



## CKJ REVIEW

# The role of psychological factors in fatigue among end-stage kidney disease patients: a critical review

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## Abstract

Fatigue is a common and debilitating symptom, affecting 42–89% of end-stage kidney disease patients, persisting even in pre-dialysis care and stable kidney transplantation, with huge repercussions on functioning, quality of life and patient outcomes. This paper presents a critical review of current evidence for the role of psychological factors in renal fatigue. To date, research has concentrated primarily on the contribution of depression, anxiety and subjective sleep quality to the experience of fatigue. These factors display consistent and strong associations with fatigue, above and beyond the role of demographic and clinical factors. Considerably less research is available on other psychological factors, such as social support, stress, self-efficacy, illness and fatigue-specific beliefs and behaviours, and among transplant recipients and patients in pre-dialysis care. Promising evidence is available on the contribution of illness beliefs and behaviours to the experience of fatigue and there is some indication that these factors may vary according to treatment modality, reflecting the differential burdens and coping necessities associated with each treatment modality. However, the use of generic fatigue scales casts doubt on what specifically is being measured among dialysis patients, illness-related fatigue or post-dialysis-specific fatigue. Therefore, it is important to corroborate the available evidence and further explore, qualitatively and quantitatively, the differences in fatigues and fatigue-specific beliefs and behaviours according to renal replacement therapy, to ensure that any model and subsequent intervention is relevant and grounded in the experiences of patients.

**Key words:** anxiety, depression, fatigue, kidney disease, sleep quality

## Introduction

Fatigue is a complex array of symptoms that has been described as 'extreme and persistent tiredness, weakness or exhaustion-mental, physical, or both' [1–3]. It has consistently emerged as a common and debilitating symptom across chronic conditions [4–7]. Likewise, fatigue is a common complaint in end-stage kidney disease (ESKD), affecting from 42% to 89% of patients, and is present across the full spectrum of chronic kidney disease (CKD), affecting patients not yet requiring renal support, to

patients on dialysis, and persisting in patients who have subsequently received a renal transplant [3, 8].

In ESKD, fatigue has huge repercussions on functioning and quality of life, further impairing patients' daily functioning, motivation and social engagement [9–14], and contributing to poorer sleep quality and increased bodily pain [13–17]; however, these associations are likely to be bidirectional. Above all, there is also evidence to suggest that fatigue may contribute directly to clinical outcomes, increasing the risk of cardiac events [18] and mortality

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[19]. Given the significance of fatigue and its consequences on patient outcomes and quality of life, timely and effective management of fatigue represents a clinical priority. Currently, no consistent and theory-led treatment model of fatigue exists, with management relying primarily on pharmacological treatments targeting anaemia or involving patients in exercise [3]. A review of pharmacological treatments for fatigue among dialysis patients reached the conclusion that no medications can be recommended for the prevention of fatigue, and complete and prolonged relief from fatigue is rare [8]. Exercise-based interventions, on the other hand, have been criticized for being unsuitable for patients with multi-morbidities, disabilities and in poorer health [20].

To date, a number of reviews have attempted to synthesize the available research on the factors associated with fatigue in this patient population [3, 8, 21, 22]. These reviews provided interesting insights on the prevalence of renal fatigue [3, 8], the type of fatigue measurements relied upon [3, 8, 22] and the outcomes associated with fatigue [3, 8, 22]. Overall, these reviews unanimously indicate that the findings are often mixed and inconclusive, with little success in identifying demographic, social-situational and clinical factors that are consistently associated with the experience of fatigue.

These reviews concentrated mainly on dialysis patients and did not differentiate between studies reporting fatigue versus vitality outcomes [3, 8, 21, 22]. The concept of vitality is considered to be at the opposite end to fatigue on a fatigue–vitality continuum [3]. Some debate exists on the comprehensiveness of the concept of vitality, capturing a reduction in energy levels, but not necessarily the negative aspects of fatigue, such as weakness, lack of motivation and difficulty with concentration [22]. Given that the vitality subscale of the SF-36 is the most widely used instrument in the dialysis population as a marker of fatigue [23, 24], it is important to assess whether systematic differences exist in factors associated with fatigue versus vitality.

Overall, the evidence for the role of demographic and social-situational factors in the experience of fatigue is mostly weak and inconsistent (e.g. [25–34]). Similarly, in relation to clinical factors, there is generally a lack of evidence for the significant variation in fatigue according to dialysis adequacy, serum albumin, haemoglobin or other clinical factors [e.g. 27, 29, 33, 35]. This may be due to the relative homogeneity of clinical values, maintained within the recommended ranges across many studies [3, 8]. However, indisputably, poorly managed patients are likely to report worse outcomes and exacerbated symptoms, including fatigue [e.g. 36–40]. Findings are generally in agreement on the negative impact of physical inactivity [31–33, 41] and comorbidities on fatigue [28, 29, 33, 35, 42]. A greater number of concomitant conditions may lead to worse overall health and functioning, and increased stress and burden imposed by additional treatment requirements [3]. While, poor physical functioning may contribute to fatigue, fatigue may also lead to inability to engage in activities; therefore, the direction of this association is unclear given the prevalence of cross-sectional research [8].

To our knowledge, this is the first narrative review providing a more comprehensive and in-depth overview of the role of psychological and cognitive-behavioural factors in the experience of fatigue in the renal population. Also, differences in factors associated with fatigue as compared with vitality and variations by renal replacement therapy (RRT) were explored. In order to develop theory-based and effective interventions for fatigue in ESKD, it is important to identify potentially modifiable factors that contribute to fatigue above and beyond the influence of demographic, social-situational and clinical factors, in each treatment modality.

## Review questions

- (i) What is the available evidence for the role of psychological and cognitive behavioural factors in ESKD fatigue?
- (ii) Are there any differences in factors depending on outcome used: fatigue versus vitality?
- (iii) Are there any differences in factors associated with fatigue/vitality depending on the type of RRT?

## Materials and methods

### Search

In anticipation of a large volume of research examining the association between depression, anxiety, subjective sleep quality and fatigue, a narrative review approach was selected to synthesize the evidence on the aforementioned factors and capture what other psychological factors have been explored to date. This narrative review was guided by principles and methods of a systematic review. To identify relevant articles, the following databases were searched: (i) Embase (via Ovid), (ii) Medline (via Ovid), (iii) PsycInfo (via Ovid), (iv) Global Health (via Ovid) and (v) Web of Science. A combination of ESKD and fatigue terms was used (please see Box 1, in [Supplementary Appendix A](#)). The search strategy was adapted to each database. Alongside the electronic search, a manual search was also conducted to identify any additional articles. The search was limited to full-text articles to allow for adequate appraisal of the findings ([Table 1](#)). The studies were included if the sample consisted of adult (aged 18 years or older) ESKD patients, with their glomerular filtration rate (GFR) falling below 60 mL/min/1.73 m<sup>2</sup>, regardless of the RRT they were receiving or if they were in pre-dialysis care. Only articles that measured fatigue or vitality and reported explicit findings related to potential predictors of fatigue/vitality, measured by independent instruments, and not within-scale correlations, were included in this review. Psychological factors were defined as cognitive, emotional or behavioural factors typically considered modifiable in the context of psychosocial interventions. Intervention studies, studies assessing the consequences of fatigue on functioning, mortality or quality of life, or articles that included a fatigue subscale but failed to report discernible fatigue findings were excluded. Please see [Supplementary Appendix B](#) for further information.

### Quality assessment

All identified studies underwent a quality assessment using a modified version of the Effective Public Health Practice Project (EPHPP) quality assessment tool that covers any quantitative study design to provide a descriptive overview of the quality of the current evidence base. Overall quality scores for each study were not computed. Relevant considerations appropriate to the studies were added to the assessment list, in particular: what study design was used, whether a power calculation was reported, what type of recruitment was used, what percentage of selected individuals agreed to participate, whether participants could be deemed representative of the population, whether reliable and valid instruments were used, whether analyses were appropriate, whether the P-value was adjusted for multiple analyses and whether confidence intervals were reported (where appropriate). A full description of the ratings for each study can be found in [Supplementary Appendix C](#).

### Analysis

Data from the included studies were extracted using a data extraction form that was adapted from the data collection

Table 1. Summary of instruments used to measure fatigue, depression, anxiety and subjective sleep quality

Reference	RRT	Fatigue	Depression	Anxiety	Subjective sleep quality
(1) Bai et al. [31]	HD	Lin's Fatigue scale [43]	CES-D		
(2) Bossola et al. [44]	HD	SF-36 vitality	BDI	HARS	Athens Insomnia Scale
(3) Bossola et al. [45]	HD	SF-36 vitality	BDI	HARS	
(4) Bossola et al. [46]	HD	SF-36 vitality	BDI		
(5) Bossola et al. [47]	HD	Six closed questions, pertaining to the domains of general tiredness, emotional tiredness, cognitive tiredness, sleepiness, weakness and lack of energy	GDS		
(6) Bossola et al. [48]	HD	SF-36 vitality	BDI	HARS	
(7) Cardenas and Kutner [49]	HD & PD	VAS-F	SDS		
(8) Chan et al. [29]	Tx	MFI-20	HADS-D	HADS-A	PSQI
(9) Chen et al. [50]	HD	SF-36 vitality & CFQ	HADS-D	HADS-A	
(10) Chilcot et al. [33]	HD	CFQ	HADS-D	HADS-A	
(11) DePasquale et al. [51]	HD	SF-36 vitality	SCL-90 R-Depression	SCL-90 R-Anxiety	
(12) Dubin et al. [52]	HD	Two closed questions around fatigue after dialysis sessions. Severe PDF was defined as a 'yes' answer to the latter question.	Deemed depressed if: (i) diagnosis of depression, mood disorder in medical history, or (ii) prescribed antidepressants.		
(13) Garcia et al. [53]	HD	SF-36 vitality	HDRS		
(14) Garcia-Llana et al. [14]	HD	SF-36 vitality	BDI	STAI	Sleeping problems were assessed using the subscale sleep/rest of the SIP
(15) Goedendorp et al. [32]	Tx	CIS	BDI-PC		
(16) Jhamb et al. [15]	HD & PD	SF-36 vitality	Antidepressants	Benzodiazepines	Three items assess sleep initiation ('Have trouble falling asleep?'), sleep maintenance ('Awaken during sleep and have trouble falling asleep again?') and sleep adequacy ('Get enough sleep to feel rested upon waking in the morning?').
(17) Jhamb et al. [16]	HD	SF-36 vitality	PHQ-9		KDQoL sleep quality and sleeping pills
(18) Jhamb et al. [35]	Pre-dialysis, HD & PD	FACIT-F			PSQI
(19) Joshwa et al. [54]	HD	FSS	BDI		PSQI
(20) Kalender et al. [55]	CKD conservative management, HD & CAPD	SF-36 vitality	BDI		
(21) Karakan et al. [56]	HD	PFS	BDI		
(22) Kim and Son [40]	HD	VAS-F	SDS		
(23) Koyama et al. [18]	HD	Fatigue Scale (developed by Fukuda et al. [57])			KDQoL sleep quality
(24) Leinau et al. [58]	HD	BFI	PHQ-9		
(25) Letchmi et al. [30]	HD	MFI-20	DASS 21	DASS 21	
(26) Lin et al. [59]	CAPD	SF-36 vitality and presence or absence of fatigue was studied according to the monthly clinical records of the primary nurses	BDI		

(continued)

Table 1. Continued

Reference	RRT	Fatigue	Depression	Anxiety	Subjective sleep quality
(27) Liu [26]	HD	Mandarin Chinese Fatigue Assess Scale (Chung [60])	Taiwanese Depression Questionnaire		
(28) Lobbedez et al. [42]	HD & PD	MFI-20	GDS		
(29) Martinez-Sanchis et al. [61]	HD, CAPD, & Tx	SF-36 vitality	HADS-D	HADS-A	PSQI
(30) Martins et al. [62]	HD	SF-36 vitality		Cognitive-Somatic Anxiety Scale (Silva et al. [63])	
(31) McCann and Boore [41]	HD	MFI-20, VAS-F, SF-36 vitality	HADS-D	HADS-A	Overall Sleep Problems Index
(32) Oliveira et al. [64]	HD	SF-36 vitality	BDI		
(33) Rodrigue et al. [34]	Pre- and post-Tx	FSI & MFI-20	CES-D		PSQI
(34) Santos [65]	HD	SF-36 vitality	BDI	STAI	
(35) Sayin et al. [28]	HD, PD, & Tx	SF-36 vitality	BDI		
(36) Senol et al. [12]	PD	FSS, SF-36 vitality	BDI		
(37) Sklar et al. [66]	HD	Patients were regarded to suffer from PDF if they spontaneously offered this complaint when asked the open-ended question, 'Do you feel better or worse after dialysis? If worse, please specify in which way(s)'. A complaint of fatigue would then be probed further with questions directed at its duration, frequency, and intensity, allowing for the creation of a fatigue index (one third of the sum of these three parameters, each rated from 1 to 5).			
(38) Taskapan et al. [67]	HD	SF-36 vitality	HDRS	HARS	Three items assess sleep initiation ('Have trouble falling asleep?'), sleep maintenance ('Awaken during sleep and have trouble falling asleep again?'), and sleep adequacy ('Get enough sleep to feel rested upon waking in the morning?').
(39) Unruh et al. [68]	HD & PD	SF-36 vitality			
(40) Vazquez et al. [69]	HD	SF-36 vitality	BDI	STAI-S	
(41) Wang et al. [70]	HD	FACIT-F	HADS-D		
(42) Wang et al. [71]	HD	FACIT-F	HADS-D	HADS-A	PSQI
(43) Wang et al. [72]	HD	FACIT-F			PSQI
(44) Williams et al. [73]	HD	VAS-F	HADS-D	HADS-A	

HD, haemodialysis; PD, peritoneal dialysis; Tx, transplant; CAPD, continuous ambulatory peritoneal dialysis; CES-D, Center for Epidemiological Studies Depression; BDI, Beck Depression Inventory; HARS, Hamilton Anxiety Rating Scale; GDS, Geriatric Depression Scale; VAS-F, fatigue visual analogue scale; SDS, Self-Rating Depression Scale; MFI-20, Multi-dimensional Fatigue Inventory; HADS, Hospital Anxiety and Depression Scale; PSQI, Pittsburgh Sleep Quality Index; CFQ, Chalder Fatigue Questionnaire; SCL-90 R, Symptom Checklist-90-Revised; PDF, post-dialysis fatigue; HDRS, Hamilton Depression Rating Scale; STAI, State-Trait Anxiety Inventory; CIS, Checklist Individual Strength; BDI-PC, Beck Depression Inventory-Primary Care; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; PHQ-9, The Patient Health Questionnaire; FSS, Fatigue Severity Scale; PFS, Piper Fatigue Scale; DASS 21, Depression Anxiety Stress Scale; KDQoL, The Kidney Disease Quality of Life Questionnaire; FSI, Fatigue Symptom Inventory; BFI, Brief Fatigue Inventory; SIP, Sickness Impact Profile 8.

checklist by the Cochrane Effective Practice and Organisation of Care Review Group to suit the purpose of this review. Key aspects of data extraction included: patient demographics, clinical and illness-related information, fatigue instrument used, investigated psychological factors, data analyses, and results for the associations between the investigated psychological factors and fatigue as an outcome. A narrative synthesis was conducted to provide a textual summary of the findings, pertaining to the reported associations between psychological factors and fatigue as an outcome, across all the included studies, and to identify any difference according to treatment modality and fatigue measurement used [74].

## Results

Fifty-four studies were identified that reported on the association between psychological variables and fatigue, mainly within investigations of the predictors of quality of life in this setting, rather than fatigue-specific studies. The vast majority of these studies were cross-sectional ( $N = 46$ ), relying on single-centre recruitment ( $N = 35$ ). Sample sizes ranged from 33 [74] to 1798 [16]. On the whole, there was a lack of consideration of power across the studies. Similarly, in most studies ( $N = 52$ ) alpha was not adjusted for multiple analyses. There was great variability in inclusion and exclusion criteria from study to study, especially evident with regards to dialysis vintage (see [Supplementary Appendix C](#)). Samples varied considerably, owing to the differences in research aims, participant selection criteria and RRT from study to study (see [Supplementary Appendix C](#)). Forty-three studies were exclusive to dialysis patients, with four studies consisting of mixed samples of both dialysis patients and transplant recipients. Only four studies included solely transplant recipients, and one study followed patients from pre-transplantation to post-transplantation. None of the studies consisted exclusively of patients in pre-dialysis care, but two studies included patients not undergoing dialysis alongside dialysis patients. Although there was variation in the instruments used, predominantly studies relied on established and validated instruments. Analyses were in general appropriate given the different research aims across the studies (see [Supplementary Appendix C](#)).

### Psychological and cognitive behavioural factors

To date, attention has been predominantly paid to depression, anxiety and subjective sleep quality with regard to fatigue, mainly among dialysis patients ( $N = 44$ ; see [Table 1](#)). From here onwards, studies from [Table 1](#) are referred to using their assigned reference numbers. Limited research is available regarding other psychological and cognitive constructs that have been previously implicated in fatigue in other chronic illnesses [75–78].

**Depression and anxiety.** Depression and fatigue overlap significantly in how they are experienced, and depression often manifests itself in lethargy and a feeling of weakness and tiredness in the general population, as well as in patient populations [8, 79–83]. Therefore, drawing conclusive interpretations as to the causality of this association is not possible [3]. Thirty-eight studies were identified that looked at the relationship between depression and fatigue/vitality. The majority ( $N = 36$ ) found a consistent significant association between the two, with depressed patients reporting greater levels of fatigue and lower

vitality (study numbers 1–10, 12–16, 18–22, 24, 26–29, 31–32, 34–38, 40–42, 44 in [Table 1](#)).

There is also evidence to suggest a significant association between anxiety and fatigue among dialysis patients and transplant recipients, where out of 18 studies reporting on this association, 15 found a significant positive association between the two (study numbers 2, 3, 6, 8–10, 14, 16, 30, 31, 35, 38, 40, 42, 44 in [Table 1](#)). Overall, some studies found that depression and other mood disorders can explain up to 38–46% of the variance in fatigue (study numbers 27, 44 in [Table 1](#)).

Only a small minority of studies failed to corroborate the association between depression, anxiety and fatigue. This may be explained by sample differences, where Letchmi *et al.* (2011)'s study (study number 25 in [Table 1](#)) was conducted in Malaysia and the lack of association between these factors may be explained by cultural differences and stigma associated with psychological distress in Asian cultures [84, 85]. In fact, the prevalence of anxiety and depression was low in Letchmi *et al.*'s sample (study numbers 25 in [Table 1](#)). Any inconsistent findings may also be explained by the great variability in the measurement of fatigue, depression and anxiety, the likely reason for the disparity in DePasquale *et al.*'s study (study number 11 in [Table 1](#)).

**Subjective sleep quality.** Even though the evidence for the role of objective sleep parameters, such as total sleep duration (e.g. study number 35 in [Table 1](#)) in the experience of fatigue seems to be weak, 13 studies were identified that examined the association between subjective sleep quality and fatigue. There was unanimous agreement with regards to the significant association between poorer subjective sleep quality and greater fatigue and lower vitality (study numbers 2, 8, 15–19, 23, 31, 33, 39, 42–43 in [Table 1](#)). Only one study failed to find a significant association between self-reported daytime sleepiness and vitality among peritoneal dialysis patients [86], whereas two studies were in support of this association [35, 54]. The prevalence of daytime sleepiness was low and the presence of restless leg syndrome (RLS), sleep apnoea and other sleep-disturbing factors were selected as exclusion criteria in the former study [86].

**Social support.** The relationship between social support and fatigue in renal patients has not been studied extensively [3, 21]. Out of 11 studies identified here, 7 found that severely fatigued renal patients perceive lower social support from friends and family [32, 72, 87–90]; this was further elaborated by Akin *et al.* (2014) [25] reporting that as levels of loneliness and fatigue increased, self-care abilities decreased, suggesting that greater fatigue severity and lower social support can have a detrimental influence on functioning and wellbeing. However, other studies did not find a significant association between social support and fatigue/vitality in the renal patient population [28, 40, 66, 73]. Great variability was evident in the measurement of social support, from studies using different self-report social support-specific scales [32, 40, 62, 66, 72, 73, 87] or social support scores extrapolated from other instruments, like the Health-Promoting Lifestyle Profile scale [88]. Given the mixed and limited evidence pool, drawing any conclusions is premature, as any differences can be also confounded by other factors, such as cultural differences and marital status.

**Cognitive behavioural factors.** Illness and symptom perceptions and associated behaviours have often emerged as dominant constructs in adjustment, quality of life and outcomes across

chronic conditions [90, 91]. Illness perceptions refer to organized beliefs about a particular condition, which can then determine coping behaviours [92, 93]. Illness perceptions consist of five dominant dimensions: (i) identity (how symptoms are experienced and attributed to the illness); (ii) cause (beliefs about causes of the illness); (iii) timeline (beliefs about the duration of the illness, cyclical, acute or chronic); (iv) consequences (beliefs about the impact of the illness); and (v) control/cure (beliefs regarding the controllability/curability of the illness) [92, 93]. The contribution of illness perceptions and coping behaviours to the experience of fatigue has been extensively documented in the literature across a range of chronic conditions (e.g. study numbers [75, 94] in Table 1). However, these factors have been so far overlooked in ESKD. Two studies examined the contribution of beliefs about the illness to fatigue; holding a severe illness identity and greater consequence beliefs were associated with lower levels of vitality in a hierarchical regression model, but none of the other illness beliefs—timeline, personal control, illness coherence, and emotional representations—emerged as significant with regards to vitality [27]. The second study examined appraisals of the illness among haemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) patients. Only the appraisal of the illness as a threat was significantly correlated with greater fatigue in CAPD, whereas appraisal of the illness neither as a loss nor as a challenge were associated with fatigue [95].

No research is currently available regarding fatigue-specific beliefs and behaviours in this patient population. A prospective study, led by the authors, is currently underway, evaluating fatigue severity and fatigue-related functional impairment over time and assessing what fatigue beliefs and behaviours, alongside demographic and clinical variables, contribute to fatigue over

time. The baseline cross-sectional data from this study revealed that an overall negative perception of fatigue, all-or-nothing and avoidance/resting behaviours in response to fatigue were significant predictors of greater fatigue severity, above and beyond the role of demographic and clinical factors, as well as distress [33].

**Other psychological factors.** Six studies have explored additional psychological factors in relation to fatigue/vitality. There is evidence in support of the negative influence of worrying and stress on energy levels [14, 88, 96]. One study also reported a significant association between self-efficacy and decreased fatigue [96] and illness intrusiveness and greater fatigue [97]. Additionally, there is some indication that greater perception of health responsibility and health-promoting behaviours can contribute to higher levels of energy in transplant recipients [88].

An interesting insight emerged from Sayin et al.'s study [28], demonstrating a link between illness knowledge and energy levels, where poorer illness knowledge was associated with lower vitality. Support for this link was evident in a trial, where following an educational intervention, illness knowledge became significantly associated with lower fatigue; however, no association between the two was evident at baseline [98].

A recent study indicated that subjective perception of exertion following exercise was the only independent predictor of physical fatigue in transplant (Tx) recipients, irrespective of objective parameters of physical fitness [99].

### The role of fatigue measurement

Across the literature, the evidence for the role of psychological factors in fatigue seems to be generally consistent regardless of instruments used. In particular, studies that used the vitality

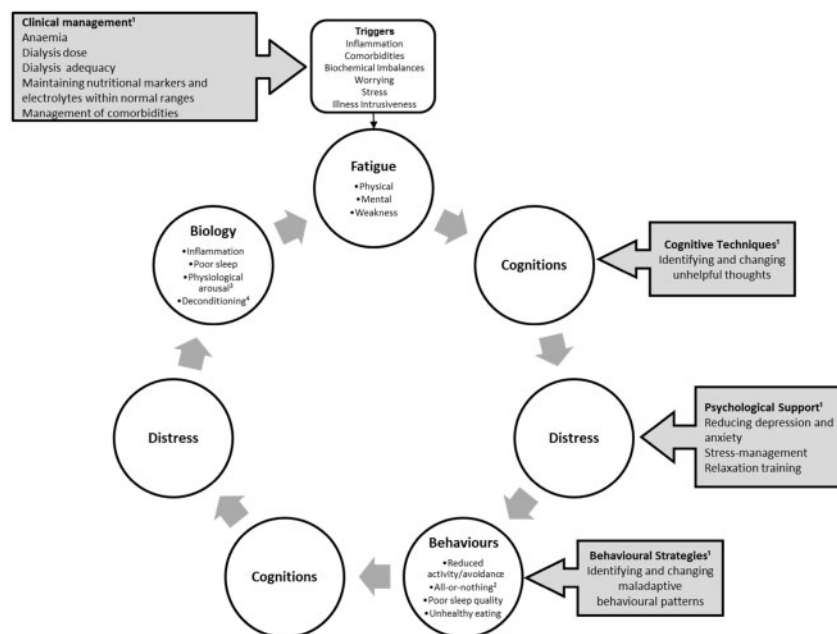


Fig. 1. Preliminary biopsychosocial model of fatigue in end-stage kidney disease. This figure illustrates how fatigue can be triggered by illness, biochemical imbalances, or stress and worrying, and it can then be perpetuated and maintained by a vicious cycle of negative beliefs, depression and/or anxiety and maladaptive behavioural patterns. <sup>1</sup>Grey boxes with arrows exemplify potential areas for intervention. Clinical management revolves around illness control and maintaining biochemical values within optimal ranges, as well as management of comorbidities. Cognitive techniques can be used to identify and change negative beliefs (e.g. catastrophizing) and to reduce depression and anxiety. Behavioural strategies, as part of psychotherapy, or physiotherapy can support patients in developing a stable activity pattern, and healthy sleep and dietary habits. <sup>2</sup>All-or-nothing = behaviour characterized by bursts of activity followed by rest. <sup>3</sup>Physiological arousal = in response to stress, chronic activation of the central and autonomic nervous systems as well as the endocrine system. <sup>4</sup>Deconditioning = changes in body systems due to physical inactivity and disuses, such as loss in muscle strength and tone.

sub-scale of the SF-36 reported comparable findings. In fact, high correlations exist between fatigue and vitality [12, 35, 41], supporting the use of vitality as a marker of fatigue. An interesting finding emerged from one study, where only subscales of the Multi-dimensional Fatigue Inventory, specifically general fatigue and mental fatigue, were significantly associated with anxiety, but there was no association between anxiety and fatigue measured by the vitality subscale of the SF-36 and visual analogue scale [41]. Fatigue-specific instruments may capture a wider spectrum of manifestations of tiredness as compared with the vitality subscale of the SF-36 or any single item scales. In fact, since the vitality subscale consists of only four items, whether it can adequately represent all the facets of fatigue is questionable [100]. There is a lack of studies comparing directly the vitality subscale of the SF-36 with fatigue-specific instruments to discern whether subtle systematic differences exist in the instruments' abilities to capture relationships between the experience of fatigue and psychological predictors. Additionally, none of the currently available fatigue instruments have been specifically developed for renal fatigue. The qualitative experience of fatigue may differ between different patient populations. Therefore, the content of generic fatigue instruments may fail to capture the relevant to renal patients' fatigue-related experiences [101], in particular with regards to illness-related fatigue and post-dialysis-specific fatigue experiences.

## Discussion

The aim of this narrative review was to build on previous reviews, by concentrating exclusively on the currently available evidence on the role of psychological factors in renal fatigue, across the full spectrum of ESKD. There was agreement between studies on the important role of depression, anxiety and subjective sleep quality in the experience of fatigue. Considerably less research is available on other psychological factors, such as social support, stress, self-efficacy, beliefs and behaviours. Promising evidence is available on the contribution of illness beliefs and behaviours to the experience of fatigue and there is some indication that these factors may vary according to treatment modality, reflecting the differential burdens and coping necessities associated with each treatment modality. Prolonged perception of the illness as a threat may lead patients to feeling burnt out, but this held only among CAPD, but not HD patients [95]. Differential burdens and challenges imposed by each treatment modality may explain why illness beliefs and fatigue levels vary. In fact, a recent study found that self-care HD patients have significantly greater personal control and illness coherence beliefs compared with in-centre patients [102]. There was also evidence for the role of stress and worrying in fatigue, suggesting that any additional burden, emotional or physical, may have detrimental effects on energy levels. Poorer illness knowledge may indirectly contribute to vitality via treatment non-adherence and greater illness-related distress.

Across studies, when cognitive-behavioural and psychological factors were introduced into the models, many demographic and clinical factors ceased to be significant, with cognitive-behavioural and psychological factors explaining 14.6–46% of unique fatigue/vitality variance [26, 27, 29, 31, 33, 47, 73]. Furthermore, the association between some demographic, social-situational and clinical factors may be explained by means of psychological factors. For example, the positive relationship between age and fatigue has been conventionally explained by age-related factors like differences in dialysis vintage, physical functioning and increased comorbidities [3]. However, this age-

fatigue relationship has not been support unanimously across studies in ESKD [30, 103]. This inconsistency may be explained by psychological factors, with younger patients possibly perceiving a greater impact of the illness on their lives and functioning, therefore holding more severe and maladaptive illness beliefs, which in turn leading to greater fatigue. Similarly, any link between marital status and fatigue may be the product of differences in social support, acting on fatigue indirectly. Employment status can act as a marker of age and physical activity, but it simultaneously may be an indication of the perceived role of patients and can also act as a distraction. In relation to education, patients with low educational attainment may find it more difficult to understand their illness and the importance of adhering to every aspect of treatment, while patients with greater educational attainment may be more aware of the severity and consequences of the illness. Similarly, some studies have reported a link between worsening renal function and fatigue in Tx recipients [29, 104]. A possible explanation may be that for Tx recipients worsening renal function represents a risk for graft loss, possibly leading to increased distress, worry and fear [104]. Overall, these findings suggest that the degree of renal function may not directly impact on energy levels, but rather through increased distress. Therefore, as Figure 1 postulates, clinical factors may trigger fatigue, but it is likely to be maintained by psychological processes, leading to a vicious cycle of negative illness and fatigue beliefs, increased distress and maladaptive behaviours. This is based on integrated fatigue models formulated in other chronic conditions, in particular Chronic Fatigue Syndrome and multiple sclerosis (MS) [105, 106].

## Limitations and future directions

Although there is promising evidence with regards to the role of psychological factors in the experience of fatigue in this setting, it is important to emphasize that most of the evidence originates from cross-sectional studies and therefore, no conclusive interpretations in relation to causality can be drawn. Considerably less research is available on psychological factors in fatigue among transplant recipients and patients in pre-dialysis care. Corroboration of the evidence for the role of social support, self-efficacy and illness intrusiveness in fatigue is necessary. Also, longitudinal studies are warranted to provide causal evidence, particularly for the associations between depression, anxiety, subjective sleep quality and fatigue. Given the evidence for differences in illness beliefs depending on RRT, it would be valuable for future research to compare fatigue-specific beliefs according to what RRT patients are receiving.

## Conclusion

Fatigue is a prevalent and debilitating symptom across the whole spectrum of renal disease. Previous narrative reviews have mainly concentrated on fatigue in dialysis patients, indicating at present a poor understanding of the pathogenesis and risk factors of fatigue in this patient population. Given the important role psychological and cognitive-behavioural factors have played in cancer and MS fatigue, this review concentrated exclusively on the current evidence for the role of these factors in renal fatigue. The most consistent evidence emerged with regards to the role of depression; anxiety and subjective sleep quality in the experience of fatigue, in many studies the role of these factors was above and beyond that of demographic, social-situational and clinical factors. Considerably less research is available on other psychological constructs, but there are some promising findings on the role of

illness perceptions and behavioural patterns in the experience of fatigue. Differences in illness beliefs and behaviours depending on RRT may also manifest themselves in the experience of fatigue, reflecting the differential burdens and restrictions of each treatment modality. However, the evidence base consists of single studies, and corroboration of these findings is warranted, particularly by longitudinal studies. Additionally, the currently available generic fatigue instruments may be unable to capture the differences between illness-related fatigue and post-dialysis-specific fatigue; therefore, it is unclear what exactly the currently used fatigue instruments are measuring, possibly contributing to the incongruities in the literature. Given the modifiable nature of psychological and cognitive-behavioural factors, these can be targeted in interventions, as has been previously successfully done in other chronic conditions, in order to alleviate the levels of fatigue in patients with renal failure.

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## Conflict of interest statement

None declared.

## Supplementary data

Supplementary data are available online at <http://ckj.oxfordjournals.org>.

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