



# International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher  
SciFormat Publishing Inc.  
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,  
Calgary, Alberta, T3E0A7,  
Canada  
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**ARTICLE TITLE** PSYCHOLOGICAL BURDEN IN RENAL REPLACEMENT THERAPY:  
COMPARATIVE OUTCOMES ACROSS HEMODIALYSIS,  
PERITONEAL DIALYSIS, AND KIDNEY TRANSPLANTATION

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**DOI** [https://doi.org/10.31435/ijitss.1\(49\).2026.4814](https://doi.org/10.31435/ijitss.1(49).2026.4814)

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**RECEIVED** 17 January 2026

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**ACCEPTED** 25 March 2026

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**PUBLISHED** 30 March 2026

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# PSYCHOLOGICAL BURDEN IN RENAL REPLACEMENT THERAPY: COMPARATIVE OUTCOMES ACROSS HEMODIALYSIS, PERITONEAL DIALYSIS, AND KIDNEY TRANSPLANTATION

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## ABSTRACT

Chronic kidney disease affects approximately 9.5% of the global population, with end-stage kidney disease requiring renal replacement therapy (RRT). This narrative review synthesizes evidence from recent meta-analyses and landmark studies comparing psychological and psychosocial outcomes across hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation (KTx). Depression prevalence is approximately 35% in both HD and PD patients, but significantly lower (25%) in KTx recipients, a difference primarily attributable to modality rather than patient characteristics. Cognitive impairment affects 53% of HD patients versus lower rates in PD patients; intradialytic cerebral ischemia emerges as a plausible mechanism, yet paradoxically, PD patients show faster brain atrophy while maintaining better cognitive test performance. Health-related quality of life follows a consistent hierarchy: KTx provides superior outcomes, followed by PD, then HD, with effects most pronounced in kidney-disease-specific domains. Critically, immunosuppressive medication side effects, not graft function, emerge as the strongest predictor of post-transplant quality of life. Major psychosocial domains including employment, sexual function, and sleep quality remain unstudied when stratified by modality. Current modality selection relies on clinical and logistical factors without considering psychological fit. This review identifies substantial evidence gaps and proposes that future practice integrate psychological assessment into pre-dialysis education and develop validated tools to personalize modality selection based on coping capacity and psychological resilience.

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## KEYWORDS

Dialysis, Kidney Transplantation, Depression, Cognitive Function, Quality of Life, Psychological Burden

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## CITATION

Damian Zienkiewicz, Gabriela Makulec, Karolina Domosud, Weronika Walendziak, Natalia Mordal, Kacper Ściebura, Wiktoria Wiśniewska, Magdalena Ostaszewska, Milena Majchrzyk, Anna Malczyk. (2026) Psychological Burden in Renal Replacement Therapy: Comparative Outcomes Across Hemodialysis, Peritoneal Dialysis, and Kidney Transplantation. *International Journal of Innovative Technologies in Social Science*. 1(49). doi: 10.31435/ijitss.1(49).2026.4814

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## 1. Introduction

Chronic kidney disease (CKD) is a common problem. Median worldwide prevalence of CKD was estimated to be 9,5%, reaching 12,8% in Eastern and Central Europe (Bello et al., 2024). End-stage kidney disease (ESKD) is the last, fifth stage of CKD. It's defined by a drop in glomerular filtration rate below 15 ml/min/1.73 m<sup>2</sup>. In 2016 the number of patients treated for ESKD reached 2,455,004 according to United States Renal Data System. The data is based on the reports created in different countries. The problem is probably more prevalent, with plenty of undiagnosed cases worldwide, especially in Africa or regions with poorer healthcare (Thurlow et al., 2021). The 5-year survival of ESKD varies and correlates with the healthcare system properties. For example, in US it was estimated to be 39% while it was 60% in Japan, even though on average patients in Japan were older (Thurlow et al., 2021).

Classically besides conservative management there are three possible effective renal replacement therapy (RRT) options: hemodialysis (HD), peritoneal dialysis (PD) and kidney transplantation (KTx). HD is inherently connected with rigid schedule and partial loss of autonomy. Patients are required to visit dialysis center three times weekly. The sole process takes a few hours, after which patients often report fatigue, blood pressure drops, dizziness, cramps, feel cold and experience "dialysis fog", described as having lowered cognitive capabilities and sleepiness. However, the effectiveness of HD is undoubted, and the patient might not feel alone with the problem, since the healthcare providers take care of them. PD on the other hand seems more flexible, because the patient is independent from having to attend the dialysis in specific place – the procedure takes usually place at patient's home, often overnight. However, the patient is responsible for the correct procedure performance. Some people may feel overwhelmed and insecure about their incompetence in the field of medicine. KTx is the gold standard, since it wholly solves the problem of kidney failure, and often for a long time. The problem lies mainly in the scarcity of the donated organs.

Clinical outcomes of those three, including mortality rates, dialysis adequacy, graft survival, and hemodynamic stability are well-known. However, their psychosocial and psychological impacts are not documented this well, and the evidence remains fragmented.

Recent meta-analyses have examined specific psychosocial outcomes in dialysis and transplant patients. Zaragoza-Fernández et al. (2025) compared depression prevalence between hemodialysis, peritoneal dialysis, and kidney transplant recipients across 16 studies involving 26,301 patients. Malik et al. (2025) examined cognitive function and dementia risk across dialysis modalities in a meta-analysis of 326,216 patients, finding significant differences between HD and PD. Nassar et al. (2025) reviewed psychosocial outcomes specific to kidney transplant recipients. To the best of our knowledge, no single comprehensive review has synthesized these findings. Each meta-analysis examines a single outcome in isolation, without integrated comparison of how multiple psychosocial domains vary across the three modalities. Moreover, major psychosocial domains remain completely unstudied when stratified by modality. Employment outcomes, sexual health and intimacy, sleep quality, and long-term psychological trajectories have not been systematically compared across HD, PD, and KTx. These domains directly impact quality of life and treatment success, yet comparative data is rather poor or non-existent. And finally, choice of modality is still based determined by clinical and logistical availability and is not personalized based on psychological profile. Psychological readiness, personality type, social support availability, and coping style likely influence which patients thrive in home-based PD and which do it in-center HD. No evidence-based psychological assessment exists to guide this personalization.

This narrative review aims to:

1. Briefly summarize mortality and key complications across hemodialysis, peritoneal dialysis, and kidney transplantation, providing necessary context for interpreting psychological findings.
2. Compare depression, anxiety, cognitive function, and quality of life across the three modalities by synthesizing recent meta-analyses and key comparative studies, identifying similarities, differences, and clinically relevant patterns in psychological burden.
3. Examine well-documented psychosocial outcomes, where comparative data exists, while acknowledging the limitations, heterogeneity, and sparse evidence base for these domains.
4. Identify understudied psychosocial domains where comparative data between modalities is minimal or absent, highlighting these as high-priority gaps for future research.

In this narrative review we synthesized recent peer-reviewed literature (primarily 2020–2025), prioritizing high-quality meta-analyses where available to establish the strongest comparative evidence. For domains where meta-analyses do not exist, we identified key comparative studies and relevant observational data, explicitly acknowledging methodological limitations and sparse sample sizes. Our focus was primarily on English-language publications. Studies examining specific populations (e.g., pediatric dialysis, high-income versus low-income countries, or specialized dialysis modalities) were included where they provided comparative psychosocial outcome data but are noted where findings may not generalize to broader populations.

## 2. Clinical Overview: Treatment Regimens and Physiological Stressors

### 2.1 Survival and prognosis

The choice between HD and PD is often viewed as a lifestyle decision. The prognostic reality however creates a psychological hierarchy among RRTs. Large propensity-matched analyses generally demonstrate that mortality risks are similar between HD and PD, particularly with adjustment for comorbidities and residual renal function (Elsayed et al., 2020). KTx is different as it shows a vast shift in survival probability. Systematic reviews indicate that KTx recipients experience a 55% reduction in mortality risk (HR 0.45; 95% CI 0.39-0.54; Chaudhry et al., 2022) compared to candidates remaining on dialysis.

Suitable candidates often perceive dialysis not as a sustainable long-term therapy, but as a bridge to transplantation. Consequently, the psychological burden on dialysis patients is frequently intensified by lingering anxiety regarding waiting list status and the scarcity of organs. Although transplant recipients avoid the immediate mortality risks associated with dialysis, they face a demanding long-term phase of graft maintenance. Failure would mean returning to a therapy with higher mortality, generating a distinct form of anxiety rather than a general fear of death.

## **2.2 Hemodialysis: Hemodynamic Variability and Systemic Fatigue**

While HD effectively prevents uremic mortality, it is clearly “unphysiological” due to its intermittent nature. It is a source of stress burden on the cardiovascular and central nervous systems. The standard HD regimen means rapid fluid removal over a short 4-hour window, creating significant hemodynamic variability. Intradialytic hypotension is a frequent complication, occurring even in 10,1-11,6% of sessions depending on the definition used (Kuipers et al., 2019). This recurrent hemodynamic instability does not only mean temporary dizziness, but it induces repetitive subclinical ischemic injury to the heart and brain. This phenomenon is called "myocardial and cerebral stunning" (McGuire et al., 2019).

These ischemic episodes and the fluctuations of solute clearance explain the post-dialysis fatigue, often described by patients as being "washed out". It can take several hours for the organism to return from this state to normal (Time to Recovery, TIRD). This physical crash is aggravated by chronic anemia management. HD patients typically require significantly higher doses of erythropoiesis-stimulating agents compared to PD patients to maintain satisfactory hemoglobin levels (van Lieshout et al., 2024), which may be due to hemodilution, erythrocyte loss and quicker loss of residual renal function in hemodialyzed patients. The cumulative ischemic burden of "stunning," could be a physiological mechanism for cognitive slowing and depressive symptoms that frequently overlap with uremic fatigue.

## **2.3 Peritoneal Dialysis: Autonomy and Responsibility**

In contrast to the hemodynamic variability of HD, PD offers a physiological profile closer to kidney function. PD, thanks to its continuous nature, allows for stable removal of solute and fluid. Due to that, the patients avoid the "sawtooth" uremic fluctuations seen in intermittent therapies. What is important is that PD is associated with better preservation of residual renal function (RRF) compared to HD (Zhao, 2023), which is a factor that strongly correlates with improved survival. The dietary restrictions are also reduced. This physiological stability, along with the convenience of home-based therapy, theoretically supports greater patient autonomy and lifestyle flexibility.

However, this independence comes at the cost of "medicalizing" the home environment. Thus, the entire burden of clinical safety shifts onto the patient. The International Society for Peritoneal Dialysis (ISPD) has lowered the target peritonitis rate to <0.40 episodes per year (Li et al., 2022), and the real-world registry data shows mean rates ranging from 0,301 to 0.304 episodes/patient-year worldwide (Marshall, 2022). Consequently, the threat of infection could be a constant psychological stressor for a fraction of patients; every fever or abdominal discomfort might trigger a fear of technique failure and potential forced transfer to HD ("technique failure anxiety"). Furthermore, the glucose-based dialysate relates to some metabolic burden. Systemic glucose absorption can lead to hyperglycemia and metabolic syndrome (Kim et al., 2013), which not only drive cardiovascular risk but can exacerbate depressive symptoms through neuroinflammatory pathways.

## **2.4 Kidney Transplantation: Imperfect Solution**

KTx is universally regarded as the gold standard for ESKD management. It grants superior correction of uremic complications and longer life expectancy compared to dialysis (Tonelli et al., 2011). Recipients of the kidney typically regain almost normal hemodynamics, improved anemia control without the need for high doses of erythropoiesis-stimulating agents, and stabilization of mineral-bone disease parameters. This physiological recovery is associated with substantial improvements in quality of life in the first post-transplant year.

Viewing the KTx as a "cure" is somewhat incorrect, since it would be more accurately described as a chronic condition managed by lifelong immunosuppression. This relief is unfortunately not permanent. Current registry data indicate that predicted half-life is 19.2 years for living donor recipients and 11,7 years for deceased donor recipients transplanted in era 2014–2017 (Poggio et al., 2021). This limit may create a prolonged lingering fear of losing the graft. This anxiety, observed by us in clinical practice, is characterized by hyper-vigilance regarding, for example, creatinine levels and a persistent concern about returning to dialysis, which many patients perceive as a major decline in quality of life. As a result, transplantation replaces dependence on dialysis with lifelong dependence on immunosuppressive therapy, which can itself become a source of ongoing anxiety.

### 3. Depression, Anxiety & Distress

#### 3.1 Comparative Prevalence: HD vs. PD vs. KTx

Depression prevalence in RRT is dependent on the treatment modality. A meta-analysis of 16 observational studies that involved 26,301 patients by Zaragoza-Fernández et al. (2025) found depression prevalence of 35.56% (95% CI: 34.2–37.0%) in hemodialysis patients and 35.09% (95% CI: 33.5–36.7%) in peritoneal dialysis patients – no statistically significant difference. In contrast, kidney transplant recipients had remarkably lower depression prevalence at 25.33% (95% CI: 24.0–26.6%). This is an approximate 10-percentage-point reduction compared to dialysis. Variables like mean age, treatment duration, diabetes and hypertension occurrence, and measurement instruments were not significantly associated with depression prevalence. This suggests that the RRT method is the main driver of these differences (Zaragoza-Fernández et al., 2025).

#### 3.2 Depression as a Clinical Outcome in Peritoneal Dialysis

Surprisingly, contrary to the expectation that depression has prognostic meaning in dialysis patients, a meta-analysis of 11 studies on PD patients found that depression was not a significant independent predictor of mortality (HR: 1.22; 95% CI: 0.86–1.72; Xu & Zhang, 2024). Similarly, depression showed no statistically significant association with technique survival (OR: 1.28; 95% CI: 0.38–4.35) based on 2 studies, nor with peritonitis risk (OR: 1.89; 95% CI: 0.82–4.33) across 3 studies (Xu & Zhang, 2024). These findings suggest that while depression is highly prevalent in PD patients (Zaragoza-Fernández et al., 2025), its presence does not predict worse clinical outcomes in this population on its own. It should not be viewed as a marker of imminent treatment failure or mortality risk. Anyway, depression in patients requiring RRT remains a serious psychiatric condition and requires clinical recognition and treatment, no matter if it is associated with dialysis-specific mortality or not.

#### 3.3 Temporal Changes in Psychiatric Symptoms: Pre- vs. Post-Transplant

KTx grants measurable improvements in depression and cognitive function in one month after surgery. In a prospective pre-post study of 100 transplant recipients using validated instruments (DASS-21 for depression/anxiety/stress, Montreal Cognitive Assessment for cognition), mean depression scores significantly declining from 5.18 to 4.44 ( $p < 0.001$ ). However, depression prevalence decreased insignificantly from 19% pretransplant to 13% posttransplant ( $p > 0.05$ ; Mukherjee & Chaudhury, 2024). Anxiety and stress showed modest, insignificant reductions: anxiety prevalence decreased from 14% to 11%, and stress from 23% to 20% ( $p > 0.05$ ; Mukherjee & Chaudhury, 2024). Cognitive impairment (CI) is a frequently overlooked outcome in transplant populations. In this study it showed significant, however slight improvement, with mean Montreal Cognitive Assessment scores rising from 25.76 to 26.62 ( $p < 0.001$ ; Mukherjee & Chaudhury, 2024). Besides, KTx correlated significantly with various improvements in quality of life domains, including emotional well-being, social interaction, sleep and energy/fatigue. These findings suggest that transplantation provides early psychiatric benefits apart from its effect on survival.

#### 3.4 Clinical Correlates of Anxiety in Transplant Recipients

Anxiety in kidney transplant recipients is associated with measurable biochemical markers. This suggests a physiological input to psychological distress. In a cross-sectional study of 161 transplant recipients, abnormal anxiety was observed in 24.3% (HADS-Anxiety score  $\geq 11$ ) with an additional 13% classified as borderline (Nassar et al., 2025), defined as score 8–10 out of 21. Anxiety correlated significantly with elevated serum creatinine ( $r = 0.164$ ,  $p = 0.039$ ). Thus, serum creatinine appears to be an independent predictor of higher anxiety scores in patients after KTx. Additionally, anxiety showed a significant inverse relationship with hemoglobin levels ( $r = -0.16$ ,  $p = 0.043$ ), suggesting that anemia may also be a modifiable risk factor for anxiety in transplant recipients (Nassar et al., 2025). Moreover, female gender, physical inactivity, and the presence of post-transplant psychiatric comorbidities were independent predictors of higher anxiety scores (all  $p < 0.05$ ; Nassar et al., 2025). What is important is that patients with abnormal anxiety reported impaired quality of life, which makes the findings of Nassar et al. (2025) worth keeping in mind.

### 3.5 Heterogeneity and Limitations

Depression assessment tools vary across studies. This may distort the perception of true differences between modalities. Study populations differ in age, dialysis duration, comorbidities, and time since transplant. All of this makes comparisons difficult. Few studies directly compare depression across HD, PD, and KTx in the same patients. The Zaragoza meta-analysis pools separate studies rather than examining simultaneous comparisons within cohorts. Anxiety appears to have received more attention in transplant recipients than in dialysis patients, with limited evidence on anxiety prevalence and correlates in dialysis populations.

## 4. Cognitive Function

### 4.1 Comparative Prevalence and Risk

CI is highly prevalent in dialysis-dependent patients. HD patients show 53% CI prevalence (Zhang et al., 2024) compared to a median of 19% in the general population (adults over 50 years old; Pais et al., 2020). Despite this substantial burden, cognitive impairment remains clinically underrecognized and infrequently documented in medical records, limiting clinical awareness and intervention (Mobushar et al., 2025). A meta-analysis of 26 studies (326,216 patients) by Malik et al. (2025) found PD patients had in general much better cognitive function compared to HD patients (SMD  $-0.46$ ; 95% CI  $-0.62$  to  $-0.29$ ;  $p < 0.00001$ ). Dementia risk was 1.68-fold higher in hemodialysis versus peritoneal dialysis (OR 1.68; 95% CI 1.25 to 2.25;  $p = 0.0006$ ; Malik et al., 2025).

However, big heterogeneity ( $I^2 = 94\%$  for dementia) makes this data not so strong. Scientists that conducted a population-based study in Taiwan adjusted for age and comorbidities. This attenuated the difference between PD and HD to non-significance (Lin et al., 2015). This suggests patient selection bias may partially explain the different effects of both RRT methods and the true impact they have may be smaller than estimates suggest.

### 4.2 Intradialytic Cerebral Ischemia

HD is a source of acute hemodynamic stress that hypothetically could lead to cognitive decline. MacEwen et al. (2017) used real-time cerebral oxygenation monitoring during 635 sessions of HD and found cerebral ischemia ( $>15\%$  oxygenation relative drop) in 23.5% of sessions. Intradialytic cerebral ischemia, but not blood pressure itself, predicted executive cognitive decline at 12-month follow-up (Trail Making Test B,  $p = 0.03$ ).

Interestingly, this hemodynamic mechanism does not fully explain differences between RRT methods in cognitive outcomes. Tsuruya et al. (2024) conducted prospective MRI studies comparing brain atrophy in PD and HD patients. Surprisingly PD patients showed 2.4-fold greater gray matter volume loss per year compared to patients undergoing HD ( $-0.68$  vs.  $-0.28$  percentage-points/year,  $p = 0.011$ ).

It is unclear why this phenomenon occurs, even though PD avoids intradialytic ischemia. And mysteriously, despite this structural brain tissue loss, PD patients maintain better cognitive function compared to HD patients. This indicates that brain volume change does not correlate with cognitive outcomes in dialysis populations.

These findings imply that mechanisms behind the cognitive advantage of PD must be explained by something else than only hemodynamic stability and they are not completely understood.

### 4.3 Post-Transplant Recovery: Evidence and Limits

Other curious findings suggest that transplantation could grant partial cognitive reversibility. A meta-analysis of 10 pre-post transplant studies found, for example, large improvements in verbal memory ( $g = 0.759$ ) and visual memory ( $g = 0.690$ ) within 1–2 years. Unfortunately, compared to healthy controls, transplant recipients remained impaired in verbal fluency ( $g = -0.657$ ;  $p < 0.001$ ), executive function ( $g = -0.283$ ;  $p = 0.030$ ) and language ( $g = -0.573$ ;  $p = 0.032$ ; Joshee et al., 2018).

Van Sandwijk et al. (2020) identified the very probable mechanism for reversible cognitive gains. White matter volume increase and NAA/Cr restoration (neuronal integrity marker) correlated with improvements in cognitive tasks. The researchers used kidney donors as controls (to exclude learning effects) and showed transplant recipient improvements in attention and working memory exceeded donor improvements. How was it possible? They proved that osmotic normalization allows water shift from extracellular to intracellular compartment, which restored brain osmolytes and white matter structure (Van Sandwijk et al., 2020). Sadly, some deficits persist, suggesting chronic ischemic white matter damage from years of dialysis is only partially reversible.

## 5. Quality of Life

### 5.1 Hierarchy and methods

Health-related quality of life (HRQoL) is a multi-factor assessment of physical, mental, social, and disease-specific well-being. It is possible to notice a pattern across HD, PD, and KTx: kidney transplantation grants the best HRQoL. It is followed by peritoneal dialysis, and hemodialysis is generally associated with the lowest measured quality of life. This hierarchy is supported by direct comparative evidence as well as meta-analytic synthesis of disease-specific and generic QoL instruments (Czyżewski et al., 2014; Chuasuwan et al., 2020; Wang et al., 2021).

Comparative assessments include mainly two types of instruments. Generic measures, particularly the SF-36 (Short Form 36 Health Survey) and EQ-5D (EuroQol 5-Dimension), capture physical, mental, social, and role functioning in various populations. The second type of instruments are kidney-specific measures, that is the Kidney Disease Quality of Life (KDQOL-SF or KDQOL-36). They evaluate domains relevant to ESKD and its treatment, such as disease burden, work status or quality of social interaction. The clinical significance of differences that can be observed varies; a change of 5 points on SF-36 subscales is considered rather meaningful, but on kidney-specific scales larger changes are expected.

There are some limitations that affect interpretation. No large, contemporary study compares HD, PD, and KTx simultaneously using identical instruments and standardized follow-up time in the same cohort. The hierarchy is in fact deduced from cross-sectional and longitudinal studies conducted in different populations, different healthcare systems, and different time periods. There is a significant heterogeneity across studies by country income level, patient age structure, comorbidities, and so on. Additionally, selection bias influences modality-specific cohorts: PD and kidney transplant recipients often are generally younger, more motivated, and clinically fitter patients than HD populations, which may overestimate QoL advantages for home-based and transplant modalities. And although the overall QoL ranking is supported by available evidence, individual differences are important. Average differences may not apply to specific patient populations or healthcare contexts. RRT method choice involves trade-offs that are not just about average HRQoL scores and must include patient preferences, social support, and feasibility in the local setting (Chuasuwan et al., 2020; Wang et al., 2021).

### 5.2 PD vs HD

A meta-analysis of 21 studies (29,000 patients) found PD brought advantages over HD in SF-36 and in KDQOL. Pooled USMD of SF-36 favored PD, with more pronounced effect for mental component – 1.86 (0.47, 3.24) – and nonsignificant for physical component summary scores (Chuasuwan et al., 2020). Importantly, the pooled USMD of KDQOL for burden of kidney disease was 9.67 (5.67, 13.68), and 2.10 (0.07, 4.13) for symptoms – smaller effect (Chuasuwan et al., 2020). However, the effect sizes in other domains were insignificant. Generic utility scores (EQ-5D) showed minimal, nonsignificant difference, though subjective health rating measured employing Visual Analogue Scale (VAS) favored PD by 3.56 points (1.73, 5.39). Besides, some of the results were highly heterogeneous (Chuasuwan et al., 2020).

A recent Indonesian study (2024) partially confirmed these findings in a recent cohort of 466 HD and 147 PD patients. The researchers used KDQOL-36 tool, and PD showed significantly better physical component scores (40.3 vs 37.2,  $p < 0.001$ ) and it was better in terms of “effects of kidney disease” component (77.5 vs 71.3,  $p = 0.004$ ; Rokhman et al., 2025). All other components of KDQOL did not reach the point of significance. PD also showed better EQ-5D utility score (0.78 vs 0.67,  $p = 0.003$ ; Rokhman et al., 2025).

On average, PD shows modest, clinically meaningful advantages in perceived disease burden and physical functioning compared to HD, but mental and social domains remain similar (Chuasuwan et al., 2020; Rokhman et al., 2025). Individual variation is large; differences are most pronounced in older, high-income populations (Chuasuwan et al., 2020).

### 5.3 KTx vs Dialysis

Kidney-specific quality of life is substantially improved thanks to KTx in comparison to dialysis. A 5-year Norwegian longitudinal study of 110 patients transitioning from dialysis to transplant showed improvement of “overall health” item rating of KDQOL-SF from 58 to 68 ( $p < 0.001$ ; von der Lippe et al., 2014). Significant improvements were seen in burden of kidney disease, work status and a few other kidney-specific domains (von der Lippe et al., 2014). Cognitive functions, however, did not change significantly after KTx (von der Lippe et al., 2014). Importantly, transplant recipients remained largely below the general

population, for example 9-23 points lower (significantly) in physical functioning, role limitations, and general health perception (von der Lippe et al., 2014).

Another Dutch study showed, that in adults  $\geq 65$  years old, transplant recipients at 1 year post-KTx had significantly higher SF-36 Physical Component Summary scores than waitlisted dialysis patients (52.1 vs 47.4;  $p < 0.001$ ). Patients with the lowest pre-transplant quality of life experienced the largest post-transplant gains (de Boer et al., 2024).

A systematic review of 44 studies (6,929 patients) confirmed transplant recipients had much higher quality of life than dialysis patients, particularly in disease-specific domains. When compared to the general population however, transplant recipients showed similar HRQOL at 1–2 years post-transplant but significantly lower physical HRQOL in studies with longer post-transplant time (Wang et al., 2021).

Transplantation provides plenty of improvements in kidney-specific domains but does not normalize physical quality of life compared to the general population. Greatest gains occur in those with worst pre-transplant quality of life.

#### 5.4 QoL after KTx – immunosuppression

A prospective cohort of older transplant recipients showed an intriguing finding. The researchers evaluated the impact of several variables on both mental and physical HRQoL. The number of self-reported immunosuppressive medication side effects was the single strongest predictor of post-transplant HRQoL ( $\beta = -0.36$ ;  $p < 0.001$  for mental QoL and  $\beta = -0.55$ ;  $p < 0.001$  for physical QoL; de Boer et al., 2024), stronger even than acute rejection ( $\beta = 0.33$ ;  $p < 0.001$  for mental QoL, no significant effect on physical QoL; de Boer et al., 2024). This suggests that graft function alone does not determine QoL, as regimen tolerability is also impactful. A comprehensive narrative review identified symptoms in kidney transplant recipients that are highly prevalent and affect negatively QoL. It appears that 40-50% patients experience fatigue, 88-92% suffer from some gastrointestinal symptoms, ~33% male and ~50% female recipients have sleep disturbance and 48–66% report sexual dysfunction (Knobbe et al., 2025). This proves that even though KTx is an excellent therapy that cures CKD in a way, it is inherently connected with a set of new problems affecting the QoL.

### 6. Discussion

This narrative review synthesizes psychological outcomes across three renal replacement modalities. Rather than treating depression, cognition, and quality of life as separate phenomena, we believe these outcomes are interconnected expressions of how each modality uniquely stresses the body and mind. Our analysis reveals that treatment choice involves more than clinical logistics. It involves a fundamental exchange of burdens that patients must understand and clinicians must help manage.

#### 6.1 The Burden of Depression Across Modalities

Depression affects roughly 35 percent of dialysis patients regardless of modality. Yet in peritoneal dialysis, depression shows no association with mortality, technique failure, or infection risk. We believe this paradox reflects something important about dialysis psychology. Depression in dialysis may be an understandable psychological response to a difficult situation rather than a marker of clinical deterioration. In other words, feeling depressed while managing dialysis at home is not inherently predictive of clinical decline. The absence of prognostic significance does not diminish the clinical importance of depression as a contributor to suffering and reduced quality of life. We recommend routine screening and treatment for depression in all dialysis patients, informed by the understanding that depression may be more about existential burden than imminent clinical failure.

#### 6.2 The Cognition-Brain Volume Dissociation

The cognitive findings present the greatest interpretive challenge. Hemodialysis patients experience more cognitive decline than PD patients, and intradialytic cerebral ischemia is a believable mechanism. Yet PD patients show faster brain tissue loss per year while maintaining better cognitive test performance. We believe this dissociation reveals that cognition depends on factors beyond simple brain volume or acute ischemic episodes. Better preserved residual renal function in PD patients, more stable osmolar environments, and perhaps superior nutritional status may protect against the cognitive decline that brain atrophy alone would predict. Alternatively, the cognitive tests used in research may not detect the specific deficits caused by gray matter loss.

We emphasize that cognitive impairment remains understudied and underrecognized in clinical dialysis practice despite affecting half of hemodialysis patients. We recommend that nephrologists screen cognition in all dialysis patients, particularly older individuals and those with recurrent intradialytic hypotension. Transplantation partially reverses cognitive deficits, supporting early referral in eligible candidates. However, some damage persists, suggesting that preventing cognitive decline during dialysis is preferable to attempting reversal after transplant.

### **6.3 Quality of life: the real trade-off**

The quality of life hierarchy (KTx better than PD better than HD) is robust when measured by kidney-disease-specific scales but largely disappears in generic health measures. We interpret this to mean that the modality advantage is not about becoming healthier overall, but about relief from kidney-specific burdens. This distinction matters for patient counseling. When we tell patients that transplant improves quality of life, we should specify that it improves their quality of life as someone with kidney disease, not necessarily your overall health or life satisfaction.

The most striking finding is that immunosuppressive side effects, not graft function, predict post-transplant quality of life. This reframes transplantation. We believe it should not be presented as a "cure" or return to health, but as an exchange. Patients trade the rigid schedule and dialysis fatigue of in-center hemodialysis, or the burden of home management in peritoneal dialysis, for a different burden: lifelong medication side effects including fatigue, gastrointestinal symptoms, and sexual dysfunction. This is a meaningful improvement for many patients, but it is not normalization.

In dialysis, quality of life differences between modalities are small and highly variable. We note that PD's flexibility benefits certain populations more than others, particularly older and wealthier patients with stable housing. However, we suspect that observed PD advantages partially reflect selection bias. PD patients are often younger and more motivated than hemodialysis patients. We believe the true modality difference in quality of life is smaller than studies suggest, and patient motivation, coping style, and social support probably matter as much as treatment type.

### **6.4 Psychological profiling at modality selection**

Current practice assigns modalities based on clinical factors (vascular access, residual function, comorbidities) with little attention to psychological fit. We believe this is a missed opportunity. Peritoneal dialysis suits patients who value autonomy and have the cognitive capacity and stable housing to manage self-care. Hemodialysis suits those who prefer professional supervision or lack the ability for self-management. Transplantation offers superior outcomes but demands sustained medication adherence.

To the best of our knowledge, validated psychological screening tools for modality selection do not yet exist. Until they do, we recommend that pre-dialysis education assess patient coping styles and health literacy. Nephrology teams should then tailor support accordingly: cognitive monitoring and intradialytic hypotension prevention for hemodialysis patients, anxiety management and realistic immunosuppression counseling for transplant recipients, and enhanced technical training for peritoneal dialysis patients. The choice of RRT method should be a shared decision that incorporates psychological resilience and preference, not just clinical availability.

### **6.5 Interpreting Heterogeneity Across Contexts**

Our review highlights substantial variation in outcomes across studies, populations, and healthcare systems. We believe this heterogeneity is not simply noise to be overcome. It reflects real differences in how modalities perform in different contexts. Transplant access varies globally. Home support systems for peritoneal dialysis differ. Cultural attitudes toward self-management shape success. These differences mean that findings from one healthcare system may not apply to another. We caution against universal prescriptive statements and instead recommend that local clinicians consider their own patient populations and resources when weighing modality options.

### 6.6 Future directions

Major psychological domains remain unstudied when stratified by modality: employment, sexual function, sleep quality, and long-term psychological adjustment. We believe prospective studies using consistent measurement instruments across modalities would clarify whether observed differences reflect true modality effects or patient selection. Advanced neuroimaging studies may resolve the cognitive paradox. Validation of psychological assessment tools could transform modality selection from a logistical decision into a person-centered process.

We conclude that RRT choice profoundly shapes psychological experience. Depression, cognitive function, and quality of life are not independent outcomes but interconnected manifestations of how each modality engages the body and mind. Future practice should acknowledge these connections and help patients understand not which modality is "best," but which burden pattern aligns with their psychology, values, and life circumstances. This requires moving beyond survival statistics and comorbidity algorithms toward a more human understanding of what dialysis and transplantation demand from patients and what they gain in return.

### 7. Conclusions

The psychological burden of RRT is not a secondary outcome, but it is central to patient experience and underinvested in clinical decision-making. Our review demonstrates that depression, cognitive dysfunction, and reduced quality of life are not separate phenomena but expressions of how each modality structures daily life and body-mind demands. Yet modality selection remains driven by vascular access, residual function, and clinic logistics, with psychological fit treated as an afterthought.

Three barriers prevent implementation of psychology-informed modality selection. First, no validated instruments exist to assess psychological readiness for home-based self-management (PD) versus supervised center-based care (HD). Second, renal programs lack training in systematic psychological screening during pre-dialysis counseling. Third, the evidence base for unstudied domains such as employment, sexual function, sleep or long-term adjustment, remains too sparse to guide personalization. Until these barriers are addressed, clinical recommendations cannot be made with confidence.

Immediate priorities are clear. Nephrology teams should integrate structured assessment of patient coping capacity, health literacy, and social stability into pre-dialysis education, not as optional content but as standard of care. This assessment need not await new instruments; validated measures for coping (Brief COPE), health literacy (HLQ), and social support (MSPSS) already exist and can be adapted for dialysis populations. Patients should understand before treatment begins that they will experience psychological burden, but that burden takes different forms across modalities. This shift from "which is best?" to "which fits you?" requires candid conversation, not data dumping.

Future research must address the evidence gaps that currently prevent evidence-based personalization. Prospective cohort studies should measure cognitive function, depression, sleep quality, and employment outcomes simultaneously across modalities using harmonized instruments. These studies should include baseline psychological assessment to distinguish modality effects from patient selection effects. Intervention trials testing pre-treatment psychological preparation tailored to modality choice could demonstrate whether aligned burden expectations improve adherence and psychological resilience.

The deepest issue remains unresolved: whether we view RRT as a medical intervention that preserves life or a life restructuring that patients must learn to inhabit. Our findings suggest it is both. Kidney transplantation offers the closest return to baseline function, but only for those with access and with stable immune tolerance. Hemodialysis provides reliable organ replacement but extracts weekly rhythmic sacrifice. Peritoneal dialysis preserves autonomy but requires sustained self-discipline and vigilance. No modality "solves" kidney failure, because each trades one set of constraints for another. The evidence we have reviewed shows that patients who thrive are those who understood these trade-offs beforehand and chose the burden pattern they could bear.

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