Subjective cognitive complaints in end-stage renal disease: a systematic review and meta-analysis

Frederick H. F. Chan[1], Zack Z. S. Goh[1], Xiaoli Zhu[1,2], Lorainne Tudor Car[1,3], Stanton Newman[4], Behram A. Khan[5,6], Konstadina Griva[1*]

[1] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

[2] Nursing Services, National Healthcare Group Polyclinics, Singapore

[3] Department of Primary Care and Public Health, Imperial College London School of Public Health, London, UK

[4] School of Health Sciences, Division of Health Services Research and Management, City University of London, London, UK

[5] National Kidney Foundation, Singapore

[6] Yong Loo Lin School of Medicine, National University of Singapore, Singapore

[*] Corresponding author: Konstadina Griva, konstadina.griva@ntu.edu.sg

Authors' Contributions: research idea and study design: FC, LTC, KG; data acquisition: FC, ZG, XZ; data analysis/interpretation: FC, KG; supervision or mentorship: LTC, KG; manuscript drafting and revision: FC, ZG, XZ, LTC, SN, BK, KG.

Funding: This work was support by the Venerable Yen Pei-National Kidney Foundation Research Fund, Singapore (NKFRC/2021/01/02).

Financial disclosure: The authors declare that they have no relevant financial interests.

Data availability statement: The authors have full control of data and agree to allow the journal to review the data if requested.

Abstract

Cognitive impairment is common in patients with end-stage renal disease (ESRD) and is associated with compromised quality of life and functional capacity, as well as worse clinical outcomes. Most previous research and reviews in this area were focused on objective cognitive impairment, whereas patients' subjective cognitive complaints (SCCs) have been less well-understood. This systematic review aimed to provide a broad overview of what is known about SCCs in adult ESRD patients. Electronic databases were searched from inception to January 2022, which identified 221 relevant studies. SCCs appear to be highly prevalent in dialysis patients and less so in those who received kidney transplantation. A random-effects meta-analysis also shows that haemodialysis patients reported significantly more SCCs than peritoneal dialysis patients (standardised mean difference -0.20, 95% confidence interval -0.38 to -0.03). Synthesis of longitudinal studies suggests that SCCs remain stable on maintenance dialysis treatment but may reduce upon receipt of kidney transplant. Furthermore, SCCs in ESRD patients have been consistently associated with hospitalisation, depression, anxiety, fatigue, and poorer quality of life. There is limited data supporting a strong relation between objective and subjective cognition but preliminary evidence suggests that this association may be domain-specific. Methodological limitations and future research directions are discussed.

Keywords: subjective cognitive complaint; end-stage renal disease; dialysis; kidney transplantation; systematic review; meta-analysis

Introduction

Chronic kidney disease is a progressive disease defined as the presence of kidney damage or reduced kidney function for at least three months (Levey et al., 2009). It is now recognised as a global health concern, with prevalence rates rising steadily (Eckardt et al., 2013; Jha et al., 2013). According to the level of glomerular filtration rate, which is a measure of kidney function, chronic kidney disease can be classified into five stages, with stage 5 (glomerular filtration rate < 15 mL/min/1.73 m²) being the most severe stage where kidneys are no longer able to remove waste products and toxins from the body effectively (Levey & Coresh, 2012). Stage 5 chronic kidney disease is also known as end-stage renal disease (ESRD) or kidney failure. At this stage, life expectancy is drastically shortened if kidney replacement therapy is not initiated (Bello et al., 2022).

There are three main modalities of kidney replacement for ESRD patients: kidney transplantation (KTx), haemodialysis (HD), and peritoneal dialysis (PD). KTx is the preferred treatment option because it completely replaces kidney function and is associated with lower mortality risk and improved quality of life (Fleming, 2011; Sawinski & Poggio, 2021). However, due to the shortage of donor organs, dialysis remains the predominant modality globally (Himmelfarb et al., 2020). HD is an intermittent treatment that typically entails three- to four-hour-long sessions thrice-weekly in dialysis centres, during which blood is circulated and filtered through a dialyser (Fleming, 2011; Vadakedath & Kandi, 2017). In contrast, PD uses a paracorporeal method where patients' own peritoneum serves as a natural semipermeable membrane to filter blood either through three to five manual exchanges daily or overnight by a PD cycler (Fleming, 2011; Vadakedath & Kandi, 2017). PD offers more flexibility as it can be performed at home (self-care or assisted PD) and allows for regular/daily clearance of waste products and excess fluid (Fleming, 2011; Vadakedath & Kandi, 2017). ESRD entails various treatment transitions such as initiation onto renal

replacement therapies, or switching from one modality to another with receipt of KTx or return back to dialysis following acute or chronic rejection of transplant graft.

While medical innovation related to renal replacement therapies has transformed ESRD from an acute life-limiting illness to a chronic disease, treatment and symptom burden remain extremely high in ESRD and especially dialysis patients. Dialysis patients are required to adhere to complex guidelines concerning their diet, fluid intake, and medication, and to permanently rearrange their schedules to accommodate treatment. On average, dialysis patients report 9-12 symptoms or treatment side effects (e.g., fatigue, pain, insomnia, etc.) at any given time (Himmelfarb et al., 2020), contributing to impaired daily functioning, poor quality of life, and psychological distress (Goh & Griva, 2018; Hedayati & Finkelstein, 2009; K. Zhang et al., 2020).

An additional burden of ESRD is the cognitive impairments that start to manifest in early renal dysfunction with progressive deterioration (Berger et al., 2016; Brodski et al., 2019) and persist upon dialysis initiation or KTx (Joshee et al., 2018; San et al., 2017; Shea et al., 2019; Wolfgram, 2018). ESRD patients are at significantly greater risks of cardiovascular disease and related factors such as hypertension and diabetes, and cerebrovascular disease such as stroke and white matter disease, which may all contribute to cognitive decline (Crowe et al., 2021; Drew et al., 2019; Murray, 2008). The accumulation of uraemic toxins in ESRD patients also has pathological effects on the neurological system (Crowe et al., 2021). In addition, the dialysis treatment itself may further accelerate cognitive decline by inducing repetitive cerebral ischemia (i.e., reduction of cerebral blood flow) during HD sessions, which in the long term may result in neurological injury (Crowe et al., 2021; Cukor et al., 2020; Drew et al., 2019; Murray, 2008). Cognitive impairments in ESRD patients involve deficits in various domains such as attention, memory, and executive function, with severity ranging from mild impairments to dementia (Berger et al., 2016; Kurella Tamura et al., 2017;

O'Lone et al., 2016; Viggiano et al., 2020). Compared to age-matched healthy controls, HD patients are more than three times more likely to have severe cognitive impairments (Murray et al., 2006). Both HD and PD patients have poorer cognitive performance than patients at earlier stages of chronic kidney disease and healthy controls (O'Lone et al., 2016; Vanderlinden et al., 2019). In contrast, KTx patients have better cognitive performance than dialysis patients and non-dialysis-dependent chronic kidney disease patients, but still perform worse than healthy controls in areas such as executive function, suggesting that KTx is also unable to fully restore cognition to a premorbid level (Joshee et al., 2018).

Cognitive impairments in ESRD patients are associated with increased hospitalisation (Murray, 2008; Murray & Knopman, 2010; Sehgal et al., 1997; Shea et al., 2019) and mortality risks (Griva et al., 2010; Kurella et al., 2006; Murray, 2008), and ultimately increased cost of care. Cognitive impairments may also interfere with patients' daily functioning, treatment adherence, self-management skills, and decision-making capacities because all these processes hinge upon patients' cognition (Iyasere et al., 2017; Murray & Knopman, 2010; Wolfgram, 2018). Given the high prevalence and potential consequences of cognitive impairments in ESRD patients, substantial research has been conducted in the past two decades, with evidence synthesised in several recent systematic reviews and meta-analyses (Ali et al., 2020; Brodski et al., 2019; Joshee et al., 2018; Shea et al., 2019; Tian et al., 2019; Vanderlinden et al., 2019). However, all these reviews were focused on objective cognitive function assessed by standardised neuropsychological tests, which albeit sensitive in detecting cognitive impairments, may provide limited understanding of patients' subjective experience with cognitive difficulties in everyday context.

The concept of subjective cognitive complaints (SCCs), or subjective cognitive decline, refers to self-reported difficulties in one or more cognitive domains (e.g., memory, attention, etc.) experienced in one's daily life or a perceived decrease in cognitive capacity in

comparison with a previously normal status (Jessen et al., 2014; Mendonça et al., 2015; Molinuevo et al., 2017; Pullens et al., 2010; Van Rijsbergen et al., 2014). In 2014, a group of Alzheimer's disease researchers published a conceptual model for SCCs, which proposed that SCCs occur at the preclinical stage of cognitive impairments where individuals experience increasing compensatory cognitive efforts and subtle cognitive decline not yet detectable by objective testing (Jessen et al., 2014). SCCs are therefore considered as an indicator of the earliest symptomatic manifestation of cognitive impairments (Jessen et al., 2014) which may be present as long as 15 years before the onset of objective impairments (Molinuevo et al., 2017; Rabin et al., 2017). However, as individuals progress to more advanced stages of cognitive impairments (i.e., dementia), SCCs may gradually level off, consistent with anosognosia (i.e., lack of self-awareness about cognitive impairments) (Rabin et al., 2017). This may be related to the presence of cognitive impairments interfering with an individual's ability to detect everyday cognitive task failure, to consolidate the experience of failure, and to accurately estimate one's own cognitive ability compared to previous knowledge (Mazancieux et al., 2019; Morris & Mograbi, 2013).

Although SCCs may attenuate along the course of cognitive decline, these complaints have been shown to be associated with objective markers of cognitive impairments (Farias et al., 2013; Rueda et al., 2015) and are considered as a reliable predictor of future progression to dementia (Farias et al., 2017; Y. C. Lee et al., 2020; Liew, 2020a, 2020b; Mendonça et al., 2015; Mitchell et al., 2014; Neto & Nitrini, 2016). The importance of SCCs is also exemplified by its inclusion as a core feature of mild cognitive impairment in consensus reports (Winblad et al., 2004). SCCs may have potential value in identifying patients at risk of cognitive impairments before these cognitive changes become more severe and irreversible (Jessen et al., 2014).

SCCs are also important as they reflect individuals' accumulative everyday experience rather than cognitive performance at a single time point as assessed by objective neuropsychological tests (Rabin et al., 2017). Studies on ESRD patients have found that SCCs are indeed better predictors of real-world outcomes including functional capacity (Song et al., 2015) and decision-making (Jayanti et al., 2016) compared to objective cognition, and are consistently associated with psychological well-being and quality of life (Duarte et al., 2005; Song et al., 2018). The self-awareness of cognitive deficits may also influence judgements about behavioural efficacy, self-care ability, and independence of daily living (Crowe et al., 2021; Morris & Mograbi, 2013). Understanding SCCs may thus be essential in improving patient-centred care for ESRD-related cognitive impairments (Crowe et al., 2021).

To date, a fair amount of research has been conducted to examine SCCs in ESRD patients, but the results have not been drawn together to provide a broad overview of what is known about these complaints in the context of ESRD. As such, we conducted a systematic review and meta-analysis to synthesise existing data on SCCs in ESRD patients. Specifically, the aims of this review include: (1) to identify instruments assessing SCCs used in ESRD research; (2) to quantify the frequency and severity of SCCs as measured by these different instruments in the target population(s); (3) to compare differences (if any) in SCCs between renal replacement modalities (i.e., HD, PD, and KTx); (4) to evaluate the course of SCCs over time and across treatment transitions; and (5) to synthesise evidence on the associations of SCCs with sociodemographic profile, clinical characteristics, clinical and patient-reported outcomes (e.g., hospitalisation, quality of life, etc.), and objective cognitive function. Based on previous research on objective cognition, we hypothesised that KTx patients would have lower frequency and severity of SCCs than dialysis patients and that SCCs will improve with KTx; as evidence on cognitive impairments across dialysis modalities (HD vs. PD) is mixed no a priori hypotheses were formulated.

Methods

The protocol was registered within the PROSPERO database (registration number: CRD42021250125). Findings were reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline (Moher et al., 2009; Page et al., 2021).

Eligibility criteria

Studies were included if they (1) involved adult patients (≥ 18 years) diagnosed with ESRD (stage 5 chronic kidney disease with glomerular filtration rate < 15 mL/min/1.73 m²) either on renal replacement therapy (any dialysis modality or kidney transplantation), conservative management (i.e., management without renal replacement therapy where the goal is to minimise symptoms and maximise the quality and length of life), or with ERSD but not yet initiated treatment, (2) used at least one measure of SCCs, and (3) reported data on frequency/severity of SCCs, differences in SCCs between treatment modalities, changes in SCCs over time, or associations of SCCs with sociodemographic and/or clinical characteristics, clinical and/or patient-reported outcomes, and/or objective cognitive function.

Studies that included only children or adolescents (under 18 years of age) or patients in stages 1-4 of chronic kidney disease were excluded. We defined SCCs as the self-reported difficulties in one or more cognitive domains or a perceived decrease in cognitive capacity in comparison with a previously normal status (Jessen et al., 2014; Mendonça et al., 2015; Molinuevo et al., 2017; Pullens et al., 2010; Van Rijsbergen et al., 2014). SCCs can be measured using self- or proxy-reported questionnaires assessing individuals' perceptions about cognitive capacity or experience of cognitive difficulties (e.g., "How much of the time in the past four weeks did you become confused?"). Self-reported measures of daily functioning (e.g., managing finances, shopping, etc.) were not considered as measures of SCCs because the capacity to carry out these activities does not solely rely on cognitive

skills. Studies using a composite measure (e.g., a measure of quality of life or depression that has a subdomain of SCCs) were included if they reported the separate SCC domain score. Studies that reported only the composite score that included the SCC domain were excluded. Unpublished studies and grey literature were excluded due to the absence of peer review. Non-English articles were excluded due to resource constraints and the research team's language skills. Only published journal articles with available English full-text were included in the final sample.

Search strategy & selection process

To identify relevant studies the following databases were searched (inception to 21 April 2021): CINAHL (EBSCOhost), Ovid – All Resources (Books@Ovid, Journals@Ovid Full Text, Your Journals@Ovid, EBM Reviews, Embase, MEDLINE), MEDLINE (PubMed), PsycINFO (EBSCOhost), and Web of Science. The search terms included exact words or synonyms of: subjective cognitive complaints, end-stage renal disease, dialysis, and kidney transplantation. We also included "kidney disease quality of life" as one of the keywords because a large number of studies in this area assessed SCCs using a subscale within this measure. Subject headings were not used because there was no subject heading in the selected databases specific to the concept of SCCs, and the use of relevant terms such as "Cognitive Dysfunction" and "Quality of Life" may decrease the specificity of the search. We performed the search in all fields including full-text because previous studies showed that full-text search is more sensitive than title/abstract search (Lin, 2009; Penning de Vries et al., 2020). An updated search was conducted to retrieve records published between the end date of the initial search and 11 January 2022. The detailed search strategy is presented in Table S1.

Titles and abstracts were scanned independently by two authors (FC & ZG) using Covidence (https://www.covidence.org) to exclude studies that were irrelevant. Full-texts of

the remaining articles were then independently screened by FC and ZG to determine eligibility. Discrepancies between the two reviewers were resolved by discussion with a third reviewer (KG). The reference lists of included articles were also examined to identify additional studies.

Data extraction

Due to the large number of relevant articles included in the current review, we adopted an accelerated approach to data extraction recommended by Cochrane (Moons et al., 2021). One reviewer (FC) extracted data from all individual studies. The correctness and completeness of extracted data were then verified by two independent reviewers (ZG & XZ). Any errors detected by the two reviewers were discussed among the three reviewers and corrected if necessary.

The following data items were extracted: article citation, study location, study design, sample size, participant characteristics (i.e., gender, age, treatment modality, etc.), measure of SCCs, frequency and severity of SCCs, differences in SCCs between treatment modality groups, longitudinal change in SCCs over time, associations of SCCs with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition. If data concerning the outcomes were missing or unclear from an article, the review team contacted the corresponding authors to obtain original data or for clarification.

Quality assessment

The quality of selected studies were assessed using the quality assessment tools developed by the National Institute of Health (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). This tool provides study design-specific items to assess methodological quality of observational cohort and cross-sectional studies, controlled intervention studies, and before-after (pre-post) studies with no control group (Ma et al., 2020). Reviewers could select “yes”, “no”, “not reported”, “cannot determine”, or “not applicable” in response to

each item for each individual study. Similar to data extraction, the first author (FC) rated each item for each included study, with verification performed by two other reviewers (ZG & XZ). Discrepancies in quality ratings between the reviewers were resolved by discussion and consensus.

Data synthesis

We first performed qualitative narrative synthesis of the included studies. We summarised patient responses to SCC measures that indicate different levels of frequency/severity of SCCs. For this specific aim, the mean values reported by cross-sectional studies and baseline scores in longitudinal studies were used. We also summarised the number of studies that reported significant ($p < .05$) or non-significant differences between treatment modalities (i.e., HD, PD and KTx), as well as the direction of these differences. The longitudinal course of SCCs was determined based on observational cohort studies that analysed changes in SCCs over time and intervention studies that reported changes in the control groups. Furthermore, the number of studies reporting positive, negative, or null associations of SCCs with sociodemographic, clinical and patient-reported variables, as well as objective cognitive function, were synthesised.

Meta-analyses were further conducted where data were sufficient (i.e., at least two studies using similar measurement and analysis methods). Specifically, we conducted a random-effects meta-analysis with a restricted maximum likelihood estimator to compare differences in SCCs between HD and PD patients based on the reported means, standard deviations, and sample sizes of each treatment group. Standardised mean differences and corresponding 95% confidence intervals were calculated. Meta-analyses comparing other treatment modalities (e.g., HD vs. KTx) were not performed due to the small number of studies reporting these findings. We also performed random-effects meta-analyses of correlation coefficients between SCCs and 10 patient-reported outcomes (i.e., depression,

anxiety, overall health rating, general health perception, pain, fatigue, physical functioning, social functioning, role limitation due to physical health, and role limitation due to emotional problems). The Fisher's *r*-to-*z* transformed correlation coefficient and corresponding 95% confidence intervals were calculated. Meta-analyses of correlation between SCCs and sociodemographic/clinical variables and objective cognition were not deemed possible due to the unavailability of original data and heterogeneity across studies in terms of the measurement and analyses methods of these variables. For all meta-analyses, heterogeneity was determined by forest plots, including summary effects along with the 95% confidence intervals and 95% prediction intervals, as well as the Q and I^2 statistics (IntHout et al., 2016). Small study effects were examined through Egger's linear regression test of funnel plot asymmetry. All meta-analyses were performed using the "metafor" package (Viechtbauer, 2010) in R 4.1.2 (R Core Team, 2018).

Results

Study selection

The search flow is illustrated in Figure 1 (Page et al., 2021). The initial search (21 April 2021) retrieved 5248 records, of which 2435 were duplicates. Two reviewers (FC & ZG) independently screened titles and abstracts of the remaining 2813 articles and excluded 1543 irrelevant records. A total of 1027 full-text papers were assessed for eligibility, of which 814 were excluded due to reasons presented in Figure 1. The updated search (11 January 2022) identified eight additional relevant articles. Thus, a total of 221 studies were included.

Study characteristics

Tables S2 present characteristics and key findings of each individual study, as well as the full reference list of included studies. The 221 studies represented 105064 patients with ESRD, with the majority (N = 89188) receiving haemodialysis (HD), 9113 patients on peritoneal dialysis (PD) and 4449 patients who received kidney transplantation (KTx). Studies were

mainly conducted in the United States (k = 33), Brazil (k = 29), Japan (k = 19), South Korea (k = 13), United Kingdom (k = 11), Canada (k = 11), Iran (k = 10), Norway (k = 10) and mainland China (k = 8). Over half of the studies (k = 134) used an observational cross-sectional design, while 49 used an observation cohort design. Moreover, there were 30 controlled intervention studies and eight pre-post studies with no control group.

Quality assessment

The quality ratings of each individual study is presented in Tables S3-S6. Quality ratings were reported separately for observational cross-sectional (Table S3), observational cohort (Table S4), controlled intervention (Table S5), and pre-post studies (Table S6).

Within the 134 cross-sectional studies, only 22.4% fulfilled at least 70% of the criteria list, whereas 31.3% fulfilled less than 50% of the criteria. Some key methodological shortcomings of the cross-sectional studies included insufficient description of patient recruitment procedure, absence of sample size justification, and outcome assessors not blinded to exposure status where possible. Methodological quality of observational cohort studies appeared to be higher compared to cross-sectional studies, with 49.0% and 93.9% fulfilling at least 70% and 50% of the criteria, respectively. Main methodological shortcomings of observational cohort studies were similar to those identified in cross-sectional studies, but include additionally the high rate of or inadequate information on loss to follow-up.

Regarding controlled intervention studies, only 26.7% of the 30 studies met at least 70% of the criteria. Areas of improvement include inadequacy of randomisation, allocation concealment, and blinding, as well as insufficient/unjustified sample size and absence of intention-to-treat analysis. Finally, within the eight pre-post studies with no control group, the majority of studies did not report response rate or provide sample size justification, and had

high rates of loss to follow-up. Despite these limitations, almost all included studies, regardless of the design, adopted reliable and valid outcome measures of SCCs.

Measures of SCCs

Thirteen measures of SCCs were identified and the characteristics of these measures are presented in Table 1. Of these, six questionnaires were developed specifically for SCCs, whereas the remaining were multidomain measures of quality of life or symptom checklist that included an SCC subscale/item. All measures identified in the current review were validated except for Henry et al. (2018) where four items from two validated questionnaires were selected and used as a measure of SCCs. The most commonly used measure (k = 207, 93.7%) was the Kidney Disease Quality of Life Cognitive Function subscale (KDQOL-CF), a 3-item scale that assesses patients' experience of slow reaction, concentration difficulty, and confusion in the past four weeks (Hays et al., 1994; Kurella et al., 2004), followed by the Patient's Assessment of Own Functioning Inventory (k = 3, 1.4%) (Chelune et al., 1986) and a single item assessing concentration difficulty from Dialysis Symptom Index (k = 2, 0.9%) (Weisbord et al., 2004). All other measures were only used once. Number of items ranged from 1 to 39 and instruments varied in cognitive domains assessed: attention/concentration (11 measures), memory (10 measures), language/comprehension (five measures), and problem-solving (four measures). Measures mainly assessed severity (seven measures) and frequency (six measures) of SCCs.

Frequency and severity of SCCs

We first synthesised data on frequency of SCCs (i.e., number of times patients experienced SCCs within a given timeframe) in ESRD patients. The KDQOL-CF data across treatment modalities (HD: k = 120, N = 37212; PD: k = 42, N = 6304; KTx: k = 17, N = 2693) were synthesised by comparing the distribution of mean scores across modalities (see Table 2). The majority of studies on HD and PD patients reported mean KDQOL-CF scores between

60 and 100 (HD: 103 studies, 85.8%; PD: 38 studies, 90.5%), indicating that SCCs were noted from "none of the time" to "some of the time" during the past month. In contrast, the majority of studies on KTx patients reported mean KDQOL-CF scores between 80 and 100 (11 studies, 64.7%), indicating that SCCs were reported from "none of the time" to "a little of the time" during the past month. When analysing Table 2 in terms of number of patients, the majority of HD (N = 28431, 76.4%) and PD (N = 4409, 69.9%) patients reported mean scores lower than 80, indicating that SCCs were experienced sometimes or more often. In contrast, the majority of KTx patients (N = 1922, 71.4%) reported mean scores higher than 80, indicating SCCs no more than "a little of the time".

Considering other measures assessing frequency of SCCs, three studies found that SCCs in HD patients were experienced from "rarely" to "sometimes" on average (Brickman et al., 1996; Fan et al., 2020; Jassal et al., 2006), which were similar to findings from KDQOL-CF. Additionally, using the concentration difficulty item in the Dialysis Symptom Index (yes/no), 30.2% to 32.3% of HD patients in Columbia reported the presence of concentration difficulties during a one-year course (Alarcon et al., 2021), whereas 57.8% of HD patients in Korea reported presence of these difficulties (Cho et al., 2018).

There is a paucity of research on severity of SCCs in ESRD (i.e., level of difficulty in performing cognitive tasks or degree of seriousness). Five studies were identified and these had used different indices assessing different cognitive domains. One study used the cognition subscale of the WHO Disability Assessment Schedule and noted that HD patients reported "no difficulty" to "mild difficulty" in daily cognitive tasks (i.e., concentration, memory, problem-solving, learning, comprehension, conversation) (Castro et al., 2018). Another study used a single item in Dialysis Symptom Index and HD patients reported that their concentration difficulties were "somewhat bothersome" to "quite bothersome" (Cho et al., 2018). A further study used the cognition subscale of Health Utilities Index Mark 3,

where HD patients reported on average that they were "somewhat forgetful, but able to think clearly and solve everyday problems" (Gorodetskaya et al., 2005). When using the British Columbia Cognitive Complaints Inventory which assesses SCC severity in six domains (i.e., memory, concentration, thought expression, word finding, thinking, problem-solving) and classifies patients into four levels of severity (0-4: normal; 5-9: mild; 10-14: moderate; 15-18: severe), one study reported that 86.9% of HD patients had mild to severe SCCs (Zubair & Butt, 2017). No study assessed severity of SCCs in PD patients. The only study to assess SCC severity in KTx used the cognition subscale of ESRD Symptom Checklist and concluded that SCCs in concentration and memory were only very mild in the first year following KTx (M = 13.0-14.3 on a scale of 0 = not at all - 100 = extreme) (Ortega et al., 2007).

Differences in SCCs between treatment modalities

Of the 23 studies which compared frequency of SCCs between HD and PD patients, 17 reported no difference (Chen et al., 2021; Czyżewski et al., 2014; Frimat et al., 2006; Fructuoso et al., 2011; Gonçalves et al., 2015; Kang et al., 2017; Kostro et al., 2016; Kutner, Zhang, Barnhart, et al., 2005; Malekmakan et al., 2016; Manavalan et al., 2017; Molsted et al., 2007; Neumann et al., 2018; Okpechi et al., 2013; Rebollo Rubio et al., 2017; Song et al., 2015; Tannor et al., 2017; Wright & Wilson, 2015), whereas six reported more frequent SCCs in HD compared to PD patients (Carmichael et al., 2000; Chrifi Alaoui et al., 2022; Kutner, Zhang, & Brogan, 2005; A. J. Lee et al., 2005; Tanaka et al., 2020; Türk et al., 2020).

Of these 23 studies, 20 provided data necessary for a random-effects meta-analysis (see Figure 2). All 20 studies used the KDQOL-CF as the measure of SCCs. There was a small but significant difference between the HD and PD groups (standardised mean difference -0.20, 95% confidence interval -0.38 to -0.03), with HD patients reporting more frequent SCCs than PD patients. The prediction interval for this comparison was large and included

zero (95% prediction interval -0.92 to 0.51). There was high heterogeneity across studies (Q = 90.81, df = 19, $p < .001$; $I^2 = 89.5\%$). Egger's test did not detect funnel plot asymmetry ($z = -0.52$, $p = .600$). It is of note however that this significant difference may be mainly driven by one study with a particularly large sample size (total N = 3302) that almost equals the total sample sizes of the rest of the studies (Kutner, Zhang, & Brogan, 2005).

Four studies using the KDQOL-CF compared frequency of SCCs between HD and KTx patients, with three reporting no difference (Barotfi et al., 2006; Czyżewski et al., 2014; Painter et al., 2012) and one reporting more frequent SCCs in HD patients (A. J. Lee et al., 2005). Two studies compared KDQOL-CF scores between PD and KTx patients and both reported no difference (Czyżewski et al., 2014; A. J. Lee et al., 2005). No study compared severity of SCCs among HD, PD and KTx patients.

Course of SCCs

A subset of included studies (k = 46) reported on changes in SCCs over time in ESRD patients. These include observational cohort studies (k = 26), pre-post studies (k = 1), and intervention studies that reported changes in the control groups (k = 19).

Twenty studies assessed SCCs at multiple time points in patients on HD, with 19 reporting no change over time (Alarcon et al., 2021; Boudville et al., 2009; Duarte et al., 2009; Frimat et al., 2006; Hayashi et al., 2017; Korevaar et al., 2002; L. C. C. Lopes et al., 2019; Maynard et al., 2019; Mazairac et al., 2013; Neumann et al., 2018; Painter et al., 2012; Poulsen et al., 2017; Scott et al., 2009; Shahnavazi et al., 2018; Simic-Ogrizovic et al., 2009; Soares et al., 2017; Unruh et al., 2004; Wu et al., 2014; Zheng et al., 2019). The follow-up periods of these studies ranged from six weeks to six years. Similarly, 11 out of 12 studies on PD patients with follow-up periods ranging from one month to three years also reported no change in SCCs over time (Chow & Wong, 2010; Frimat et al., 2006; Jiao et al., 2017; Jung et al., 2016; Korevaar et al., 2002; Li et al., 2014; Lo et al., 1998; Michels et al., 2011;

Neumann et al., 2018; Uchiyama et al., 2019; Wong et al., 2010). Of note, all these studies reporting no change in SCCs in dialysis patients adopted the KDQOL-CF which only contains three items. When using a more comprehensive measure (i.e., Patient's Assessment of Own Functioning Inventory), Song et al. (2018) found a significant reduction in SCCs over a one-year course in both HD and PD patients.

Regarding the effect of KTx, there is evidence of a significant reduction in SCCs among HD, PD, or pre-emptive patients from pre- to post-KTx (Kostro et al., 2016; McAdams-DeMarco et al., 2018; Ortega et al., 2007; Peipert et al., 2020; Rajkumar et al., 2019; Tsarpali et al., 2021). Following KTx, SCCs appear to be stable over time and may be maintained for up to six years post-KTx (Costa-Requena et al., 2017; Czyżewski et al., 2014; Hernández Sánchez et al., 2021; Lønning et al., 2018; Ortega et al., 2007; Peipert et al., 2020; Ryu et al., 2021; Tsarpali et al., 2021).

The effect of transplant graft rejection and return to dialysis and the effect of dialysis initiation on SCCs could not be synthesised since there is a paucity of research comparing SCCs across these treatment transitions (i.e., KTx to dialysis and pre- to post-initiation of dialysis).

Associations with sociodemographic, clinical, and patient-reported variables

Evidence concerning associations of SCCs with sociodemographic, clinical, and patient-reported variables were synthesised by the number and percentage of studies that reported a positive, negative, or null association with each variable (see Table 3). There was high heterogeneity in terms of the quantification of these variables. Study authors were contacted for data on correlations or between-group comparisons but the response rate was very low. Associations with sociodemographic and clinical variables were therefore not meta-analysed due to the lack of data.

Among sociodemographic variables, the majority of studies found no association between SCCs and age, gender, marital status, household income, and smoking status. Regarding education level, seven studies reported that lower education was associated with higher SCCs (Brickman et al., 1996; Duarte et al., 2005; Kontodimopoulos & Niakas, 2005; Kutner et al., 2007; A. A. Lopes et al., 2007; Ortega et al., 2007; Song et al., 2015) whereas seven others found no association (Anees et al., 2018; Bouidida et al., 2014; Fan et al., 2020; Ho et al., 2013; Neumann et al., 2018; Sorensen et al., 2012; Zubair & Butt, 2017). It appeared that the seven studies reporting a significant association with education had generally larger sample sizes, and adopted more lengthy and comprehensive measures of SCCs, compared to studies reporting null associations. In terms of employment status, four studies found a significant association between SCCs and unemployment (de Oliveira et al., 2012; A. A. Lopes et al., 2007; Ortega et al., 2007; Vázquez et al., 2005) and these studies had generally larger sample sizes compared to the two that reported no association (Anees et al., 2018; Neumann et al., 2018).

Clinical parameters were largely unrelated to SCCs as shown in Table 3, where null associations were reported in at least 70% of the studies for most variables. However, hospitalisation was consistently associated with SCCs in all six studies assessing this outcome. Specifically, four cross-sectional studies reported that patients with more frequent and/or longer hospitalisation events in the preceding 12 months reported higher frequency of ensuing SCCs (Hays et al., 1994; Kontodimopoulos & Niakas, 2005; Poulsen et al., 2017; Türk et al., 2020). Two other prospective cohort studies with very large sample sizes (N = 6151 and 10030 respectively) reported that higher SCCs at baseline were associated with significantly greater risk of future hospitalisation (A. A. Lopes et al., 2003; Mapes et al., 2003).

In terms of patient-reported outcomes (see Table 3), SCCs have been consistently associated higher depressive symptoms (18 studies, 85.7%), higher anxious symptoms (9 studies, 90.0%), higher bodily pain (6 studies, 85.7%), higher fatigue symptoms (6 studies, 100.0%), worse physical functioning (5 studies, 83.3%), more overall physical symptoms (5 studies, 100.0%), poorer sleep quality (3 studies 75.0%), and lower functional capacity (3 studies 75.0%). Results regarding some other quality-of-life domains (i.e., overall health rating, social functioning, general health perception, role limitation due to physical health or emotional problems, and physical inactivity) were less consistently reported but still showed an overall association between higher SCCs and worse quality of life.

For 10 of these patient-reported outcomes (i.e., depression, anxiety, overall health rating, general health perception, bodily pain, fatigue, physical functioning, social functioning, role limitation due to physical health, and role limitation due to emotional problems) where data were sufficient, random-effects meta-analyses of correlation coefficients were further conducted to determine the strength of associations. Results and forest plots of these meta-analyses are presented in Figures S1-S10. The pooled effects showed significant correlations between SCCs and all 10 patient-reported outcomes (95% confidence interval not including zero). The strength of these associations ranged from small (0.22) to moderate (0.49), with depressive symptoms (correlation coefficient 0.46, 95% confidence interval 0.39 to 0.53), anxious symptoms (correlation coefficient 0.40, 95% confidence interval 0.33 to 0.47), fatigue symptoms (correlation coefficient 0.49, 95% confidence interval 0.45 to 0.54), and role limitation due to emotional problems (correlation coefficient 0.43, 95% confidence interval 0.37 to 0.48) showing the strongest correlations with SCCs. Details with regards to the prediction interval, heterogeneity, and funnel plot asymmetry, are presented in Figures S1-S10.

Association with objective cognitive function

Only five studies evaluated association between SCCs and objective cognitive function in ESRD patients (Brickman et al., 1996; Henry et al., 2018; Jayanti et al., 2016; Song et al., 2015; Sorensen et al., 2012). Some studies assessed objective cognition using global screening tests that provides a total sum score across cognitive domains such as the Mini-Mental State Examination (Henry et al., 2018; Sorensen et al., 2012) and the Modified Mini-Mental State test (Jayanti et al., 2016), while others used individual neuropsychological tests assessing specific domains, such as the Trail-Making Test and the Digit Span Task (Brickman et al., 1996; Henry et al., 2018; Jayanti et al., 2016; Sorensen et al., 2012).

When operationalising objective cognition and/or SCCs as a single construct (i.e., calculating only the total score of global cognitive tests or sum score of SCC measures), studies generally found no association between objective and subjective cognition (Brickman et al., 1996; Henry et al., 2018; Jayanti et al., 2016; Song et al., 2015; Sorensen et al., 2012). However, there is preliminary evidence suggesting that this association may be domain-specific. In particular, although Henry et al. (2018) found no association between overall SCCs and global cognitive test scores, complaints about slow reaction in this study was associated with poorer performance on Digit Span Task (short-term verbal memory) and Trail-Making Test (attention/concentration and executive function), and self-reported confusion was also associated with poorer performance on Digit Span Task, Visual Retention Test (visual memory), and Trail-Making Test. Similarly, Jayanti et al. (2016) found that self-reported concentration difficulties (but not memory complaints) were associated with poorer performance in the Trail-Making Test (but not performance on global cognitive test).

All five studies assessing the association between objective tests and subjective complaints adopted a cross-sectional design (Brickman et al., 1996; Henry et al., 2018; Jayanti et al., 2016; Song et al., 2015; Sorensen et al., 2012). Therefore, it was not possible to determine whether SCCs in ESRD patients may predict future risks of progression to mild

cognitive impairments or dementia. We were also unable to determine the relationship between objective and subjective cognition over time and how they may interact with one another along the course of kidney disease, renal replacement therapies, and/or treatment transitions.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis on SCCs in patients with ESRD. By including 221 relevant articles, we provided a comprehensive overview of this commonly experienced but poorly understood problem. We synthesised evidence of the frequency, severity, and course of SCCs in ESRD patients, differences between treatment modalities, associations of SCCs with sociodemographic, clinical, and patient-reported variables, and relationship between subjective and objective cognition. Although there is substantial heterogeneity across studies in terms of the study design, sample characteristics, and measures used to assess SCCs, some preliminary conclusions can be drawn. First, SCCs are highly prevalent in dialysis patients, with over two thirds of HD (76.4%) and PD (69.9%) patients reporting SCCs sometimes or more often. Within dialysis patients, those who are on HD experience significantly more frequent SCCs compared to those on PD, with a small effect size. In contrast, SCCs are much less prevalent in KTx patients with over two thirds (71.4%) reporting these complaints only a little of time or never. When analysing the longitudinal course, SCCs appear relatively stable over time on HD and PD treatments but may reduce significantly upon receipt of KTx. In addition, there is either no or mixed evidence on associations between SCCs and most sociodemographic/clinical variables, except for hospitalisation which has been consistently associated with higher SCCs. Patient-reported outcomes including depression, anxiety, fatigue, and quality of life in various domains appear to be more consistently associated with SCCs, with small to medium magnitude. Finally, the association between subjective and objective cognition in ESRD

patients could not be established due to the lack of data but there is preliminary evidence suggesting domain-specificity of this association.

Our findings regarding the prevalence of SCCs and differences between treatment modalities are generally in line with the objective cognition literature. Two recent meta-analyses have confirmed that PD patients have better performance on objective cognitive tests and lower risk of cognitive impairments compared to HD patients (Ali et al., 2020; Tian et al., 2019). Our meta-analysis extends these findings to subjective reports. PD, by being a daily treatment, offers a more gentle and continuous clearance of toxins and waste products, without the more acute and variable haemodynamic changes and fluid shifts reported in HD (Viggiano et al., 2020). As such, PD is expected to provoke fewer and less severe instances of brain injury, hence better preserving cognitive function (Drew et al., 2019; Murray, 2008; Tian et al., 2019). However, caution is needed when interpreting this meta-analysis since the prediction interval was very wide and contained zero, suggesting that the comparison in future similar studies can fluctuate across a wide range of effects (IntHout et al., 2016). It is also important to note that according to our quality assessment, the outcome assessors in studies comparing HD and PD groups were often not blinded to patients' exposure status, which may introduce experimenter bias where the assessors expect HD patients to have more SCCs than PD patients. Furthermore, it is possible that this observed difference is a mere reflection of pre-existing differences between those who opt for HD versus PD (Crowe et al., 2021). One included study found that more severe SCCs in pre-dialysis patients were associated with a higher likelihood of choosing fully-assisted (i.e., HD) over self-care dialysis (i.e., PD) (Jayanti et al., 2016). These confounding factors are important to address in future studies as they may undermine interpretation of the true effect of dialysis modality on cognition. To date, transplantation remains the optimal treatment for restoring cognition in ESRD patients as it completely replaces the kidneys and has been associated with cerebral

benefits and improvements in objective cognitive performance (Crowe et al., 2021; Joshee et al., 2018). Our review further supported the advantages of KTx by showing a lower prevalence rate of SCCs in KTx than in dialysis patients, and a reduction in SCCs from pre- to -post-KTx.

Regarding the longitudinal course, SCCs appear relatively stable in patients receiving HD or PD treatments. This conclusion was inconsistent with the objective cognition literature where several longitudinal studies showed a significant decline in executive function over the course of HD/PD (Drew et al., 2017; Iyasere et al., 2017; Kurella Tamura et al., 2017). The majority of studies assessing change in SCCs in our review used the KDQOL-CF measure which does not assess executive function and thus may have missed the opportunity to observe changes in complaints about this important domain. Indeed, one study used a more comprehensive questionnaire that includes memory, language, sensory-perceptual, and executive function domains and found a significant reduction in overall SCCs over a one year course in both HD and PD patients (Song et al., 2018). This again seems to contradict the studies using objective tests in the direction of change. However, according to the conceptual model of SCCs mentioned earlier, SCCs may be the most evident during preclinical cognitive impairments when objective performance is still within normal limits (Jessen et al., 2014). As cognitive impairments become more severe, SCCs may recede due to diminished accuracy in estimating own cognitive abilities (Mazancieux et al., 2019; Morris & Mograbi, 2013; Rabin et al., 2017). In the context of ESRD, the decline in executive function over the dialysis treatment course may interfere with patients' ability to monitor everyday task performance and detect failure/lapses which are essential for updating self-perception of cognitive ability (Morris & Mograbi, 2013), thus contributing to decreasing SCCs. Besides the course of SCCs on dialysis, future longitudinal investigations are also needed to determine the effect of dialysis initiation on SCCs, as well as change in SCCs shifting across treatment modalities

(e.g., shifting from HD to PD) since SCCs may become particularly frequent/severe during these transition periods due to the associated symptoms, side effects, complications, and changes to treatment and self-care requirements (Broers et al., 2015).

The analyses of associations between SCCs and sociodemographic/clinical variables revealed mainly no or mixed evidence. Hospitalisation was the only variable shown to be consistently associated with higher SCCs across six studies (Hays et al., 1994; Kontodimopoulos & Niakas, 2005; A. A. Lopes et al., 2003; Mapes et al., 2003; Poulsen et al., 2017; Türk et al., 2020), in line with previous research which showed significantly greater hospitalisation risks in dialysis patients with objective cognitive impairments compared to those without (Murray, 2008; Sehgal et al., 1997; Shea et al., 2019; Y. Zhang et al., 2018). It is noteworthy that this relation may be bi-directional. On one hand, hospitalisation entails potential surgical procedures, associated need for anaesthesia, heightened risks for infection and other adverse events, medication exposure, and depression and sleep difficulty that may all contribute to cognitive impairments (Mathews et al., 2014). On the other hand, SCCs reflect everyday cognitive difficulties that may interfere with patients' independence in daily functioning, medication taking, diet and fluid control, and other self-care activities and may therefore result in poor disease management which may increase hospitalisation risk (Murray & Knopman, 2010). Future studies that include serial assessments and long-term follow-ups are needed to confirm the nature and direction of this relation.

Similarly, the observed associations of SCCs with patient-reported outcomes are likely to be bi-directional. The strongest and most consistent associations were found between SCCs and depression, anxiety, and fatigue, consistent with previous research in other patient populations, including cancer, stroke, and Alzheimer's (O'Farrell et al., 2017; Pullens et al., 2010; Rabin et al., 2017; Van Rijsbergen et al., 2014). SCCs often overlap with psychological distress and fatigue and are considered as symptoms of these problems. For example, the

Chalder Fatigue Scale includes items assessing concentration difficulties, memory, and word finding (Cella & Chalder, 2010). The experience of cognitive difficulties or failure in daily living may also increase individuals' distress and worry about these problems. In addition, individuals with depression and anxiety exhibit attentional biases toward negative information and therefore may be hypersensitive to cognitive failure, resulting in an overreporting of SCCs (Rabin et al., 2017). Future longitudinal studies are required to disentangle whether these mood and fatigue symptoms are the precursors, consequences, or concurrent factors of SCCs.

There is very limited data concerning the relation between objective and subjective cognition in ESRD patients. Overall studies indicated no or weak association between these two assessment methods, yet we found some preliminary evidence that the relationship between SCCs and objective cognition may be domain-specific. For example, one study suggests that SCCs specific to concentration ability (e.g., "I am good at concentrating when reading") were associated with poorer performance in part B of the Trail-Making Test, which is a measure of attention/concentration and executive function (Jayanti et al., 2016). Studies in the Alzheimer's disease literature have also found support for the domain-specificity hypothesis of the objective-subjective cognition relation (Farias et al., 2008, 2013) and therefore may be worth replicating in the context of ERSD. Future studies should adopt multi-domain measures of objective and subjective cognition and should align the specific SCC items/domains with the corresponding objective cognitive domain tests (e.g., association between memory complaints and delayed recall task performance).

Nevertheless, there are several reasons why SCCs may not be consistently associated with objective cognition. First, SCCs are reported based on accumulative everyday experience whereas objective tests may only reflect performance in a controlled environment at a single time point (Molinuevo et al., 2017; Rabin et al., 2015, 2017). Second, theories

suggest that SCCs may recede as objective cognitive impairments progress due to anosognosia (Jessen et al., 2014; Morris & Mograbi, 2013; Rabin et al., 2017). The relationship between subjective and objective cognition may therefore be expected to be modest and may vary along the course of cognitive decline and renal replacement therapies. SCCs have been proposed as a more accurate and meaningful measure at preclinical and early stages of cognitive impairments, whereas objective tests become increasingly sensitive at advanced stages (Jessen et al., 2014). Relatedly, informant-reports of SCCs may be a useful alternative to self-reports at stages of established cognitive impairments. In the current review, we did not identify any study using an informant measure of SCCs, but research has shown that informant-reports are more closely linked to objective test scores and markers such as brain atrophy compared to self-reports (Rueda et al., 2015), and may also predict future progression (Farias et al., 2017). Longitudinal studies assessing objective performance and self- and informant-reported SCCs at multiple time points are needed to understand the temporal dynamic relations among various cognitive assessment tools in ESRD patients.

It is important to note that the disconnect between subjective ratings and objective assessments has been shown not just in terms of cognition, but also other symptoms and functioning outcomes. For example, subjective (e.g., questionnaires) and objective measures of sleep quality (e.g., polysomnography) are typically weakly associated, yet subjective sleep complaint remains an essential component of insomnia diagnosis (Savard & Ganz, 2016). Research has also shown that the intensity of physical symptoms is not always associated with the meaning that individuals attribute to the symptoms (Petersen et al., 2011) and that clinical markers of disease severity are not always correlated with individuals' perceptions of severity (Haverstock & Feldman, 2006). According to Leventhal's Common-Sense Model, individuals construct meanings or mental representations for their illness or symptoms (Hagger & Orbell, 2003; Leventhal et al., 1984, 2016). These representations include

individuals' interpretations and beliefs about illness/symptom identity (i.e., frequency/severity), as well as perceived causes, anticipated timeline, consequences, and controllability of these illness/symptoms (Leventhal et al., 2016). These representations can appear inconsistent with medical models or clinical indicators, but may determine how patients respond to or cope with the illness/symptoms (Donovan et al., 2008; Hagger & Orbell, 2003; Leventhal et al., 2016). The lack of association between subjective and objective cognition therefore does not necessarily imply that SCCs are inaccurate because SCCs can also be viewed as patients' representations of cognitive failure/lapses which influence their coping or compensatory responses.

A key limitation of studies included in this review is the overreliance on the KDQOL-CF measure. The KDQOL-CF contains three items assessing the frequency of slow reaction, concentration difficulties, and confusion in the past four weeks (Kurella et al., 2004). Despite its ease of administration and potential value in clinical settings, KDQOL-CF is limited in its content as it fails to cover domains such as memory and executive function shown to be most impaired in ESRD patients (Joshee et al., 2018; O'Lone et al., 2016). Therefore, the reported prevalence of SCCs are most likely underestimated and the comparison between treatment modalities may fail to capture differences in certain important domains. Additional limitations of the KDQOL-CF include the use of double-barrelled items (e.g., did you have difficulty concentrating or thinking) which may undermine accuracy of responses, and the use of generic/broad wording (e.g., did you become confused) rather than specific items (e.g., do you have difficulty recalling conversations a few days later) (Rabin et al., 2015). There is hence a need to refine existing or develop new SCC measures specifically for ESRD that capture multiple cognitive domains (in particular memory and executive function) and include specific items that are simple and easy to understand (Rabin et al., 2015).

It should be acknowledged that non-English articles and grey literature were excluded from the current review and therefore some relevant papers may have been missed. Also, within the included studies, there was limited information on the severity of SCCs, effect of treatment transitions (i.e., dialysis initiation or return to dialysis after KTx rejection) on SCCs, and associations of SCCs with key outcomes such as treatment adherence, self-care capacity, dementia risk, and mortality. In addition, we were not able to perform meta-analyses for all research questions because data were not always reported in the included studies and there was high heterogeneity in terms of how SCCs and other factors were operationalised. Although study authors were contacted for original data or additional analyses, the response rate was very low.

Despite the limitations, we believe that this paper provides a comprehensive overview of current evidence regarding the extent and course of SCCs, as well as factors associated with these complaints in patients living with ESRD. This field of research remains in its infancy since the majority of studies only considered SCCs as a secondary outcome that reflects a subdomain of quality of life or overall symptoms. We call for further research on SCCs in ESRD patients that are well-grounded in relevant theories, utilise longitudinal designs, adopt valid and reliable measures of multiple cognitive domains and symptom representation dimensions, and include both patients and informants. Improving our understanding of SCCs in ESRD patients have important clinical implications because subjective reports may improve the clinical meaningfulness of objective tests and may allow early detection and early intervention for patients with higher risk of progression to objective cognitive impairments.

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Table 1. *Measures used to assess SCCs in ESRD patients.*

Measures	No. of Items	Recall Period	Response Format	Measurement Dimensions	Content Dimensions	Frequency of Use
SCC-specific measures						
Brief Metacognition Questionnaire	9	N/A	5-point Likert - Strongly disagree - Disagree - Neither agree nor disagree - Agree - Strongly agree	Severity of SCCs	1. Memory 2. Concentration	1
British Columbia Cognitive Complaints Inventory (BC-CCI)	6	Past 7 days	4-point Likert - Not at all - Some - Quite a bit - Very much	Severity of SCCs	1. Memory 2. Concentration 3. Thought Expression 4. Word Finding 5. Thinking Speed 6. Problem Solving	1
Cognitive Difficulties Scale (CDS)	39	Past month	5-point Likert - Not at all - Rarely - Sometimes - Often - Very often	Frequency of SCCs	1. Attention & Concentration 2. Praxis 3. Prospective Memory 4. Speech 5. People's Names 6. Temporal Orientation	1

Measures	No. of Items	Recall Period	Response Format	Measurement Dimensions	Content Dimensions	Frequency of Use
Henry et al., 2017	4	Current	Smartphone-based electronic diary reports (6 times/day for a week) with 6-point Likert - None of the time - A little of the time - Some of the time - A good bit of the time - Most of the time - All of the time	Frequency of SCCs	1. Reaction time 2. Concentration & Thinking 3. Confusion 4. Decision Making	1
Patient's Assessment of Own Functioning Inventory (PAOFI)	33	Recent	6-point Likert - Almost always - Very often - Fairly often - Once in a while - Very infrequently - Almost never	Frequency of SCCs Change in SCCs	1. Memory 2. Language & Communication 3. Use of Hands 4. Sensory-Perceptual 5. Higher Level Cognitive & Intellectual Functions	3
Perceived Deficits Questionnaire 5-item version (PDQ-5)	5	Past 7 days	5-point Likert - Never - Rarely - Sometimes - Often - Almost always	Frequency of SCCs	1. Attention 2. Retrospective memory 3. Prospective memory 4. Planning & Organization	1

Measures	No. of Items	Recall Period	Response Format	Measurement Dimensions	Content Dimensions	Frequency of Use
Composite measures with SCC subscale						
Dialysis Symptom Index (DSI)	1	Past 7 days	Yes/No; 5-point Likert - Not at all bothersome - A little bothersome - Somewhat bothersome - Quite bothersome - Very bothersome	Presence of SCCs Severity of SCCs	1. Concentration	2
End-Stage Renal Disease Symptom Checklist (ESRD-SCL)	5	N/A	5-point Likert - 0 = Not at all - 4 = Extremely	Severity of SCCs	1. Concentration 2. Memory 3. Moodiness	1
Health Utilities Index Mark 3 (HUI3)	1	N/A	6 levels ranging from "Able to remember most things, think clearly and solve day to day problems." to "Unable to remember anything at all, and unable to think or solve day to day problems."	Severity of SCCs	1. Memory 2. Thinking 3. Problem Solving	1
Kidney Disease Quality of Life (KDQOL)	3	Past 4 weeks	6-point Likert - None of the time - A little of the time - Some of the time - A good bit of the time - Most of the time - All of the time	Frequency of SCCs	1. Reaction time 2. Concentration & Thinking 3. Confusion	207

Measures	No. of Items	Recall Period	Response Format	Measurement Dimensions	Content Dimensions	Frequency of Use
Patient-Reported Outcomes Measurement Information System (PROMIS)	4 to 12	Past 7 days	5-point Likert - Never - Rarely (Once) - Sometimes (Two or three times) - Often (About once a day) - Very often (Several times a day)	Frequency of SCCs	1. Mental Acuity 2. Concentration 3. Verbal and Nonverbal Memory 4. Verbal Fluency 5. Interference with Daily Functioning 6. Other People's Observation 7. Impact on Quality of Life	1
Visual Analogue Scale (10 items of quality of life)	1	Current	Visual Analogue Scale (0-100)	Severity of SCCs	1. Memory	1
WHO Disability Assessment Schedule (WHODAS 2.0)	6	Past 30 days	5-point Likert - No difficulty - Mild difficulty - Moderate difficulty - Severe difficulty - Extreme difficulty or inability to do	Severity of SCCs	1. Concentration 2. Memory 3. Problem Solving 4. Learning 5. Communication	1

Notes. SCCs = Subjective cognitive complaints; ESRD = End-stage renal disease.

Table 2. *Distribution of mean KDQOL-CF scores within different ranges across treatment modalities.*

Score Range	In-centre Haemodialysis		Peritoneal Dialysis		Kidney Transplantation	
	k (%)	N (%)	k (%)	N (%)	k (%)	N (%)
0-19	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (11.8%)	119 (4.4%)
20-39	7 (5.8%)	796 (2.1%)	2 (4.8%)	955 (15.1%)	0 (0.0%)	0 (0.0%)
40-59	10 (8.3%)	1058 (2.8%)	2 (4.8%)	97 (1.5%)	0 (0.0%)	0 (0.0%)
60-79	52 (43.3%)	26577 (71.4%)	19 (45.2%)	3357 (53.3%)	4 (23.5%)	652 (24.2%)
80-100	51 (42.5%)	8781 (23.6%)	19 (45.2%)	1895 (30.1%)	11 (64.7%)	1922 (71.4%)
Overall	120 (100.0%)	37212 (100.0%)	42 (100.0%)	6304 (100.0%)	17 (100.0%)	2693 (100.0%)

Notes. Studies that reported medians were not included in this table; For longitudinal studies that reported mean KDQOL-CF scores at multiple time points, only the baseline data were included; A score of 0, 20, 40, 60, 80, and 100 on the KDQOL-CF indicates that cognitive difficulties are experienced all of the time, most of the time, a good bit of the time, some of the time, a little of the time, and none of the time, respectively; KDQOL-CF = Cognitive Function subscale of the Kidney Disease Quality of Life questionnaire; k = Number of studies that reported means within each range; N = Total sample size of studies that reported means within each range.

Table 3. *Associations of subjective cognitive complaints with sociodemographic, clinical, and patient-reported variables reported by at least two studies.*

Variables	Total	Higher SCCs	Lower SCCs	No Association
	Number of studies (percentage)			
Sociodemographic				
Older age	29	2 (6.9%)	2 (6.9%)	25 (86.2%)
Female gender	17	2 (11.8%)	-	15 (88.2%)
Lower education level	14	7 (50.0%)	-	7 (50.0%)
Unemployment	6	4 (66.7%)	-	2 (33.3%)
Marital status	4	-	-	4 (100.0%)
Lower household income	3	1 (33.3%)		2 (66.7%)
Smoking	3	-	-	3 (100.0%)
Clinical				
Longer dialysis vintage	15	1 (6.7%)	2 (13.3%)	12 (80.0%)
Comorbidity	13	4 (30.8%)	-	9 (69.2%)
Higher albumin	13	2 (15.4%)	3 (23.1%)	8 (61.5%)
Higher dialysis adequacy	11	1 (9.1%)	1 (9.1%)	9 (81.8%)
Higher haemoglobin	8	1 (12.5%)	1 (12.5%)	6 (75%)
Diabetes	8	-	1 (12.5%)	7 (87.5%)
BMI	8	-	-	8 (100.0%)
Hospitalisation	6	6 (100.0%)	-	-
Mortality	6	2 (33.3%)	-	4 (66.7%)
Higher GFR	5	1 (20.0%)	-	4 (80.0%)
Higher creatinine	3	2 (66.7%)	-	1 (33.3%)
Higher phosphorus	3	1 (33.3%)	-	2 (66.7%)
Hematocrit	3	-	-	3 (100.0%)
nPNA	3	-	-	3 (100.0%)
Lower SGA score	3	1 (33.3%)	-	2 (66.7%)
Lower systolic blood pressure	3	1 (33.3%)	-	2 (66.7%)
Time after KTx	2	-	-	2 (100.0%)
Cancer	2	-	-	2 (100.0%)
Sarcopenia	2	-	-	2 (100.0%)
Sodium	2	-	-	2 (100.0%)
Calcium	2	-	-	2 (100.0%)
Cholesterol	2	-	-	2 (100.0%)
cPENS	2	-	-	2 (100.0%)
Higher TNF-α	2	1 (50.0%)	-	1 (50.0%)
Higher IL-6	2	1 (50.0%)	-	1 (50.0%)
Higher Ferritin	2	1 (50.0%)	-	1 (50.0%)
Patient-reported				
Higher depressive symptoms	21	18 (85.7%)	1 (4.8%)	2 (9.5%)
Higher anxious symptoms	10	9 (90.0%)	1 (10.0%)	-

Variables	Total	Higher SCCs	Lower SCCs	No Association
	Number of studies (percentage)			
Lower overall health rating	9	6 (66.7%)	-	3 (33.3%)
Higher level of pain	7	6 (85.7%)	-	1 (14.3%)
Higher fatigue symptoms	6	6 (100.0%)	-	-
Worse physical functioning	6	5 (83.3%)	-	1 (16.7%)
Worse social functioning	6	4 (66.7%)	-	2 (33.3%)
Worse perceived general health	5	3 (60.0%)	-	2 (40.0%)
Role limitation due to physical health	5	3 (60.0%)	-	2 (40.0%)
Role limitation due to emotional problems	5	3 (60.0%)	-	2 (40.0%)
More overall symptoms	5	5 (100.0%)	-	-
Poorer sleep quality	4	3 (75.0%)	-	1 (25.0%)
Lower functional capacity	4	3 (75.0%)	-	1 (25.0%)
Physical inactivity	3	2 (66.7%)	-	1 (33.3%)
Medication adherence	2	-	-	2 (100.0%)

Notes. SCCs = Subjective cognitive complaints; BMI = Body mass index; GFR = Glomerular filtration rate; nPNA = Normalised protein nitrogen appearance; SGA = Subjective global assessment; KTx = Kidney transplantation; cPENS = Composite score on protein-energy nutritional status; TNF-α = Tumour Necrosis Factor alpha; IL-6 = Interleukin 6.

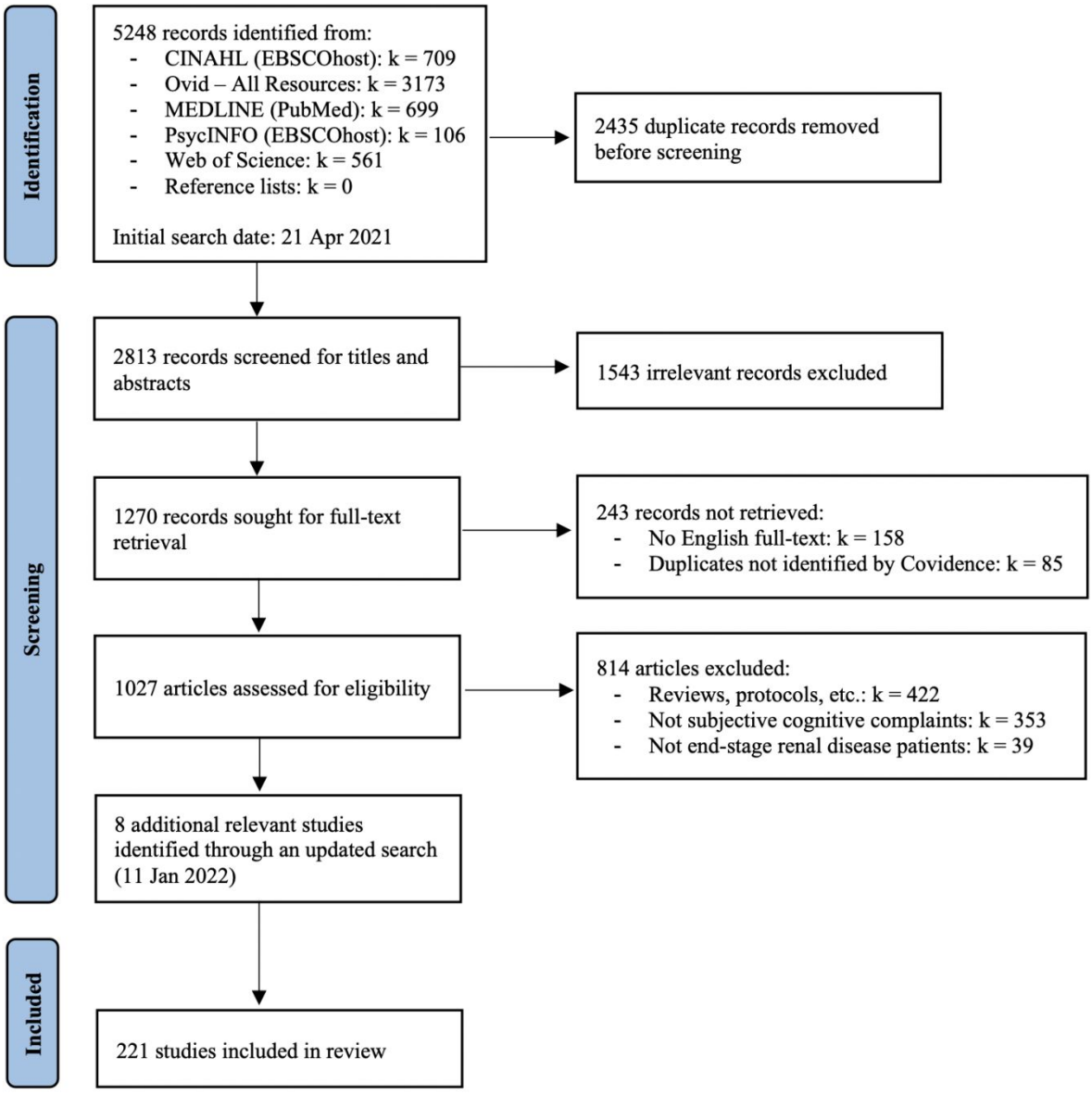

Figure 1. PRISMA flow diagram

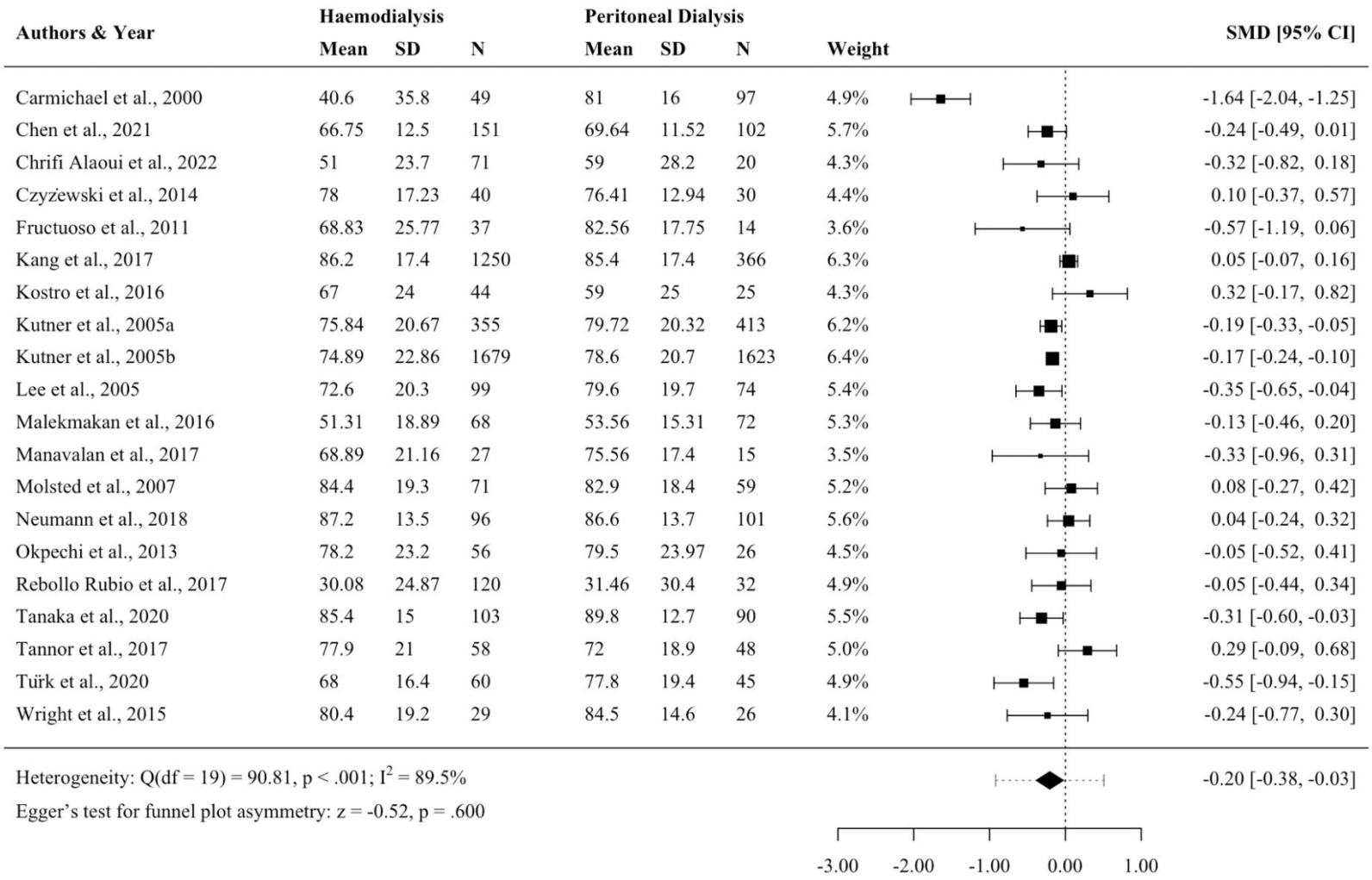

Figure 2. Forest plot showing the results of 20 studies examining difference in subjective cognitive complaints between haemodialysis and peritoneal dialysis patients. SD = Standard deviation; SMD = Standardised mean difference; CI = Confidence interval.

Table S1. *Search strategy*

Database	S#	Search Terms
CINAHL (EBSCOhost)	1	TX (“subjective cogniti*” OR “self-reported cogniti*” OR “patient-reported cogniti*” OR “self-perceived cogniti*” OR “patient-perceived cogniti*” OR “cognitive complaint*” OR “cognitive concern*” OR “cognitive failure*” OR “cognitive difficult*” OR “everyday cogniti*” OR metacogniti* OR “kidney disease quality of life” OR KDQOL OR “patient’s assessment of own functioning” OR PAOF*)
	2	TX (“chronic kidney disease*” OR “end-stage kidney disease*” OR “end-stage renal disease*” OR “renal insufficien*” OR “kidney failure” OR dialy* OR hemodia* OR haemodia* OR “renal transplant*” OR “kidney transplant*” OR “renal replacement” OR “kidney replacement” OR “artificial kidney”)
	3	#1 AND #2
Ovid – All Resources (Books@Ovid, Journals@Ovid Full Text, Your Journals@Ovid, EBM Reviews, Embase, MEDLINE)	1	(“subjective cogniti*” or “self-reported cogniti*” or “patients-reported cogniti*” or “self-perceived cogniti*” or “patient-perceived cogniti*” or “cognitive complaint*” or “cognitive concern*” or “cognitive failure*” or “cognitive difficult*” or “everyday cogniti*” or “metacogniti*” or “kidney disease quality of life” or KDQOL or “patient's assessment of own functioning” or PAOF*).mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, fx, hw, tn, dm, mf, dv, kf, dq, nm, ox, px, rx, an, ui, ds, on, sy]
	2	(“chronic kidney disease*” or “end-stage kidney disease” or “end-stage renal disease” or “renal insufficien*” or “kidney failure” or dialy* or hemodia* or haemodia* or “renal transplant*” or “kidney transplant*” or “renal replacement” or “kidney replacement” or “artificial kidney”).mp. [mp=tx, bt, ti, ot, ab, ct, sh, kw, fx, hw, tn, dm, mf, dv, kf, dq, nm, ox, px, rx, an, ui, ds, on, sy]
	3	#1 AND #2
MEDLINE (PubMed)	1	“subjective cogniti*”[All Fields] OR “self reported cogniti*”[All Fields] OR “patient reported cogniti*”[All Fields] OR “self perceived cogniti*”[All Fields] OR “patient perceived cogniti*”[All Fields] OR “cognitive complaint*”[All Fields] OR “cognitive concern*”[All Fields] OR “cognitive failure*”[All Fields] OR “cognitive difficult*”[All Fields] OR “everyday cogniti*”[All Fields] OR “metacogniti*”[All Fields] OR “kidney disease quality of life”[All Fields] OR “KDQOL”[All Fields] OR “patient’s assessment of own functioning”[All Fields] OR “PAOF*”[All Fields]
	2	“chronic kidney disease*”[All Fields] OR “end stage kidney disease*”[All Fields] OR “end stage renal disease*”[All Fields] OR “renal insufficien*”[All Fields] OR “kidney failure”[All Fields] OR “dialy*”[All Fields] OR “hemodia*”[All Fields]

		OR “haemodia*”[All Fields] OR “renal transplant*”[All Fields] OR “kidney transplant*”[All Fields] OR “renal replacement”[All Fields] OR “kidney replacement”[All Fields] OR “artificial kidney”[All Fields]
	3	#1 AND #2
PsycINFO (EBSCOhost)	1	TX (“subjective cogniti*” OR “self-reported cogniti*” OR “patient-reported cogniti*” OR “self-perceived cogniti*” OR “patient-perceived cogniti*” OR “cognitive complaint*” OR “cognitive concern*” OR “cognitive failure*” OR “cognitive difficult*” OR “everyday cogniti*” OR metacogniti* OR “kidney disease quality of life” OR KDQOL OR “patient’s assessment of own functioning” OR PAOF*)
	2	TX (“chronic kidney disease*” OR “end-stage kidney disease*” OR “end-stage renal disease*” OR “renal insufficien*” OR “kidney failure” OR dialy* OR hemodia* OR haemodia* OR “renal transplant*” OR “kidney transplant*” OR “renal replacement” OR “kidney replacement” OR “artificial kidney”)
	3	#1 AND #2
Web of Science	1	(ALL=(“subjective cogniti*” OR “self-reported cogniti*” OR “patient-reported cogniti*” OR “self-perceived cogniti*” OR “patient-perceived cogniti*” OR “cognitive complaint*” OR “cognitive concern*” OR “cognitive failure*” OR “cognitive difficult*” OR “everyday cogniti*” OR metacogniti* OR “kidney disease quality of life” OR karol OR “patient’s assessment of own functioning” OR PAOF*)) AND ALL=(“chronic kidney disease*” OR “end-stage kidney disease*” OR “end-stage renal disease*” OR “renal insufficien*” OR “kidney failure” OR dialy* OR hemodia* OR haemodia* OR “renal transplant*” OR “kidney transplant*” OR “renal replacement” OR “kidney replacement” OR “artificial kidney”)

Notes. Kidney Disease Quality of Life (KDQOL) was included in the keywords because it contains a cognitive function subscale and has been frequently used in patients with end-stage renal disease. Patient’s Assessment of Own Functioning (PAOF) is a comprehensive questionnaire of subjective cognitive complaints that has been used in several key studies relevant to this review.

Table S2. *Characteristics and key findings of included studies.*

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Abbasi Abianeh et al., 2020, Iran (1)	Pre-post study with no control group	HD: 45, 58.5 (10.0), 46.7%	KDQOL-CF	HD: M = 58.56	N/A	N/A	N/A
Ahmadzadeh et al., 2017, Iran (2)	Pre-post study with no control group	HD: 53, 54.0 (N/A), 41.5%	KDQOL-CF	HD: M = 62.66	N/A	N/A	N/A
AL-Jumaih et al., 2011, Saudi Arabia (3)	Observational cross-sectional study	HD: 100, 53.4 (10.3), 31.3%	KDQOL-CF	HD: M = 25.60	N/A	N/A	N/A
Alarcon et al., 2021, Colombia (4)	Observational cohort study	HD: 992, 60.5 (15.1), 37.6%	DSI-Difficulty Concentrating	HD: prevalence = 30.23%	N/A	No change in SCCs from baseline (high-flux) to 6 and 12 months (medium cut-off) in HD patients	No difference in SCCs between high-flux and medium cut-off HD
Amro et al., 2014, Norway (5)	Observational cross-sectional study	HD & PD: 243 (HD), 58 (PD), 59.8 (16.2), 33.9%	KDQOL-CF		N/A	N/A	SCCs positively associated with three symptom clusters: uraemic (nausea, lack of appetite, dizziness/faintness, feeling squeezed out, shortness of breath, chest pain), neuromuscular (numbness in extremities, sore muscles, cramps) and skin (itching, dry skin)
Anees et al., 2016, Pakistan (6)	Observational cross-sectional study	HD: 130, 43.1 (13.5), 35.9%	KDQOL-CF	HD: Median = 33.33	N/A	N/A	N/A
Anees et al., 2018, Pakistan (7)	Observational cohort study	HD: 135, N/A (N/A), N/A	KDQOL-CF	HD: M = 31.78	N/A	N/A	SCCs not associated with education level, employment status, household income, funding for dialysis, or mortality at 2 years
Aoun et al., 2020, Lebanon (8)	Observational cohort study	HD: 71, 68.4 (13.1), 36.6%	KDQOL-CF	HD: M = 83.00	N/A	N/A	SCCs not associated with mortality at 1 year or at 2 years; SCCs not associated with Duchenne smile
Aramwit et al., 2012, Thailand (9)	Pre-post study with no control group	HD: 47, 49.6 (11.2), 63.8%	KDQOL-CF	HD: M = 65.53	N/A	N/A	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Bacci et al., 2018, Brazil (10)	Observational cross-sectional study	HD: 30, 41.0 (N/A), 55.0%	KDQOL-CF	HD: Median = 5.00	N/A	N/A	SCCs not associated with inflammatory markers (TNF-alpha, IL-6, CRP, Hcy, Ferritin) or anthropometric parameters (abdominal circumference, BMI, triceps skinfold, arm circumference)
Bagasha et al., 2021, Uganda (11)	Observational cross-sectional study	HD: 124, N/A (N/A), 34.2%; Conservative management: 240, N/A (N/A), 42.6%	KDQOL-CF	HD: M = 63.66; Conservative management: M = 67.39	No difference in SCCs between HD and conservative management patients	N/A	N/A
Bakewell et al., 2001, UK (12)	Observational cross-sectional study	HD: 40, 52.5 (14.8), 35.0%; PD: 40, 49.0 (14.4), 30.0% KTx: 40, 46.0 (10.4), 30.0%	KDQOL-CF	N/A	N/A	N/A	Asian patients reported more SCCs than white patients
Barbosa et al., 2017, Brazil (13)	Observational cross-sectional study	HD: 47, 50.9 (13.3), 44.7%	KDQOL-CF	HD: M = 80.14	N/A	N/A	No difference in SCCs between patients on HD < 3 years and patients on HD > 3 years
Barotfi et al., 2006, Hungary (14)	Observational cross-sectional study	HD: 418, 53.0 (14.0), 44.0%; KTx:418, 49.0 (12.0), 41.0%	KDQOL-CF	HD: M = 78.00; KTx: M = 79.00	No difference in SCCs between HD and KTx patients	N/A	SCCs associated with lower overall health rating and higher depressive symptoms; SCCs not associated with age or GFR
Barzegar et al., 2017, Iran (15)	Observational cross-sectional study	HD: 246, 56.5 (12.8), 41.5%	KDQOL-CF	HD: M = 54.30	N/A	N/A	No difference in SCCs between patients on HD < 3 years and patients on HD > 3 years
Bataclan et al., 2009, Philippines (16)	Observational cross-sectional study	HD: 80, 53.0 (2.0), 56.0%	KDQOL-CF	HD: M = 89.11	N/A	N/A	SCCs not associated with overall health rating
Bawazier et al., 2018, Indonesia (17)	Observational cohort study	HD: 39, N/A (N/A), 53.8%	KDQOL-CF	HD: M = 82.05	N/A	N/A	Patients reported more SCCs with reusable dialyser than with single-use dialyser
Bele et al., 2012, India (18)	Observational cross-sectional study	HD: 54, 42.1 (13.5), 27.8%	KDQOL-CF	HD: M = 71.85	N/A	N/A	SCCs associated with greater concerns about death, hopelessness, meaninglessness, and futility

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Bettoni et al., 2017, Brazil (19)	Observational cross-sectional study	HD: 100, 53.3 (14.7), 34.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower perceived self-care capacity
Boudville et al., 2009, Australia (20)	Controlled intervention study	HD: 33, 59.1 (19.4), 39.0%	KDQOL-CF	N/A	N/A	No change in SCCs switching between dialysers in HD patients	No difference in SCCs between FX and HF80 dialysers
Bouidida et al., 2014, Morocco (21)	Observational cross-sectional study	HD & PD: 62 (HD), 18 (PD), 43.9 (14.2), N/A	KDQOL-CF	N/A	N/A	N/A	Females reported more SCCs than males; SCCs associated with lower overall health rating; SCCs not associated with age, education level, or dialysis vintage
Braga et al., 2011, Brazil (22)	Observational cross-sectional study	HD: 223, 69.5 (7.1), 43.5%	KDQOL-CF	HD: M = 84.78	N/A	N/A	N/A
Brickman et al., 1996, US (23)	Observational cross-sectional study	HD: 426, 42.9 (12.7), 59.0%	CDS	HD: M = 33.80	N/A	N/A	SCCs associated with lower education level, higher haemoglobin, higher depressive symptoms, higher state anxiety, and neuroticism; SCCs negatively associated with extraversion; SCCs not associated with age, sex, race, first language, marital status, HD vintage, albumin, diabetes, glucose, sodium, or creatinine; SCCs not associated with performance on WAIS-R Vocabulary Scale, Trail Making Test Part B, Stroop Color-Word Interference Test, Continuous Performance Test, WAIS-R Digit Symbol, WAIS-R Digit Span, Enhanced Cued Recall, or Wechsler Memory Test-Revised
Carmichael et al., 2000, UK (24)	Observational cross-sectional study	HD: 49, 57.8 (13.0), 34.7%; PD: 97, 57.0 (15.0), 40.2%	KDQOL-CF	HD: M = 40.6; PD: M = 81.0	HD patients reported more SCCs than PD patients	N/A	SCCs not associated with age or haemoglobin

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Castro et al., 2018, Brazil (25)	Observational cross-sectional study	HD: 51, 54.6 (15.8), 39.2%	KDQOL-CF; WHODAS 2.0-Cognition	HD (KDQOL-CF): M = 93.72; HD (WHODAS 2.0-Cognition): M = 11.17	N/A	N/A	SCCs (KDQOL-CF) associated with poorer quality of life in getting alone, life activities, and participation domains of WHODAS 2.0; SCCs (KDQOL-CF) not associated with mobility or self-care domains of WHODAS 2.0; SCCs (WHODAS 2.0-Cognition) associated with poorer quality of life in physical, psychological, social, and environmental domains of WHOQOL-BREF; SCCs (WHODAS 2.0-Cognition) associated with poorer quality of life in symptom/problem list, burden of kidney disease, physical functioning, pain, emotional well-being, and energy/fatigue domains of KDQOL; SCCs (WHODAS 2.0-Cognition) not associated with effects of kidney disease, work status, quality of social interaction, sexual function, sleep, social support, dialysis staff encouragement, overall health rating, patient satisfaction, role physical, general health perceptions, role emotional, and social function domains of KDQOL
Cavalcante et al., 2013, Brazil (26)	Observational cross-sectional study	HD: 291, N/A (N/A), 44.7%	KDQOL-CF	HD: Median = 93.30	N/A	N/A	N/A
Cepeda Marte et al., 2019, Dominican Republic (27)	Observational cross-sectional study	HD: 21, N/A (N/A), 19.0%	KDQOL-CF	HD: M = 26.35	N/A	N/A	N/A
Chan et al., 2010, Hong Kong (28)	Observational cross-sectional study	PD: 153, 60.0 (14.0), 45.8%	KDQOL-CF	PD: M = 72.11	N/A	N/A	N/A
Chen et al., 2021, Mainland China (29)	Observational cohort study	HD: 151, 56.5 (17.0), 46.4%; PD: 102, 59.7 (17.3), 51.0%	KDQOL-CF	HD: M = 66.75; PD: M = 69.64	No difference in SCCs between HD and PD patients	N/A	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Cheung et al., 2012, Singapore (30)	Observational cohort study	Conservative management: 78, N/A (N/A), 44.9%	KDQOL-CF	Conservative management: M = 92.10	N/A	N/A	SCCs not associated with GFR; SCCs associated with functional disability assessed by Karnofsky Performance Status, self-rated change of general health compared to one year ago, and poorer quality of life in the physical functioning, role physical, emotion well-being, role emotional, and energy/fatigue domains of RAND 36; SCCs not associated with quality of life in the pain, general health, and social function domains of RAND 36
Cho et al., 2018, Korea (31)	Observational cross-sectional study	HD: 230, 60.5 (14.0), 47.4%	DSI-Difficulty Concentrating	HD: M = 2.08; prevalence = 57.8%	N/A	N/A	N/A
Chow et al., 2010, Hong Kong (32)	Controlled intervention study	PD: 85, 56.9 (13.5), 38.8%	KDQOL-CF	PD: M = 66.18	N/A	No change in SCCs from baseline to 6 and 12 weeks in PD patients (control group)	N/A
Chrifi Alaoui et al., 2022, Morocco (33)	Observational cross-sectional study	HD: 71, N/A (N/A), 52.1%; PD: 20, N/A (N/A), 40.0%	KDQOL-CF	HD: Median = 53.30; PD: Median = 60.00	HD patients reported more SCCs than PD patients	N/A	N/A
Costa-Requena et al., 2017, Spain (34)	Observational cohort study	KTx: 124, 53.2 (14.2), 32.3%	KDQOL-CF	N/A	N/A	SCCs reduced from 1 to 6 months post-KTx; no change in SCCs from 6 to 24 months post-KTx	N/A
Czyżewski et al., 2014, Poland (35)	Observational cohort study	HD: 40, N/A (N/A), 42.5%; PD: 30, N/A (N/A), 50.0%; KTx:47, N/A (N/A), 44.7%	KDQOL-CF	HD: M = 78.00; PD: M = 76.41; KTx: M = 68.89	No difference in SCCs between HD, PD, and KTx patients	No change in SCCs from 3 to 12 months post-KTx	N/A
Czyzewski et al., 2018, Poland (36)	Observational cross-sectional study	KTx: 118, 45.0 (N/A), 53.4%	KDQOL-CF	KTx: M = 68.50	N/A	N/A	No difference in SCCs between patients who received KTx < 1 year, patients who received KTx between 1 and 10 years, and patients who received KTx > 10 years

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
D'Onofrio et al., 2017, Italy (37)	Observational cross-sectional study	HD: 103, 66.2 (N/A), 37.9%	KDQOL-CF	HD: M = 70.00	N/A	N/A	N/A
Dai et al., 2020, Mainland China (38)	Controlled intervention study	HD (thrice-weekly): 70, 50.6 (4.9), 40.0%; HD (twice-weekly): 70, 50.9 (4.3), 44.3%	KDQOL-CF	HD: M = 73.10	N/A	N/A	Thrice-weekly HD associated with more SCCs than twice-weekly HD
de Oliveira Cordeiro et al., 2020, Brazil (39)	Observational cross-sectional study	KTx: 222, 45.8 (12.8), 39.6%	KDQOL-CF	KTx: M = 82.80	N/A	N/A	N/A
de Oliveira et al., 2012, Brazil (40)	Observational cross-sectional study	PD: 82, 61.0 (N/A), 61.0%	KDQOL-CF	PD: M = 83.23	N/A	N/A	Patients who do not work reported more SCCs than patients who work
de Roij van Zuijdewijn et al., 2016, Netherlands, Norway, and Canada (41)	Observational cross-sectional study	HD: 489, 63.3 (13.8), 39.5%	KDQOL-CF	HD: M = 77.00	N/A	N/A	SCCs associated with higher Malnutrition Inflammation Score, lower Subjective Global Assessment score, and higher creatinine; SCCs not associated with Geriatric Nutritional Risk Index, Composite Score on Protein-Energy Nutritional Status, albumin, BMI, or Normalized Protein Nitrogen Appearance
Debnath et al., 2018, US (42)	Observational cross-sectional study	HD: 40, N/A (N/A), 65.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with higher depressive symptoms
Dehesa-Lopez et al., 2016, Mexico (43)	Observational cross-sectional study	HD: 194, 54.0 (16.0), 45.4%	KDQOL-CF	HD: M = 21.80	N/A	N/A	SCCs associated with higher serum phosphorus and serum albumin; SCCs not associated with age, HD vintage, haemoglobin, serum calcium, or dialysis adequacy (Kt/V)
Dehghan et al., 2020, Iran (44)	Observational cross-sectional study	HD: 113, 58.1 (13.6), 40.7%	KDQOL-CF	HD: M = 68.35	N/A	N/A	SCCs not associated with use of relaxation methods
Diamant et al., 2011, Canada (45)	Observational cross-sectional study	HD: 277, 65.9 (14.8), 41.8%	KDQOL-CF	HD: M = 79.28	N/A	N/A	No difference in SCCs between patients receiving HD in satellite units and in-center units

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Duarte et al., 2005, Brazil (46)	Observational cross-sectional study	HD & PD: 53 (HD), 41 (PD), 49.0 (13.0), 45.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated lower education level; SCCs not associated with age, HD vintage, number of comorbidities, or hematocrit; SCCs associated with poorer quality of life in the level of energy, pain, emotional reaction, sleep, social isolation, and physical capacity domains of the Nottingham Health Profile; SCCs associated with poorer quality of life in the physical symptom, fatigue, depression, relationship with others, and frustration domains of the Kidney Disease Questionnaire; SCCs not associated with functional disability assessed by Karnofsky Performance Status
Duarte et al., 2009, Brazil (47)	Controlled intervention study	HD: 85, 53.2 (14.3), 58.8%	KDQOL-CF	HD: M = 66.83	N/A	No change in SCCs from baseline to 3 and 9 months in HD patients (control group)	N/A
Fan et al., 2020, Taiwan (48)	Observational cross-sectional study	HD: 200, 62.0 (11.4), 49.5%	PDQ-5	HD: M = 1.80	N/A	N/A	SCCs associated with older age, lower serum albumin, and higher depressive symptoms; SCCs not associated with sex, education level, marital status, family history of mental disorders, BMI, HD vintage, dialysis adequacy (urea reduction ratio), smoking, alcohol use, diabetes, cardiovascular disease, hypertention, cancer, serum sodium, haemoglobin, cholesterol, triglycerides, or uric acid
Fiderkiewicz et al., 2011, Poland (49)	Observational cross-sectional study	HD: 196, 63.9 (13.2), 39.8%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with irritable bowel syndrome symptoms
Foley et al., 2009, Canada (50)	Controlled intervention study	HD: 596, 50.8 (N/A), 39.6%	KDQOL-CF	HD: M = 66.62	N/A	N/A	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Fong et al., 2007, Canada (51)	Observational cross-sectional study	PD: 57, 61.0 (13.0), 45.0% NHD: 36, 49.0 (12.0), 33.0%	KDQOL-CF	PD: M = 81.40; NHD: M = 75.60	No difference in SCCs between PD and NHD patients	N/A	N/A
Frimat et al., 2006, France (52)	Observational cohort study	HD: 284, 67.6 (11.3), 40.1%; PD: 103, 70.8 (11.4), 43.7%	KDQOL-CF	HD: M = 63.50; PD: M = 63.40	No difference in SCCs between HD and PD patients at any time point	No change in SCCs from predialysis to 6 or 12 months post-initiation of HD/PD	N/A
Fructuoso et al., 2011, Portugal (53)	Observational cross-sectional study	HD: 37, 67.3 (14.9), 43.2%; PD: 14, 38.9 (13.3), 42.9%	KDQOL-CF	HD: M = 68.83; PD: M = 82.56	No difference in SCCs between HD and PD patients	N/A	N/A
Fukuhara et al., 2003, US, France, Germany, Italy, Spain, UK, and Japan (54)	Observational cross-sectional study	HD: 7378, 59.4 (N/A), 42.7%	KDQOL-CF	HD: M = 77.30	N/A	N/A	European patients reported more SCCs than Japanese and US patients
G. B. Lopes et al., 2014, Brazil (55)	Observational cross-sectional study	HD: 800, 49.0 (13.9), 39.6%	KDQOL-CF	HD: Median = 86.70	N/A	N/A	Patients who reported needing some time to recover after HD sessions had more SCCs than patients who felt well immediately after the end of HD sessions
Garcia et al., 2010, Brazil (56)	Observational cross-sectional study	HD: 47, 39.4 (8.9), 0.0%	KDQOL-CF	HD: Median = 93.30	N/A	N/A	SCCs not associated with depressive symptoms
Giglio et al., 2018, Brazil (57)	Observational cross-sectional study	HD: 170, 70.6 (7.2), 34.7%	KDQOL-CF	HD: Median = 86.70, 87.00, 80.00, 93.30, 80.00, 93.00 in patients with low and appropriate muscle mass, low and appropriate muscle strength, and with and without sarcopenia, respectively	N/A	N/A	SCCs associated lower muscle strength; SCCs not associated with muscle mass or sarcopenia status

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Goldfarb-Rumyantzev et al., 2006, US (58)	Pre-post study with no control group	HD (week 1-4) switching to DHD (week 5-12) and then to HD (week 13-16): 12, 52.0 (18.0), 50.0%	KDQOL-CF	HD: M = 74.50; DHD: M = 84.80	No difference in SCCs between HD (week 1-4 & 13-16) and DHD (week 5-12)	No change in SCCs switching from HD (weeks 1-4) to DHD (weeks 5-12) and back to HD (weeks 13-16)	N/A
Gonçalves et al., 2015, Brazil (59)	Observational cross-sectional study	HD: 222, 54.4 (15.2), N/A; PD: 116, 58.0 (13.9), N/A	KDQOL-CF	HD: M = 79.64; PD: M = 81.09	No difference in SCCs between HD and PD patients	N/A	N/A
Gorodetskaya et al., 2005, US (60)	Observational cohort study	HD: 38, 57.3 (16.5), 34.0%	HUI3-Cognition	HD: M = 0.93	N/A	N/A	N/A
Green et al., 2001, Japan (61)	Observational cross-sectional study	HD & PD: 690 (HD), 103 (PD), 55.0 (N/A), 45.9%	KDQOL-CF	N/A	N/A	N/A	Patients who received assistance in filling out the survey had more SCCs than those who filled out the survey themselves
Griva et al., 2012, UK (62)	Observational cross-sectional study	KTx: 218, 49.7 (12.3), 40.4%	KDQOL-CF	N/A	N/A	N/A	SCCs not associated with medication adherence
Gumprecht et al., 2010, Poland (63)	Observational cross-sectional study	HD: 114, 55.7 (15.1), 47.4%	KDQOL-CF	HD: M = 75.89	N/A	N/A	SCCs not associated with diabetes
Hasan et al., 2021, Egypt (64)	Observational cohort study	HD: 100, 48.8 (5.9), 49.0%	KDQOL-CF	HD: M = 84.27	N/A	N/A	SCCs associated with lower dialysis adequacy (Kt/V); improvement of Kt/V associated with reduction of SCCs over 3 months
Hayashi et al., 2017, Japan (65)	Controlled intervention study	HD: 18, 54.7 (13.6), 35.0%	KDQOL-CF	HD: M = 86.54	N/A	No change in SCCs from baseline to 16 weeks in HD patients (control group)	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Hays et al., 1994, US (66)	Observational cross-sectional study	HD: 165, 53.0 (N/A), 52.0%	KDQOL-CF	HD: M = 78.51	N/A	N/A	SCCs associated with number of hospital days in the past 6 months; SCCs associated with number of good days in the last seven days, number of bad days in the last seven days, rating of one's life compared with people without kidney disease, extent to which the individual is able to do everything they want to do, days health caused one to stay in bed for one-half day or longer during the last 30 days, and overall health rating
Henry et al., 2018, US (67)	Observational cross-sectional study	HD: 26, 42.7 (15.8), 57.7%	Four items from KDQOL-CF and BDI	HD: M = 0.27 for reaction time, M = 0.36 for concentration and thinking, M = 0.12 for confusion, and M = 0.12 for decision-making	N/A	N/A	Patients reported more SCCs of confusion on dialysis days than non-dialysis days; patients reported more SCCs of reaction time on short interdialytic interval than on day 2 of the long interdialytic interval; SCCs of reaction time associated with poorer performance in Digit Span Task and Trail Making Test B; SCCs of confusion associated with poorer performance in Digit Span Task, Visual Retention Test, and Trail-Making Test B; SCCs not associated with MMSE scores
Hernández Sánchez et al., 2021, Spain (68)	Controlled intervention study	KTx: 16, 49.2 (9.8), 43.8%	KDQOL-CF	KTx: M = 12.00	N/A	No change in SCCs from baseline to 10 weeks in KTx patients (control group)	
Ho et al., 2013, Malaysia (69)	Observational cross-sectional study	HD: 72, N/A (N/A), 58.3%	KDQOL-CF	HD: M = 83.70	N/A	N/A	Non-Malays reported more SCCs than Malays; SCCs not associated with age, sex, education level, or presence of comorbidities
Hornik et al., 2019, Poland (70)	Observational cross-sectional study	HD: 72, 57.8 (16.0), 50.0%	KDQOL-CF	HD: M = 71.30	N/A	N/A	SCCs not associated with adherence to recommended physical activity
Hyodo et al., 2004, Japan (71)	Observational cross-sectional study	HD: 21, 55.9 (11.3), 0.0%	KDQOL-CF	HD: M = 89.27	N/A	N/A	No difference in SCCs between patients who desired Slidenafil and patients who did not

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
J. M. Lopes et al., 2014, Brazil (72)	Observational cross-sectional study	HD: 101, 56.4 (14.4), 32.0%	KDQOL-CF	HD: M = 89.31	N/A	N/A	N/A
Jansz et al., 2018, Netherlands (73)	Observational cross-sectional study	NHD: 31, 53.9 (12.5), 38.0%; KTx: 41, 54.0 (13.8), 25.0%	KDQOL-CF	NHD: M = 78.00 KTx: M = 81.00	No difference in SCCs between NHD and KTx patients	N/A	N/A
Jassal et al., 2006, Canada (74)	Observational cohort study	HD (baseline) switching to NHD (6 month): 12, 39.6 (3.3), 50.0%	PAOFI	HD (baseline): M = 36.90; NHD (6 months): M = 26.70	Patients reported more SCCs on HD (baseline) than on NHD (6 months)	SCCs reduced after switching from HD (baseline) to NHD (6 months)	N/A
Jayanti et al., 2016, UK (75)	Observational cross-sectional study	Predialysis: 204, 59.4 (13.0), 38.7%	Brief Metacognition Questionnaire	Predialysis: M = 17.84 for metamemory; M = 14.48 for metaconcentration	N/A	N/A	SCCs of concentration (not memory) associated with lower odds of choosing self-care dialysis (PD/HHD) over a fully assisted dialysis modality (HD); SCCs of concentration (not memory) associated with poorer performance in the Trail Making Test part B (not part A or 3MS)
Jiao et al., 2017, Mainland China (76)	Controlled intervention study	PD: 118, 58.0 (7.0), 44.1%	KDQOL-CF	PD: M = 67.32	N/A	No change in SCCs from baseline to 6 and 12 weeks in PD patients (control group)	N/A
Joshi et al., 2010, Singapore (77)	Observational cross-sectional study	HD: 980, 56.0 (21.0), 43.9%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower overall health rating
Jung et al., 2016, Korea (78)	Observational cohort study	APD: 80, 50.9 (11.2), 33.7%; CAPD: 80, 51.4 (11.8), 35.0%	KDQOL-CF	APD: M = 83.42; CAPD: M = 79.08; PD (combining two groups): M = 81.25	No difference in SCCs between APD and CAPD at either time point	No change in SCCs from 1 to 12 months post-initiation of PD	N/A
Kanamori et al., 2012, Japan (79)	Observational cohort study	HD: 211, 59.0 (12.3), 37.4%	Visual Analogue Scale of Memory (0-100)	HD: Median = 45 and 51 in elderly and non-elderly patients	N/A	N/A	SCCs of memory not associated with age or mortality at 3 years

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Kang et al., 2017, Korea (80)	Observational cohort study	HD: 1250, 56.4 (13.2), 43.4%; PD: 366, 54.1 (11.9), 46.7%	KDQOL-CF	HD: M = 86.20; PD: M = 85.40	No difference in SCCs between HD and PD patients	N/A	N/A
Kim et al., 2011, Korea (81)	Pre-post study with no control group	HD: 24, 51.9 (7.2), 41.7%	KDQOL-CF	HD: M = 81.94	N/A	N/A	N/A
Kim et al., 2020, Korea (82)	Observational cohort study	HD: 1461, 58.3 (14.2), 38.3%	KDQOL-CF	HD: M = 82.79	N/A	N/A	CVC associated with more SCCs than AVF at 3 months post-initiation of HD; No difference in SCCs between AVF and AVG, or between AVG and CVC at 3 months; No difference in SCCs between the three access types at 12 months
Kim et al., 2021, Korea (83)	Observational cross-sectional study	HD: 1247, 56.4 (13.2), 43.5%; PD: 364, 54.1 (11.9), 46.4%	KDQOL-CF	HD: Median = 93.00 and 95.00 in patients with non-high and high physical activity; PD: Median = 93.00	N/A	N/A	HD patients with low physical activity reported more SCCs than HD patients with high physical activity; SCCs not associated with physical activity in PD patients
Knudsen et al., 2016, Denmark (84)	Observational cross-sectional study	HD: 81, 66.0 (13.0), 32.1%	KDQOL-CF	HD: M = 85.00	N/A	N/A	N/A
Ko et al., 2007, US (85)	Observational cross-sectional study	HD: 112, 55.5 (16.9), 58.0%	KDQOL-CF	HD: M = 78.70	N/A	N/A	N/A
Kontodimopoulos et al., 2005, Greece (86)	Observational cross-sectional study	HD: 483, 59.9 (14.6), 38.8%	KDQOL-CF	HD: M = 74.49	N/A	N/A	SCCs associated with female gender, older age, lower education level, presence of comorbidities, and more times of hospitalisations in the past year; SCCs associated with poorer quality of life in the physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health domains of SF-36

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Korevaar et al., 2002, Netherlands (87)	Observational cohort study	HD & PD: 234 (HD), 141 (PD), 60.0 (16.0), 39.0%	KDQOL-CF	N/A	N/A	No change in SCCs from 3 to 12 months post-initiation of HD/PD	SCCs associated with number of comorbidities; SCCs associated with higher dialysis adequacy (Kt/V) in HD but not PD patients; SCCs not associated with GFR; increase in SCCs from 3 to 12 months post-initiation of dialysis associated with reduction in serum albumin; SCCs associated with lower overall health rating
Kostro et al., 2016, Poland (88)	Observational cohort study	HD switching to KTx: 44, 49.0 (N/A), 31.8%; PD switching to KTx: 25, 42.0 (N/A), 44.0%	KDQOL-CF	HD (before KTx): M = 67.00; PD (before KTx): M = 59.00; KTx (combining two groups): M = 75.91	No difference in SCCs between HD and PD patients	SCCs reduced from pre-KTx (HD/PD) to 12 months post-KTx	N/A
Krishnasamy et al., 2019, Australia (89)	Observational cross-sectional study	HD: 32, 71.4 (10.6), 37.5%	KDQOL-CF	HD: M = 83.15	N/A	N/A	Isolation due to multidrug-resistant organisms not associated with SCCs
Kurella et al., 2004, US (90)	Observational cross-sectional study	HD: 79, 61.2 (14.4), 41.0%	KDQOL-CF	HD: Median = 73.00	N/A	N/A	SCCs positively associated with benzodiazepine use and stroke; SCCs negatively associated with beta-blocker use; SCCs associated with higher depressive symptoms
Kusumoto et al., 2008, Brazil (91)	Observational cross-sectional study	HD: 194, N/A (N/A), 36.6%	KDQOL-CF	HD: M = 80.83	N/A	N/A	No difference in SCCs between adults (< 60 years) and elderly (> 60 years)
Kutner et al., 2005a, US (92)	Observational cohort study	HD: 455, 61.2 (15.6), 43.3%; PD: 413, 56.1 (14.7), 47.2%	KDQOL-CF	HD: M = 75.84; PD: M = 79.72	No difference in SCCs between HD and PD patients at any time point	N/A	
Kutner et al., 2005b, US (93)	Observational cross-sectional study	HD: 1679, 61.6 (15.4), 46.9%; PD: 1623, 56.4 (15.3), 47.0%	KDQOL-CF	HD: M = 74.89; PD: M = 78.60	HD patients reported more SCCs than PD patients	N/A	SCCs not associated with sex or race
Kutner et al., 2007, US (94)	Observational cross-sectional study	HD & PD: 1170 (HD), 1116 (PD), 60.0 (16.0), 39.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower education level, sleep medication prescription, self-reported sleep difficulty, higher depressive symptoms, and more bodily pain

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Lai et al., 2018, Italy (95)	Observational cohort study	PD: 51, 63.1 (14.6), 45.1%	KDQOL-CF	PD: M = 88.60	N/A	N/A	SCCs not associated with age
Lazarus, 2019, Oman (96)	Controlled intervention study	HD: 150, 48.8 (10.3), 44.7%	KDQOL-CF	HD: M = 61.50	N/A	N/A	N/A
Lee et al., 2005, UK (97)	Observational cross-sectional study	HD: 99, 63.0 (14.2), 39.4%; PD: 74 58.7 (15.3), 48.6%; KTx: 209, 52.8 (13.9), 40.2%	KDQOL-CF	HD: M = 72.60; PD: M = 79.60; KTx: M = 80.90	HD patients reported more SCCs than PD and KTx patients; No difference in SCCs between PD and KTx patients	N/A	N/A
Lee et al., 2020, Korea (98)	Observational cohort study	HD: 568, 60.8 (13.5), 38.4%	KDQOL-CF	N/A	N/A	N/A	SCCs not associated with mortality at 5 years
Leone et al., 2021, Brazil (99)	Observational cross-sectional study	HD: 162, N/A (N/A), 37.1%	KDQOL-CF	HD: M = 81.28	N/A	N/A	SCCs not associated with patient activation
Li et al., 2014, Mainland China (100)	Controlled intervention study	PD: 135, 56.3 (12.4), 41.5%	KDQOL-CF	PD: M = 73.09	N/A	No change in SCCs from baseline to 6 and 12 weeks in PD patients (control group)	N/A
Li et al., 2016, US (101)	Observational cross-sectional study	HD: 72, 52.0 (13.0), 32.0%	KDQOL-CF	HD: M = 82.20	N/A	N/A	SCCs associated with depressive and anxious symptoms (BAI, BDI, HADS); SCCs associated self-reported physical inactivity, but not associated with physical inactivity measured by a physical activity monitor; SCCs not associated with physical performance assessed by 6-minute walk test, sit-to-stand test, and stair climbing test
Lim et al., 2020, Korea (102)	Controlled intervention study	HD: 49, 63.0 (14.4), 32.7%	KDQOL-CF	HD: M = 83.11	N/A	N/A	No difference in SCCs between medium cut-off and high-flux dialysers

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Lo et al., 1998, Hong Kong (103)	Controlled intervention study	PD: 20, 45.7 (11.1), 50.0%	KDQOL-CF	PD: M = 63.18	N/A	No change in SCCs from baseline to 12 weeks in PD patients (control group)	N/A
Lønning et al., 2018a, Norway (104)	Observational cohort study	KTx: 120, 71.6 (4.3), 29.0%	KDQOL-CF	N/A	N/A	No change in SCCs from pre-KTx (HD/PD/preemptive) to 2, 6, and 12 months post-KTx	Longer waiting time for KTx associated with increase in SCCs; Change in SCCs not associated with age, sex, comorbidity, pre-KTx dialysis vintage, GFR, donor age, or HLA-DR
Lønning et al., 2018b, Norway (105)	Observational cohort study	KTx waiting list: 261, 71.2 (4.1), 33.0%	KDQOL-CF	N/A	N/A	No change in SCCs between baseline (KTx acceptance) to 6 and 12 months on KTx waiting list	N/A
Loos-Ayav et al., 2008, France (106)	Observational cohort study	HD & PD: 161 (HD), 34 (PD), 54.6 (12.8), 39.0%	KDQOL-CF	N/A	N/A	N/A	Non-autonomous patients reported more SCCs than autonomous (independent, self-care) patients at 12 months post-initiation of HD/PD
Lopes et al., 2003, US (107)	Observational cohort study	HD: 6151, 60.1 (15.5), 46.8%	KDQOL-CF	HD: M = 77.29	N/A	N/A	Hispanic patients had more SCCs than white patients: SCCs associated with hospitalisation and mortality only in white patients
Lopes et al., 2007, US, France, Germany, Italy, Spain, UK, and Japan (108)	Observational cross-sectional study	HD: 9526, 59.5 (14.8), 41.5%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower household income, lower education level, unemployment, cerebrovascular or neurological disease, cardiac disease, and psychiatric disease; SCCs not associated with age, sex, marital status, living status, serum albumin, haemoglobin, dialysis adequacy (Kt/V), dialysis access, predialysis SBP, BMI, peripheral vasculopathy, diabetes, lung disease, or cancer

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Lopes et al., 2019, Brazil (109)	Controlled intervention study	HD: 50, 54.2 (12.4), 40.0%	KDQOL-CF	HD: M = 87.38	N/A	No change in SCCs from baseline to 12 weeks in HD patients (control group)	N/A
Ma et al., 2021, China (110)	Observational cross-sectional study	HD: 190, 61.7 (13.4), 38.4%	KDQOL-CF	HD: M = 32.81	N/A	N/A	SCCs associated with lower scores in the average positive factors, somatisation, obsessive compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism domains of the SCL-90
Macedo et al., 2021, Brazil (111)	Observational cross-sectional study	HD: 170, 70.6 (7.2), 34.7%	KDQOL-CF	HD: M = 79.66	N/A	N/A	SCCs not associated with sarcopenia (muscle mass and muscle strength) or malnutrition (Subjective Global Assessment)
Madariaga et al., 2016, US (112)	Observational cross-sectional study	KTx: 21, 34.4 (8.9), 52.4%	KDQOL-CF	KTx: M = 80.32	No difference in SCCs between conventional KTx patients maintained on chronic immunosuppression and KTx patients who achieved long-term immunosuppression-free renal allograft survival after combined kidney and bone marrow transplantation	N/A	N/A
Malekmakan et al., 2016, Iran (113)	Observational cross-sectional study	HD: 68, 54.9 (12.1), 57.4%; PD: 72, 52.4 (12.1), 50.0%	KDQOL-CF	HD: M = 51.31; PD: M = 53.56	No difference in SCCs between HD and PD patients	N/A	N/A
Malindretos et al., 2010, Greece (114)	Observational cross-sectional study	HD: 200, 62.9 (14.7), 45.0%	KDQOL-CF	HD: M = 70.06	N/A	N/A	SCCs associated with number of comorbidities (Index of Coexistent Disease)

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Manavalan et al., 2017, India (115)	Observational cross-sectional study	Predialysis: 57, 51.1 (12.5), 33.3%; HD & PD: 27 (HD), 15 (PD), 42.0 (13.4), 35.7%	KDQOL-CF	Predialysis: M = 62.22; HD: M = 68.89; PD: M = 75.56	No difference in SCCs between predialysis, HD, and PD patients	N/A	N/A
Manju et al., 2020, India (116)	Observational cross-sectional study	HD: 112, 60.6 (11.8), 33.9%	KDQOL-CF	HD: M = 68.86	N/A	N/A	N/A
Manns et al., 2002, Canada (117)	Observational cross-sectional study	HD: 128, 61.8 (N/A), 43.7%	KDQOL-CF	HD: M = 78.70	N/A	N/A	SCCs not associated with dialysis adequacy (Kt/V)
Mansouri et al., 2020, Iran (118)	Controlled intervention study	HD: 60, 49.7 (N/A), 11.67%	KDQOL-CF	HD: M = 45.79	N/A	N/A	N/A
Mapes et al., 2003, US, France, Germany, Italy, Spain, UK, and Japan (119)	Observational cohort study	HD: 10030, 58.9 (14.9), 42.4%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with mortality and hospitalisation
Marinho et al., 2017, Brazil (120)	Observational cross-sectional study	HD: 105, N/A (N/A), 42.9%	KDQOL-CF	HD: M = 86.41	N/A	N/A	N/A
Martin et al., 2000, UK (121)	Observational cross-sectional study	PD: 72, 51.4 (14.6), 36.1%	KDQOL-CF	PD: M = 78.60	N/A	N/A	SCCs associated with higher depressive and anxious symptoms (HADS) and external locus of control orientation
Martin et al., 2001, UK (122)	Observational cross-sectional study	PD: 48, 54.0 (13.9), 33.3%	KDQOL-CF	PD: M = 80.22	N/A	N/A	SCCs not associated with dialysis adequacy (Kt/V)
Martin-Alemañy et al., 2016, Mexico (123)	Controlled intervention study	HD: 36, 34.0 (N/A), 58.3%	KDQOL-CF	HD: M = 35.03	N/A	N/A	N/A
Masina et al., 2016, Malawi (124)	Observational cross-sectional study	HD: 22, 44.8 (16.0), 40.9%	KDQOL-CF	HD: M = 83.00	N/A	N/A	N/A
Maynard et al., 2019, Brazil (125)	Controlled intervention study	HD: 40, 46.5 (13.6), 45.0%	KDQOL-CF	HD: M = 82.65	N/A	No change in SCCs from baseline to 12 weeks in HD patients (control group)	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Mazairac et al., 2011, Netherlands, Norway, and Canada (126)	Observational cross-sectional study	HD: 589, 64.0 (14.0), 38.0%	KDQOL-CF	HD: M = 79.00	N/A	N/A	SCCs associated with lower albumin and higher creatinine; SCCs not associated with Subjective Global Assessment score, Normalized Protein Nitrogen Appearance, BMI, cholesterol, or Composite Score on Protein-Energy Nutritional Status
Mazairac et al., 2012, Netherlands (127)	Observational cross-sectional study	HD: 570, 64.0 (14.0), 38.0%	KDQOL-CF	HD: M = 80.00	N/A	N/A	N/A
Mazairac et al., 2013, Netherlands, Norway, and Canada (128)	Controlled intervention study	HD: 356, 64.0 (13.0), 35.0%; HDF: 358, 64.0 (14.0), 40.0%	KDQOL-CF	HD: M = 78.00; HDF: M = 80.00	No difference in SCCs between HD and HDF patients at either time point	No change in SCCs over 2 years in HD patients; SCCs increased over 2 years in HDF patients	N/A
McAdams-DeMarco et al., 2018, US (129)	Observational cohort study	KTx: 443, 52.0 (14.1), 37.3%	KDQOL-CF	KTx: M = 86.70	N/A	SCCs reduced from pre-KTx (HD/PD/preemptive) to 3 months post-KTx	SCCs associated with frailty; SCCs not associated with donor type or kidney donor profile index
Medeiros et al., 2017, Brazil (130)	Observational cross-sectional study	HD: 6, 47.2 (14.9), 66.7%	KDQOL-CF	HD: M = 86.66	N/A	N/A	N/A
Mentari et al., 2005, US (131)	Observational cohort study	HD: 1600, N/A (N/A), 47.0%	KDQOL-CF	HD: M = 81.10	N/A	N/A	No impact of change in Medicare reimbursement on SCCs
Michels et al., 2011, Netherlands (132)	Observational cohort study	APD: 64, 52.0 (17.8), 21.9% CAPD: 486, 53.6 (14.2), 35.2%	KDQOL-CF	N/A	No difference in SCCs between APD and CAPD at any time point	No change in SCCs from baseline to 6, 12, 18, 24, 30, and 36 months in PD patients	N/A
Milan Manani et al., 2020, Italy (133)	Observational cross-sectional study	PD: 73, N/A (N/A), 26.1%	KDQOL-CF	PD: Median = 80.00 and 83.30 for patients with and without remote monitoring	N/A	N/A	No difference in SCCs between PD patients with and without remote monitoring

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Moist et al., 2008, US, France, Germany, Italy, Spain, UK, and Japan (134)	Observational cross-sectional study	HD: 20994, 60.7 (14.8), 42.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with longer travel time to HD sessions
Molsted et al., 2007, Denmark (135)	Observational cross-sectional study	HD: 71, 59.0 (16.0), 24.0%; PD: 59, 59.0 (13.0), 44.0%	KDQOL-CF	HD: M = 84.40; PD: M = 82.90	No difference in SCCs between HD and PD patients	N/A	SCCs associated with lower blood haemoglobin, lower plasma albumin, longer dialysis vintage, and comorbidity; SCCs not associated with age, sex, or dialysis adequacy (Kt/V)
Montinaro et al., 2010, Italy (136)	Observational cross-sectional study	HD: 30, 57.8 (14.1), 33.0%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with higher IL-6, TNF-alpha, and IL-10; SCCs associated with higher depressive and anxious symptoms (HADS)
Moura et al., 2014, Portugal (137)	Observational cross-sectional study	HDF: 322, 64.9 (14.3), 40.4%	KDQOL-CF	HDF: M = 77.70	N/A	N/A	CVC associated with more SCCs than AVF; SCCs not associated with diabetes or location of AVF (right forearm, left forearm, right upper arm, left upper arm)
Moura et al., 2015a, Portugal (138)	Observational cross-sectional study	HDF: 322, 64.9 (14.3), 40.4%	KDQOL-CF	HDF: M = 77.77	N/A	N/A	N/A
Moura et al., 2015b, Portugal (139)	Observational cross-sectional study	HDF: 305, 64.9 (14.3), 40.3%	KDQOL-CF	HDF: M = 78.26	N/A	N/A	SCCs not associated with age or sex
Naderifar et al., 2019, Iran (140)	Observational cross-sectional study	HD: 200, 48.4 (14.9), 50.0%	KDQOL-CF	HD: M = 48.36	N/A	N/A	N/A
Nagasawa et al., 2018a, Japan (141)	Observational cross-sectional study	HD: 51, 67.7 (12.1), 29.4%	KDQOL-CF	HD: M = 91.20	N/A	N/A	SCCs not associated with caregivers' quality of life (EQ-5D, SF-36)
Nagasawa et al., 2018b, Japan (142)	Observational cross-sectional study	HD: 92, 67.0 (11.6), 22.8%	KDQOL-CF	HD: M = 94.10	N/A	N/A	SCCs not associated with medication adherence
Nayana et al., 2017, India (143)	Observational cross-sectional study	HD: 50, 51.9 (14.7), 20.0%	KDQOL-CF	HD: M = 61.86	N/A	N/A	N/A
Neumann et al., 2018, Germany (144)	Observational cohort study	HD: 96, 51.9 (15.9), 25.0%; PD: 101, 55.7 (14.7), 35.6%	KDQOL-CF	HD: M = 87.20; PD: M = 86.60	No difference in SCCs between HD and PD patients	No change in SCCs from baseline to 12 months in HD/PD patients	SCCs not associated with age, comorbidity, psychotropic drug intake, education level, employment status, or dialysis vintage; SCCs associated with higher depressive symptoms

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Ohtake et al., 2014, Japan (145)	Controlled intervention study	HD: 68, 69.7 (10.8), 33.8%	KDQOL-CF	HD: M = 84.65	N/A	N/A	N/A
Okpechi et al., 2013, South Africa (146)	Observational cross-sectional study	HD: 56, 38.6 (1.4), 53.6%; PD: 26, 36.0 (2.2), 34.6%	KDQOL-CF	HD: M = 78.20; PD: M = 79.50	No difference in SCCs between HD and PD patients	N/A	N/A
Oliveira et al., 2016, Brazil (147)	Observational cross-sectional study	HD: 286, 54.7 (14.1), 39.9%	KDQOL-CF	HD: M = 80.97	N/A	N/A	SCCs associated with more missed HD sessions
Orozco-González et al., 2021, Mexico (148)	Observational cross-sectional study	PD: 151, 36.8 (16.2), 43.7%	KDQOL-CF	PD: Median = 87.00, 67.00, and 67.00 in patients with normal nutrition, mild to moderate protein-energy wasting, and severe protein-energy wasting	N/A	N/A	SCCs associated with worse nutrition (more severe protein-energy wasting)
Ortega et al., 2007, Spain (149)	Observational cohort study	KTx: 307, 51.6 (12.0), 40.8%	ESRD-SCL-Limited Cognitive Capacity	KTx: M = 14.3	N/A	SCCs reduced from pre-KTx to 3 months post-KTx; no change in SCCs from 3 to 6 and 12 months post-KTx	SCCs associated with lower education levels, longer duration on RRT, and nonactive working status; SCCs associated with poorer quality of life in the physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health domains of SF-36; SCCs associated with poorer quality of life assessed by EuroQol-5D
Østhus et al., 2012, Norway (150)	Observational cross-sectional study	HD & PD: 301, 59.8 (16.2), 33.9%	KDQOL-CF	N/A	N/A	N/A	No difference in SCCs between patients accepted for KTx waiting list, permanently rejected for KTx, and pending for KTx acceptance
Ottaviani et al., 2016, Brazil (151)	Observational cross-sectional study	HD: 100, 53.3 (14.7), 34.0%	KDQOL-CF	HD: M = 88.06	N/A	N/A	SCCs associated with higher depressive and anxious symptoms (HADS)

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Painter et al., 2012, US (152)	Observational cohort study	HD: 13, 45.5 (10.4), 15.4%; HD switching to DHD: 10, 42.6 (12.4), 10.0%; HD switching to KTx: 20, 43.5 (10.9), 15.0%	KDQOL-CF	HD: M = 89.70; DHD: 91.30; KTx: 88.30	No difference in SCCs between HD, DHD, and KTx patients	No change in SCCs from baseline to 6 months in HD patients; No change in SCCs switching from HD (baseline) to DHD or KTx (6 months)	N/A
Pakpour et al., 2011, Iran (153)	Observational cross-sectional study	HD: 212, 57.5 (14.7), 43.8%	KDQOL-CF	HD: M = 55.70	N/A	N/A	SCCs not associated with overall health rating
Palanova et al., 2019, Czech Republic (154)	Pre-post study with no control group	PD: 14, 61.9 (8.7), 57.1%	KDQOL-CF	PD: M = 91.90	N/A	N/A	N/A
Paniagua et al., 2005, Mexico (155)	Controlled intervention study	PD: 923, 47.1 (13.9), 42.3%	KDQOL-CF	PD: M = 28.20	N/A	N/A	PD patients with enhanced creatinine clearance target reported more SCCs at 6 months than patients on standard PD; presence of diabetes associated with fewer SCCs; SCCs not associated with age, sex, serum albumin, GFR, dialysis vintage, hematocrit, or nPNA
Park et al., 2007, Korea (156)	Observational cross-sectional study	HD & PD: 132 (HD), 32 (PD), 54.1 (13.0), 41.5%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower overall health rating
Park et al., 2012, Korea (157)	Observational cross-sectional study	PD: 105, 49.3 (13.6), 47.6%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with higher depressive symptoms (BDI)
Park et al., 2017, Korea (158)	Observational cohort study	HD (thrice-weekly): 207, 61.7 (13.4), 40.1%; HD (incremental): 105, 60.2 (13.3), 41.9%	KDQOL-CF	HD: M = 83.24	N/A	N/A	No difference in SCCs between thrice-weekly and incremental HD
Parsons et al., 2006, Canada (159)	Pre-post study with no control group	HD: 13, 53.0 (18.0), 38.5%	KDQOL-CF	HD: M = 92.00	N/A	N/A	N/A
Peipert et al., 2020, US (160)	Observational cohort study	KTx: 477, 49.0 (N/A), 40.0%	KDQOL-CF	KTx: M = 81.99	N/A	SCCs reduced from pre-KTx (HD/PD/preemptive) to 3 months post-KTx; No change in SCCs from 3 to 12 months post-KTx	Increase in SCCs from 3 to 12 months post-KTx associated with death-censored graft failure; Change in SCCs associated with age at KTx, and use of HD or PD prior to KTx; Change in SCCs not associated with sex, race, education level, or BMI

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Pereira et al., 2019, Brazil (161)	Observational cross-sectional study	HD: 258, 56.8 (14.5), 59.7%	KDQOL-CF	HD: M = 94.16	N/A	N/A	N/A
Portela et al., 2020, Brazil (162)	Observational cross-sectional study	HD: 103, 84.4 (3.9), 38.8%	KDQOL-CF	HD: M = 81.00	N/A	N/A	N/A
Rosegger et al., 2020, Brazil (163)	Observational cross-sectional study	KTx waiting list: 57, 36.7 (6.1), 28.1%; KTx: 103, 40.0 (8.2), 48.5%	KDQOL-CF	KTx: M = 8.80	N/A	N/A	No difference in SCCs between patients who received KTx < 1 year, patients who received KTx between 1 and 3 years, and patients who received KTx > 3 years
Poulsen et al., 2017, Denmark (164)	Observational cohort study	HD: 82, 62.0 (15.0), 32.0%	KDQOL-CF	N/A	N/A	No change in SCCs from baseline to 6 and 12 months in HD patients	SCCs associated with lower age, increased hospitalisation, higher GFR, and higher albumin; SCCs not associated with sex, diabetes, number of comorbidities, or number of serious adverse events
Pucheu et al., 2004, France (165)	Observational cross-sectional study	PD: 47, 56.6 (17.4), 38.3%	KDQOL-CF	PD: M = 68.20	N/A	N/A	N/A
Rajkumar et al., 2019, Australia (166)	Observational cohort study	KTx: 75, 47.0 (13.0), 44.0%	KDQOL-CF	KTx: M = 81.00	N/A	SCCs reduced from pre-KTx (HD/PD/preemptive) to 12 months post-KTx	N/A
Ramatillah et al., 2017, Malaysia (167)	Observational cross-sectional study	HD: 78, N/A (N/A), 38.5%	KDQOL-CF	HD: M = 75.66	N/A	N/A	SCCs not associated with age, sex, or race
Rebollo Rubio et al., 2017, Spain (168)	Observational cross-sectional study	HD & PD: 120 (HD), 32 (PD), 62.5 (14.1), 28.3%	KDQOL-CF	HD: M = 30.08; PD: M = 31.46	No difference in SCCs between HD and PD patients	N/A	N/A
Romano-Zelekha et al., 2017, Israel (169)	Observational cross-sectional study	HD: 1102, 65.5 (14.2), 48.8%	KDQOL-CF	HD: M = 71.70	N/A	N/A	SCCs not associated with race
Ryu et al., 2021, Korea (170)	Observational cohort study	KTx: 842, 45.3 (11.7), 36.9%	KDQOL-CF	N/A	N/A	No change in SCCs from 2 to 4 and 6 years post-KTx	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Salamon et al., 2018, Australia (171)	Controlled intervention study	PD: 13, N/A (N/A), 54.0%	KDQOL-CF	PD: Median = 73.33	N/A	N/A	N/A
Sawada et al., 2021, Japan (172)	Observational cross-sectional study	KTx: 67, N/A (N/A), 40.3%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with poorer quality of life (EQ-5D-5L)
Scott et al., 2009, US (173)	Controlled intervention study	HD: 88, 54.7 (14.7), 46.6%	KDQOL-CF	HD: M = 76.50	N/A	No change in SCCs from baseline to 3 months in HD patients (control group)	N/A
Seica et al., 2009, Romania (174)	Observational cross-sectional study	HD: 606, 51.7 (12.6), 45.3%	KDQOL-CF	HD: M = 78.80	N/A	N/A	N/A
Shahnavazi et al., 2016, Iran (175)	Observational cross-sectional study	HD: 98, N/A (N/A), 41.9%	KDQOL-CF	HD: M = 42.88	N/A	N/A	N/A
Shahnavazi et al., 2018, Iran (176)	Controlled intervention study	HD: 43, N/A (N/A), 41.9%	KDQOL-CF	HD: M = 40.76	N/A	No change in SCCs from baseline to 6 and 12 weeks in HD patients (control group)	N/A
Shimoyama et al., 2003, Japan (177)	Observational cross-sectional study	PD: 26, 49.8 (14.7), 34.0%	KDQOL-CF	PD: M = 82.90	N/A	N/A	SCCs associated with worse quality of life in the bodily pain, general health, vitality, and mental health domains of SF-36; SCCs not associated with the physical functioning, role physical, social functioning, or role emotional domains of SF-36
Sihombing et al., 2017, Indonesia (178)	Observational cohort study	HD: 113, N/A (N/A), 46.9%	KDQOL-CF	HD: M = 84.13	N/A	N/A	N/A
Simic-Ogrizovic et al., 2009, Serbia (179)	Observational cohort study	HD: 102, 55.4 (13.8), 53.9%	KDQOL-CF	N/A	N/A	No change in SCCs from baseline to 3 and 6 years in HD patients	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Soares et al., 2017, Brazil (180)	Controlled intervention study	HD: 50, 51.4 (13.3), 0.0%	KDQOL-CF	HD: M = 87.39	N/A	No change in SCCs from baseline to 6 months in HD patients (control group)	N/A
Song et al., 2015, US (181)	Observational cross-sectional study	HD & PD: 125 (HD), 10 (PD), 58.4 (12.8), 46.7%	PAOFI	N/A	No difference in SCCs between HD and PD patients	N/A	SCCs associated with fewer years of education; SCCs not associated with age, history of stroke, comorbidity, dialysis vintage, or dialysis adequacy (Kt/V); SCCs associated with more severe pain and other symptoms (ESAS), worse physical functioning (ADL, IADL), and higher depressive (CES-D-SF) and anxious symptoms (STAI); SCCs associated with poorer performance in backward counting task in BTACT; SCCs not associated with performance in other tests in BTACT
Song et al., 2018, US (182)	Observational cohort study	HD & PD: 216 (HD), 11 (PD), 58.7 (12.6), 48.0%	PAOFI	N/A	N/A	SCCs reduced from baseline to 12 months in HD and PD patients	White patients reported more SCCs than nonwhite patients; SCCs not associated with age or comorbidity; SCCs associated with more severe overall symptoms (ESAS), worse physical functioning (ADL, IADL), worse emotional well-being (CESD-SF, SAI, PANAS-PA), and worse spiritual well-being (FACIT-Sp)
Sørensen et al., 2007, Denmark (183)	Observational cross-sectional study	HD & PD: 66 (HD), 12 (PD), 62.5 (12.5), 25.6%	KDQOL-CF	N/A	N/A	N/A	SCCs not associated with diabetes

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Sorensen et al., 2012, US (184)	Observational cross-sectional study	HD: 168, 62.0 (17.0), 49.0%	KDQOL-CF	HD: M = 76.00	N/A	N/A	SCCs associated with lower SBP; SCCs not associated with age, sex, race, education level, HD vintage, cause of ESRD, smoking status, comorbidity, DBP, BMI, dialysis adequacy (Kt/V), albumin, or phosphorus; SCCs associated with higher depressive symptoms (CES-D); SCCs associated with immediate recall (from the Wechsler Memory Scale-III); SCCs not associated with MMSE score, verbal IQ, delayed recall, short delay, percent retention, recognition, block design, digit symbol, digit span, Trail Making Test A & B, COWAT, or mental alterations
Stavrianou et al., 2007, Greece (185)	Observational cross-sectional study	HD: 146, 57.0 (15.7), N/A	KDQOL-CF	HD: M = 84.00	N/A	N/A	N/A
Stumm et al., 2019, Brazil (186)	Pre-post study with no control group	HD: 63, 58.9 (13.1), 33.3%	KDQOL-CF	HD: M = 86.98	N/A	N/A	N/A
Sturgill et al., 2020, US (187)	Observational cross-sectional study	HD & PD & HHD: 71 (HD), 14 (PD), 7 (HHD), 56.1 (14.8), 40.2%	PROMIS-Cognition	HD: M = 49.57	N/A	N/A	SCCs not associated with dialysis adequacy (Kt/V), albumin, or haemoglobin
Tamilselvan et al., 2021, India (188)	Controlled intervention study	HD: 37, 47.5 (11.6), 35.1%	KDQOL-CF	HD: M = 48.50	N/A	N/A	N/A
Tanaka et al., 2020, Japan (189)	Observational cross-sectional study	HD: 103, 62.7 (13.8), 20.4%; PD: 90, 65.5 (12.3), 31.1%; HD+PD: 36, 57.4 (9.1), 25.0%	KDQOL-CF	HD: M = 85.40; PD: M = 89.80; HD+PD: M = 91.70	HD patients reported more SCCs than PD and HD+PD patients; No difference in SCCs between PD and HD+PD patients	N/A	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Tannor et al., 2017, South Africa (190)	Observational cross-sectional study	HD: 58, 42.8 (9.8), 70.7%; PD: 48, 36.1 (10.7), 56.3%	KDQOL-CF	HD: M = 77.90; PD: M = 72.00	No difference in SCCs between HD and PD patients	N/A	N/A
Ting et al., 2003, US (191)	Observational cohort study	HD switching to DHD: 42, 59.9 (16.7), 33.0%	KDQOL-CF	HD: M = 71.60; DHD: M = 85.10	Patients reported more SCCs on HD (baseline) than on DHD (3 and 12 months)	SCCs reduced after switching from HD (baseline) to DHD (3 months); No change in SCCs from 3 to 12 months post-initiation of DHD	N/A
Tsarpali et al., 2021, Norway (192)	Observational cohort study	KTx: 136, 71.5 (4.1), 30.1%	KDQOL-CF	KTx: M = 92.10	N/A	SCCs reduced from pre-KTx (HD/PD/preemptive) to 1 year post-KTx; no change in SCCs from 1 to 3 years post-KTx	N/A
Türk et al., 2020, Turkey (193)	Observational cross-sectional study	HD: 60, 56.6 (14.1), 41.7%; PD: 45, 52.0 (13.2), 51.1%	KDQOL-CF	HD: M = 68.00; PD: M = 77.80	HD patients reported more SCCs than PD patients	N/A	SCCs associated with number of hospitalisation, duration of hospitalisation, and higher serum ferritin levels
Uchiyama et al., 2019a, Japan (194)	Controlled intervention study	PD: 47, 64.1 (9.3), 25.5%	KDQOL-CF	PD: M = 91.33	N/A	No change in SCCs from baseline to 12 weeks in PD patients (control group)	N/A
Uchiyama et al., 2019b, Japan (195)	Observational cross-sectional study	PD: 50, 63.8 (9.6), 26.0%	KDQOL-CF	PD: M = 90.40	N/A	N/A	SCCs associated with poorer exercise capacity (Incremental Shuttle Walking Test, handgrip strength, quadriceps strength)
Unruh et al., 2004, US (196)	Controlled intervention study	HD: 1813, 57.6 (14.0), 56.3%	KDQOL-CF	HD: M = 75.40	N/A	No change in SCCs from baseline to 1, 2, and 3 years in HD patients	No effect of HD dose (Kt/V 1.05 vs. 1.45) or flux membranes (high vs. low) on SCCs
Unruh et al., 2008, US (197)	Observational cohort study	HD: 1813, 57.6 (14.0), 56.3%	KDQOL-CF	N/A	N/A	N/A	SCCs not associated with age at baseline; Patients aged 70 and older reported larger increase in SCCs over 3 years than patients younger than 70 years old

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
van Doorn et al., 2004, Belgium (198)	Observational cross-sectional study	HD: 70, 67.9 (N/A), N/A	KDQOL-CF	HD: M = 81.10	N/A	N/A	SCCs not associated with age
van Eps et al., 2010, Australia (199)	Observational cohort study	HD switching to NHD: 63, 52.0 (13.0), 21.0%	KDQOL-CF	HD: Median = 13.33; NHD: Median = 6.67	No difference in SCCs between HD (baseline) and NHD (6-12 months)	No change in SCCs switching from HD (baseline) to NHD (6-12 months)	N/A
Varela et al., 2011, Spain (200)	Observational cross-sectional study	PD: 53, 49.5 (17.0), 54.7%	KDQOL-CF	PD: M = 77.73	N/A	N/A	SCCs associated with higher depressive and anxious symptoms (HADS)
Vázquez et al., 2005, Spain (201)	Observational cross-sectional study	HD: 194, 48.6 (16.1), 56.7%	KDQOL-CF	HD: M = 78.82	N/A	N/A	SCCs associated with unemployment; SCCs not associated age, sex, social class, comorbidity, albumin, or haemoglobin; SCCs associated with higher anxious symptoms (STAI-T); SCCs not associated with depressive symptoms (CDI)
von der Lippe et al., 2014, Norway (202)	Observational cross-sectional study	HD & PD: 301, 59.8 (16.2), 33.9%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with lower age; SCCs associated with previous renal graft loss; SCCs not associated with comorbidity, BMI, dialysis vintage
von der Lippe et al., 2016, Norway (203)	Observational cohort study	KTx: 142, 51.0 (15.5), 32.4%	KDQOL-CF	KTx: M = 88.00	No change in SCCs from pre-KTx (HD/PD) to post-KTx	N/A	
Walters et al., 2002, US (204)	Observational cross-sectional study	HD: 422, 59.0 (15.8), 46.4%	KDQOL-CF	HD: M = 75.16	N/A	N/A	SCCs not associated with age or sex; SCCs associated with higher depressive symptoms
Wang et al., 2008, Canada (205)	Controlled intervention study	HD: 18, 56.0 (N/A), 5.6%	KDQOL-CF	HD: M = 81.35	N/A	N/A	No difference in SCCs between standard HD, HD with increased dialysate flow, HD with increased session time, and HD with 2 dialysers
Warsame et al., 2018, US (206)	Observational cross-sectional study	HD: 431, 54.0 (13.0), 35.3%	KDQOL-CF	N/A	N/A	N/A	SCCs not associated with intradialytic activity levels

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Watanabe et al., 2014, Japan (207)	Observational cross-sectional study	HD: 34, 57.1 (7.6), 23.6%; HHD: 46, 54.0 (8.3), 13.0%	KDQOL-CF	HD: M = 87.50; HHD: M = 90.10	No difference in SCCs between HD and HHD patients	N/A	N/A
Watanabe et al., 2018, Japan (208)	Observational cohort study	PD switching to HD+PD: 10, 53.3 (7.8), 50.0%	KDQOL-CF	PD: M = 83.30; HD+PD: M = 88.70	No difference in SCCs between PD (baseline) and HD+PD (12 months)	No change in SCCs switching from PD (baseline) to HD+PD (12 months)	N/A
Wong et al., 2010, Singapore (209)	Controlled intervention study	PD: 98, 62.4 (N/A), 46.9%	KDQOL-CF	PD: M = 76.60	N/A	No change in SCCs from baseline to 7 and 13 weeks in PD patients (control group)	N/A
Woźniak et al., 2018, Poland (210)	Observational cross-sectional study	KTx: 136, 50.4 (N/A), 45.6%	KDQOL-CF	KTx: M = 81.35	N/A	N/A	SCCs not associated with number of prescribed drugs
Wright et al., 2015, US (211)	Observational cross-sectional study	HD: 29, N/A (N/A), 44.8%; PD: 26, N/A (N/A), 61.5%; HHD: 22, N/A (N/A), 40.9%	KDQOL-CF	HD: M = 80.40; PD: M = 84.50; HHD: M = 81.20	No difference in SCCs between HD, PD, and HHD patients	N/A	N/A
Wu et al., 2014, Mainland China (212)	Controlled intervention study	HD: 65, 48.8 (13.9), 15.4%	KDQOL-CF	HD: M = 65.32	N/A	No change in SCCs from baseline to 12 weeks in HD patients (control group)	N/A
Yamana, 2009, Japan (213)	Observational cross-sectional study	HD: 44, 57.0 (13.8), 27.3%	KDQOL-CF	HD: Median = 93.30	N/A	N/A	SCCs associated with shorter HD vintage; SCCs not associated with age, sex, primary disease, complications, length of HD sessions, IDWG, cardiothoracic ratio, hematocrit, albumin, systolic blood pressure, potassium, phosphorus, or calcium
Yang et al., 2021, Mainland China (214)	Observational cohort study	HD: 273, 59.9 (14.4), 41.4%	KDQOL-CF	N/A	N/A	N/A	SCCs associated with higher posttraumatic stress symptoms
Yıldırım et al., 2007, Turkey (215)	Observational cross-sectional study	HD: 82, 51.0 (12.0), 65.0%	KDQOL-CF	HD: M = 83.21	N/A	N/A	N/A

Author & Year & Location	Study Design	Sample Characteristics (Modality: N, Age M (SD), % Female)	SCC Measure	Frequency/Severity of SCCs	Modality Difference	Course of SCCs	Association with sociodemographic and clinical variables, patient-reported outcomes, and objective cognition
Yoon et al., 2016, Korea (216)	Observational cohort study	PD: 481, 51.3 (11.1), 46.8%	KDQOL-CF	PD: M = 83.50	N/A	N/A	SCCs associated with increased hydration status
Zabel et al., 2012, Australia (217)	Observational cross-sectional study	HD: 62, 63.0 (16.0), 60.0%	KDQOL-CF	HD: M = 80.00	N/A	N/A	SCCs associated with poorer self-reported appetite
Zheng et al., 2019, Mainland China (218)	Controlled intervention study	HD: 46, 78.0 (5.1), N/A	KDQOL-CF	HD: M = 68.87	N/A	No change in SCCs from baseline to 3 months in HD patients (control group)	N/A
Ziaja et al., 2009, Poland (219)	Observational cross-sectional study	KTx: 38, N/A (N/A), N/A	KDQOL-CF	KTx: Median = 80.00; KTx (simultaneous pancreas transplantation): Median = 93.33	KTx patients reported more SCCs than patients who received simultaneous pancreas and kidney transplantation	N/A	N/A
Zimmerman et al., 2003, Canada (220)	Observational cohort study	HD switching to HF: 7, 60.0 (N/A), 14.3%	KDQOL-CF	HD: M = 81.90; HF: M = 93.33	No difference in SCCs between HD (baseline) and HF (4 weeks)	No change in SCCs switching from HD (baseline) to HF (4 weeks)	N/A
Zubair et al., 2017, Pakistan (221)	Observational cross-sectional study	HD: 137, N/A (N/A), 27.7%	BC-CCI	HD: prevalence = 86.90%	N/A	N/A	SCCs associated with shorter HD vintage and poorer sleep quality (PSQI); SCCs not associated with age, sex, family income, marital status, HD frequency, smoking status, education level, BMI, occupation, or use of naswar

Notes. ESRD = End-Stage Renal Disease; HD = Haemodialysis; PD = Peritoneal Dialysis; KTx = Kidney Transplantation; NHD = Nocturnal Haemodialysis; HHD = Home Haemodialysis; DHD = Daily Haemodialysis; HDF = Hemodiafiltration; HF = Hemofiltration; HD+PD = Combined haemodialysis and peritoneal dialysis therapy; APD = Automated Peritoneal Dialysis; CAPD = Continuous Ambulatory Peritoneal Dialysis; RRT = Renal Replacement Therapy; SCC = Subjective Cognitive Complaint; PAOFI = Patient's Assessment of Own Functioning Inventory; BC-CCI = British Columbia Cognitive Complaints Inventory; CDS = Cognitive Difficulties Scale; PDQ = Perceived Deficits Questionnaire; KDQOL-CF = Kidney Disease Quality of Life Cognitive Function subscale; HUI = Health Utilities Index; WHODAS = World Health Organisation Disability Assessment Schedule; PROMIS = Patient-Reported Outcomes

Measurement Information System; DSI = Dialysis Symptoms Index; ESRD-SCL = End-Stage Renal Disease Symptom Checklist; MMSE = Mini-Mental State Examination; 3MS = Modified Mini-Mental State test; WAIS-R = Wechsler Adult Intelligence Scale-Revised; BTACT = Brief Test of Adult Cognition by Telephone; COWAT = Controlled Oral Word Association Test; WHOQOL-BREF = Abbreviated World Health Organisation Quality of Life questionnaire; SF-36 = 36-item Short Form survey; BDI = Beck Depression Inventory; CES-D = Centre for Epidemiologic Studies Depression scale; HADS = Hospital Anxiety and Depression Scale; STAI = State-Trait Anxiety Inventory; ESAS = Edmonton Symptom Assessment System; ADL = Activities of Daily Living; IADL = Instrumental Activities of Daily Living; PSQI = Pittsburgh Sleep Quality Index; BMI = Body Mass Index; GFR = Glomerular Filtration Rate; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; AVF = Arteriovenous Fistula; AVG = Arteriovenous Graft; CVC = Central Venous Catheter; IDWG = Interdialytic Weight Gain; M = Mean; SD = Standard Deviation; N = Sample size.

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Table S3. *Quality assessment of observational cross-sectional studies.*

Author & Year	1. Was the research question or objective in this paper clearly stated?	2. Was the study population clearly specified and defined?	3. Was the participation rate of eligible persons at least 50%?	4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	5. Was a sample size justification, power description, or variance and effect estimates provided?	6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	10. Was the exposure(s) assessed more than once over time?	11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	12. Were the outcome assessors blinded to the exposure status of participants?	13. Was loss to follow-up after baseline 20% or less?	14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?
AL-Jumaih et al., 2011	Y	Y	NR	N	N	NA	NA	N	N	NA	Y	NA	NA	N
Amro et al., 2014	Y	Y	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Anees et al., 2016	Y	Y	NR	Y	N	NA	NA	N	N	NA	Y	NA	NA	N
Bacci et al., 2018	Y	N	Y	Y	N	NA	NA	Y	Y	N	Y	Y	NA	N
Bagasha et al., 2021	Y	N	Y	N	Y	NA	NA	N	N	NA	Y	NR	NA	N
Bakewell et al., 2001	Y	N	CD	CD	N	NA	NA	Y	N	NA	Y	NA	NA	N
Barbosa et al., 2017	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Barotfi et al., 2006	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Barzegar et al., 2017	Y	Y	NR	Y	N	NA	NA	Y	Y	NA	Y	N	NA	N
Bataclan et al., 2009	Y	N	NR	CD	Y	NA	NA	Y	Y	N	Y	N	NA	N
Bele et al., 2012	Y	Y	Y	Y	N	NA	NA	Y	N	N	Y	NR	NA	N
Bettoni et al., 2017	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Bouidida et al., 2014	Y	N	NR	NR	N	NA	NA	Y	Y	N	Y	NR	NA	N
Braga et al., 2011	Y	Y	Y	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Brickman et al., 1996	Y	N	NR	NR	N	NA	NA	Y	Y	N	Y	N	NA	Y
Carmichael et al., 2000	Y	N	Y	NR	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Castro et al., 2018	Y	Y	NR	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Cavalcante et al., 2013	Y	N	Y	NR	N	NA	NA	N	Y	NA	Y	NA	NA	N
Cepeda Marte et al., 2019	Y	Y	NR	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Chan et al., 2010	Y	Y	NR	Y	Y	NA	NA	Y	Y	N	Y	N	NA	Y
Cho et al., 2018	Y	Y	Y	Y	Y	NA	NA	N	Y	NA	Y	NA	NA	N
Chrifi Alaoui et al., 2022	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Czyzewski et al., 2018	Y	Y	NR	N	N	NA	NA	Y	Y	NA	Y	NR	NA	N
D'Onofrio et al., 2017	Y	Y	Y	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
de Oliveira Cordeiro et al., 2020	Y	Y	Y	N	N	NA	NA	NA	Y	NA	Y	NA	NA	N

de Oliveira et al., 2012	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
de Roij van Zuijdewijn et al., 2016	Y	Y	NR	N	N	NA	NA	Y	Y	Y	Y	NR	NA	Y
Debnath et al., 2018	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Dehesa-Lopez et al., 2016	Y	N	NR	CD	N	NA	NA	Y	N	NR	Y	NR	NA	N
Dehghan et al., 2020	Y	N	Y	N	Y	NA	NA	Y	Y	N	Y	N	NA	N
Diamant et al., 2011	Y	Y	Y	N	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Duarte et al., 2005	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	N
Fan et al., 2020	Y	Y	NR	Y	N	NA	NA	Y	Y	Y	Y	NR	NA	Y
Fiderkiewicz et al., 2011	Y	N	Y	CD	N	NA	NA	Y	Y	N	Y	N	NA	Y
Fong et al., 2007	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Fructuoso et al., 2011	Y	N	Y	NR	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Fukuhara et al., 2003	Y	N	Y	N	N	NA	NA	Y	Y	NA	Y	NA	NA	Y
G. B. Lopes et al., 2014	Y	Y	NR	N	N	NA	NA	Y	N	N	Y	N	NA	Y
Garcia et al., 2010	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	N
Giglio et al., 2018	Y	Y	NR	Y	N	NA	NA	Y	Y	N	Y	Y	NA	N
Gonçalves et al., 2015	Y	N	NR	N	Y	NA	NA	Y	Y	NA	Y	NR	NA	CD
Green et al., 2001	Y	N	NR	N	N	NA	NA	Y	Y	NA	Y	NA	NA	N
Griva et al., 2012	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Gumprecht et al., 2010	Y	Y	Y	N	N	NA	NA	NA	Y	NR	Y	NR	NA	N
Hays et al., 1994	N	Y	Y	CD	N	NA	NA	Y	Y	N	Y	N	NA	N
Henry et al., 2017	Y	N	NR	N	N	NA	NA	Y	Y	N	N	Y	NA	N
Ho et al., 2013	Y	Y	Y	Y	Y	NA	NA	Y	Y	NA	Y	NA	NA	N
Hornik et al., 2019	Y	N	NR	NR	N	NA	NA	N	Y	N	Y	N	NA	N
Hyodo et al., 2004	N	Y	NR	Y	N	NA	NA	N	Y	N	Y	N	NA	N
J. M. Lopes et al., 2014	Y	N	NR	N	N	NA	NA	N	Y	NA	Y	NA	NA	N
Jansz et al., 2018	Y	Y	Y	N	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Jayanti et al., 2016	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Joshi et al., 2010	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Kim et al., 2021	Y	Y	NR	N	N	NA	NA	N	Y	N	Y	N	NA	Y
Knudsen et al., 2016	Y	Y	Y	N	N	NA	NA	N	N	NA	Y	NA	NA	N
Ko et al., 2007	Y	Y	Y	N	N	NA	NA	N	N	NA	Y	NA	NA	N
Kontodimopoulos et al., 2005	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Krishnasamy et al., 2019	Y	N	NR	N	N	NA	NA	N	Y	NA	Y	NR	NA	N
Kurella et al., 2004	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Kusumoto et al., 2008	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	N	NA	N
Kutner et al., 2005b	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NA	NA	Y
Kutner et al., 2007	N	Y	NR	Y	N	NA	NA	Y	N	N	Y	N	NA	Y
Lee et al., 2005	Y	Y	N	NR	N	NA	NA	Y	Y	NA	Y	N	NA	N
Leone et al., 2021	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	Y
Li et al., 2016	Y	N	NR	NR	N	NA	NA	Y	Y	N	Y	N	NA	Y
Lopes et al., 2007	Y	Y	NR	N	Y	NA	NA	Y	Y	N	Y	NR	NA	Y
Ma et al., 2021	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Macedo et al., 2021	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Madariaga et al., 2016	Y	Y	NR	CD	N	NA	NA	Y	Y	NA	Y	Y	NA	N
Malekmakan et al., 2016	Y	N	NR	CD	Y	NA	NA	Y	Y	NA	Y	NR	NA	N
Malindretos et al., 2010	Y	N	Y	CD	Y	NA	NA	Y	Y	N	Y	NR	NA	N
Manavalan et al., 2017	Y	Y	NR	Y	N	NA	NA	Y	Y	NA	Y	N	NA	N

Manju et al., 2020	Y	Y	Y	Y	Y	NA	NA	N	Y	NA	Y	NA	NA	N
Manns et al., 2002	Y	Y	Y	CD	N	NA	NA	Y	Y	Y	Y	Y	NA	N
Marinho et al., 2017	Y	Y	Y	Y	Y	NA	NA	N	Y	NA	Y	NA	NA	N
Martin et al., 2000	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Martin et al., 2001	Y	N	NR	CD	Y	NA	NA	Y	Y	N	Y	NR	NA	N
Masina et al., 2016	Y	Y	Y	N	N	NA	NA	N	Y	NA	Y	NA	NA	N
Mazairac et al., 2011	Y	Y	NR	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Mazairac et al., 2012	Y	N	NR	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Medeiros et al., 2017	Y	Y	N	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Milan Manani et al., 2020	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Moist et al., 2008	Y	Y	Y	N	N	NA	NA	Y	Y	NA	Y	N	NA	Y
Molsted et al., 2007	Y	Y	Y	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Montinaro et al., 2010	Y	N	NR	N	N	NA	NA	Y	Y	N	N	N	NA	N
Moura et al., 2014	Y	N	NR	N	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Moura et al., 2015a	Y	N	NR	N	N	NA	NA	N	Y	NA	Y	NA	NA	N
Moura et al., 2015b	Y	N	NR	N	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Naderifar et al., 2019	Y	Y	NR	Y	Y	NA	NA	N	Y	NA	Y	NA	NA	N
Nagasawa et al., 2018a	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Nagasawa et al., 2018b	Y	Y	Y	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Nayana et al., 2016	Y	Y	Y	Y	Y	NA	NA	N	Y	NA	Y	NA	NA	N
Okpechi et al., 2013	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	NR	NA	N
Oliveira et al., 2016	Y	Y	NR	Y	Y	NA	NA	Y	Y	N	Y	Y	NA	N
Orozco-González et al., 2021	Y	Y	NR	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Østhus et al., 2012	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Ottaviani et al., 2016	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Pakpour et al., 2011	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	N
Park et al., 2007	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	N
Park et al., 2012	Y	Y	Y	CD	N	NA	NA	Y	Y	N	Y	N	NA	N
Pereira et al., 2019	Y	Y	Y	N	N	NA	NA	Y	Y	N	Y	NR	NA	CD
Portela et al., 2020	Y	Y	NR	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Posegger et al., 2019	Y	N	Y	N	N	NA	NA	Y	Y	NA	Y	CD	NA	N
Pucheu et al., 2004	Y	Y	NR	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Ramatillah et al., 2017	Y	N	NR	N	N	NA	NA	Y	Y	NA	Y	N	NA	N
Rebollo Rubio et al., 2017	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Romano-Zelekha et al., 2017	Y	Y	Y	Y	Y	NA	NA	Y	Y	NA	Y	NA	NA	Y
Sawada et al., 2020	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	N	NA	N
Seica et al., 2009	Y	N	Y	N	N	NA	NA	N	N	NA	Y	NA	NA	N
Shahnavazi et al., 2016	Y	Y	NR	Y	N	NA	NA	N	Y	NA	Y	NA	NA	N
Shimoyama et al., 2003	Y	Y	Y	CD	N	NA	NA	Y	Y	N	Y	N	NA	N
Song et al., 2015	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	Y
Sørensen et al., 2007	Y	Y	Y	N	N	NA	NA	N	Y	N	Y	NR	NA	N
Sorensen et al., 2012	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Stavrianou et al., 2007	Y	Y	Y	CD	N	NA	NA	N	N	NA	Y	NA	NA	N
Sturgill et al., 2020	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	Y	NA	Y
Tanaka et al., 2020	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	Y
Tannor et al., 2017	Y	Y	Y	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Türk et al., 2020	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y

Uchiyama et al., 2019b	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
van Doorn et al., 2004	Y	Y	Y	N	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Varela et al., 2011	Y	N	Y	N	N	NA	NA	Y	Y	N	Y	N	NA	Y
Vázquez et al., 2005	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
von der Lippe et al., 2014	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Walters et al., 2002	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Warsame et al., 2018	Y	Y	NR	CD	N	NA	NA	Y	Y	N	Y	N	NA	Y
Watanabe et al., 2014	Y	Y	NR	Y	N	NA	NA	Y	Y	NA	Y	NR	NA	N
Wozniak et al., 2018	Y	N	NR	N	N	NA	NA	Y	Y	N	Y	NR	NA	Y
Wright et al., 2015	Y	N	Y	N	Y	NA	NA	Y	Y	NA	Y	N	NA	N
Yamana, 2009	Y	Y	NR	Y	N	NA	NA	Y	Y	N	Y	NR	NA	N
Yıldırım et al., 2007	Y	N	NR	N	N	NA	NA	N	N	NA	Y	NA	NA	N
Zabel et al., 2012	Y	Y	N	Y	N	NA	NA	Y	Y	N	Y	N	NA	N
Ziaja et al., 2009	Y	N	Y	N	N	NA	NA	Y	Y	NA	Y	Y	NA	N
Zubair et al., 2017	Y	Y	Y	Y	N	NA	NA	Y	Y	N	Y	N	NA	Y

Notes. Quality assessment was performed using the quality assessment tool for observational cohort and cross-sectional studies developed by the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH); Y = Yes; N = No; NR = Not reported; CD = Cannot determine; NA = Not applicable.

Table S4. *Quality assessment of observational cohort studies.*

Author & Year	1. Was the research question or objective in this paper clearly stated?	2. Was the study population clearly specified and defined?	3. Was the participation rate of eligible persons at least 50%?	4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	5. Was a sample size justification, power description, or variance and effect estimates provided?	6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	10. Was the exposure(s) assessed more than once over time?	11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	12. Were the outcome assessors blinded to the exposure status of participants?	13. Was loss to follow-up after baseline 20% or less?	14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?
Alarcon et al., 2021	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N	N
Anees et al., 2018	Y	N	NR	Y	N	Y	Y	Y	Y	N	Y	Y	NR	N
Aoun et al., 2020	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	Y	NR	Y
Bawazier et al., 2018	N	Y	NR	Y	Y	Y	CD	Y	Y	Y	N	N	NR	Y
Chen et al., 2021	Y	Y	Y	Y	N	NR	CD	Y	Y	CD	Y	NR	NR	N
Cheung et al., 2012	Y	Y	NR	Y	Y	N	N	Y	Y	Y	Y	N	Y	N
Costa-Requena et al., 2017	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NA	N	N
Czyżewski et al., 2014	Y	Y	NR	N	N	Y	Y	Y	Y	Y	Y	NR	NR	N
Frimat et al., 2006	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Gorodetskaya et al., 2005	Y	Y	NR	N	N	Y	Y	Y	N	Y	Y	NR	Y	Y
Hasan et al., 2021	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	NR	Y	N
Jassal et al., 2006	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N
Jung et al., 2016	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Kanamori et al., 2012	Y	N	Y	N	N	Y	Y	Y	Y	N	Y	NA	NA	Y
Kang et al., 2017	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y	NR	NA	Y
Kim et al., 2020	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Korevaar et al., 2002	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	N	Y
Kostro et al., 2016	Y	N	NR	N	N	Y	Y	Y	Y	Y	Y	NR	NR	N
Kutner et al., 2005a	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Lai et al., 2018	Y	Y	NR	Y	N	Y	Y	N	Y	NA	Y	NR	NR	N
Lee et al., 2020	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	NA	NA	Y
Lønning et al., 2018a	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Lønning et al., 2018b	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NR	N	N
Loos-Ayav et al., 2008	Y	Y	NR	N	N	Y	Y	NA	Y	Y	Y	N	N	Y
Lopes et al., 2003	Y	Y	NR	N	N	Y	CD	Y	Y	N	Y	NA	NA	Y

Mapes et al., 2003	Y	Y	Y	N	N	Y	Y	Y	Y	N	Y	NA	NA	Y
McAdams-DeMarco et al., 2018	Y	Y	NR	N	N	Y	N	Y	Y	N	Y	NR	NR	Y
Mentari et al., 2005	Y	Y	NR	N	N	Y	CD	NA	Y	NA	Y	N	NR	N
Michels et al., 2011	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	NR	N	Y
Neumann et al., 2018	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Ortega et al., 2007	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	N
Painter et al., 2012	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	N	CD
Park et al., 2017	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y
Peipert et al., 2020	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Poulsen et al., 2017	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y
Rajkumar et al., 2019	Y	Y	NR	Y	N	Y	Y	N	Y	Y	Y	NA	N	N
Ryu et al., 2021	Y	Y	NR	CD	N	Y	Y	N	Y	Y	Y	NR	Y	N
Sihombing et al., 2017	Y	Y	NR	Y	N	Y	CD	N	Y	Y	Y	NR	NR	N
Simic-Ogrizovic et al., 2009	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	NA	N	N
Song et al., 2018	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	N	Y	Y
Ting et al., 2003	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	N	N
Tsarpali et al., 2021	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	N	Y
Unruh et al., 2008	Y	Y	Y	N	N	Y	Y	Y	Y	NA	Y	NA	N	Y
van Eps et al., 2010	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	Y	N	N
von der Lippe et al., 2016	Y	Y	NR	N	N	Y	Y	N	Y	Y	Y	NR	N	N
Watanabe et al., 2018	Y	N	NR	N	N	Y	Y	Y	N	Y	Y	NR	NR	N
Yang et al., 2021	Y	Y	NR	N	N	N	CD	Y	Y	CD	Y	CD	Y	N
Yoon et al., 2016	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y
Zimmerman et al., 2003	Y	N	NR	N	N	Y	N	Y	Y	Y	Y	NR	Y	N

Notes. Quality assessment was performed using the quality assessment tool for observational cohort and cross-sectional studies developed by the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH); Y = Yes; N = No; NR = Not reported; CD = Cannot determine; NA = Not applicable.

Table S5. *Quality assessment of controlled intervention studies.*

Author & Year	1. Was the study described as randomized, a randomized clinical trial, or an RCT?	2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	3. Was the treatment allocation concealed (so that assignments could not be predicted)?	4. Were study participants and providers blinded to treatment group assignment?	5. Were the people assessing the outcomes blinded to the participants' group assignments?	6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	9. Was there high adherence to the intervention protocols for each treatment group?	10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?
Boudville et al., 2009	Y	Y	Y	N	N	NR	Y	NR	NR	NR	Y	N	Y	CD
Chow et al., 2010	Y	Y	NR	NR	NR	Y	Y	Y	Y	Y	Y	Y	Y	N
Dai et al., 2020	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
Duarte et al., 2009	Y	N	Y	Y	Y	N	Y	Y	Y	NR	Y	N	Y	CD
Foley et al., 2009	Y	CD	Y	Y	Y	Y	N	NR	Y	Y	Y	Y	Y	Y
Hayashi et al., 2017	N	N	N	NR	NR	N	N	Y	Y	NR	Y	N	Y	N
Hernández Sánchez et al., 2021	Y	Y	Y	NR	NR	Y	Y	Y	Y	NR	Y	N	Y	Y
Jiao et al., 2017	N	Y	Y	N	N	Y	Y	Y	NR	NR	Y	N	Y	N
Lazarus, 2019	Y	N	Y	Y	Y	Y	Y	Y	NR	NR	Y	Y	Y	Y
Li et al., 2014	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	Y	N
Lim et al., 2020	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	N
Lo et al., 1998	N	N	N	N	N	Y	Y	N	NR	Y	Y	N	CD	N
Lopes et al., 2019	Y	N	NR	N	Y	Y	N	Y	Y	Y	Y	N	Y	N
Mansouri et al., 2020	N	N	Y	N	NR	Y	Y	Y	Y	Y	Y	Y	Y	N
Martin-Alemañy et al., 2016	Y	Y	NR	N	NR	Y	Y	Y	Y	NR	Y	N	Y	N
Maynard et al., 2019	Y	Y	Y	N	NR	Y	Y	Y	Y	Y	Y	Y	Y	N
Mazairac et al., 2013	Y	N	N	N	N	Y	N	Y	N	Y	Y	N	CD	Y
Ohtake et al., 2014	Y	N	NR	NR	NR	Y	Y	Y	Y	Y	Y	N	Y	N
Paniagua et al., 2005	Y	NR	NR	NR	NR	Y	N	Y	NR	NR	Y	N	Y	Y
Salamon et al., 2017	Y	Y	Y	NR	NR	Y	N	Y	NR	NR	Y	N	Y	N
Scott et al., 2009	N	N	N	N	NR	Y	Y	Y	Y	NR	Y	Y	Y	N
Shahnavazi et al., 2018	Y	Y	NR	NR	NR	Y	Y	Y	Y	Y	Y	N	Y	N
Soares et al., 2017	Y	CD	Y	NR	NR	CD	N	N	NR	NR	Y	N	Y	N
Tamilselvan et al., 2021	N	Y	NR	NR	NR	CD	Y	NR	NR	NR	Y	Y	Y	N
Uchiyama et al., 2019a	Y	N	NR	N	N	Y	Y	Y	N	NR	Y	Y	Y	Y
Unruh et al., 2004	Y	CD	NR	NR	Y	Y	N	NR	NR	NR	Y	N	Y	N

Wang et al., 2008	Y	CD	Y	Y	Y	NR	N	NR	Y	NR	Y	N	Y	Y
Wong et al., 2010	Y	CD	NR	NR	Y	Y	Y	Y	Y	NR	Y	Y	Y	N
Wu et al., 2014	N	Y	NR	NR	NR	Y	Y	Y	NR	NR	Y	N	Y	N
Zheng et al., 2019	Y	Y	NR	NR	NR	Y	Y	Y	Y	Y	Y	N	Y	N

Notes. Quality assessment was performed using the quality assessment tool for controlled intervention studies developed by the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH); Y = Yes; N = No; NR = Not reported; CD = Cannot determine; NA = Not applicable.

Table S5. *Quality assessment of before-after (pre-post) studies with no control group.*

Author & Year	1. Was the study question or objective clearly stated?	2. Were eligibility/selection criteria for the study population prespecified and clearly described?	3. Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	4. Were all eligible participants that met the prespecified entry criteria enrolled?	5. Was the sample size sufficiently large to provide confidence in the findings?	6. Was the test/service/intervention clearly described and delivered consistently across the study population?	7. Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	8. Were the people assessing the outcomes blinded to the participants' exposures/interventions?	9. Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	10. Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	11. Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	12. If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?
Abbasi Abianeh et al., 2020	Y	Y	Y	NR	CD	Y	Y	NR	NR	Y	N	NA
Ahmadzadeh et al., 2017	Y	Y	Y	NR	CD	Y	Y	NR	N	Y	N	NA
Aramwit et al., 2012	Y	Y	Y	NR	CD	Y	Y	Y	N	N	N	NA
Goldfarb-Rumyantzev et al., 2006	N	Y	Y	N	CD	Y	Y	NR	Y	Y	Y	NA
Kim et al., 2011	Y	Y	Y	Y	CD	Y	Y	Y	Y	Y	Y	NA
Palanova et al., 2019	N	Y	Y	N	CD	Y	Y	NR	N	Y	N	NA
Parsons et al., 2006	Y	Y	Y	NR	N	Y	Y	NR	N	N	Y	NA
Stumm et al., 2019	Y	Y	Y	Y	CD	Y	Y	N	Y	Y	N	NA

Notes. Quality assessment was performed using the quality assessment tool for before-after (pre-post) studies with no control group developed by the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH); Y = Yes; N = No; NR = Not reported; CD = Cannot determine; NA = Not applicable.

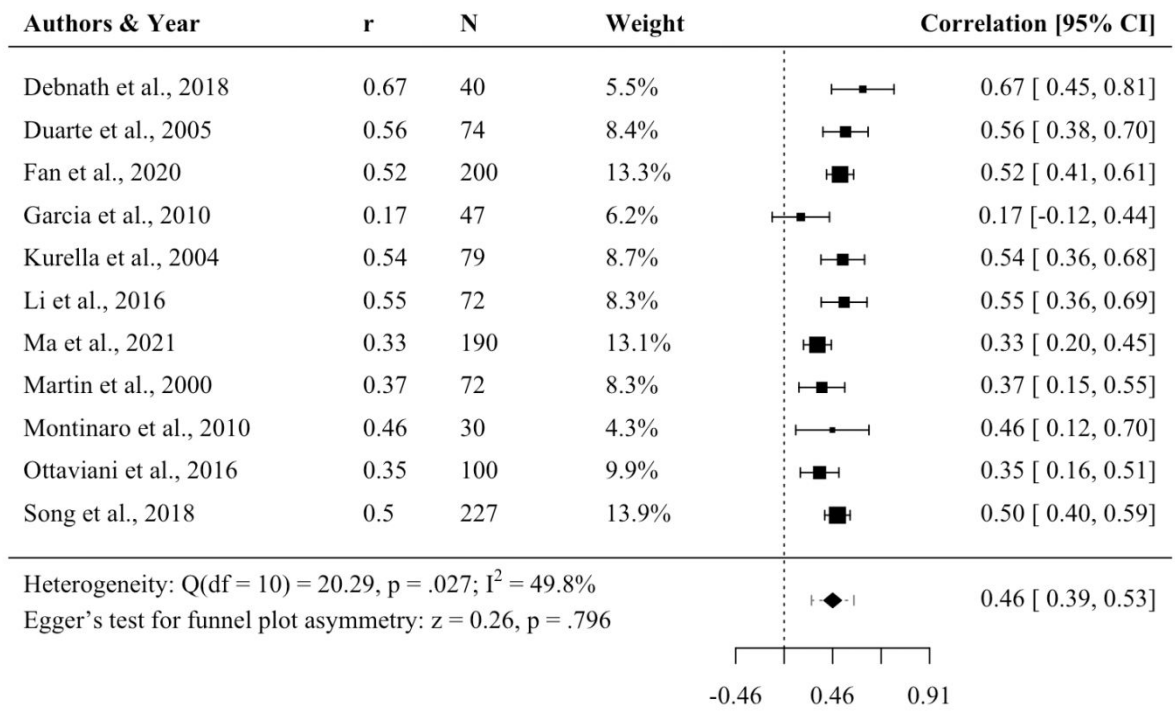

Figure S1. Forest plot showing the results of 11 studies reporting correlation coefficients between subjective cognitive complaints and depressive symptoms. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.46 (95% confidence interval 0.39 to 0.53; 95% prediction interval 0.27 to 0.62), suggesting that subjective cognitive complaints were associated with higher depressive symptoms. There was evidence of heterogeneity across studies (Q = 20.29, df = 10, p = .027; I^2 = 49.8%). Egger's test did not detect funnel plot asymmetry (z = 0.26, p = .796).

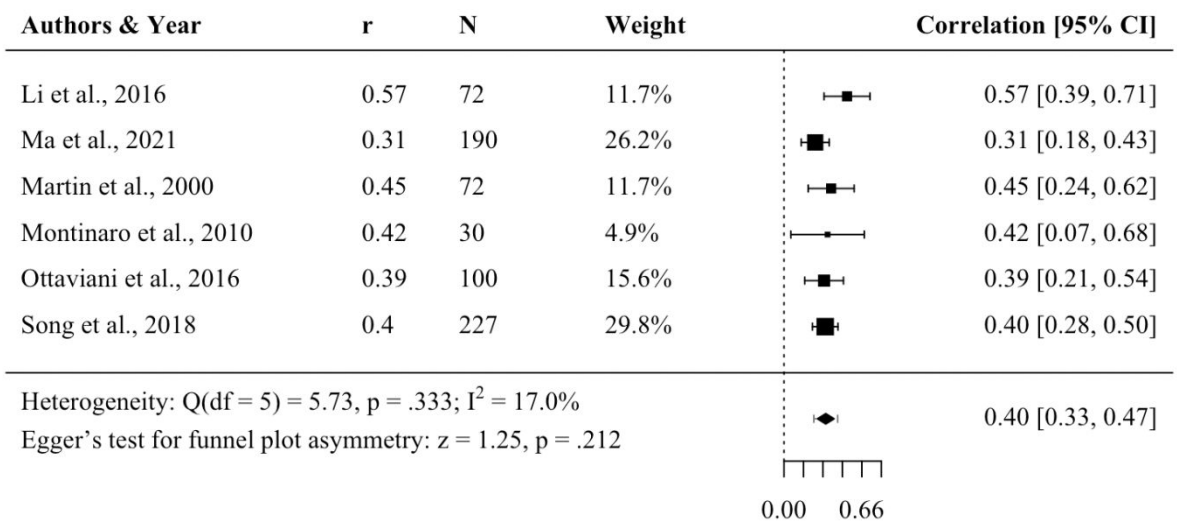

Figure S2. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and anxious symptoms. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.40 (95% confidence interval 0.33 to 0.47; 95% prediction interval 0.30 to 0.50), suggesting that subjective cognitive complaints were associated with higher anxious symptoms. There was no evidence of heterogeneity across studies (Q = 5.73, df = 5, p = .333; I^2 = 17.0%). Egger's test did not detect funnel plot asymmetry (z = 1.25, p = .212).

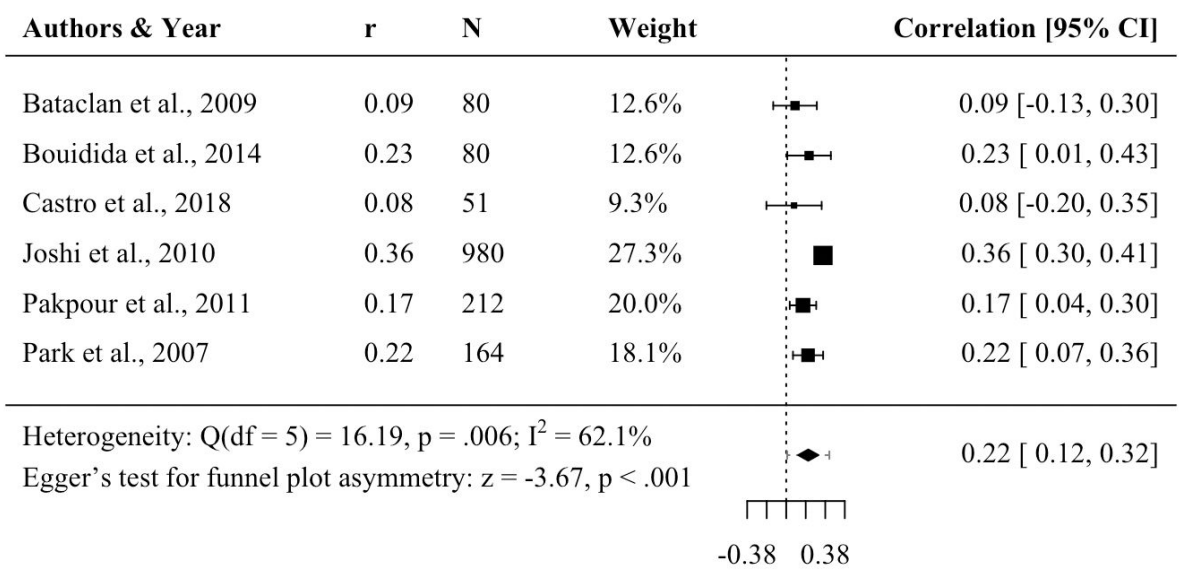

Figure S3. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and overall health ratings. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.22 (95% confidence interval 0.12 to 0.32; 95% prediction interval 0.01 to 0.42), suggesting that subjective cognitive complaints were associated with worse overall health ratings. There was evidence of heterogeneity across studies (Q = 16.19, df = 5, p = .006; I^2 = 62.1%). Egger's test detected funnel plot asymmetry (z = -3.67, p < .001).

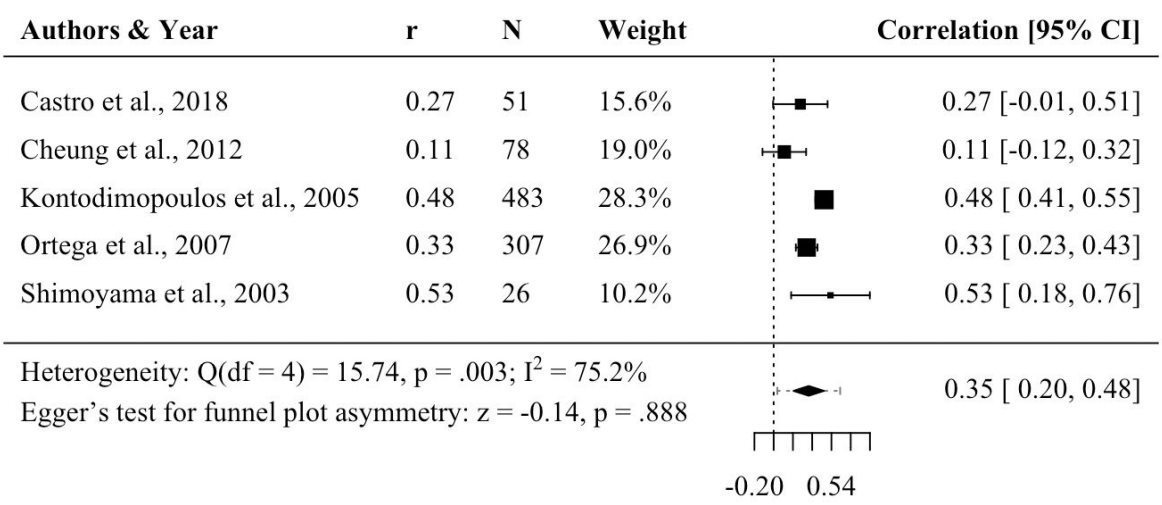

Figure S4. Forest plot showing the results of five studies reporting correlation coefficients between subjective cognitive complaints and general health perception. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.35 (95% confidence interval 0.20 to 0.48; 95% prediction interval 0.04 to 0.60), suggesting that subjective cognitive complaints were associated with worse perceived general health. There was evidence of heterogeneity across studies (Q = 15.74, df = 4, p = .003; I^2 = 75.2%). Egger's test did not detect funnel plot asymmetry (z = -0.14, p = .888).

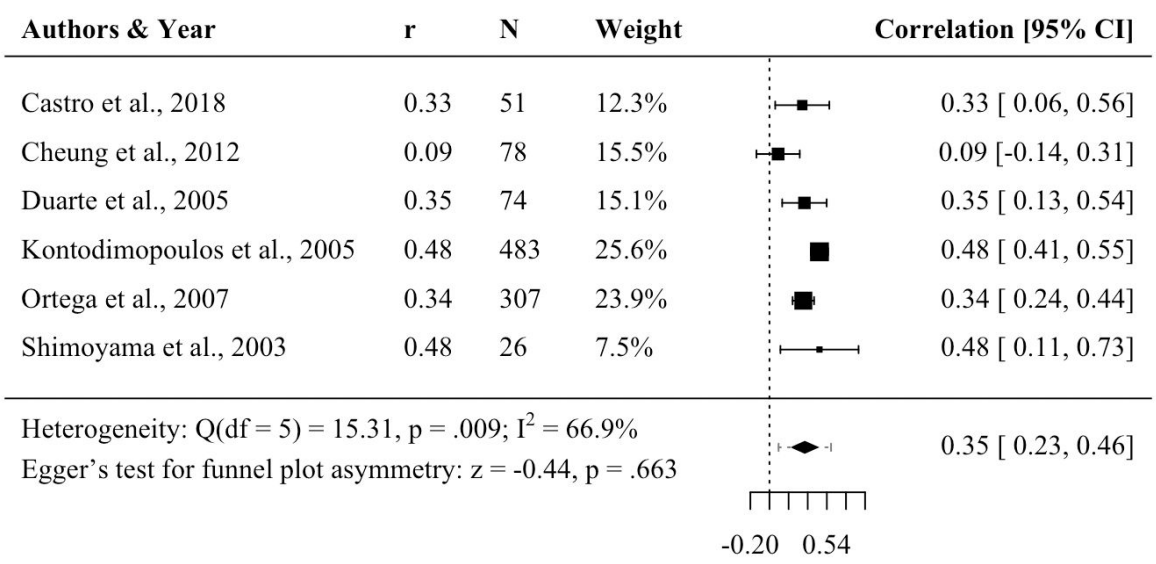

Figure S5. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and bodily pain. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.35 (95% confidence interval 0.23 to 0.46; 95% prediction interval 0.09 to 0.57), suggesting that subjective cognitive complaints were associated with higher level of bodily pain. There was evidence of heterogeneity across studies (Q = 15.31, df = 5, p = .009; I^2 = 66.9%). Egger's test did not detect funnel plot asymmetry (z = -0.44, p = .663).

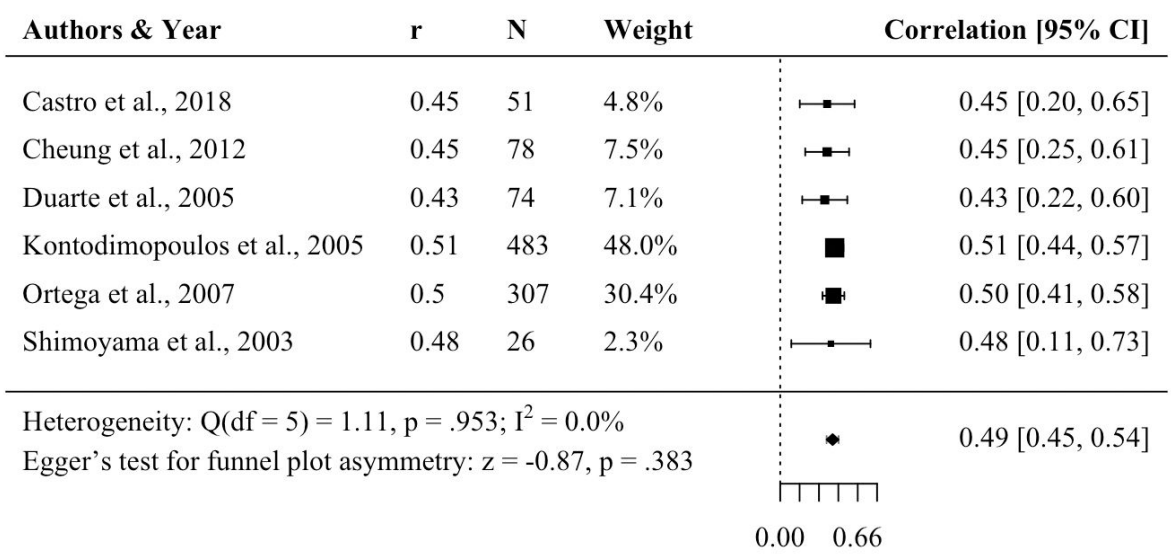

Figure S6. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and fatigue symptoms. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.49 (95% confidence interval 0.45 to 0.54; 95% prediction interval 0.45 to 0.54), suggesting that subjective cognitive complaints were associated with higher fatigue symptoms. There was no evidence of heterogeneity across studies (Q = 1.11, df = 5, p = .953; I^2 = 0.0%). Egger's test did not detect funnel plot asymmetry (z = -0.87, p = .383).

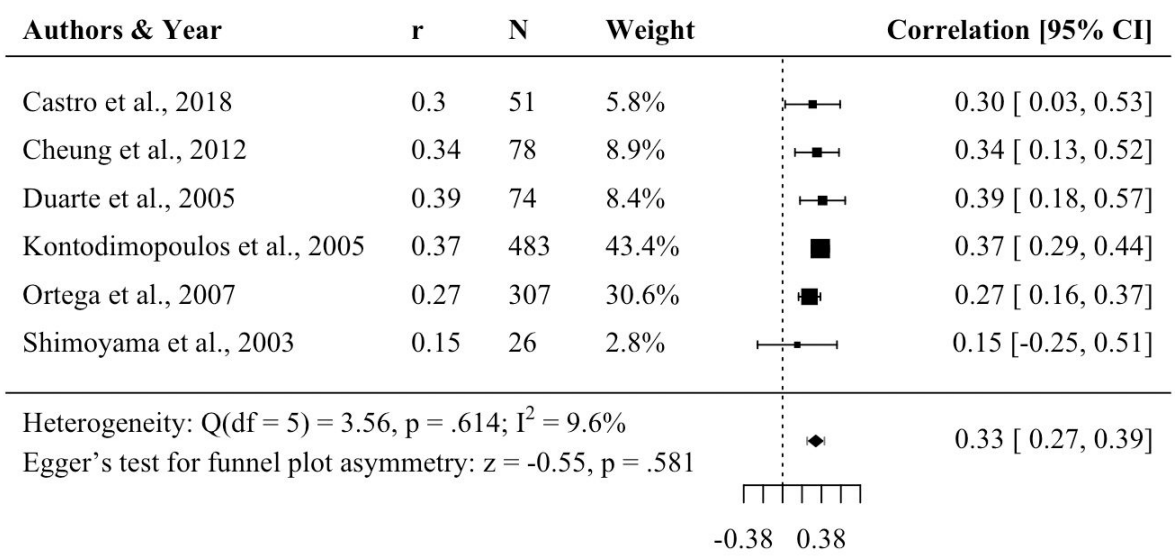

Figure S7. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and self-reported physical functioning. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.33 (95% confidence interval 0.27 to 0.39; 95% prediction interval 0.25 to 0.41), suggesting that subjective cognitive complaints were associated with worse physical functioning. There was no evidence of heterogeneity across studies (Q = 3.56, df = 5, p = .614; I^2 = 9.6%). Egger's test did not detect funnel plot asymmetry (z = -0.55, p = .581).

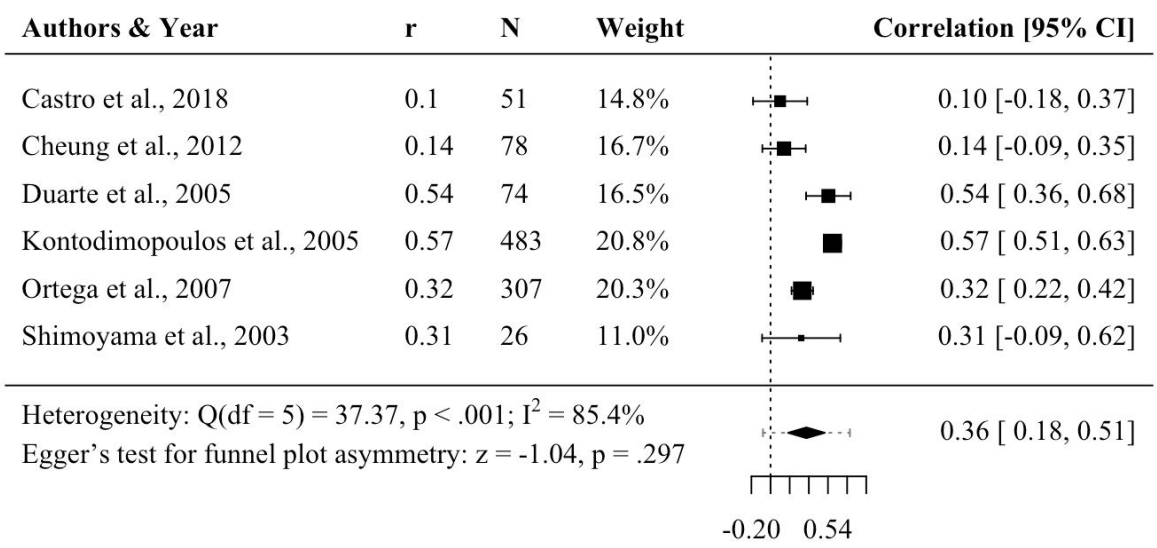

Figure S8. Forest plot showing the results of six studies reporting correlation coefficients between subjective cognitive complaints and social functioning. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.36 (95% confidence interval 0.18 to 0.51; 95% prediction interval -0.08 to 0.68), suggesting that subjective cognitive complaints were associated with worse social functioning. There was evidence of heterogeneity across studies (Q = 37.37, df = 5, $p < .001$; $I^2 = 85.4\%$). Egger's test did not detect funnel plot asymmetry ($z = -1.04$, $p = .297$).

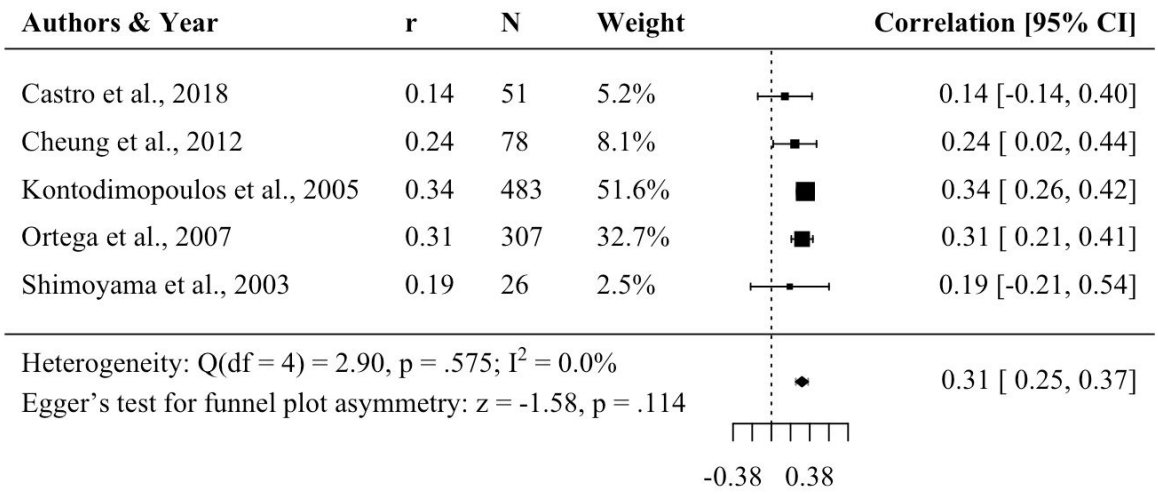

Figure S9. Forest plot showing the results of five studies reporting correlation coefficients between subjective cognitive complaints and role limitation due to physical health. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.31 (95% confidence interval 0.25 to 0.37; 95% prediction interval 0.25 to 0.37), suggesting that subjective cognitive complaints were associated with role limitation due to physical health. There was no evidence of heterogeneity across studies (Q = 2.90, df = 4, p = .575; I^2 = 0.0%). Egger's test did not detect funnel plot asymmetry (z = -1.58, p = .114).

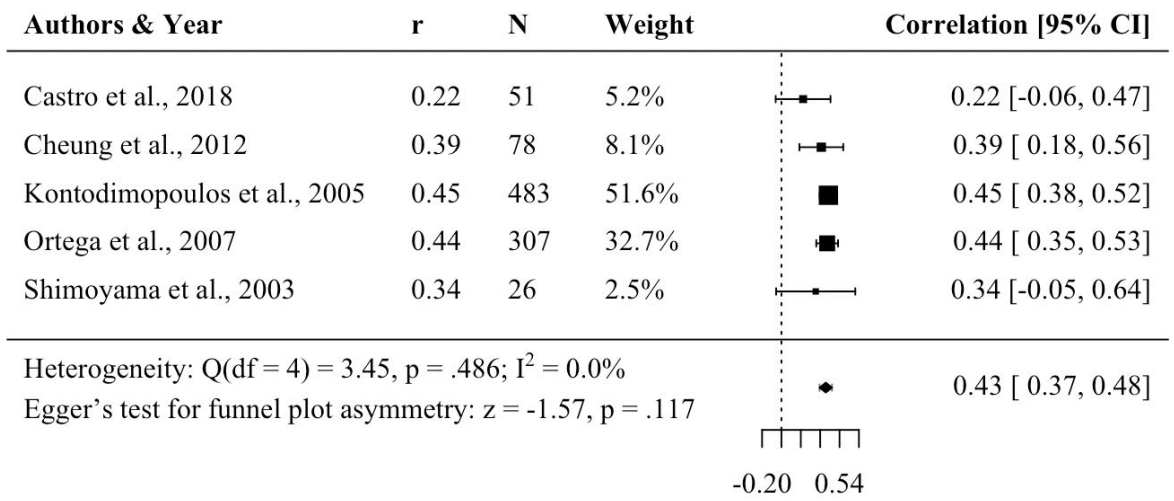

Figure S10. Forest plot showing the results of five studies reporting correlation coefficients between subjective cognitive complaints and role limitation due to emotional problems. r = Correlation coefficient; CI = Confidence interval. The pooled correlation coefficient was 0.43 (95% confidence interval 0.37 to 0.48; 95% prediction interval 0.37 to 0.48), suggesting that subjective cognitive complaints were associated with role limitation due to emotional problems. There was no evidence of heterogeneity across studies (Q = 3.45, df = 4, p = .486; I^2 = 0.0%). Egger's test did not detect funnel plot asymmetry (z = -1.57, p = .117).