Psychosocial and clinical correlates of fatigue in haemodialysis patients: the importance of patients' illness cognitions and behaviours

Joseph Chilcot PhD CPsychol[1], Rona Moss-Morris PhD CPsychol[1], Micol Artom MSc[1], Larissa Harden MSc[1], Federica Picariello MSc[1], Hector Hughes MB ChB[2], Sarah Bates BSc[1], Iain C Macdougall MD FRCP[2]

[1]Health Psychology Section, Psychology Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK
[2]Department of Renal Medicine, King's College Hospital, London, UK

Corresponding author: Dr Joseph Chilcot; Health Psychology Section, Psychology Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK; Email: joseph.chilcot@kcl.ac.uk; Tel: 02071880184

Abstract

Purpose: Fatigue is commonly experienced in end-stage kidney disease (ESKD) and is associated with poor outcomes. Currently little research has examined the psychosocial correlates of fatigue severity and its impact in renal disease patients. We predicted that psychological factors (distress, cognitions and behaviours) would be associated with fatigue severity and impairment in ESKD patients even when controlling for clinical and disease factors.

Methods: 174 haemodialysis patients completed the Chalder Fatigue Questionnaire (fatigue severity) and the Work and Social Adjustment Scale (fatigue-related impairment) in addition to measures evaluating distress, fatigue perceptions, symptom beliefs and behaviours. Demographic and clinical data were also collected.

Results: Fatigue severity was not related to haemogloblin levels, serum albumin, or dialysis vintage. In hierarchical regression models demographic and clinical factors explained 20% of the variance in fatigue (ethnicity, Body Mass Index, exercise, log C-reactive protein and multi-morbidity). Psychological distress (beta=0.21, p<0.01), negative beliefs about fatigue (beta=0.10, p=0.01) and unhelpful behaviours (all-or-nothing behaviour [beta=0.28, p<0.01] and avoidance [beta=0.16, p<0.01]), explained an additional 36.4% of the variance. Fatigue related impairment was associated with psychological distress, perceptions that symptoms indicate damage, avoidance behaviour and the level of fatigue severity.

Conclusions: Patients' mood, beliefs and behaviours are associated with fatigue in dialysis patients. Psychological interventions to alter these factors may reduce fatigue severity and fatigue related disability in ESKD patients.

Introduction

Fatigue is a common symptom reported by individuals with End-Stage Kidney Disease (ESKD) treated with dialysis, which can be defined as "extreme and persistent tiredness, weakness or exhaustion- mental, physical or both" [1, 2]. Prevalence rates of fatigue in ESKD are comparable to other long-term conditions [3, 4] with estimates of clinically meaningful fatigue ranging from 42 to 89 per cent [5, 6]. Fatigue is a substantial contributor to impaired quality of life (QoL) [7] and poor clinical outcomes among dialysis patients [8]. For example, in a recent study, symptoms of vitality, which includes fatigue, was associated with increased mortality risk, independent of the effect of depression[9]. Given this, fatigue management is a high clinical priority for dialysis patients.

Fatigue in ESKD is associated with a range of factors including older age [10-12, 5, 8, 13-18] and ethnicity [8, 19, 20]. With regards to biochemical, haematological and treatment-related factors, fatigue has been shown to be related with lower haemoglobin (Hb) [21-24, 16], greater levels of inflammation [5, 25], poor nutrition [26, 5, 27, 22], dialysis adequacy markers [28, 16] and multimorbidity [5, 25, 8]. Despite this results are mixed and not always consistent [4]. Accordingly there is considerable variation in fatigue severity that is not well explained by socio-demographic and disease-related factors among dialysis patients.

There is increasing recognition regarding the importance of psychological factors in the perpetuation and maintenance of fatigue symptoms in long-term medical conditions [29]. Within ESKD, the majority of studies investigating the relationship between fatigue and psychosocial factors have focused on depression [30] and anxiety [31]. Depression and anxiety are common in ESKD patients affecting approximately a third of patients [32-34] and is associated with poor clinical outcomes including

increased risk of hospitalization and mortality[35].Fatigue and depression are interrelated and depression may manifest itself as feelings of tiredness and lack of energy [36]. Despite the strong bidirectional links between the two, evidence to support the relationship between depression and fatigue in haemodialysis (HD) patients is not always consistent [37]. Rather, recent advances in other conditions, including multiple sclerosis (MS) have identified the importance of cognitive and behavioural factors in the aetiology of fatigue [38], which when modified in psychological interventions led to significant improvements in fatigue symptoms and disability [39, 40]. Of particular importance appears to be the role of illness perceptions and individual beliefs and behaviours in response to symptoms. Illness perceptions refer to organized beliefs about a particular condition or symptom(s) (in the present study perceptions surrounding fatigue), which then determines coping behaviours and procedures undertaken in response to manage the condition. Illness perceptions consist of five dominant dimensions: (1) *identity* (how symptoms are experienced and attributed to the illness); (2) *cause* (beliefs about causes of the illness); (3) *timeline* (beliefs about the duration of the illness, cyclical, acute or chronic); (4) *consequences* (beliefs about the impact of the illness), and (5) *control/cure* (beliefs regarding the controllability/curability of the illness). The contribution of illness perceptions and coping behaviours to the experience of fatigue has been documented in the literature across a range of long-term physical conditions [41, 29, 42, 43]. For example, in MS illness perceptions are associated with fatigue and disability, even when controlling for disease-related factors [44]. In the present study we measured perceptions of fatigue, rather than illness perceptions of ESKD, in order to evaluate how patients understand their fatigue and allow us to better identify

beliefs related to their symptoms, which could serve as therapeutic targets in future work.

The complexity of symptoms experienced by dialysis patients and their interpretation is challenging. Responses to symptoms as signs of disease and bodily damage can lead to maladaptive coping strategies such as catastrophizing and fearful thoughts, as well as distress and negative emotions [29, 45-47]. These in turn can manifest themselves in maladaptive behavioural patterns, such as all-or-nothing or avoidance behaviours, creating a vicious cycle which ultimately impacts on experience symptoms [29, 48, 45, 46]. All-or-nothing behaviours are characterized by an inconsistent pattern of activity with episodes of over-exertion followed by excessive rest, while avoidance is defined by a marked reduction in activity altogether [29, 49, 48, 45]. Such an inconsistent approach to activity can disrupt the sleep-wake cycle and impair functioning, in turn exacerbating and maintaining fatigue [50]. Alongside negative cognitive representations of an illness, engaging in all-or-nothing or excessive rest or avoidance behaviours was predictive of greater fatigue severity and disability in MS [49].

Despite promising findings in other patient populations, no studies have yet explored the ways patients perceive, interpret and react to fatigue symptoms in dialysis patients. Furthermore, given the success of tailored psychological interventions in other long-term conditions [51-53], it is all the more important to investigate whether there may be a role for such strategies in the management of fatigue in the dialysis population. Accordingly, the overarching objective of this study was to assess the severity of fatigue in haemodialysis patients and consider factors associated with the variation in fatigue severity and fatigue related impairment. Given

the findings of past studies investigating fatigue in other long-term conditions we tested the following hypotheses:

1. Psychological distress as measured by depression and anxiety symptoms, would be associated with greater fatigue severity and higher levels of fatigue related impairment.

2. Negative perceptions of fatigue (symptom perceptions) would be associated with greater fatigue severity and higher levels of fatigue related impairment.

3. Higher levels of catastrophizing and fear avoidance, greater use of all-or-nothing behaviour and avoidance behaviours would be associated with greater fatigue severity and higher levels of fatigue related impairment.

Methods

Study Design and procedure

The study employed a cross-sectional design. The primary outcome variable was self-reported fatigue severity, as measured by the Chalder Fatigue Scale [54]. The secondary outcome variable was functional impact of fatigue as measured by the Work and Social Adjustment Scale (WSAS) [55]. Patients completed these and other questionnaires (described below) during a stable dialysis session at least 20 minutes after the initiation of treatment. The study received approved by an NHS research ethics committee.

Patients

Haemodialysis patients were recruited from the renal service of King's College Hospital. Patients were approached for study inclusion providing they had no significant visual or physical impairment preventing completion of the questionnaires, had no documented cognitive impairment, had a dialysis vintage >90 days (often a

standard inclusion criteria in renal studies, allowing patients to adjust to the treatment), and were free from serious mental health conditions as noted in the medical history (e.g. psychosis, personality disorder). Patients were not approached if they were judged to be unsuitable by the nursing staff, repeatedly unwell during the recruitment period or in the process of switching to peritoneal dialysis (PD). Details of study recruitment, inclusion, exclusion and consent rates are shown in figure 1.

Data collection: Demographic and clinical factors

Demographic information was measured by a self-report questionnaire. Medical history and laboratory data were retrieved from electronic hospital patients' records for each patient at the moment of inclusion in the study. Demographic information included age, gender, ethnicity, marital status, employment status and living arrangements. Clinical factors collected included primary renal diagnosis, dialysis vintage (length of time on dialysis; months), dialysis access type, transplant list status, perceived transplant list status, Body Mass Index (BMI kg/m^2), current smoking status (yes/no) and exercise status (exercise twice a week or more; yes or no). Routine laboratory measures included haemoglobin (g/dL), serum albumin (g/L), creatinine (umol/L), urea (mmol/L) and C-reactive protein (CRP, mg/L). Given the skewed distribution of CRP, which is a marker of inflammation, all values were logged transformed. Comorbidity was evaluated using the Charlson comorbidity score, were greater higher scores indicate greater morbidity [56].

Questionnaire Measures - Dependent variables

Fatigue (Primary outcome)

The Chalder Fatigue Questionnaire [54] is an 11-item questionnaire measuring the severity of physical and mental fatigue on two separate subscales. Seven items represent physical fatigue (items 1-7) and 4 represent mental fatigue (items 8-11). Each item is scored; better than usual (0), no worse than usual (1), worse than usual (2) and much worse than usual (3). The ratings of items are added together to calculate the total score (range = 0-33) where high scores represent greater levels of fatigue. This questionnaire has previously been used as a measure of fatigue in HD patients [57] as well as other long-term medical conditions [58, 38]. Internal reliability of the total fatigue score was excellent (α=0.91) in the data reported here

Functional impairment (Secondary outcome)

The Work and Social Adjustment Scale (WSAS) [55] is a valid and reliable self-report scale of functional impairment attributable to an identified problem (in this case fatigue). The scale consists of five items that correspond to impairment in work, home management, social activities, private leisure activities and relationships. Each item is rated on a 9-point scale ranging from 0 (not at all a problem) to 8 (very seriously impaired), with high scores indicating greater impairment (α=0 .90).

Questionnaire Measures - Independent variables

Symptom perceptions of fatigue

The Brief Illness Perceptions Questionnaire (BIPQ) [59] was used to evaluate perceptions about fatigue symptoms (fatigue symptom perceptions). Four items assess cognitions (consequences, timeline, personal control, treatment control), two of them

assess emotional responses to fatigue (concern and emotions) and one item assesses the patient's feelings about how much they understand their fatigue. The items are rated using a response scale of 0 to 10; in which higher scores represent more threatening views of fatigue. Total fatigue perception scores were included in the analysis, where a higher score indicates more unhelpful symptoms perceptions (i.e beliefs that their fatigue is ongoing, serious, uncontrollable, emotionally distressing and incomprehensible). The item "*How much do fatigue symptoms affect you currently?*" was not used in the total score, since this item overlaps with the measurement of fatigue severity.

Cognitive and Behavioural Responses to Symptoms (fatigue symptoms)

The Cognitive and Behavioural Responses to Symptoms Questionnaire (CBSQ) was used to measure patients' cognitive and behavioural responses to their fatigue symptoms [60, 38]. The CBSQ contains 40-items measured on a 5-point Likert scale. Items are added to form five cognitive subscales; fear avoidance (e.g. "Avoiding unnecessary activities is the safest thing I can do to prevent my symptoms from worsening"), embarrassment avoidance (e.g. "I am embarrassed about my symptoms"), catastrophizing about symptoms (e.g. "I think that if my symptoms get too severe they may never decrease"), beliefs that symptoms signal damage to the body (damage beliefs, e,g. "the severity of my symptoms must mean there is something serious going on in my body"), and symptom focus (e.g. "my symptoms are always at the back of my mind"). There are also two behavioural subscales; resting and avoidance of activity (e.g. "I tend to avoid activities that make my symptoms worse), and all-or-nothing behaviour (e.g. "I tend to overdo things when I feel energetic"). The measure demonstrated good psychometric properties (i.e.

internal reliabilities >0.70 and a confirmed factor structure; data not shown) within the current study.

Psychological Distress

The Hospital Anxiety and Depression Scale (HADS) is a widely used self-report instrument for assessing depression and anxiety in patients with medical illnesses [61]. It is a 14-item self-report questionnaire with 7 items relating to anxiety and 7 items relating to depression. Given the high correlation between depression and anxiety subscales, a total score is more appropriate [62], with higher scores indicating greater levels of distress (score range 0-42).

Statistical Methods

All data were analyzed using IBM SPSS version 22. Missing data analysis was performed to assess the patterns of missing data for the study. Overall 4 per cent of all values were missing (data pattern was missing at random). Missing data were handled using multiple imputation (10 imputation models), which was selected because of its effectiveness with moderate samples sizes [63]. Factors associated with fatigue and functional impairment in univariate analyses were evaluated using multiple linear regression models. Variables were entered in final regression models using a hierarchical method, using a two-block variable entry method representing partially then fully adjusted models respectively. Block 1 adjusted for relevant demographic and clinical predictors of the outcome variable (fatigue or functional impairment). In a second block, psychological variables were adjusted for (fully adjusted model). Since multiple imputation was used unstandardised regression coefficients are presented. Model improvement was evaluated using a ΔF-statistic. Improvement in explained

variance was calculated using ΔR^2. Statistical significance level was assumed at $p<$ 0.05.

Results

Patient characteristics

We approached 268 haemodialysis patients for study participation, of which 174 agreed to take part and provided informed consent. A summary of demographic and clinical information is presented in table 1 (n=174). The mean age was 58.9 (*SD* = 1.6) years and the majority of the sample was male (63.2%). The most common renal diagnosis was hypertensive renal disease (23.5%) and almost half of the sample dialysed through a brachial fistula. Only 17% of the patients were working full-time, with more than 32% of patients currently not working due to ill-health. The mean dialysis vintage was 50.6 months (minimum = 3, maximum of 303 months). Means (standard deviations) for the psychological and behavioural variables are shown in table 2.

Demographic and clinical correlates of fatigue and impairment

Both fatigue severity and fatigue related functional impairment scores showed no significant univariate associations with age, gender, smoking status, Hb, serum albumin or dialysis vintage (effect sizes all <0.13). Both fatigue severity and related functional impairment correlated with BMI (r=0.26, p=0.001 and r=0.19, p=0.02 respectively) Charlson comorbidity score (r=0.19, p=0.01 and r=0.20, p=0.01 respectively) and logCRP (r=0.16, p=0.04 and r=0.17, p=0.03 respectively), albeit these effect sizes were relatively small. Fatigue related functional impairment was not associated with white ethnicity, whereas fatigue severity scores were higher in white compared with non-white patients (mean difference 2.8 ± 0.97 (S.E.); p=0.004).

Fatigue severity (mean difference = 3.0 ± 0.96 (S.E.); p=0.002) and related functional impairment (mean difference= 8.0 ± 1.9 (S.E.); p<0.01) were lower in those who exercised compared with those who did not.

Psychological correlates of fatigue and impairment

Correlates between fatigue and functional impairment are shown in table 2, accompanied by mean and standard deviations for each variable. Fatigue severity and fatigue-related impairment correlated strongly (r=0.64, p<0.01). Both correlated significantly with distress, negative fatigue perceptions, and all the cognitive and behavioural responses to fatigue subscales (table 2).

Multivariate regression: Factors associated with fatigue severity

Factors significantly associated with fatigue severity in univariate analysis were examined in regression models. A hierarchical regression model was run in which fatigue was regressed upon demographic and clinical factors in block 1 (white ethnicity, BMI, logCRP, Charlson comorbidity score and exercise status). White ethnicity, BMI, Charlson comorbidity score and exercise status were all significantly associated with fatigue (see table 3), explaining 20 per cent of the variance in fatigue scores.

In a second block, psychological distress (HADs scores), illness perceptions, cognitive and behavioural responses to fatigue symptoms were added (table 3), which improved the model significantly (ΔF=5.9, p<0.01) explaining 56.4% of the variance in fatigue scores. Higher levels of psychological distress, more negative fatigue perceptions, and greater use of all-or-nothing behaviour and avoidance resting behaviour, were all associated with greater fatigue severity. Within this fully adjusted

model (adjustment for demographic, clinical and psychological factors), the only other factor associated with fatigue severity was white ethnicity (table 3).

Multivariate regression: Factors associated with fatigue related impairment

A hierarchical regression model was run which included all independent variables that showed univariate associations with functional impairment (WSAS). In block 1, relevant demographic and clinical factors were entered. Charlson score, logCRP and exercise were all significantly associated with functional impairment (table 4). The model explained 19.3 per cent of the variance in functional impairment.

In a second block, psychological distress, illness perceptions, cognitive and behavioural responses to fatigue symptoms were added (table 4). Fatigue severity was adjusted for, since it was important to establish whether mood, cognitions and behaviours had an association with fatigue related functional impairment beyond the influence of perceived fatigue severity. Adding these variables in block 2 significantly improved the model ($\Delta F=10.2$, $p<0.01$) explaining 63.3 per cent of the variance in functional impairment. Psychological distress, perceptions that fatigue symptoms are a sign of damage, avoidance behaviour and fatigue severity was all associated with greater fatigue related functional impairment (table 4).

Discussion

The aim of the present study was to explore and evaluate the associations between psychological factors and the experience of fatigue in haemodialysis patients. The psychological factors of interest were, distress, perceptions about fatigue, symptom beliefs and behaviours. Hypotheses regarding the association between these cognitive-behavioural factors in fatigue severity and related functional impairment

were confirmed, emerging as significant factors, above and beyond the influence of demographic and clinical factors. Higher levels of distress, negative and unhelpful fatigue perceptions, and maladaptive behaviours (all-or-nothing and avoidance resting), were associated with greater fatigue severity. Distress, perceptions that fatigue symptoms are a sign of damage, avoidance behaviour and fatigue severity were associated with fatigue-related impairment. We predicted that catastrophizing about symptoms would be associated with fatigue severity and impairment, a hypothesis only partially supported here since the association with both outcomes was non-significant in adjusted analysis.

We found that the majority of demographic variables including gender, marital status, and age, did not contribute significantly to either fatigue severity or functional impairment. Results of studies concerning the relationship between fatigue in ESKD and demographic factors have been inconsistent [4, 64, 5, 65, 31], underlining that these factors may have a lesser impact on fatigue. However, we did find that white ethnicity was associated with fatigue severity in both unadjusted and adjusted models, consistent with findings in previous studies [8, 19, 20]. White ethnicity has also been found to be a risk factor for depression in renal patients [35]. It is likely that the experience of symptoms are influenced by cultural factors and differences in healthcare experiences and social support [66, 67], factors which might explain ethnicity differences observed here. However it is important to note, due to the relatively higher exclusion rate of "non English speakers", it is likely our crude white vs. non-white comparison has underrepresentation within the non-white group, which may influence the result observed here.

Exercise was associated with reduced fatigue severity and impairment in partially adjusted analysis, remaining significant in fully adjusted models. The

beneficial effects of exercise upon fatigue has been demonstrated in dialysis patients with randomised controlled trials showing significant improvements in fatigue levels following various exercise interventions [68, 69]. However as part of unhelpful behavioural responses, fatigue may also lead to limited activity and avoidance of physical exercise. Therefore the association between exercise and fatigue is likely to be bidirectional.

With regard to clinical factors, multimorbidity was associated with fatigue severity and functional impairment but only in partially adjusted models. These findings support previous studies in haemodialysis patients [5, 8, 25] and also other conditions including cancer [70, 71], rheumatoid arthritis [72] and MS [73, 74]. These findings may also relate to depression, since depression and fatigue are closely related. Depression is know to increase as the number of morbidities increases [75], therefore it is likely that fatigue symptoms also worsen as individuals experience more disease and illness.

Additionally, BMI was significantly associated with fatigue severity and impairment at the bivariate level, but was not associated with either fatigue severity or impairment in fully adjusted models. The association between BMI and fatigue severity has been observed in other conditions including breast cancer [76, 77], MS [78] and diabetic patients [79]. The link between BMI and fatigue is also observed in the general population, with obesity associated with higher levels of fatigue [80-82]. There is also evidence to suggest that higher BMI is linked with increased levels of pro-inflammatory cytokines [83-85]; which are associated with fatigue in dialysis patients (e.g. interleukin-6) [25]. However, the majority of clinical factors, such as Hb, serum albumin, and dialysis vintage, did not contribute significantly to fatigue severity. These null effects corroborate those of others in ESKD [86, 14, 87, 88, 31,

89, 17, 37, 28] highlighting that the impact of such clinical factors upon fatigue is mixed [4]. Hb may well be weakly associated with fatigue in HD patients since there is limited variance in Hb levels due to routine anemia management, where erythropoiesis-stimulating agents are used to maintain Hb between recommended levels. We did observe a significant association between CRP (logCRP) with fatigue severity and fatigue related impairment in both univariate and partially adjusted analysis. However, once psychological factors were adjusted for CRP was only associated with functional impairment. Taken together it appears that inflammation does explain a small amount of the variance in fatigue severity and impairment in dialysis patients, yet it is important to note that CRP has relatively low sensitivity so future work should evaluate the association between ESKD fatigue with more specific markers such as high sensitivity CRP and interleukin-6.

While these findings support previous research regarding the contribution of psychological factors in fatigue across a range of chronic conditions [90, 29, 91], this is the first investigation to demonstrate that cognitive-behavioural factors are associated with the experience of fatigue in ESKD. Studies of dialysis patients have found an association between depression, anxiety and fatigue, results that are supported here [4]. Catastrophizing about symptoms only held univariate associations with both fatigue and fatigue related impairment, and not in adjusted models. Future work should examine further the role of catastrophizing cognitions in the aetiological of ESKD fatigue, since such cognitions appear to be robustly associated with fatigue in other long-term conditions [91, 76, 92, 93].

In the present study, holding negative fatigue perceptions was associated with fatigue severity, consistent with previous findings in other conditions [94, 95]. These results further support the importance of understanding patient's perceptions of illness

and symptoms [96] and suggest that targeting unhelpful beliefs maybe a viable therapeutic target. However it is important to note that the casual relationship between these negative perceptions and fatigue is not yet established in this setting. In additional, we measured perceptions of fatigue, rather than illness perceptions of ESKD in order to evaluate how patients understand their fatigue, rather than assess representations of their kidney problem. Future work should also consider the role that illness perceptions (of ESKD) have upon fatigue severity and ideally investigate multimorbidity illness representations in relation to outcomes, as others have started to examine[97].

In relation to the findings on the detrimental association between maladaptive behavioural patterns and fatigue, this has been previously documented in a range of patient populations, such as MS [49, 98]. In rheumatoid arthritis, a passive coping style, characterized by avoidance behaviours, is associated with greater fatigue severity [90]. In the present study, exercise was associated with less fatigue severity and functional impairment, further consolidating the detrimental nature of excessive avoidance of activity [99]. In HD patients, physical inactivity was associated with greater fatigue [100], in agreement with the findings here. Physical activity has been found to be inversely associated with the experience of fatigue in diverse patient populations [101], such as cancer [102] and rheumatoid arthritis [103]. Avoidance of activity is an important behaviour to tackle, although it is essential that patients do not over do activity on days when they feel better, leading to all-or-nothing behaviour (burst of activity when feeling well following by prolonged rest because of the effects of over exertion). It is possible that patients avoid activity as a strategy to control their fatigue, whilst some avoid then engage in over activity when feeling relatively well, in response to a change in symptoms, which ultimately reinforces fatigue severity and

disability over time. A recent study in dialysis patients has shown that fatigue symptoms vary over the day, and between dialysis and non-dialysis days[104]. Therefore it is possible that unhelpful behaviours enacted during the interdialytic period may led to the maintenance and perpetuation of symptoms and their impact. Consistency of behaviour should therefore be encouraged in dialysis patients. Taken together, these findings support a biopsychosocial model of ESKD fatigue (see Artom et al., 2014) and suggest the important role beliefs, emotions and behaviours may have on the experience of fatigue in HD patients.

There are several limitations in this study which merit discussion. Firstly, the cross-sectional design prevents any conclusions about causality. Longitudinal designs will allow more robust temporal associations to be evaluated and consider how fatigue symptoms vary over time. This is particularly important since the effect of several factors upon the outcomes were attenuated in fully adjusted models, *possibly* indicating mediating factors. Longitudinal designs will allow future studies to examine the associations between predictor factors in an attempt to understand the mechanisms through which biological, social and psychological factors impact upon the experience and consequences of fatigue.

Furthermore, approximately 65 per cent of eligible patients provided informed consent, highlighting the potential risk of selection bias, with the most fatigued and unwell patients possibly rejecting participation. However, as the mean fatigue score was 28.3 from a possible maximum of 33, it can be assumed that the severe-end of fatigue was captured. It should also be noted that patients completed measures on dialysis and past research has show slightly higher reports of fatigue on-dialysis days [104]. Lastly, our sample was restricted only to patients who could

complete the measures in English, and thus our findings may not be generalizable to the whole of a multi-ethnic dialysis population.

In conclusion, the present findings suggest an association between negative illness beliefs, distress and maladaptive behavioural patterns with exacerbated levels of fatigue and functional impairment. The temporal relationship between these factors need further study to test the assumptions of a biopsychosocial model of ESRD fatigue. Working with patients to identify and alter these potentially modifiable cognitive-behavioural factors may provide an additional future treatment option for ESKD patients suffering from persistent and debilitating fatigue.

Conflict of interest statement:

The authors, Joseph Chilcot, Rona Moss-Morris, Micol Artom, Larissa Harden, Federica Picariello, Hector Hughes, Sarah Bates and Iain C Macdougall declare no conflict of interest.

Ethical Statement:

All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000

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Table 1. Summary of demographic and clinical factors (n=174)

Variable	Number	Proportion (%)
Demographic data		
Female	64	36.8
Ethnicity		
Caucasian	75	43.1
Non-white	99	56.9
Marital status		
Married/living with partner/single parent	88	50.6
Divorced/separated/single/widowed/never married/other	86	49.4
Living arrangements		
With spouse/partner/relatives/friends	48	29.8
Alone	113	70.2
Employment status		
Working full-time/part-time/self-employed/housekeeping	29	17.8
Retired	60	36.8
Not working due to ill health	53	32.5
Unemployed	14	8.6
None of the above	7	4.3
Clinical data		
Smoker		
Smoker	18	10.4
Non-smoker	110	63.6
Ex-smoker	45	26
Exercise status		
Exercise	95	55.2
No exercise	77	44.3
Transplant status		
Active	33	19
Unfit reconsider/suspended/working-up	71	41
Unfit/Unfit permanent/off by patient request	69	40
Primary renal diagnosis		
Hypertensive renal disease	41	24
Type 2 diabetes	45	26
Access type (n, %)		
Haemocath	46	26.6
Brachial fistula	83	48
Radial fistula	35	20.2
Arm PTFE	9	5.2
	Mean	*Standard deviation*
Age (years)	58.9	1.2
Dialysis Vintage (months) (mean, s.d)	50.6	4.2
Haemoglobin (g/dl) (mean, s.d)	109.3	0.81
Serum Albumin (g/l) (mean, s.d)	39.1	0.28
Creatinine (umol/l) (mean, s.d)	822.8	20.9
C-reactive protein (mg/l) (mean, s.d)	29.6	2.9

Table 2: Summary statistics and intercorrelations between psychological variables

	Variable	Mean (s.d)	1	2	3	4	5	6	7	8	9	10
							Correlations					
1	Fatigue	28.3 (6.5)	-									
2	WSAS (functional impairment)	18.5 (13.0)	.641**	-								
3	HADs (distress)	13.9 (8.2)	.597**	.659**	-							
4	Fatigue Perceptions	30.3 (13.2)	.584**	.604**	.658**	-						
5	Fear avoidance	11.0 (4.4)	.279**	.395**	.402**	.331**	-					
6	Catastrophizing	7.2 (3.8)	.356**	.479**	.541**	.412**	.471**	-				
7	Damage beliefs	10.2 (3.6)	.320**	.477**	.527**	.381**	.460**	.566**	-			
8	Embarrassment avoidance	8.2 (5.5)	.407**	.482**	.621**	.407**	.382**	.542**	.553**	-		
9	Symptom focus	11.3 (5.5)	.388**	.438**	.663**	.417**	.427**	.588**	.597**	.717**	-	
10	All-or-nothing behaviour	6.1 (4.5)	.484**	.410**	.498**	.398**	.263**	.239**	.314**	.405**	.432**	-
11	Avoidance/resting behaviour	12.4 (7.0)	.537**	.608**	.580**	.519**	.444**	.394**	.386**	.476**	.442**	.504**

**p<0.01

Table 3: Factors associated with fatigue severity

Variable	Block 1 Beta	Block 1 95% CI	Block 2 Beta	Block 2 95% CI
Demographic/clinical				
Charlson score	0.50*	0.02, 0.98	0.29	-0.11, 0.68
BMI	0.20**	0.06, 0.35	0.08	-0.04, 0.20
Exercise status (yes)	-3.3**	-5.1, -1.6	-1.2	-2.7, 0.35
logCRP	0.60	-0.11, 1.3	0.27	-0.31, 0.85
White	2.4**	0.60, 4.2	2.9**	1.43, 4.50
Psychological				
HADs total			0.21**	0.06, 0.36
Fatigue perceptions			0.10*	0.01, 0.17
Fear avoidance			-0.11	-0.33, 0.12
Catastrophizing			0.08	-0.18, 0.36
Damage beliefs			0.08	-0.21, 0.37
Embarrassment avoidance			-0.02	-0.22, 0.18
Symptom focus			-0.04	-0.26, 0.17
All-or-nothing behaviour			0.28**	0.08, 0.48
Avoidance/resting behaviour			0.16**	0.02, 0.31
F-statistic	7.9**		13.8*	
R^2	0.20		0.56	

unstandardized beta's shown

CI: confidence interval

*$p<0.05$ **$p<0.01$

Table 4: Factors associated with fatigue related functional impairment

	Block 1		Block 2	
Variable	Beta	95% CI	Beta	95% CI
Demographic/clinical				
Charlson score	1.21*	0.25, 2.20	0.39	-0.34, 1.12
BMI	0.27	-0.02, 0.56	-0.01	-0.24, 0.22
Exercise status (yes)	-8.9**	-12.4, -5.3	-2.9*	-5.8, -0.01
logCRP	1.6*	0.21, 3.0	0.61	-0.44, 1.7
Psychological				
HADs total			0.35*	0.06, 0.64
Fatigue perceptions			0.12	-.06, 0.30
Fear avoidance			0.05	-0.35, 0.44
Catastrophizing			0.29	-0.21, 0.79
Damage beliefs			0.54*	0.01, 1.10
Embarrassment avoidance			0.09	-0.28, 0.46
Symptom focus			-0.28	-0.68, 0.13
All-or-nothing behaviour			0.05	-0.33, 0.43
Avoidance/resting behaviour			0.31*	0.03, 0.58
Fatigue severity			0.49**	0.20, 0.77
F-statistic	9.7**		19.9**	
R^2	0.19		0.63	

Unstandardized beta's shown

CI: confidence interval

*$p < 0.05$ **$p < 0.01$
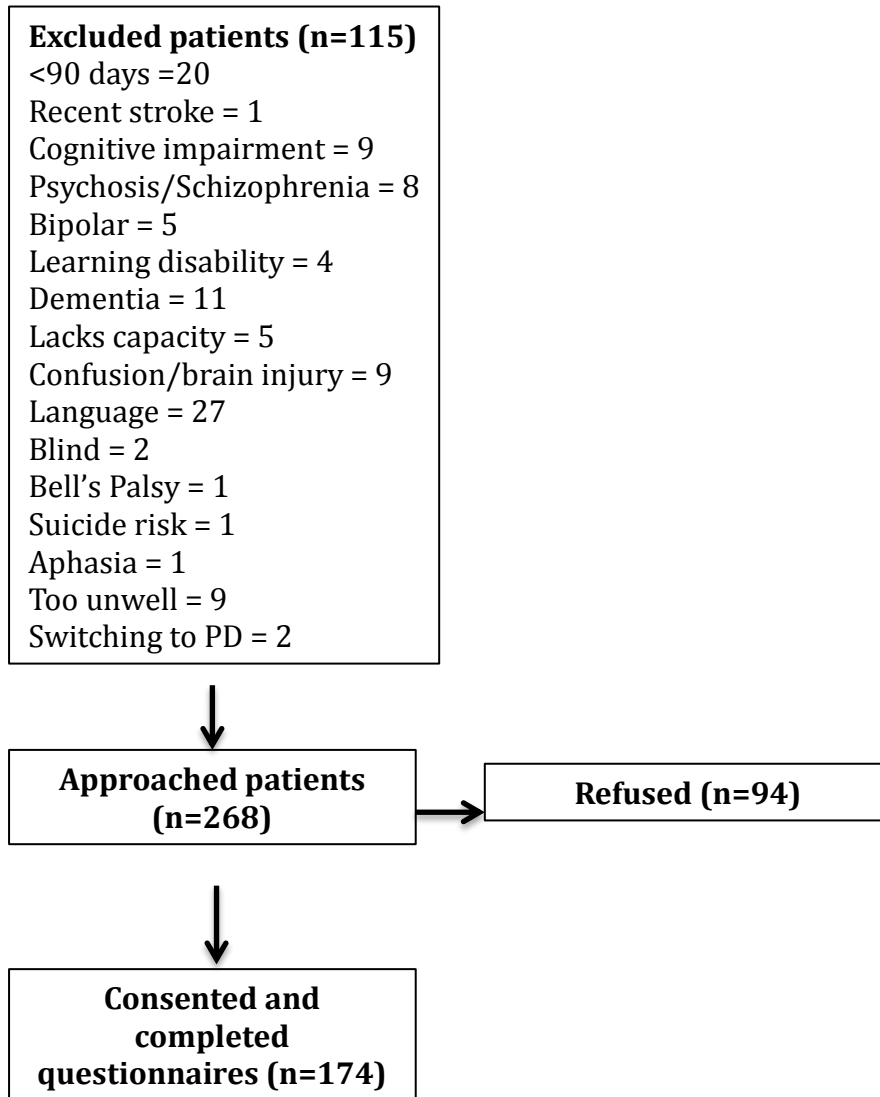
Figure 1: Patient recruitment flow chart