HRQoL. ■

Author Disclosure Statement

Dr Queeley and Dr Campbell have no conflicts of interest to report.

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STAKEHOLDER PERSPECTIVE



Dialysis Procedures and Health-Related Quality of Life: The Challenge of Creating Evidence-Based Healthcare in End-Stage Renal Disease

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Evidence-based healthcare integrates research evidence derived from many sources with clinical expertise and patient values. Ascending through a pyramid of reports and sequentially more comprehensive and sophisticated studies,¹ meta-analyses combine data from independent studies that address comparable questions with similar methodology. The quantitative estimates of treatment effects expressed as relative risk, odds ratio, or risk difference examine moderating variables on patient outcomes that extend the original impact of primary research potentially influencing the practice of medicine.² Queeley and Campbell illustrate the process in end-stage renal disease related to health-related quality-of-life (HRQoL) assessments and the differential effects of peritoneal dialysis versus hemodialysis.³

RESEARCHERS: HRQoL has assumed increasing importance for the evaluation of treatment effectiveness given the improved survival of patients with chronic kidney disease (CKD). As a multidimensional construct, HRQoL incorporates physical health, psychological well-being, and social dimension scores, which progressively worsen as CKD progresses.⁴ The frequency of assessments has little to no impact on HRQoL,⁵ although observational research and randomized controlled trials (RCTs) suggest that feedback with intervention yield improvements in care.⁶ The International Society of Nephrology and the Kidney Disease: Improving Global Outcomes recommend periodic assessments of HRQoL as a standard of care for patient-centered delivery, emphasizing nonpharmacologic interventions as a first-line intervention.⁷

Research methodology for meta-analyses provides a framework for data extraction and analyses, with residual areas of uncertainty and debate. Methodologic rigor is enhanced by multiple independent raters selecting relevant publications using eligibility criteria in a transparent study selection process. Differences in baseline risk, concomitant therapy, and outcome definition across studies represent challenges in data aggregation and analyses, and exploring the impact of heterogeneity across studies is challenging. Formal examination of heterogeneity de-

termines if differences across studies can be expected by chance. Identification of confounding variables that could modify trial results is essential, and sensitivity analysis evaluates study groups based on methodological or clinical characteristics likely to influence outcomes.

Conforming to PRISMA guidelines,⁸ Queeley and Campbell systematically address all eligibility criteria, including publication date, access to original data for effect-size analyses, use of recognized and sanctioned HRQoL measures, and duration of hemodialysis and peritoneal dialysis. They included small and larger studies without restriction, provided other eligibility criteria were satisfied. A random-effects model was used to test for homogeneity because of the variability in the extracted studies; an alternative approach using fixed-effects modeling assumes homogeneity of the intervention effect, leading to differences in point estimates and confidence intervals between these procedures.⁹ Standardized Cohen effect sizes were calculated with exploration of moderator variables (eg, more recent vs older articles, country of origin). The impact of standards of care and healthcare system by the country of origin were not assessed; 13 of the 15 studies were conducted outside of the United States. The most dominant quality of life (QoL) measures Queeley and Campbell noted was the Kidney Disease QoL Short Form 36 (SF-36) survey (used cross-sectionally), the World Health Organization Quality of Life Survey 100, and their variants, with 4318 patients considered. The 3 major HRQoL domains were separately presented with the 2 methods of dialysis.

When contrasting peritoneal dialysis with hemodialysis, a majority of studies suggested that peritoneal dialysis had a more favorable impact across all 3 domains of HRQoL. However, summary effect sizes from the meta-analysis indicated significant variation based on time of publication and study location (non-US studies were recent and favored peritoneal dialysis; US studies were older, larger, and nominally favored hemodialysis). Aggregate results, therefore, did not permit conclusions regarding peritoneal dialysis versus hemodialysis impact on HRQoL.

STAKEHOLDER PERSPECTIVE *Continued*

PAYERS: Health plans inform formulary placement, coverage, and reimbursement by using clinical evidence, including systematic reviews and meta-analysis. RCTs and observational studies also contribute to the decision process, acknowledging differences in implications that could be drawn from conclusions. For example, RCTs may exaggerate benefit for individual patients given the design features of an RCT, whereas implications from meta-analyses can differ based on the method used to extract and analyze the data.¹⁰ Translating analyses into policy is particularly difficult when heterogeneity across studies precludes practical clinical interpretation on a patient level.

Nephrology guidelines infrequently reference meta-analyses; when nephrologists are asked about the perceived role of meta-analyses in evidence-based medicine and their influence on patient care, the majority accept meta-analyses, acknowledge their contribution to guidelines, and indicate that they can influence patient care, although meta-analyses are not ranked higher in importance than RCTs.¹¹

Extrapolation from non-US studies into the US healthcare system is a limitation of the present analysis, given the dominance of non-US information and the impact of publication date on the results.³ Country- or region-specific moderators are ubiquitous in interventional and observational studies, and these are often impactful, unless they are anticipated in design and/or incorporated into analysis. Although not addressed in the present meta-analysis,³ studies also have inconsistently demonstrated cost-effective differences contrasting continuous ambulatory peritoneal dialysis, hemodialysis, and automated peritoneal dialysis,¹² which are possibly attributable to varying standards of care by country.¹³ Additional independent studies in different delivery settings permitting meta-analyses that sample a larger portfolio of studies are required to determine whether cost-effective dialysis procedures also provide the greatest HRQoL enhancements.

PATIENTS: Across indications, the impetus for disease-specific patient-related outcomes is pronounced. Individualized HRQoL measures are attractive, because they permit patients to identify domains pertinent to their individual condition. These data increasingly are captured electronically and are integrated into electronic medical records. Modifying factors for individualized QOL, such as race and age, can suggest differences based on method of dialysis.¹⁴ Correlations between the more frequently used SF-36 and individualized HRQoL can be

robust; however, for systematic reviews and meta-analyses, the use of standardized measures is preferred.

Acknowledging the adage that “researchers live at the mean, while clinicians live within standard deviations,” the importance of patient-specific measures looms large in the delivery of healthcare. For example, in CKD, patient differences in HRQoL between peritoneal dialysis and hemodialysis are noted at trend levels of statistical significance, with patients using peritoneal dialysis more likely to identify kidney health and disease as QOL factors. In addition, individual symptoms (eg, pruritus, depressive symptoms, sleep disorder, and sexual dysfunction) rather than domain scores also influence individualized patient care and tend to be underestimated by healthcare providers precluding early effective intervention.¹⁵ Although the preservation of residual renal function, correction of anemia, and physical therapy and rehabilitation are known to preserve HRQoL, identifying systematic differences between the methods of dialysis and subjective measures, such as HRQoL assessments, remains elusive. ■

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