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Sex-related Differences in Health Related Quality of Life Among Hemodialysis Patients: A Systematic Review and Meta Analysis

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Abstract

Background: Health-related quality of life (HRQoL) is a key patient-centered outcome in hemodialysis (HD) care, but sex-related differences remain poorly quantified. This systematic review and meta-analysis are focused on comparing HRQoL scores between female and male HD patients across generic (SF-36) and kidney-specific (KDQOL-SF) domains.

Methods: This systematic review and meta-analysis followed PRISMA 2020 guidelines and was registered in PROSPERO (CRD420251078233). PubMed, Cochrane Library, Embase, and Google Scholar were searched for observational studies reporting HRQoL by sex in adult HD patients published from January 2000 to June 2025. Two reviewers independently screened studies, extracted data, and assessed risk of bias. Mean differences (Females–Males) were pooled using REML random-effects models (95% CI), heterogeneity was quantified using I^2 and the Q-test, and small-study bias was evaluated using funnel plots and Egger's regression.

Results: Nineteen studies (N=6025; 2713 female, 3312 males) were included. In SF-36 domains, females scored lower than males across all eight scales, most notably in Bodily Pain (P<0.001), Role-Physical (P<0.001), and Physical Functioning (P<0.001). Egger's test indicated small-study bias only for Bodily Pain and General Health. In KDQOL domains, females reported worse "Symptoms and Problems" (P=0.0653) and "Effects on Daily Life" (P=0.0087), with no other significant sex differences.

Conclusion: Female HD patients consistently experience poorer HRQoL than males across multiple SF-36 and select KDQOL domains. These findings highlight the need for sex-sensitive interventions, such as tailored pain management and psychosocial support, to improve quality of life in females receiving HD.

Keywords: Hemodialysis, HRQoL, Chronic kidney disease, SF-36, Sex-related differences

Conflicts of Interest: *None declared*
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Introduction

Chronic kidney disease (CKD) is a global public health concern related to the gradual and irreversible decline of kidney function (1). By the year 2040, CKD is expected to become the fifth leading cause of years of life lost (YLL) worldwide (2). As CKD progresses to the final stage, end-stage renal disease (ESRD), patients experience almost

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↑What is "already known" in this topic:
Health-related quality of life (HRQoL) is a critical patient-centered outcome in hemodialysis (HD), encompassing physical, mental, and social well-being. Previous studies suggest that females generally report poorer HRQoL than males, influenced by biological factors such as inflammation and anemia, and psychosocial aspects like depression and caregiving burden. However, findings across HD populations have been inconsistent and lack quantitative synthesis.

→What this article adds:
This systematic review and meta-analysis integrates data from 19 studies involving over 6000 HD patients to clarify sex-related disparities in HRQoL. Female patients were found to have significantly lower scores across most domains, particularly physical functioning, pain, and emotional well-being, indicating a consistent disadvantage. These findings underscore the importance of incorporating sex-sensitive assessments and personalized interventions to improve the quality of life among females undergoing hemodialysis.

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complete kidney failure and require renal replacement therapy, usually in the form of hemodialysis (HD) (3). While HD effectively removes waste products and maintains fluid and electrolyte balance, it places substantial physical, emotional, and social strain on patients (4). These challenges often result in decreased functional capacity, increased dependency, and reduced participation in daily activities (5). Therefore, there is an urgent need for care strategies that focus not only on survival but also on the overall quality of life for patients.

Considering these, traditional clinical endpoints such as mortality or routine biochemical markers (e.g., serum urea, creatinine, potassium, calcium–phosphate balance, hemoglobin, and albumin) (6, 7) are insufficient to capture the full impact of HD. Instead, health-related quality of life (HRQoL) has emerged as a critical outcome that reflects the subjective experience of physical, psychological, and social well-being of patients (8).

HRQoL in HD patients is not only a reflection of individual well-being but is also predictive of clinical outcomes, including hospitalization and mortality. According to registry and cohort data, annual mortality among maintenance HD patients is in the order of 15–20 % (and in some reports exceeding 20 %) with cardiovascular disease responsible for 40–50 % of deaths, while hospitalization rates in HD patients average around 1.4–1.5 admissions per patient-year (9–11). Beyond survival, HD patients commonly experience multiple concurrent health problems, including anemia, hypertension, CKD-mineral and bone disorder, pruritus, sleep disturbance, and sarcopenia or muscle weakness (12–15). These comorbidities, combined with psychological stress, depression, reduced physical activity, financial burden, and limited social support, are well-documented determinants of poor HRQoL in HD populations. Therefore, accurately assessing and improving HRQoL is a vital component of patient-centered care in nephrology (16, 17).

In the broader landscape of chronic illness, sex-related differences in health outcomes are well-documented. Females with chronic diseases often report worse HRQoL than males, influenced by a complex interplay of biological, psychological, and sociocultural factors (18, 19). Biologically, estrogen fluctuations, higher prevalence of anemia, and greater inflammatory responses have been associated with fatigue and reduced physical well-being in female patients (20, 21). Psychologically, females show higher rates of depression and anxiety, partly linked to illness perception and coping styles that emphasize emotional rather than problem-focused strategies (22–24). Socioculturally, females often face a lower socioeconomic status and reduced social support, which further diminishes their perceived quality of life compared to male patients (25, 26).

In the context of HD, these differences may be amplified due to sex-specific coping mechanisms, differences in social support, and perceptions of illness (27, 28). Some studies suggest that female HD patients may report lower HRQoL scores compared to males, particularly in domains related to physical functioning, emotional well-being, and social interaction (19, 29). Other studies report no significant differences or even higher HRQoL scores for females compared to males in some domains (30, 31).

Therefore, findings across individual studies are inconsistent and sometimes contradictory, making it difficult to have definitive conclusions.

Despite a growing body of literature exploring HRQoL in HD populations, there is a lack of systematic synthesis examining sex-related differences specifically. This gap limits our understanding of whether targeted, sex-sensitive interventions are needed. A comprehensive and methodologically rigorous analysis is needed to clarify the extent and nature of sex disparities in HRQoL among HD patients.

This study aims to systematically review and quantitatively synthesize the available evidence on sex-related differences in HRQoL among adults undergoing HD. By identifying consistent patterns and potential moderators, this meta-analysis seeks to inform more equitable and personalized approaches to care in the HD population.

Methods

Reporting Guidelines and Registration

This systematic review and meta-analysis follow the PRISMA 2020 guidelines. A completed checklist is provided in the supplementary materials (Appendix B). The protocol was developed before the initiation of the review to ensure methodological transparency and minimize bias. The review protocol was registered with PROSPERO under the registration number CRD420251078233. The protocol includes detailed information on the review objectives, eligibility criteria, search strategy, data extraction methods, risk bias assessment, and statistical analysis plan.

Review Framework

This systematic review was structured according to the PI/ECO framework to define the scope and eligibility criteria. Population (P): Adult patients (≥18 years) undergoing maintenance HD for CKD. Intervention/Exposure (I/E): Female sex, representing the exposure variable in assessing sex-related differences. Comparison (C): Male hemodialysis patients, serving as the reference group. Outcome (O): HRQoL, encompassing physical, psychological, and social dimensions, as measured by validated tools such as the SF-36 and KDQOL instruments. This framework guided the development of the search strategy, inclusion/exclusion criteria, and data synthesis process.

Definitions of Sex and Gender

Following the Sex and Gender Equity in Research (SAGER) guidelines (32), sex refers to the biological characteristics in humans and animals, including chromosomal complement, gonadal and reproductive anatomy, and endogenous hormone profiles. By contrast, gender refers to socially created roles, behaviors, expressions, and identities across women, men, and gender-diverse groups. Although some HD studies label their comparison groups as “gender” when offering only the binary options of female or male, these classifications reflect biological attributes rather than social identity (32). Following SAGER

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and prevailing medical research practice, therefore, all such binary female/male distinctions in this review are treated as sex-related differences, reserving "gender" for contexts in which participants' social or identity-based self-representation is explicitly measured.

Databases and Search Terms

The electronic databases PubMed, Cochrane Library, and Embase were searched, and the search engine Google Scholar was used to identify additional relevant articles. Both Medical Subject Headings (MeSH) and keyword terms were applied. The search strategy included expressions such as "life quality", "quality of life", "health-related quality of life", "HRQoL", "dialysis", and "hemodialysis". Only English-language, peer-reviewed original research articles published between January 2000 and June 2025 were eligible for inclusion (Appendix Table A1).

Study selection

Following the database search, 2,867 records were retrieved (Figure 1). The DistillerSR software was used to remove duplicates and screen articles. Titles and abstracts of the remaining 986 articles were screened independently by two research members (Y.O. and Z.G.), and 714 articles were removed at this stage. Only studies that applied the Short Form-36 (SF-36) or the Kidney Disease Quality of Life (KDQOL) instruments to assess quality of life in adult HD populations were eligible for inclusion. Full texts of 272 articles were screened independently by two research members (Y.O. and Z.G.) against inclusion and exclusion criteria. Studies that reported full quantitative data (mean±SD, median, and IQR) separately for the male and female populations of adult HD patients were included. After applying inclusion/exclusion criteria, 19 studies were selected. Final inclusion decisions were made by consensus between two independent reviewers (Y.O. and Z.G.). In cases of disagreement, a third reviewer (Sh.K) was consulted to reach a final decision.

Inclusion criteria

Observational studies (cross-sectional, cohort, case series, descriptive, or prospective) that reported HRQoL among adult patients (≥18 years) undergoing HD, using the SF-36 or KDQOL questionnaires, were included. To be eligible, studies had to report HRQoL outcomes stratified by sex, providing exact numerical values as either mean±SD or median with IQR for each sex. Only studies published in English between January 2000 and June 2025 were included.

Exclusion criteria

Studies were excluded if they were published in languages other than English, published before January 2000, or had non-eligible study designs such as reviews, letters to the editor, editorials, commentaries, expert opinions,

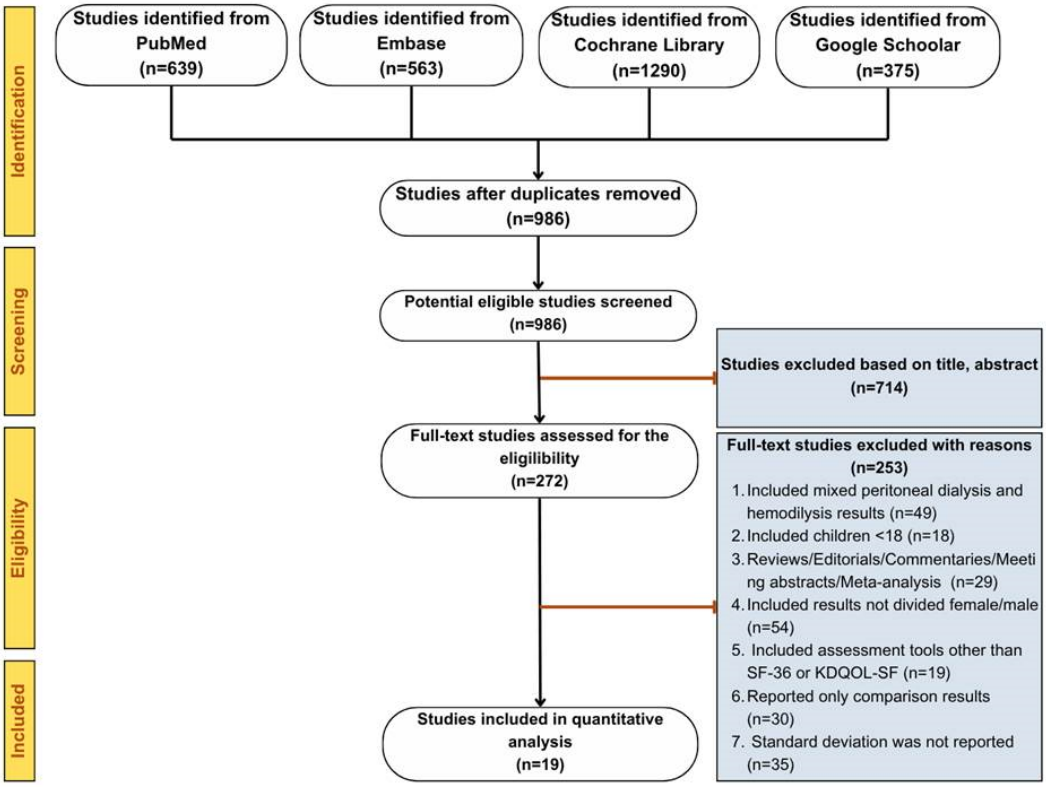

Figure 1. Flow diagram of the study selection process.

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case-control studies, randomized controlled trials, brief reports, book chapters, or theses. Studies that focused primarily on treatment effects, medications, or clinical decision-making rather than HRQoL outcomes were also excluded. Additionally, studies were excluded if they did not report HRQoL results separately for males and females, failed to use SF-36 or KDQOL-SF assessment tools, or did not provide complete numerical data (e.g., missing SDs, IQR, or full results tables).

Data Collection Tools

The SF-36 is a validated instrument that measures physical and mental health through eight domains, generating component scores (33). The KDQOL-SF includes the same 36 core questions as the SF-36, with 43 additional items specific to kidney disease. These items assess symptoms, impact on daily activities, cognitive and sexual function, social interactions, and sleep quality (34). In both tools, the score ranges from 0 (the worst) to 100 (the best) (33, 34).

Quality Assessment

The quality of the included studies was independently assessed by two reviewers (Y.O. and Z.G.) using the Newcastle–Ottawa Scale (NOS). The scale evaluates three domains: selection of study participants, comparability of groups, and outcome assessment. Each criterion was scored as 1 if clearly reported and 0 if unreported or unclear. Disagreements between reviewers were resolved through discussion or consultation with a third reviewer (Sh.K). The total quality score ranged from 0 (lowest quality) to 9 (highest quality). Studies scoring 7–9 were considered high quality, 4–6 fair quality, and those scoring below 4 were classified as low quality (35).

Data Extraction

Two independent reviewers (Y.O. and Z.G.) extracted data using a standardized data extraction form. The following information was recorded for each included study: first author's name, year of publication, country or region of study, study design, type of HRQoL instrument used, total sample size, quality assessment score, key sociodemographic characteristics of participants, and HRQoL outcomes stratified by sex. In cases of disagreement during data extraction, a third reviewer (Sh.K) was consulted to reach a consensus. Extracted data were tabulated and used for both narrative synthesis and meta-analysis.

Data Analysis

All meta-analyses were performed in RStudio (v4.2.3). For each SF-36 and KDQOL domain, we calculated the mean difference (MD) (Females–Males) and its standard error (SE) from each study and then pooled these estimates under a random-effects model (REML estimator) to accommodate both within- and between-study variation. Between-study heterogeneity was quantified by I^2, τ^2, and Cochran's Q (with k–1 degrees of freedom), and interpreted as low (<25 %), moderate (<50 %), or high (<75 %). Small-study bias was examined using both funnel plot inspection and Egger's regression (intercept, 95% CI, t-statistic, p-value). A p-value below 0.10 was interpreted as suggestive of asymmetry. All pooled MDs are accompanied by two-sided p-values ($\alpha = 0.05$), and the corresponding forest and funnel plots for each domain.

Results

Overview of meta-analysis

Data extracted from 19 studies yielded a total of 2,713 female and 3,312 male HD patients (Table 1). The included studies were published between 2000 and 2025, used either the SF-36 (n=13) or KDQOL-SF (n=6) instruments, and covered 13 different countries. Study quality (NOS) ranged from 5 to 8 (median=7). Extracted outcome data were then subjected to random-effects meta-analysis across core SF-36 domains. The next section presents pooled MD for each domain, along with heterogeneity and small-study bias assessments.

SF-36 HRQoL domains

Table 2 summarizes the pooled MD for all eight SF-36 domains, comparing female versus male HD patients.

Across domains, females consistently reported lower HRQoL scores than males, with statistically significant differences detected across Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, and Mental Health. Appendix Figures A1–16 present both forest and funnel plots, as well as corresponding heterogeneity statistics (I^2, τ^2, Q-tests) and Egger's regression results for each SF-36 domain.

Across all eight SF-36 domains, female HD patients consistently reported lower HRQoL scores than males, with a statistically significant difference observed. Between-study heterogeneity ranged from low (Role Physical, I^2=26.4%; Role Emotional, I^2=29.4%) to moderate (Mental Health, I^2=47.7%; Vitality, I^2=36.1%) and was highest for Social Functioning and Physical Functioning (I^2=53.3% and I^2=58.0%, respectively). Funnel-plot inspection and Egger's regression tests revealed no evidence of small-study bias for domains, except Bodily Pain (t_{12}=–3.47; P=0.0046) and General Health (t_{12}=–3.77; P=0.0027), which showed significant asymmetry.

Physical Component Summary

Ten studies (N=3987, 1844 females, 2143 males) contributed SF-36 Physical Component Summary (PCS) scores in HD patients (Figure 2A). Across these studies, females scored on average 2.50 points lower than males ($p<0.001$), indicating a statistically significant disadvantage in the overall physical health summary for female patients. Between-study heterogeneity was substantial (I^2=73.5%, τ^2=3.2475, Q_9=33.94). Visual inspection of the funnel plot and formal testing found no evidence of small-study bias (Egger's intercept= –3.12; 95% CI –6.52 to 0.27; t(8)=0.22; P=0.8334) (Figure 2B).

Mental Component Summary

In the Mental Component Summary (MCS), ten studies (total N =3987, 1844 females, 2143 males) were pooled (Figure 3A). Females scored, on average, 2.30 points lower than males (P=0.0028), indicating a small but statisti-

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Table 1. Characteristics of Studies Included in the Meta-Analysis

Year of publication	Authors	HRQoL instrument	Country	Type of study	Female sample size (n)	Male sample size (n)	NOS score	Ref.
2000	Rebollo et al.	SF-36	Spain	CS	82	87	6	(36)
2002	Molsted et al.	SF-36	Denmark	CS	39	70	7	(37)
2004	Chiang et al.	SF-36	Taiwan	MCS	275	222	7	(38)
2005	Kutner et al.	KDQOL-SF	US	CO	788	891	6	(39)
2010	Lopes et al.	KDQOL-SF	Brazil	CS	355	513	7	(40)
2011	Germin-Petrović et al.	SF-36	Croatia	CS	130	125	6	(41)
2013	Ho et al.	KDQOL-SF	Malaysia	DCS	42	30	6	(42)
2014	Mandoorah et al.	SF-36	Saudi Arabia	CS	82	123	6	(43)
2016	Okasha et al.	KDQOL-SF	Eqypt	DCS	76	121	5	(44)
2016	Weiss et al.	SF-12	Germany	CES	368	492	8	(45)
2017	Hajian-Tilaki et al.	SF-36	Iran	CompCS	69	85	7	(46)
2017	Zhou et al.	SF-36	China	MCS	60	65	6	(47)
2017	Alves et al.	SF-36	Brazil	ACS	76	121	8	(48)
2023	Togay et al.	SF-36	Turkey	CS	48	49	6	(49)
2024	Riehl-Tonn et al.	SF-36	Canada	CompO	26	34	7	(50)
2024	Machaca-Choque et al.	SF-36	Peru	CS	83	124	7	(51)
2024	Sahu et al.	KDQOL-SF	India	DCS	34	70	8	(52)
2024	Shinjar et al.	KDQOL-SF	Iraq	ACS	22	28	5	(53)
2024	Bodesova et al.	SF-36	Kazakhstan	PC	58	62	8	(54)

Abbreviations: CS – Cross-sectional study; DCS – Descriptive cross-sectional study; ACS – Analytical cross-sectional study; MCS – Multicenter cross-sectional study; CES – Cross-sectional epidemiological study; CO – Cohort observational study; PC – Prospective cohort study; CompCS – Comparative cross-sectional study; CompO – Comparative observational study.

Table 2. Meta-analytic summary of eight SF-36 HRQoL domains for female versus male HD patients

Domain	Definition	k	MD [95 % CI]	I^2	*P*-value
Physical Functioning	Ability to perform physical activities (e.g., walking, lifting, climbing stairs).	14	-9.78 (-12.44, -7.13)	58.0%	0.0035*
Role Physical	Role limitations at work/home due to physical health problems.	13	-5.00 (-7.32, -2.67)	26.4%	0.1776
Bodily Pain	Intensity of pain and interference with normal activities.	14	-7.46 (-9.79, -5.12)	41.6%	0.0514
General Health	Overall health perceptions and outlook (current and expected).	14	-3.97 (-5.51, -2.43)	36.4%	0.0846
Vitality	Energy and fatigue levels.	14	-4.32 (-5.95, -2.70)	36.1%	0.0867
Social Functioning	Impact of physical/emotional problems on social activities.	14	-4.06 (-6.56, -1.56)	53.3%	0.0095*
Role Emotional	Role limitations at work/home due to emotional problems.	13	-3.43 (-6.23, -0.62)	29.4%	0.1493
Mental Health	Psychological well-being (e.g., anxiety, depressed mood, positive affect).	14	-3.80 (-5.58, -2.02)	47.7%	0.0241*

k denotes the number of included studies; MD is the pooled mean difference (Females − Males) with 95 % CI; I^2 indicates the percentage of total variability due to between-study heterogeneity; and *P*-value tests whether the pooled MD differs from zero (*P<0.05).

cally significant difference in mental HRQoL scores. Between-study variability was considerable (I^2=71.3%, τ^2=3.6796, Q_9=31.40). The corresponding funnel plot did not reveal notable asymmetry, and Egger's regression test (intercept=1.74; 95% CI = –1.92 to 5.39; t_8 =–2.29; p=0.0510) provided no evidence of small-study bias (Figure 3B).

Kidney disease component summary

The KDQOL kidney disease components analyzed in this study capture dialysis-specific concerns beyond generic HRQoL. Symptoms/Problems reflect the frequency and bother of common CKD/HD symptoms (e.g., cramps, pruritus, dyspnea). Effects of Kidney Disease on Daily Life gauges how kidney disease interferes with everyday activities, time demands, and independence. Cognitive Function assesses attention, memory, and clarity of thought. Burden of Kidney Disease summarizes perceived overall burden, frustration, and time consumed by the illness. Sleep covers sleep quality, adequacy, and disturbances. Dialysis Staff Encouragement reflects perceived support, respect, and information from dialysis personnel. Social Support measures the availability and adequacy of help from family and friends. Dialysis Care Satisfaction rates overall satisfaction with dialysis care (30, 34).

Six studies (N=2920 HD patients, 1295 females, 1625 males) reported scores on the Symptoms and Problems domain of the Kidney disease component summary (KDCS). In the random-effects meta-analysis, female patients scored on average 3.70 points lower than male patients (P<0.001), indicating a statistically significant sex-related difference in symptoms and problems of kidney disease (Figure 4A). Between-study heterogeneity was moderate (I^2 =51.8%, τ^2 =3.07; Q_5 =10.38). Visual

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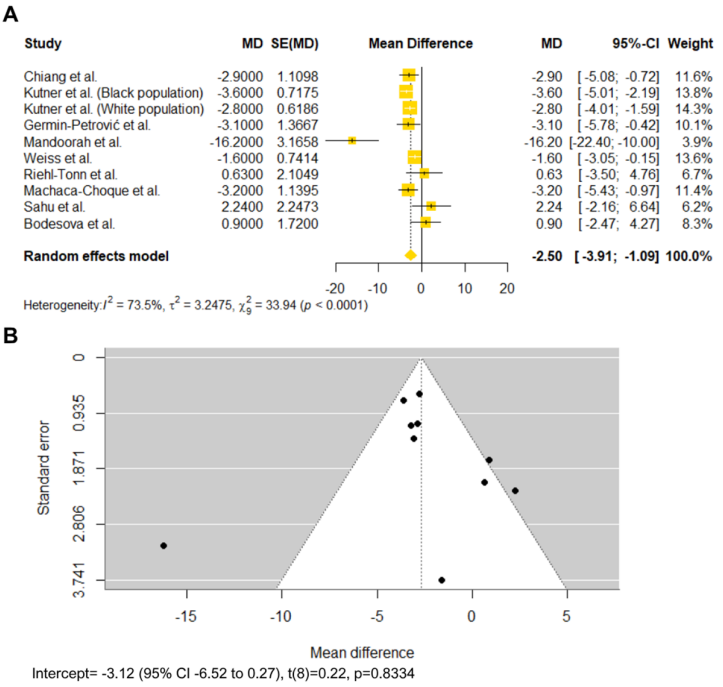

Figure 2. Forest Plot and Funnel of PCS scores in HD Patients. (A) Mean differences (Females−Males) in SF-36 PCS scores from 10 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= –2.50), and the sloping dotted lines show the 95% pseudo–confidence limits around that estimate.

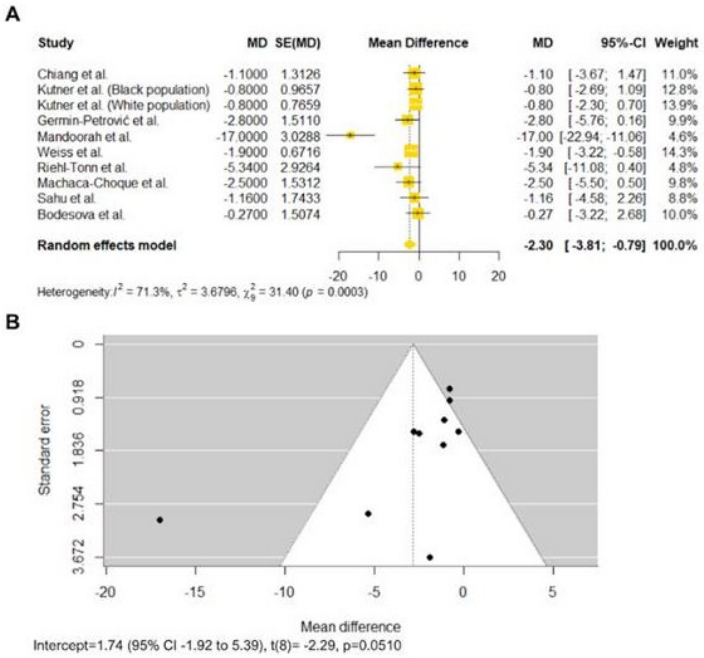

Figure 3. Forest Plot and Funnel Plot of MCS scores in HD Patients. (A) Mean differences (Females−Males) in SF-36 MCS scores from 10 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= –2.30), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

inspection of the funnel plot revealed no marked asymmetry, and Egger's regression test did not reach statistical

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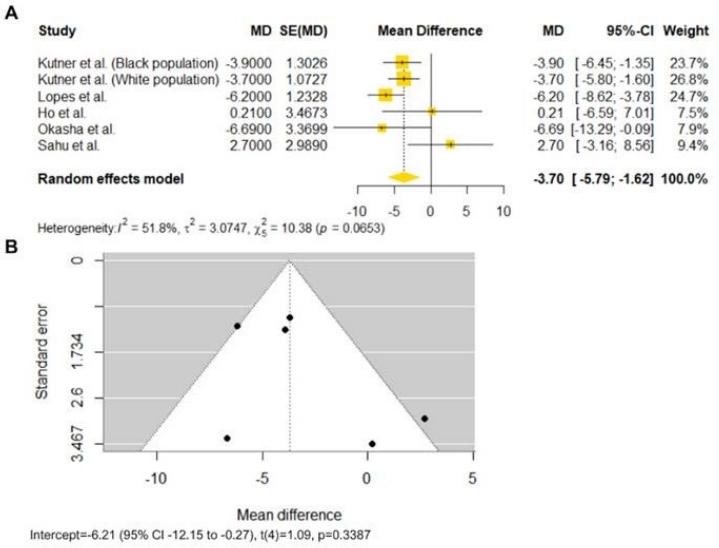

Figure 4. Forest Plot and Funnel Plot of Symptoms and Problems KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 6 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= –3.70), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

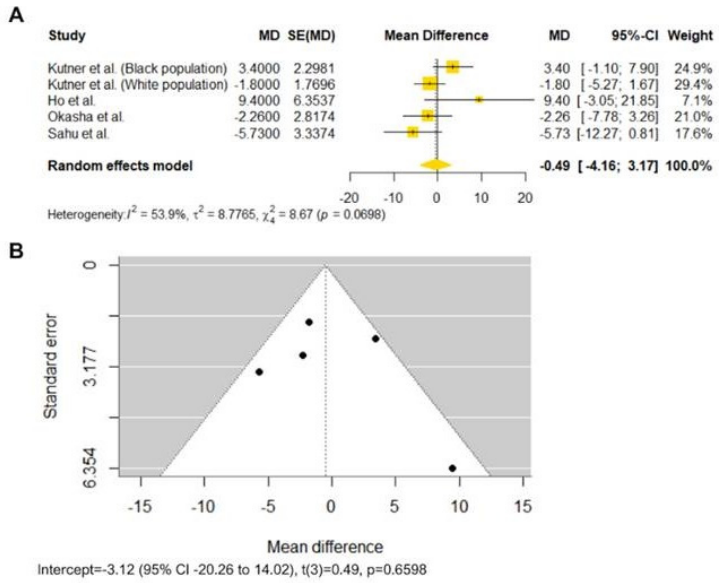

Figure 5. Forest Plot and Funnel Plot of Burden of Kidney Disease KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 5 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= –0.49), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

significance (intercept= –6.21; 95% CI –12.15 to –0.27; t_4 =1.09; *P*=0.3387), suggesting no evidence of small-study bias (Figure 4B).

Five studies (N=2052 HD patients, 940 females, 1112 males) reported scores on the Effects of kidney disease on daily life domains of KDCS. Females scored 2.41 points higher than males in the "Effects of kidney disease on daily life" domain (*P*=0.0136), indicating that females perceived the disease as having a significantly less negative impact on daily life (Figure 5A).

Four studies (N=1948 HD patients, 906 females, 1042 males) reported the Cognitive function domain; there was

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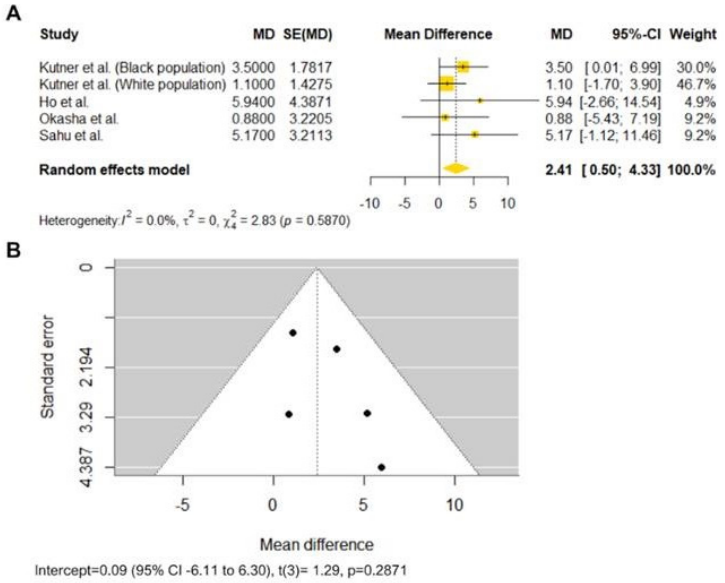

Figure 6. Forest Plot and Funnel Plot of Effects of Kidney Disease on Daily Life KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 5 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= 2.41), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

a statistically significant sex-related difference (*P*=0.0198). (Figure 6A). Between-study heterogeneity was negligible (I^2=0.0%) for both domains. Visual inspection of the funnel plots showed no meaningful asymmetry, and Egger's tests did not indicate small-study bias (both *P*>0.20) (Figure 5B and Figure 6B).

In the random-effects meta-analysis, none of the assessed domains, including kidney disease burden, sleep quality, dialysis staff encouragement, social support satisfaction, and dialysis care satisfaction, showed sex-related differences, with all *P*-values exceeding 0.05. All domains had negligible to moderate heterogeneity (I^2 = 0.0–53.9 %) and no evidence of small-study bias on Egger's regression in any domain. Forest and funnel plots for these domains can be found in Appendix Figures A17–21.

Discussion

In this comprehensive meta-analysis of 19 studies encompassing over 6000 HD patients, the consistent, statistically significant sex-related differences in HRQoL were demonstrated across most domains. Women scored lower than men by 3–8 points on average, with the largest gaps in Bodily Pain (MD=–7.46, *P*<0.001) and Physical Functioning (MD=–9.78, *P*<0.001). This indicates that female HD patients experience disproportionately greater symptoms, functional limitations, and discomfort. These sex-related differences persisted despite varying instruments (SF-36 vs. KDQOL) and geographic settings, highlighting their robustness.

Our finding of a substantial female disadvantage in physical domains accords with prior reports in non-dialysis populations (55, 56) and highlights the complex burden of HD. Potential drivers include sex differences in muscle mass, inflammatory responses, and pain perception, as well as greater psychological distress and caregiving roles among females (57–61). In the MCS (MD=–2.30, *P*=0.0028) and Role Emotional domain (MD= –3.43, *P*=0.0164), females also scored lower, suggesting that mental health and emotional role limitations are also present. These gaps may reflect sex-specific coping styles or disparities in social support networks (62–64).

Although most domains showed minimal small-study bias, significant funnel-plot asymmetry emerged for Bodily Pain and General Health, indicating that smaller studies may overestimate these sex differences. Nevertheless, the overall pattern across more than 14 studies per domain lends confidence in the generalizability of results obtained.

In the KDQOL kidney-specific component, females scored significantly lower than males in Symptoms/Problems (MD=–3.70, *P*<0.001), indicating greater symptom burden. Conversely, females showed significantly greater scoresin Effects of Kidney Disease on Daily Life (MD=+2.41, *P*=0.0136), suggesting they perceived a lesser impact of kidney disease on daily functioning. This may reflect sex-based differences in symptom processing, stress response, or health behavior. Females may engage more frequently in emotion-focused coping and seek social support, which can mitigate perceived disruption (28, 65, 66). Males, on the other hand, may experience greater functional loss or psychological burden when chronic illness limits physical performance or autonomy (56,67,68).

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A significant sex-related difference was also detected in Cognitive Function (P=0.0198). No significant differences were found for Burden of Kidney Disease, Sleep, Dialysis Staff Encouragement, Social Support, or Dialysis Care Satisfaction. The absence of differences in these latter domains may reflect adequate psychosocial or institutional support structures that buffer female patients, or may simply reflect limited study numbers.

Taken together, the domain-specific deficits observed in females, greater pain and functional limitation (Bodily Pain MD=–7.46; Physical Functioning MD=–9.78), poorer mental well-being (MCS MD=–2.30; Role Emotional MD=–3.43), and higher kidney-specific symptom burden (KDQOL Symptoms/Problems MD=–3.70), provide the empirical basis for sex-tailored interventions. In practice, this includes (i) pain-focused protocols (multimodal analgesia and symptom management) to address higher pain scores (57, 68); (ii) structured physical rehabilitation/strength training to mitigate functional limitations (57,68); and (iii) psychosocial services (screening and treatment for depression/anxiety, coping-skills training, and peer support) to target mental health and emotional role deficits (60,62). The positive difference in Effects of Kidney Disease on Daily Life (MD=+2.41) further suggests that intervention content and delivery may need to be differentiated by sex to optimize perceived daily functioning (28, 65, 66).

Future research should delineate the mechanistic underpinnings of these sex disparities, spanning hormonal regulation, inflammatory pathways, anemia/iron metabolism, and neuropsychological stress responses. Longitudinal studies are needed to test whether gaps widen or attenuate over time and whether females and males differentially benefit from interventions (e.g., structured exercise programs, symptom-targeted pain therapies). In parallel, qualitative studies (e.g., in-depth interviews, focus groups) can elicit gendered experiences of HD burden and coping that are not fully captured by quantitative instruments.

Key strengths include the large pooled sample, use of standardized HRQoL instruments, comprehensive heterogeneity and bias assessments, and pre-registration of our protocol in PROSPERO. Limitations are moderate heterogeneity in some domains (e.g., I^2 = 58 % for Physical Functioning), reliance on observational data (precluding causal inference), and underrepresentation of studies from low-resource settings. Finally, many of the primary studies used the terms “sex” and “gender” inconsistently, highlighting the need for clearer and more standardized reporting in future research.

Conclusion

Female HD patients experience significantly poorer HRQoL than males across multiple domains, particularly in physical functioning, pain, and emotional well-being. These findings underscore the need for sex-sensitive assessment and targeted interventions to improve the lived experience of females on HD.

Authors’ Contributions

Conceptualization, Y.O., Z.G., and Sh.K.; methodology, Y.O., Z.G., and Sh.K.; software, Y.O.; validation, Z.G. and Sh.K.; formal analysis, Y.O., Z.G., and Sh.K.; investigation, Y.O., Z.G., and Sh.K.; resources, Y.O.; data curation, Y.O., Z.G., and Sh.K..; writing-original draft preparation, Y.O.; writing-review and editing, Z.G. and Sh.K.; visualization, Y.O. and Z.G.,; supervision, Sh.K.; project administration, Y.O. and Sh.K; All authors have read and agreed to the published version of the manuscript.

Ethical Considerations

Ethical review and approval were not necessary for this work.

Acknowledgment

Not applicable.

Conflict of Interests

The authors declare that they have no competing interests.

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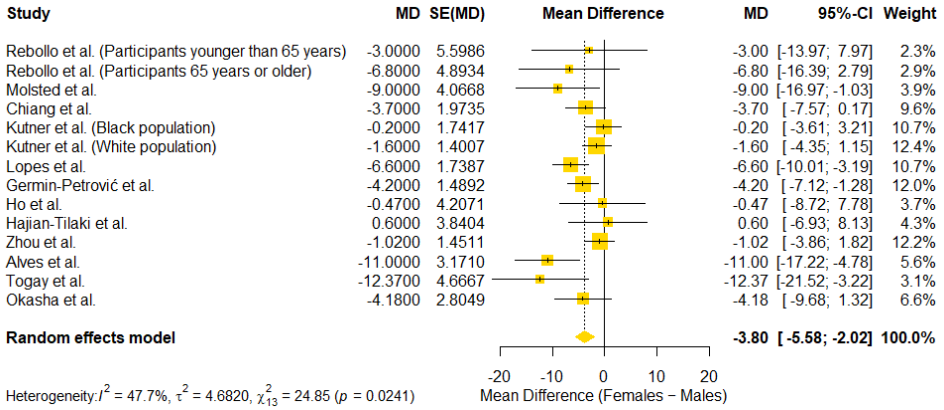
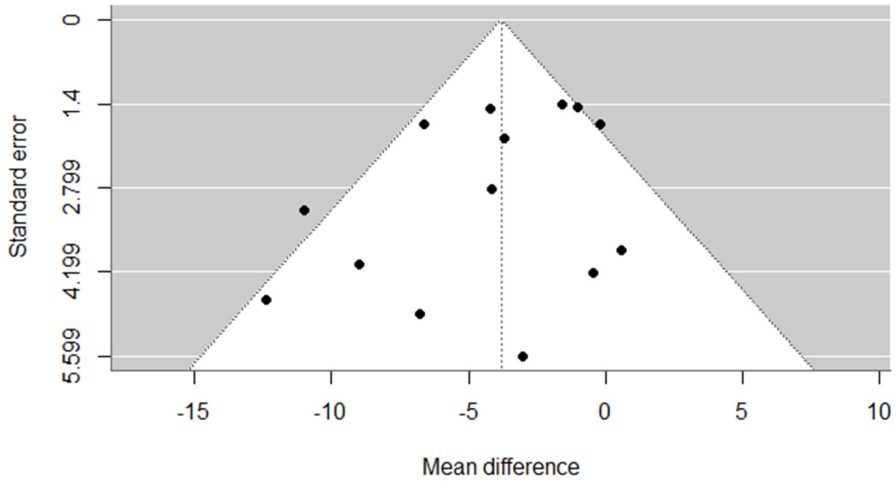
Appendix Table A1. Detailed search strategies for each database/search engine

Database/search engine	Search Query / Strategy	Filters Applied
PubMed	("hemodialysis"[MeSH Terms] OR "hemodialysis"[Title/Abstract] OR "dialysis"[Title/Abstract]) AND ("quality of life"[MeSH Terms] OR "health-related quality of life"[Title/Abstract] OR "HRQoL"[Title/Abstract] OR "life quality"[Title/Abstract])	Language: English; Publication type: Journal Article; Species: Humans; Date range: Jan 2000 – Jun 2025
Embase	('hemodialysis'/exp OR 'dialysis'/exp) AND ('quality of life'/exp OR 'health-related quality of life':ab,ti OR 'HRQoL':ab,ti OR 'life quality':ab,ti)	Language: English; Humans; Date range: 2000–2025
Cochrane Library	(hemodialysis OR dialysis) in Title, Abstract, or Keywords AND ("quality of life" OR "health-related quality of life" OR "HRQoL")	Date range: 2000–2025; Trials and Reviews only
Google Scholar	"hemodialysis" + "quality of life" + "HRQoL" + "gender difference"	Language: English; Date range: 2000–2025; first 200 results screened



Appendix Figure A1. Forest Plot of Physical Functioning domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown Figure S2.



Appendix Figure A2. Funnel Plot of Physical Functioning domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –3.80), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = –

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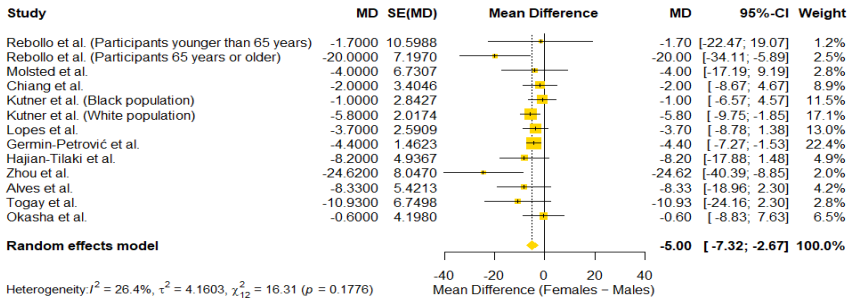
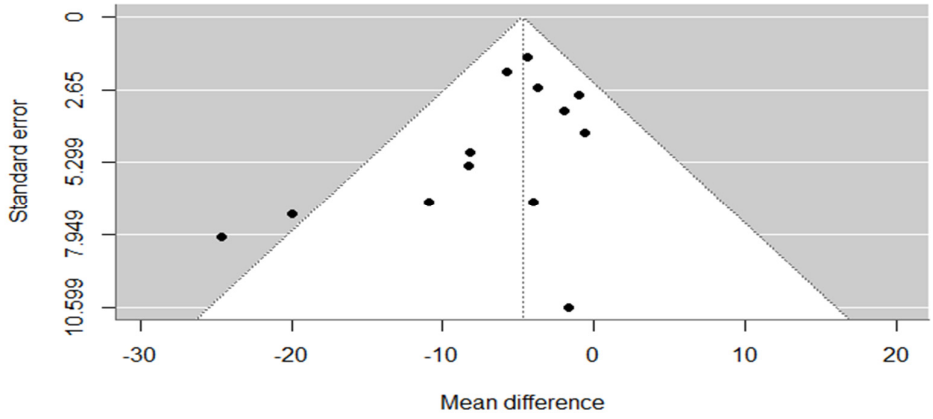
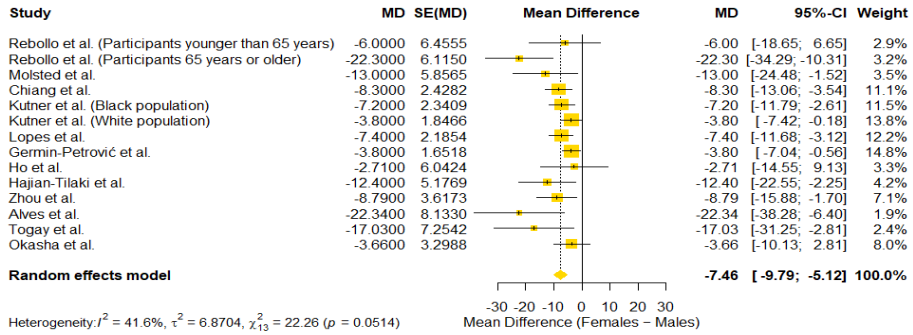


Appendix Figure A3. Forest Plot of Role Physical domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 13 studies (N = 4332; 1983 females, 2349 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.



Appendix Figure A4. Funnel Plot of Role Physical domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –5.00), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = –2.19 (95 % CI –6.24 to 1.86), t(11) = –1.61, p = 0.1347 (no evidence of small-study bias).



Appendix Figure A5. Forest Plot of Bodily Pain domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.

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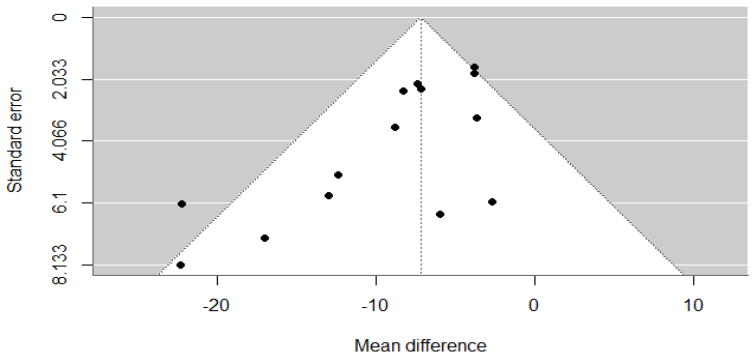
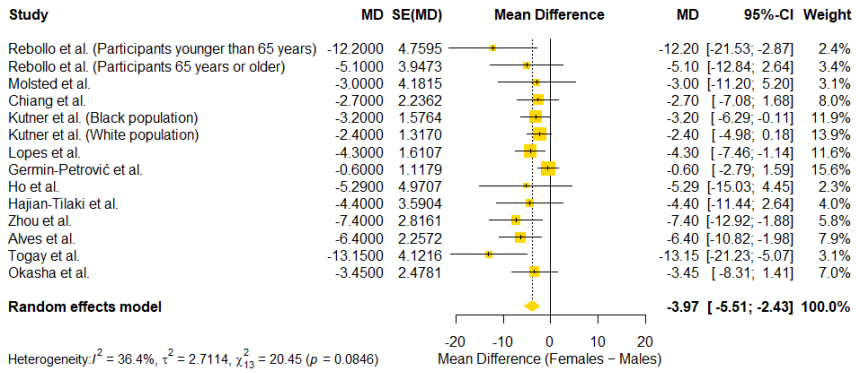
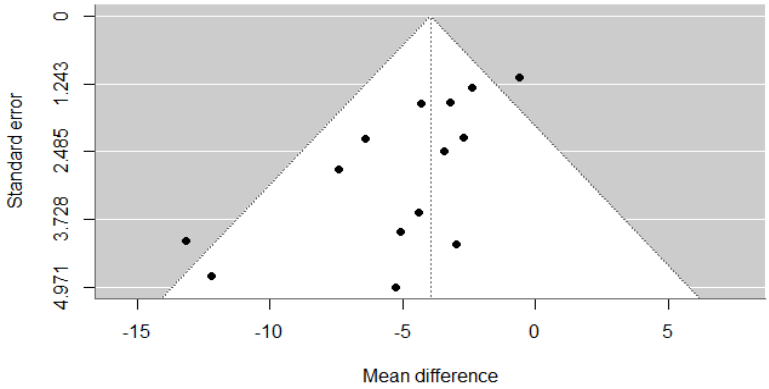


Appendix Figure A6. Funnel Plot of Bodily Pain domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –7.46), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = –1.46 (95 % CI –5.01 to 2.09), t(12) = –3.47, p = 0.0046 (indicating significant small-study effects).



Appendix Figure A7. Forest Plot of General Health domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.



Appendix Figure A8. Funnel Plot of General Health domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –3.97), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = 0.46 (95 % CI -1.96 to 2.87), t(12) = –3.77, p = 0.0027 (indicating significant small-study effects).

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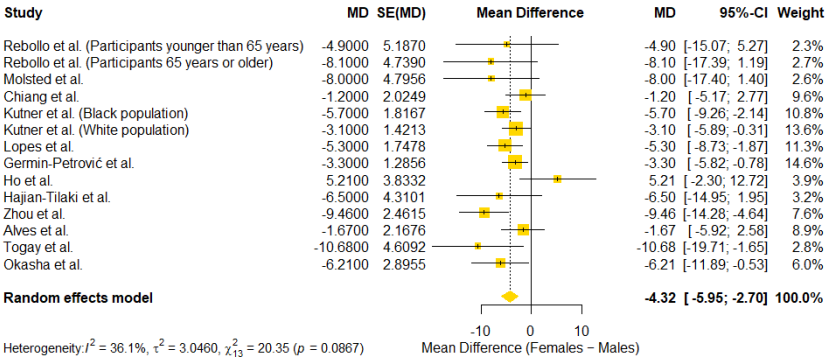
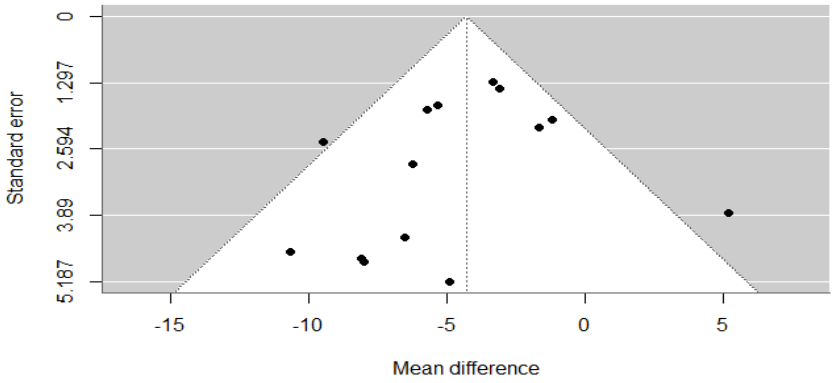
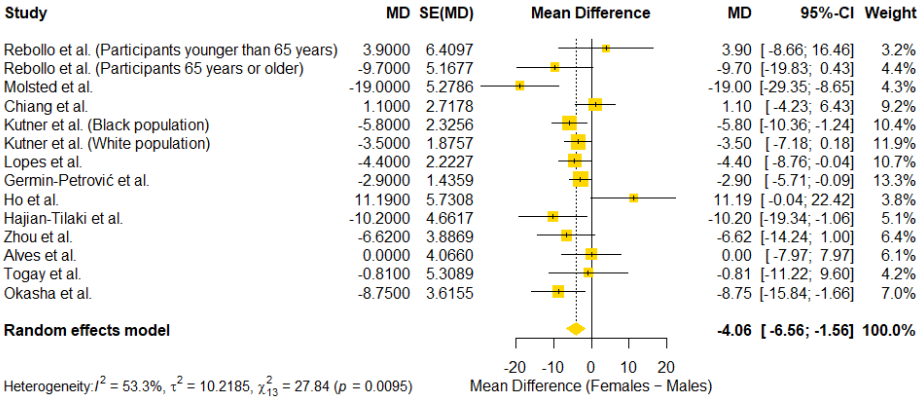


Appendix Figure A9. Forest Plot of Vitality domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.



Appendix Figure A10. Funnel Plot of Vitality domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –4.32), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = -2.50 (95 % CI -6.37 to 1.36), t(12) = –0.99, p = 0.3404 (no evidence of small-study bias).



Appendix Figure A11. Forest Plot of Social Functioning domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.

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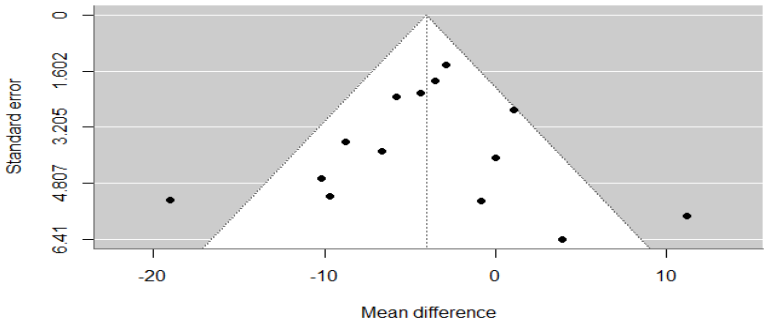
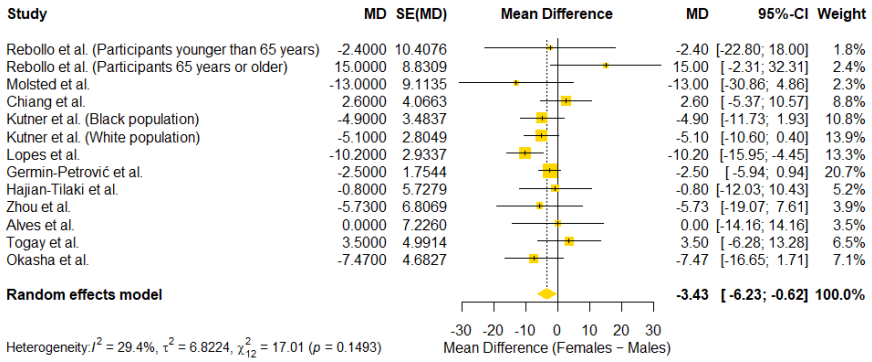
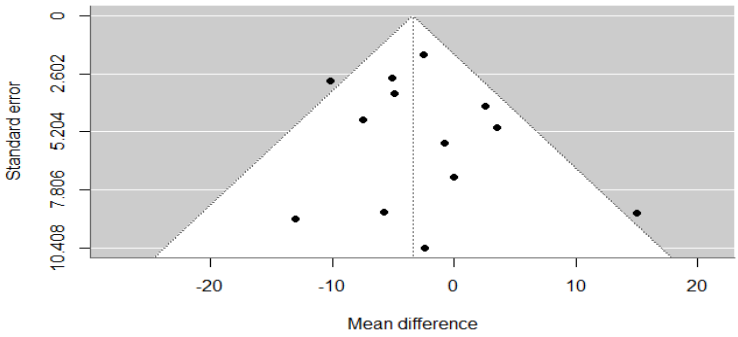
[DOI: 10.47176/mjiri.39.167]



Appendix Figure A12. Funnel Plot of Social Functioning domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –4.06), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = -3.00 (95 % CI -8.68 to 2.68), t(12) = –0.33, p = 0.7466 (no evidence of small-study bias).



Appendix Figure A13. Forest Plot of Role Emotional domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 13 studies (N = 4332; 1983 females, 2349 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.



Appendix Figure A14. Funnel Plot of Role Emotional domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –3.43), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = -5.00 (95 % CI -10.73 to 0.73), t(11) = 0.64, p = 0.5354 (no evidence of small-study bias).

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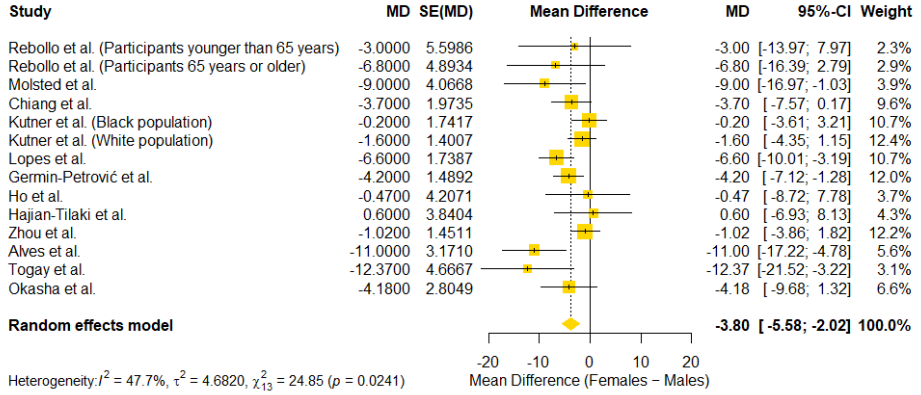
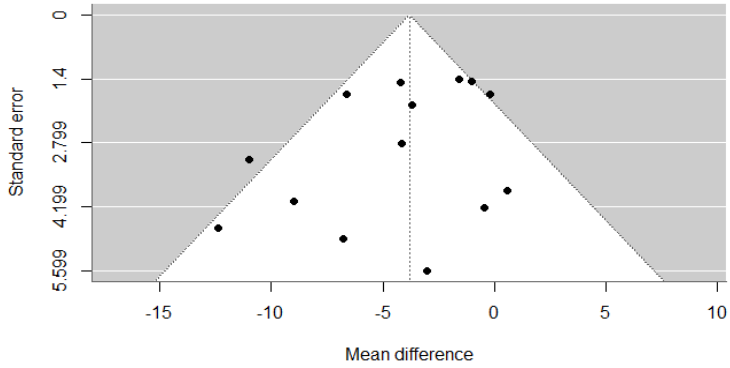


Appendix Figure A15. Forest Plot of Mental Health domain scores in HD Patients. Mean differences (Females − Males) in SF-36 PCS scores from 14 studies (N = 4419; 2040 females, 2379 males). Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below.



Appendix Figure A16. Funnel Plot of Role Emotional domain scores in HD Patients. Each point represents one study's mean difference (Females – Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD = –3.80), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate. Egger's regression test for funnel-plot asymmetry: intercept = -0.77 (95 % CI -4.72 to 3.17), t(12) = -1.54, p = 0.1494 (no evidence of small-study bias).

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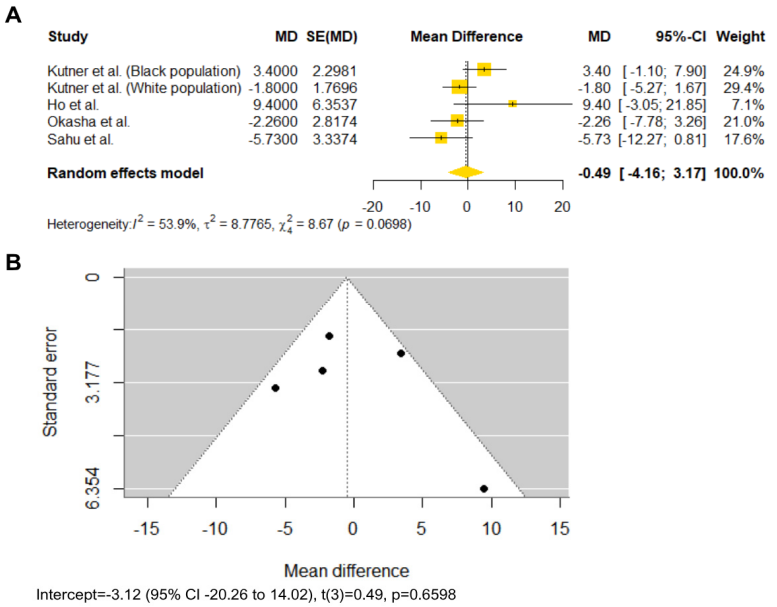
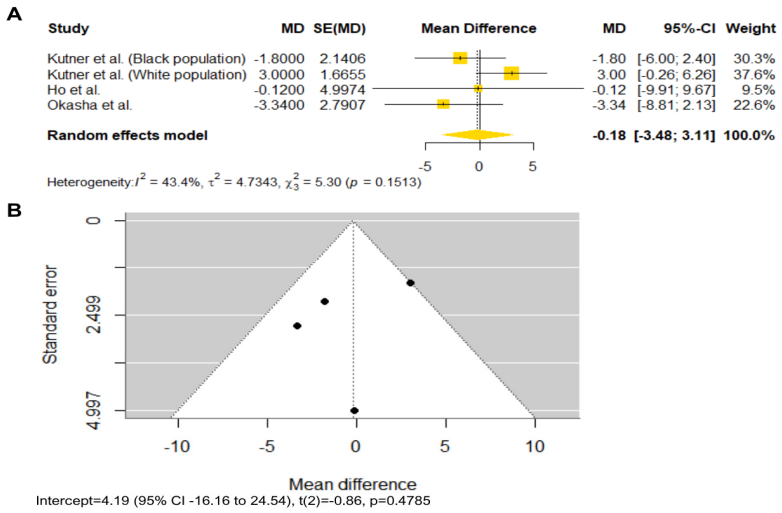


Appendix Figure A17. Forest Plot and Funnel Plot of Burden of Kidney Disease KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 5 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= –0.49), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.



Appendix Figure A18. Forest Plot and Funnel Plot of Sleep Quality KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 4 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= -0.18), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

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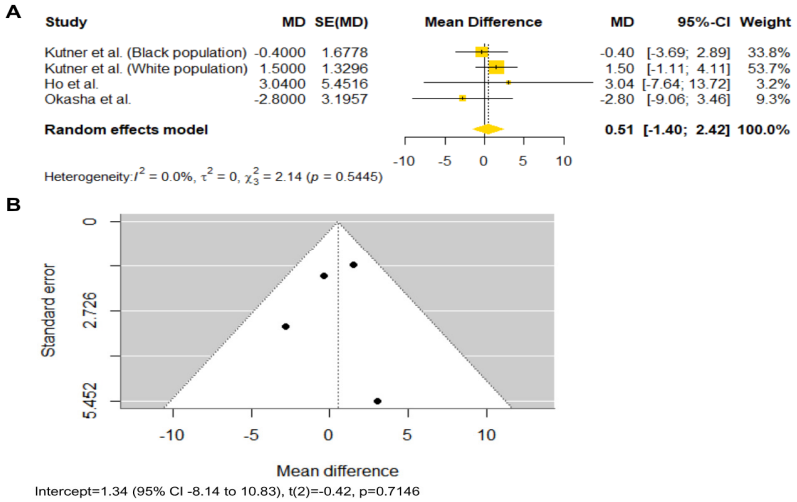
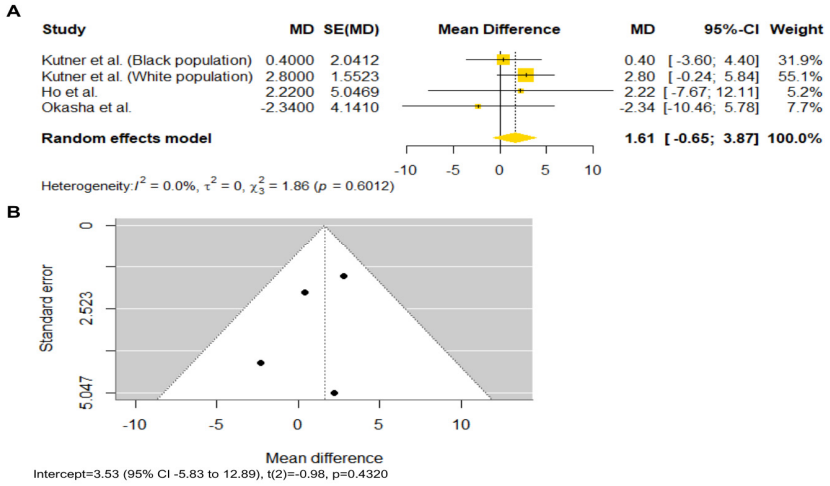


Appendix Figure A19. Forest Plot and Funnel Plot of Dialysis staff encouragement KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 4 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_3, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= 0.51), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.



Appendix Figure A20. Forest Plot and Funnel Plot of Social support satisfaction KDCS scores in HD Patients. (A) Mean differences (Females−Males) from 4 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_3, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= 1.61), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

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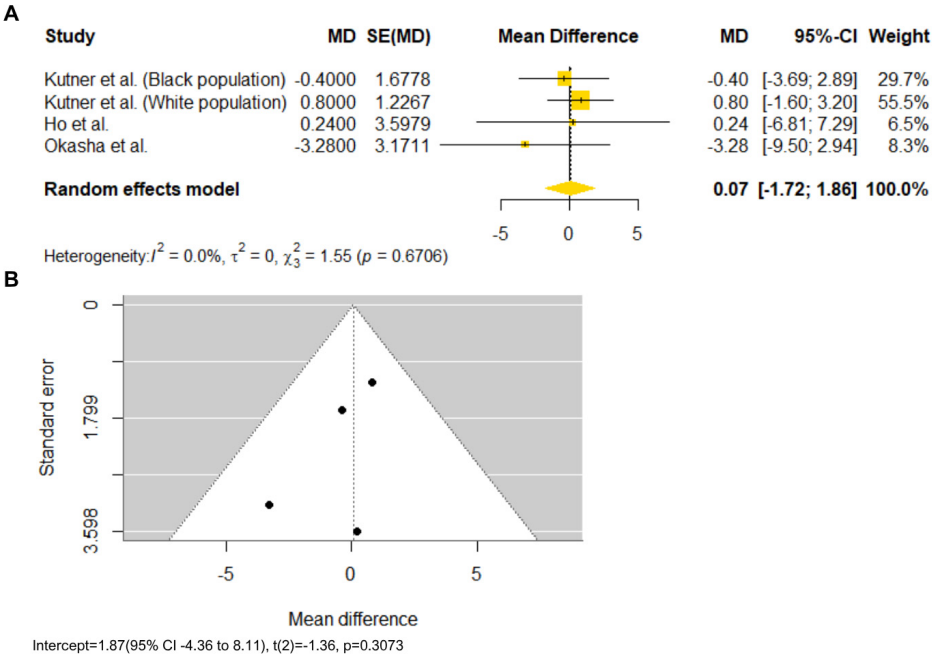

Appendix Figure A21. Forest Plot and Funnel Plot of Dialysis Care Satisfaction (KDCS) Scores in HD Patients. (A) Mean differences (Females−Males) from 4 studies. Squares show study estimates (95% CI), sized by weight; the vertical line at zero indicates no difference. The diamond shows the pooled random-effects MD (95% CI). Heterogeneity (I^2, τ^2, Q_9, p-value) is shown below. (B) Each point represents one study's mean difference (Females–Males) against its standard error. The vertical dashed line marks the overall pooled effect (MD= 0.07), and the sloping dotted lines show the 95 % pseudo–confidence limits around that estimate.

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