Sita Sharma ORCID iD: 0000-0001-9136-1810

Ann Bonner ORCID iD: 0000-0001-9920-6743

Educational or behavioural interventions for symptoms and health-related quality of life in adults receiving haemodialysis: a systematic review

Running Head: Intervention for symptoms and quality of life

Authors:

Sita Sharma[1], MN, BN, RN, PhD candidate

Theresa Green[1,2], PhD, RN, Professor

Kimberly E Alexander[1], PhD, MEdu, BN, BSc(Pub Hlth), RN, Assoc. Professor

Ann Bonner[1, 3], PhD, MA, BAppSc(Nurs), RN, Professor

Institutional affiliations:

[1] School of Nursing, Queensland University of Technology, Brisbane, Australia.

[2] Internal Medicine, Metro North Hospital and Health Service, Brisbane, Australia.

[3] Kidney Health Service, Royal Brisbane and Women's Hospital, Brisbane, Australia.

Corresponding author at:

Sita Sharma, School of Nursing, Faculty of Health, Queensland University of Technology, Kelvin Grove, QLD, 4059, Australia. Phone: +61 73138 80574; Fax: +61 73138 3814; E-mail: sita.sharma@hdr.qut.edu.au.

This is the author manuscript accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/jorc.12329.

Biodata

Sita Sharma *MN, BN, RN* is a PhD candidate at the School of Nursing, Queensland University of Technology, Australia. She obtained her Bachelor and Masters degree in Nursing from Tribhuvan University, Nepal. Her PhD research focuses on evaluating the effectiveness of an educational intervention to reduce symptom and improve health-related quality of life in adults with end-stage kidney disease receiving haemodialysis of Nepal.

Conflicts of interest: No conflict of interest has been declared by the authors.

ABSTRACT

Background: People with end-stage kidney disease (ESKD) suffer from multiple symptoms which have a negative impact on their health-related quality of life (HRQoL). Educational and behavioural interventions are being developed for this population; however, the effect of these interventions is unclear.

Aim: To evaluate the effectiveness of educational or behavioural interventions compared to standard care or alternative strategies on reducing symptoms and improving HRQoL in adults with ESKD receiving haemodialysis (HD).

Methods: An effectiveness systematic review using Joanna Briggs Institute (JBI) procedure was conducted on experimental studies (randomised controlled trials [RCTs], pseudo-RCTs and quasi-experimental designs) published in English between January 2009 to July 2019. Studies were retrieved from CINAHL, PubMed, Medline, Embase, PsycINFO, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trial) and JBI databases. Effect size (ES) at 95% confidence interval (95% CI) was calculated where possible.

Results: Eighteen studies involving 791 participants were included in this review. All studies involved behavioural interventions with the majority of studies (n=11)

targeting psychological symptoms. Interventions were categorised as either active or passive. Active interventions seemed to improve some physical symptoms, although there was very little evidence of improvements to HRQoL. Passive interventions tended to have a large effect on psychological symptoms and the mental health components of HRQoL.

Conclusion: Due to great heterogeneity between studies, meta-analyses could not be conducted further limiting the evidence to inform practice. In addition, further research on educational interventions to teach self-management strategies for symptom management and to improve HRQoL in people with ESKD receiving HD are needed.

KEYWORDS: haemodialysis**,** interventions, symptoms, quality of life

INTRODUCTION

End-stage kidney disease (ESKD) is the final stage of chronic kidney disease (CKD) where kidneys are no longer functioning to meet the body's need (Mills *et al.* 2015). In this stage, kidney replacement therapy (KRT), either regular dialysis (haemodialysis or peritoneal dialysis) or kidney transplantation, is required to sustain life (Webster *et al.* 2017). Globally haemodialysis (HD) is the most common modality of treatment for people with ESKD (Mukakarangwa *et al.* 2018).

Symptom burden in terms of number, frequency and severity of symptoms is problematic for those receiving HD (Cao *et al.* 2017). Fatigue, muscle cramps, sleep disturbance, pain, restless leg syndrome (RLS), dry skin and pruritus are common physical symptoms while depression and anxiety are common psychological symptoms (Almutary *et al.* 2013, 2016a). There is evidence that healthcare professionals often under recognise the frequency and severity of symptoms

experienced by this group of patients (Cox *et al.* 2017), and that early identification and management of symptoms ought to be integrated into routine care (Almutary *et al.* 2016b).

Health-related quality of life (HRQoL) is lower in people with ESKD receiving HD than the average healthy population (Rebollo Rubio *et al.* 2017), and this may be due to a variety of factors such as the person's age, gender, burden of disease/s, along with the effects of HD (Zyoud *et al.* 2016; Jankowska-Polańska *et al.* 2016). In addition, as the overall symptom experience increases (i.e., as the prevalence, frequency and severity of symptoms increases) in people with ESKD, there is a strong negative relationship with HRQoL (Almutary *et al.* 2017). In the HD population, both the physical and mental well-being component of HRQoL are affected by the experience of living with a high symptom burden.

Interventions targeting one or more symptoms may improve the HRQoL of those receiving HD (Shim & Cho 2018). When HRQoL is improved, there is also improvement in survival, response to treatment, and fewer hospitalisations (Jankowska-Polańska *et al.* 2016). Several systematic reviews assessing the effectiveness of interventions to reduce symptoms and to improve HRQoL among the ESKD population receiving HD have been conducted (Astroth *et al.* 2013; Chung *et al.* 2017; KauricKlein 2019; Mitrou *et al.* 2013; Xing *et al.* 2016; Zhao *et al.* 2019; Zins *et al.* 2018). These reviews do however have a narrow scope and were typically restricted to a specific symptom such as fatigue (Astroth *et al.* 2013), depression (Chung *et al.* 2017; Mitrou *et al.* 2013; Xing *et al.* 2016) or pain (Zins *et al.* 2018), while two reviews focused on physical symptoms (fatigue or pain or sleep) and psychological symptoms (anxiety and depression) (KauricKlein 2019; Zhao *et al.* 2019). In addition, most studies included in these reviews occurred more than ten

years ago. In more recent systematic reviews, KauricKlein (2019) included only two randomised controlled trials (RCTs) examining the effect of yoga, and Zhao *et al.* (2019) conducted a review including 13 RCTs evaluating the effect of exercise on physical and psychological symptoms. However, these systematic reviews assessed single interventions (i.e., yoga or exercise). Thus, a systematic review is needed to update, expand and evaluate the recent evidence of educational or behavioural interventions that reduce symptoms and improve HRQoL for people on HD.

The objectives of this systematic review were to (1) examine the educational and behavioural interventions used to reduce symptoms and improve HRQoL in people receiving HD; (2) identify the symptoms targeted by these interventions; (3) identify the instruments most commonly administered to assess symptoms and HRQoL in this population, and (4) evaluate the effectiveness of educational or behavioural interventions compared with standard care or alternative strategies on reducing symptoms and improving HRQoL in adults with ESKD receiving HD.

METHODS

We undertook a systematic review of studies in adults with ESKD undergoing HD (population), evaluating the effectiveness of educational or behavioural interventions (intervention) compared to standard care or alternative strategies (comparator) on reducing symptoms and improving HRQoL (outcomes). This systematic review was conducted according to the Joanna Briggs Institute (JBI) systematic review of effectiveness guideline (Tufanaru *et al.* 2017) and followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist (Moher *et al.* 2009). The protocol for this review was registered in PROSPERO (registration number CRD42019144763).

Eligibility Criteria

Inclusion criteria

This review examined studies that included adults aged 18 years or older diagnosed with ESKD who were receiving HD.

Exclusion criteria

Studies that included children, adults with CKD stages 1-4, and adults with CKD stage five not on HD were excluded.

Interventions

This review considered studies using educational or behavioural interventions aimed at reducing symptoms and improving HRQoL. For this review, an educational intervention was defined as either providing information or teaching skills to patients that improved their knowledge level necessary for self-management (Joboshi & Oka 2017) or included a combination of methods such as teaching or counselling (Zangi *et al.* 2015) designed to assist in understanding or recognising or managing symptoms. Correspondingly, interventions intended to change the individual's action or behaviour in regard to their health were considered as behavioural interventions. For this review, a broad range of behavioural interventions including psychosocial interventions, massage, exercise, physical activity, acupressure, music therapy, meditation, yoga, Tai Chi, mindfulness, cognitive behavioural therapy (CBT), relaxation or support group were included (Leidy *et al.* 2014; Kristy *et al.* 2018). Interventions delivered face-to-face, via telephone, mail, internet/online or via mobile phone applications in any setting as either a group or individual, provided as a single

or a series of sessions were considered. Any provider of educational or behavioural interventions was also considered.

Comparators

This review considered studies that compared the intervention with standard care (usual care with no formalised, structured intervention) or placebo or no intervention or an alternative intervention.

Outcome

The primary outcome of this review was to evaluate the effectiveness of educational or behavioural interventions aimed at reducing any symptom measured by any instrument and improving HRQoL, measured by any instrument.

Types of studies included

This review considered only experimental study designs, including Randomised control trial (RCTs), pseudo-RCTs and quasi-experimental designs.

Information Sources

A comprehensive literature search from January 2009 to July 2019 for English language studies published in electronic databases was conducted. The databases searched were CINAHL, PubMed, Medline, Embase, PsycINFO, Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trial) and JBI database.

Search Strategies

The three-phase search strategy of JBI systematic review was used to locate relevant and published studies. First, keywords were identified using two databases PubMed and CINAHL by analysing titles, abstracts and index terms. Next, database-specific searches were constructed using keywords. The search consisted of medical subject headings (MeSH) and keywords combined using Boolean, truncation and wild card

operators (see *Supplementary Table 1*). In the final phase, reference lists of all studies already retrieved were checked to identify additional studies.

Selection of Studies

Initially, titles and abstracts of studies retrieved were first checked for duplication, and after removal of duplicates, remaining studies were screened for full-text retrieval. Each author then independently assessed studies for eligibility for inclusion and any discrepancies were resolved by discussion.

Risk of bias within studies

A risk of bias assessment was conducted using the JBI critical appraisal checklists for RCTs and quasi-experimental studies (Tufanaru *et al.* 2017). Domains assessed were methods of randomisation, concealment, blinding, treatment allocation and follow up. Each domain was rated as yes, no, unclear and not applicable. A study that scored higher than 50% was considered of sufficient quality and included in the review (see *Supplementary Table 2a and 2b*). At this point, five studies were excluded (Krespi *et al.* 2009; Mortazavi *et al.* 2013; Ouzouni *et al.* 2009; Sertoz *et al.* 2009; Stanley *et al.* 2011) and the reasons for exclusion are presented in *Supplementary Table 2c*.

Data Extraction

Details regarding the publication year, setting, aim, design, participant's characteristics, sample size, interventions, the comparator, instrument, outcome measures and main results were extracted from included studies and tabulated.

Data Synthesis

Cochrane Effective Practice and Organisation of Care (EPOC) recommends reporting the effect of intervention (Cochrane Effective Practice and Organisation of Care

(EPOC) 2018). Effect size (ES) (Cohen's *d*) at 95% confidence interval (95% CI) was calculated for continuous data where possible. The effect size was interpreted as small if *d*>0.2, medium if *d*>0.5 and large if *d*>0.8. For studies with insufficient data to calculate an ES, only statistical significance was considered. There was high heterogeneity between the studies in terms of interventions, comparators, instruments and statistical analysis, thereby preventing a meta-analysis. Thus, findings are presented in a narrative form.

RESULTS

Characteristics of the included studies

A total of 987 records were identified through a comprehensive databases search, of which 253 duplicates were removed, with 18 studies included in the final review (see *Figure 1*). Basic characteristics of the studies included in this review are presented in *Table 1*. Of the studies included in the review, 14 were RCTs, and four were quasi-experimental studies. Studies were conducted in the United States, Italy, Australia, Brazil, Tunisia, Greece, UK, Iran and Taiwan, involving a total of 791 participants. The sample sizes of the studies range from 12 (Hernandez *et al.* 2018) to 93 participants (Arab *et al.* 2016). Participants' mean age varied from 41.5 (Lerma *et al.* 2017) to 71.3 years (Chan *et al.* 2016), although two studies did not report the mean age of the participants (Arab *et al.* 2016; Cukor *et al.* 2014). Fourteen of the studies included in this review had recruited more than 50% males. All of the included studies had recruited participants who had received HD for more than three months. The mean duration of HD ranged from 12.1 months (Lerma *et al.* 2017) to 76.7 months (Frih *et al.* 2017b); however, three studies did not report this characteristic

(Arab *et al.* 2016; Birdee *et al.* 2015; Henson *et al.* 2010). The earliest study included was published in 2009 (Duarte *et al.* 2009) and the latest in 2019 (Burrai *et al.* 2019).

Interventions

All 18 studies employed behavioural interventions to reduce symptom/s and improve HRQoL. As the interventions used in the studies were heterogenous, limiting comparisons and meta-analyses, we categorised interventions into two types based on whether the activity involved active bodily movement or not. The interventions were classified as those requiring physical activity (i.e. active intervention) and those not requiring any physical activity (i.e. passive intervention; see *Table 2*). Active interventions were exercise (aerobic or resistance training), muscle training and yoga (Birdee *et al.* 2015; Chan *et al.* 2016; Frih *et al.* 2017a; Giannaki *et al.* 2013; Henson *et al.* 2010; Moraes *et al.* 2015; Pellizzaro *et al.* 2013) while passive interventions were acupressure (Arab *et al.* 2016; Shen *et al.* 2017), cognitive behavioural therapy/intervention (CBT/CBI), psychological intervention (Cukor *et al.* 2014; Duarte *et al.* 2009; Hernandez *et al.* 2018; Hudson *et al.* 2017; Lerma *et al.* 2017), listening to music or Holy Qur'an (Burrai *et al.* 2019; Frih *et al.* 2017b), relaxation technique (Rambod *et al.* 2014) and breathing program (Tsai *et al.* 2015). Only one study was guided by a theoretical framework (psycho-neuro-endocrine-immunological framework (McCain & Zeller 1996) to provide a rationale for the intervention (Burrai *et al.* 2019). The duration of the interventions ranged from 15 days (Burrai *et al.* 2019) to 6 months (Giannaki *et al.* 2013; Moraes *et al.* 2015). All studies, except three (Duarte *et al.* 2009; Frih *et al.* 2017a; Lerma *et al.* 2017), delivered the interventions (i.e. acupressure, yoga, aerobic and resistance exercise, listening to music or Holy Qur'an, muscle training, relaxation technique, breathing program) during a patient's HD session. Interventions were delivered using a variety

and sometimes a combination of modes (i.e., booklets, websites, face-to-face, telephone, and audiotapes). Interventions were delivered by a range of professionals (i.e., a researcher, yoga teacher, dialysis nurse, exercise physiologist, psychologist, physiotherapist, reader, psychological wellbeing practitioner, physical educator, or traditional Chinese medicine health practitioner). Two studies did not give information about the intervention provider (Giannaki *et al.* 2013; Pellizzaro *et al.* 2013). Fifteen studies delivered the intervention on a one-to-one basis. In about half of the studies (n=8), the comparison groups were described as receiving 'standard care' or 'usual care' or ‘routine care’ or ‘no intervention’. Three studies compared the intervention with two comparison groups, an alternative intervention and a placebo-controlled group or standard care group (Arab *et al.* 2016; Giannaki *et al.* 2013; Pellizzaro *et al.* 2013).

Outcomes

All studies included in this review targeted at least one symptom and all assessed HRQoL. Depression, anxiety and sleep were the most frequently targeted symptoms (see *Table 2*).

Instruments

Instruments used to assess outcomes varied across studies. Regarding symptoms, both disease-specific and symptom-specific measures were used (see *Supplementary Table 3)*. The most commonly used instruments to measure symptoms were the Pittsburgh Sleep Quality Index (PSQI) for sleep (n=4) and Beck Depression Inventory (BDI) for depression (n=4). Cukor *et al.* (2014) used a clinician-administered instrument (Hamilton Depression Rating Scale [HAM-D]) to measure the severity of depression in adults already diagnosed with depression. Burrai *et al.* (2019) did not describe how

they measured cramps and itching in people receiving HD. For HRQoL, both generic and disease-specific measures were used (see *Supplementary Table 4*). The Short-form (SF)-36 (n=7) was the most frequently used instrument for measuring HRQoL.

Effectiveness of interventions

Overall, there was substantial heterogeneity between the studies, interventions, comparators and instruments used which precluded a meta-analysis being performed. We have calculated the ES (Cohen's *d*) at 95% CI for studies (see *Supplementary Tables 5 & 6*). As all interventions were behavioural, we categorised them into active and passive interventions based on physical activity to report on effectiveness. Active interventions were those comprising exercise (aerobic and resistance), or training (muscle or resistance) and yoga whereas CBT/CBI, psychological intervention, listening to music or the Holy Qur'an, relaxation technique and breathing program were categorised as passive interventions.

Seven studies using active intervention targeted physical symptoms (fatigue, pain, sleep, appetite and RLS) and psychological symptoms (anxiety and depression) although their results were inconsistent. Only one study (Frih *et al.* 2017a) demonstrated a significant and large effect on improving anxiety (d=1.65) and depression (d=2.72). In some studies, active interventions compared with control group significantly improved fatigue (p=0.002), sleep (p<0.001), pain (p<0.001), multiple symptoms (p=0.014; Pellizzaro *et al.* 2013); RLS (p=0.012; Giannaki *et al.* 2013); anorexia (p<0.05; Moraes *et al.* 2015); and depression (p=0.003; Giannaki *et al.* 2013) although significant ES were not found. However, other studies did not show any changes in fatigue, depression (Chan *et al.* 2016; Henson *et al.* 2010) and overall symptoms (Birdee *et al.* 2015) between groups. For HRQoL, active interventions employed in the studies significantly improved the physical health of

HRQoL, although the ES was not significant (p=0.003; Giannaki *et al.* 2013). In few studies, there were significant improvement in sub-scales of HRQoL like role physical (p<0.05; Chan *et al.* 2016; Moraes *et al.* 2015); social functioning (p=0.029); and role emotional (p<0.001; Chan *et al.* 2016). Moreover, one study with an active intervention (resistance and aerobic exercise) significantly improved both components of HRQoL, physical and mental (p=0.003 and p<0.001, respectively; Frih *et al.* 2017a). A large ES (d=1.10 and d=2.06) was also found for this study (Frih *et al.* 2017a).

The majority of studies with passive interventions focused on psychological symptoms (anxiety or depression; n=6); three studies targeted physical symptoms (pain or sleep), and two studies included both physical and psychological symptoms (sleep, anxiety and depression; Burrai *et al.* 2019; Tsai *et al.* 2015). Psychological symptoms were significantly improved by passive interventions with ES ranged from 0.14 (Hudson *et al.* 2017) to 1.60 (Frih *et al.* 2017b). Passive interventions (i.e. listening to music and Holy Qur'an, CBT/psychological intervention, breathing program) significantly improved symptoms of depression in seven studies (Burrai *et al.* 2019; Cukor *et al.* 2014; Duarte *et al.* 2009; Frih *et al.* 2017b; Hernandez *et al.* 2018; Lerma *et al.* 2017; Tsai *et al.* 2015). Likewise, anxiety was significantly reduced by passive interventions such as listening to music or Holy Qur'an or CBT (Burrai *et al.* 2019; Frih *et al.* 2017b; Lerma *et al.* 2017; p<0.001, p<0.05 and p=0.007 respectively). Moreover, passive interventions (i.e. acupressure, listening to music and relaxation technique) significantly reduced pain (Burrai *et al.* 2019; Rambod *et al.* 2014; p<0.001 and p=0.01 respectively), improved sleep (Arab *et al.* 2016; Burrai *et al.* 2019; p<0.001 and p=0.008 respectively) and other symptoms like cramps and itching (p<0.001; Burrai *et al.* 2019) although not all ESs could be calculated. Passive interventions also significantly improved HRQoL (7 out of 11

studies) with three studies (Duarte *et al.* 2009; Frih *et al.* 2017b; Tsai *et al.* 2015) showing significant improvement in the mental health of HRQoL (p=0.004, p<0.05 and p=0.02, respectively) with medium to large EFs found. Three other studies (Cukor *et al.* 2014; Lerma *et al.* 2017; Rambod *et al.* 2014) showed significant improvement in the overall HRQoL in people receiving HD (p=0.04, p=0.004 and p=0.002 respectively) although ESs were inconsistent. Furthermore, one study showed significant improvement in both physical and mental health (HRQoL) in the intervention group (p<0.001 and p<0.001 respectively; Arab *et al.* 2016) however only mental health was significantly improved by the intervention (d=0.92, 95% CI 0.39 to 1.45).

DISCUSSION

This review found 18 studies using behavioural interventions that targeted symptoms and HRQoL in people receiving HD. Behavioural interventions were either active or passive types, and the majority of studies primarily targeted psychological rather than physical symptoms. The quality of the studies varied, and there was substantial heterogeneity which precluded being able to conduct a meta-analysis. Overall, passive interventions appeared to be effective in improving psychological symptoms and the mental-health component of HRQoL. Likewise, active interventions mainly aerobic or resistance exercise were shown to be effective in improving some physical symptoms, although there was very limited evidence of improvement in HRQoL.

The current review revealed that both anxiety and depression were better managed by passive interventions (e.g. listening to music, using CBT, psychological interventions and breathing program), which are in line with the findings from a previous systematic review indicating that psychological intervention significantly reduced

symptoms of depression in people receiving HD (Xing *et al.* 2016). Based on current findings, it makes intuitive sense that improvements in symptoms could be attributed to the fact that behavioural interventions are effective, important and preferred in managing psychological symptoms. People who prefer not to or are reluctant to take more medication for their psychological symptoms may benefit from behavioural interventions. Behavioural interventions encourage active involvement in self-managing health and may assist people with better overall management of their symptoms (Allegrante *et al.* 2019; Grady & Gough 2014).

This systematic review also discovered that less attention was given to the physical symptoms experienced by adults receiving HD. A probable explanation is that severe and more distressing physical symptoms were primarily managed through pharmacological interventions (Moledina & Perry-Wilson 2015). Equally, active behavioural interventions like aerobic exercise or resistance training are also useful in managing physical symptoms such as fatigue, pain, appetite, sleep and RLS. These findings are consistent with Zhao *et al.* (2019) who reported in their systematic review that exercise training had a favourable outcome on fatigue, anxiety and depression in people with ESKD receiving HD. However, there are few studies on the effect of active interventions on other physical symptoms as well as the overall symptom burden in this population. Thus, future clinical trials targeting the most prevalent, severe and distressing physical symptoms is required.

The current review showed that passive interventions might be effective in improving mental health as well as the overall HRQoL in people undergoing HD, although our findings are inconsistent with another systematic review (Xing *et al.* 2016). Active interventions included in this systematic review inconsistently affected HRQoL. Even other systematic reviews (Chung *et al.* 2017; Sheng *et al.* 2014) also demonstrated

unclear evidence to support active interventions as a strategy to improve HRQoL. This could be due to participants not recognising the benefits of continuing to perform the active intervention at home when not on HD.

Our review did not find any eligible study that used an educational intervention targeting symptom understanding, recognition and self-management to improve HRQoL in people undergoing HD. Educational interventions provide relevant information to improve the knowledge of the patient which can assist people in modifying behaviours to better self-manage their chronic disease (Ribeiro *et al.* 2015). As such, an educational intervention alone and/or in combination with behavioural interventions could be useful in reducing symptoms like fatigue, pain, and depression. For example, educational interventions have been shown to improve cancer-related fatigue (Bennett *et al.* 2016), and fatigue and depression in people with CKD not on dialysis (Kao *et al.* 2012). In a recent RCT to manage symptoms in people with type 2 diabetes, a symptom management education program significantly decreased diabetes symptom severity, improved self-care behaviours and HRQoL (Lin *et al.* 2019). Thus, further research to evaluate the effectiveness of an educational intervention to reduce symptom burden and improve HRQoL in people receiving HD is clearly needed.

Studies included in the current systematic review applied a variety of instruments to measure symptoms and HRQoL. Symptoms were mostly assessed using CKD-specific instruments, whereas generic instruments were used to measure HRQoL. The wide variety of instruments used restricts the comparison between studies. Therefore, appropriate and consistent instruments for measuring study outcomes are required to facilitate comparison and meta-analysis, and it will be an essential step to move forward in this area of research.

LIMITATION

We acknowledge that the search was limited to articles published between 2009-2019 and only in English language. The exclusion of studies in other languages may have limited our findings. Additionally, despite identifying all papers that met our inclusion criteria, we did not search the grey literature, meaning that unpublished studies with relevant results may have been missed. Furthermore, the various types of interventions, different comparators, and a variety of instruments used to measure outcomes, restricted meta-analyses being performed. Consequently, the findings from this systematic review need to be interpreted with caution. Finally, it was difficult to estimate the ES between intervention and control groups in all studies which reduces the generalisability of the findings of this review. Nevertheless, we strictly adhered to the robust processes of conducting an effectiveness systematic review.

IMPLICATIONS FOR CLINICAL PRACTICE

Frequency and severity of symptoms experienced by people on HD profoundly reduce HRQoL. There is some evidence found in this systematic review to support the use of various behavioural interventions to manage physical and psychological symptoms and to improve HRQoL. Active interventions like exercise aerobic or resistance training during HD sessions may be effective in reducing fatigue, pain, RLS while improving sleep and HRQoL, and patients in the studies seemed to tolerate these interventions during HD. Moreover, these interventions can be integrated into routine care and are suitable for nurses to deliver and/or for supervision. Caution is needed with people who have cardiovascular disease, and these patients ought to be declared medically suitable. Likewise, passive interventions (e.g. CBT, breathing technique, and listening to music), also may reduce symptoms of anxiety and depression. These

interventions do not add to the medication burden of those on HD with multiple medications. Nonetheless, such interventions may be challenging to integrate into routine care; for instance, CBT does require training to be competent to provide it. We recommend that appropriate training for renal healthcare providers, especially dialysis nurses about mental health issues and brief interventions may be useful as an initial step in managing psychological symptoms and improving HRQoL. Of interest, the studies using educational interventions were removed from this review due to low methodological quality. Given that nephrology nurses provide formal and informal patient education during HD, robust randomised controlled trials testing educational interventions targeting symptom understanding, recognition and self-management to improve HRQoL in this populations are urgently needed.

CONCLUSION

This systematic review identified a small number of studies that evaluated the effectiveness of behavioural interventions to reduce symptoms and improve HRQoL in people receiving HD. We found inconsistent results, and there was mixed effectiveness of behavioural interventions on symptoms and HRQoL, and passive behavioural interventions, in particular, were effective in managing psychological symptoms and the mental health component of HRQoL in this population. In this patient group, the most prevalent and severe symptom, fatigue, received limited attention from researchers, and we recommend that randomised controlled trials using a range of active and passive behavioural interventions and/or education for fatigue self-management strategies is undertaken. Furthermore, it is recommended that validated patient-reported outcome measures (PROMs) are used to measure change in fatigue severity and effect on activities of daily living as primary study endpoints.

CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

REFERENCES

Allegrante J. P., Wells M. T. & Peterson J. C. (2019). Interventions to Support Behavioral Self-Management of Chronic Diseases. *Annual Review of Public Health*, **40**(1), 127-146.

Almutary H., Bonner A. & Douglas C. (2013). Symptom burden in chronic kidney disease: a review of recent literature. *Journal of Renal Care*, **39**(3), 140-150.

Almutary H., Bonner A. & Douglas C. (2016a). Which patients with chronic kidney disease have the greatest symptom burden? A Comparative study of advanced CKD stage and dialysis modality. *Journal of Renal Care*, **42**(2), 73-82.

Almutary H., Douglas C. & Bonner A. (2016b). Multidimensional symptom clusters: an exploratory factor analysis in advanced chronic kidney disease. *Journal of Advanced Nursing*, **72**(10), 2389-2400.

Almutary H., Douglas C. & Bonner A. (2017). Towards a symptom cluster model in chronic kidney disease: A structural equation approach. *Journal of Advanced Nursing*, **73**(10), 2450-2461.

Arab Z., Shariati A. R., Asayesh H., *et al.* (2016). A sham-controlled trial of acupressure on the quality of sleep and life in haemodialysis patients. *Acupuncture in Medicine*, **34**(1), 2-6.

Astroth K. S., Russell C. L. & Welch J. L. (2013). Non-pharmaceutical fatigue interventions in adults receiving hemodialysis: a systematic review. *Journal of the American Nephrology Nurses' Association*, **40**(5), 407-427.

Bennett S., Pigott A., Beller E. M., *et al.* (2016). Educational interventions for the management of cancer-related fatigue in adults. *Cochrane Database for Systematic Reviews*, **11**, Cd008144.

Birdee G. S., Rothman R. L., Sohl S. J., *et al.* (2015). Feasibility and Safety of Intradialysis Yoga and Education in Maintenance Hemodialysis Patients. *Journal of Renal Nutrition*, **25**(5), 445-453.

Burrai F., Lupi R., Luppi M., *et al.* (2019). Effects of Listening to Live Singing in Patients Undergoing Hemodialysis: A Randomized Controlled Crossover Study. *Biological Research for Nursing*, **21**(1), 30-38.

Cao X., Tian L. & Lin C. (2017). Symptom clusters in patients receiving haemodialysis: a systematic review of observational studies. *Journal of Clinical Nursing*, **26**(17-18), 2545-2557.

Chan D., Green S., Fiatarone Singh M., *et al.* (2016). Development, feasibility, and efficacy of a customized exercise device to deliver intradialytic resistance

training in patients with end stage renal disease: Non-randomized controlled crossover trial. *Hemodialysis International*, **20**(4), 650-660.

Chung Y. C., Yeh M. L. & Liu Y. M. (2017). Effects of intradialytic exercise on the physical function, depression and quality of life for haemodialysis patients: a systematic review and meta-analysis of randomised controlled trials. *Journal of Clinical Nursing*, **26**(13-14), 1801-1813.

Cochrane Effective Practice and Organisation of Care (EPOC).(2018) "Reporting the effects of an intervention in EPOC reviews." Accessed 15 January.

Cox K. J., Parshall M. B., Hernandez S. H. A., *et al.* (2017). Symptoms among patients receiving in-center hemodialysis: A qualitative study. *Hemodialysis International*, **21**(4), 524-533.

Cukor D., Ver Halen N., Asher D. R., *et al.* (2014). Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. *Journal of the American Society of Nephrology* **25**(1), 196-206.

Duarte P. S., Miyazaki M. C., Blay S. L., *et al.* (2009). Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients. *Kidney International*, **76**(4), 414-21.

Frih B., Jaafar H., Mkacher W., *et al.* (2017a). The effect of interdialytic combined resistance and aerobic exercise training on health related outcomes in chronic hemodialysis patients: The Tunisian randomized controlled study. *Frontiers in Physiology*, **8**(MAY).

Frih B., Mkacher W., Bouzguenda A., *et al.* (2017b). Effects of listening to Holy Qur'an recitation and physical training on dialysis efficacy, functional capacity, and psychosocial outcomes in elderly patients undergoing haemodialysis. *The Libyan Journal of Medicine*, **12**(1), 1372032-1372032.

Giannaki C. D., Sakkas G. K., Karatzaferi C., *et al.* (2013). Effect of exercise training and dopamine agonists in patients with uremic restless legs syndrome: a six-month randomized, partially double-blind, placebo-controlled comparative study. *BMC Nephrology*, **14**, 194-194.

Grady P. A. & Gough L. L. (2014). Self-management: a comprehensive approach to management of chronic conditions. *American Journal of Public Health*, **104**(8), e25-e31.

Henson A., Gillespie B., McCarthy A., *et al.* (2010). Intradialytic exercise: A feasibility study. *Renal Society of Australasia Journal*, **6**(1).

Hernandez R., Burrows B., Wilund K., *et al.* (2018). Feasibility of an Internet-based positive psychological intervention for hemodialysis patients with symptoms of depression. *Social Work in Health Care*, **57**(10), 864-879.

Hudson J. L., Moss-Morris R., Norton S., *et al.* (2017). Tailored online cognitive behavioural therapy with or without therapist support calls to target

psychological distress in adults receiving haemodialysis: a feasibility randomised controlled trial. *Journal of Psychosomatic Research*, **102**, 61-70.

Jankowska-Polańska B., Uchmanowicz I., Wysocka A., *et al.* (2016). Factors affecting the quality of life of chronic dialysis patients. *European Journal of Public Health*, **27**(2), 262-267.

Joboshi H. & Oka M. (2017). Effectiveness of an educational intervention (the Encourage Autonomous Self-Enrichment Program) in patients with chronic kidney disease: A randomized controlled trial. *International Journal of Nursing Studies*, **67**, 51-58.

Kao Y.-H., Huang Y.-C., Chen P.-Y., *et al.* (2012). The effects of exercise education intervention on the exercise behaviour, depression, and fatigue status of chronic kidney disease patients. *Health Education*, **112**(6), 472-484.

KauricKlein Z. (2019). Effect of yoga on physical and psychological outcomes in patients on chronic hemodialysis. *Complementary Therapies in Clinical Practice*, **34**, 41-45.

Krespi M. R., Oakley D., Bone M., *et al.* (2009). The effects of visual imagery on adjustment and quality in life of hemodialysis patients. *Turkish Journal of Psychiatry* **20**(3), 255-68.

Kristy S., Toni L. G. & Ann L. H. (2018) "Behavioural management of physical and psychological symptoms in palliative care." In *Perspectives on Behavioural Interventions in Palliative and End-of-Life Care*, edited by Brian D Carpenter Rebecca S Allen, Morgan K. Eichorst, 48-69. London: Routledge. https://doi-org.ezp01.library.qut.edu.au/10.4324/9781315212265.

Leidy N. K., Kimel M., Ajagbe L., *et al.* (2014). Designing trials of behavioral interventions to increase physical activity in patients with COPD: Insights from the chronic disease literature. *Respiratory Medicine*, **108**(3), 472-481.

Lerma A., Perez-Grovas H., Bermudez L., *et al.* (2017). Brief cognitive behavioural intervention for depression and anxiety symptoms improves quality of life in chronic haemodialysis patients. *Psychology and Psychotherapy*, **90**(1), 105-123.

Lin L. Y., Lee B. O. & Wang R. H. (2019). Effects of a Symptom Management Program for Patients With Type 2 Diabetes: Implications for Evidence-Based Practice. *Worldviews on Evidence-Based Nursing*, **16**(6), 433-443.

McCain N. L. & Zeller J. M. (1996). Psychoneuroimmunological studies in HIV disease. *Annual Review of Nursing Research*, **14**, 23-55.

Mills K. T., Xu Y., Zhang W., *et al.* (2015). A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney International*, **88**(5), 950-957.

Mitrou G. I., Grigoriou S. S., Konstantopoulou E., *et al.* (2013). Exercise training and depression in ESRD: a review. *Seminars in Dialysis*, **26**(5), 604-13.

Moher D., Liberati A., Tetzlaff J., *et al.* (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Medicine*, **6**(7), e1000097.

Moledina D. G. & Perry-Wilson F. (2015). Pharmacologic Treatment of Common Symptoms in Dialysis Patients: A Narrative Review. *Seminars in Dialysis*, **28**(4), 377-383.

Moraes C., Marinho S., Lobo J. C., *et al.* (2015). Effects of resistance exercise training on acyl-ghrelin and obestatin levels in hemodialysis patients. *Renal Failure*, **37**(5), 851-857.

Mortazavi M., Vahdatpour B., Ghasempour A., *et al.* (2013). Aerobic exercise improves signs of restless leg syndrome in end stage renal disease patients suffering chronic hemodialysis. *The Scientific World Journal*, **2013**.

Mukakarangwa M. C., Chironda G., Bhengu B., *et al.* (2018). Adherence to Hemodialysis and Associated Factors among End Stage Renal Disease Patients at Selected Nephrology Units in Rwanda: A Descriptive Cross-Sectional Study. *Nursing Research Practice*, **2018**.

Ouzouni S., Kouidi E., Sioulis A., *et al.* (2009). Effects of intradialytic exercise training on health-related quality of life indices in haemodialysis patients. *Clinical Rehabilitation*, **23**(1), 53-63.

Pellizzaro C. O., Thomé F. S. & Veronese F. V. (2013). Effect of peripheral and respiratory muscle training on the functional capacity of hemodialysis patients. *Renal Failure*, **35**(2), 189-197.

Rambod M., Sharif F., Pourali-Mohammadi N., *et al.* (2014). Evaluation of the effect of Benson's relaxation technique on pain and quality of life of haemodialysis patients: a randomized controlled trial. *International Journal of Nursing Studies*, **51**(7), 964-973.

Rebollo Rubio A., Morales Asencio J. M. & Eugenia Pons Raventos M. (2017). Depression, anxiety and health-related quality of life amongst patients who are starting dialysis treatment. *Journal of Renal Care*, **43**(2), 73-82.

Ribeiro C. D., Resqueti V. R., Lima Í., *et al.* (2015). Educational interventions for improving control of blood pressure in patients with hypertension: a systematic review protocol. *BMJ Open*, **5**(3), e006583.

Sertoz O. O., Asci G., Toz F., *et al.* (2009). Planning a social activity to improve psychological well-being and quality of life of hemodialysis patients: a pilot study. *Therapeutic Apheresis and Dialysis*, **13**(4), 366-372.

Shen K., Cho Y., Pascoe E. M., *et al.* (2017). The SIESTA trial: A randomized study investigating the efficacy, safety, and tolerability of acupressure versus sham therapy for improving sleep quality in patients with end-stage kidney disease on hemodialysis. *Evidence-based Complementary and Alternative Medicine*, **2017**.

Sheng K., Zhang P., Chen L., *et al.* (2014). Intradialytic Exercise in Hemodialysis Patients: A Systematic Review and Meta-Analysis. *American Journal of Nephrology*, **40**(5), 478-490.

Shim H. Y. & Cho M.-K. (2018). Factors influencing the quality of life of haemodialysis patients according to symptom cluster. *Journal of Clinical Nursing*, **27**(9-10), 2132-2141.

Stanley R., Leither T. W. & Sindelir C. (2011). Benefits of a holistic breathing technique in patients on hemodialysis. *Journal of the American Nephrology Nurses' Association*, **38**(2), 149-152.

Tsai S. H., Wang M. Y., Miao N. F., *et al.* (2015). CE: original research: The efficacy of a nurse-led breathing training program in reducing depressive symptoms in patients on hemodialysis: a randomized controlled trial. *The American Journal of Nursing*, **115**(4), 24.

Tufanaru C., Munn Z., Aromataris E., *et al.* (2017) "Chapter 3: Systematic reviews of effectiveness." In *Joanna Briggs Institute Reviewer's Manual*, edited by Munn Z Aromataris E: The Joanna Briggs Institute. https://reviewersmanual.joannabriggs.org/.

Webster A. C., Nagler E. V., Morton R. L., *et al.* (2017). Chronic Kidney Disease. *The Lancet*, **389**(10075), 1238-1252.

Xing L., Chen R., Diao Y., *et al.* (2016). Do psychological interventions reduce depression in hemodialysis patients?: A meta-analysis of randomized controlled trials following PRISMA. *Medicine (Baltimore)*, **95**(34), e4675.

Zangi H. A., Ndosi M., Adams J., *et al.* (2015). EULAR recommendations for patient education for people with inflammatory arthritis. *Annals of the Rheumatic Diseases*, **74**(6), 954.

Zhao Q. G., Zhang H. R., Wen X., *et al.* (2019). Exercise interventions on patients with end-stage renal disease: a systematic review. *Clinical Rehabilitation*, **33**(2), 147-156.

Zins S., Gross R. & Hooke M. C. (2018). Complementary Therapies for Pain Among Individuals Receiving Hemodialysis: A Systematic Review. *Nephrology Nursing Journal*, **45**(1), 13-23.

Zyoud S. e. H., Daraghmeh D. N., Mezyed D. O., *et al.* (2016). Factors affecting quality of life in patients on haemodialysis: a cross-sectional study from Palestine. *BMC Nephrology*, **17**(1), 44.

Figure

Figure 1: PRISMA flowchart of identified studies for inclusion (Moher *et al.* (2009)

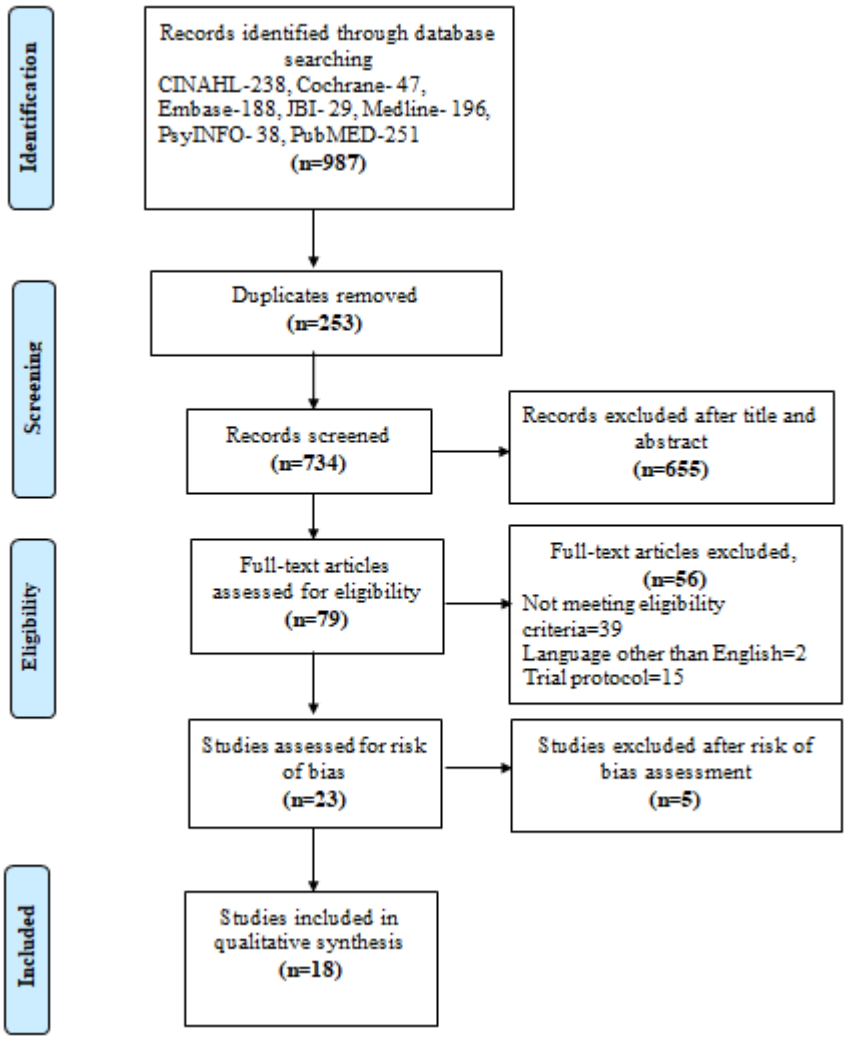

Table 1: Study Characteristics

Author/s, Year, Country	Study Design	Sample size	Baseline Characteristics of Participants (Age[years]; [Mean±SD; median (IQR)], Male [%]; Dialysis duration [DD]; [months]; [Mean±SD; median (IQR)])	Intervention/Control	Main Results	
					Symptoms	HRQoL
Arab *et al.* (201	Randomised contro	93	Age: NR	*Intervention*:	*Sleep* • Significant	• Significant

6) Iran	l trial		Male: 52.68 DD: NR		Acupressure *Comparators:* 1. Sham acupressure 2. Standard care *Format*: Individual, face-to-face during dialysis *Delivered by*: Researcher trained by the acupuncturist *Duration*: 3 times a week for 4 weeks	impro vemen t in sleep in the interve ntion group compa red with the sham acupre ssure and contro l group (p<0.001)	impro veme nt in the physi cal and menta l health of HRQ oL after acupr essure (p<0.001) • Betw een-group comp arison not report ed
Birde e *et al.* (201 5) Unite d State s	Rando mised contro l trial	31	*Interventi on group* Age: 48.2 (26.4) Male: 50 DD: NR	*Comparison group* Age: 48.0 (26) Male: 62 DD: NR	*Intervention*: Intradialytic Yoga *Comparison:* Standard dialysis education *Format*: Individual, face-to-face during dialysis *Delivered by*: Yoga teacher	*Fatigue and sleep* • No signifi cant impro vemen t in fatigue and sleep in the yoga group compa red with the educat	• No signif icant chang es in the physi cal and menta l wellb eing of HRQ oL

					Duration: 3 times a week for 12 weeks	ion group	
Burrai *et al.* (2019) Italy	A randomised control crossover trial	24	Age: 62.3± 2.8 Male:62.5 DD: 75.6±12.0		*Intervention*: Listening to live music *Control:* Standard care *Format*: Group, face-to-face during dialysis *Delivered by*: Dialysis nurse *Duration*: 15 minutes for 15 days	*Sleep, pain, cramps, itching, anxiety and depression* • Symptoms of sleep (p=0.008), pain, cramps, itching, anxiety and depression (p<0.001) significantly reduced in the intervention group compared with control	• No statistically significant changes in the physical and mental health of HRQoL
Chan *et al.* (2016) Austr	Non-randomised crossover	15	Age: 71.3± 11.0 Male:59		*Intervention*: Progressive resistance	*Depression* • No signifi	• Signif icant impro

alia	trial		DD: 24(41)	training *Control*: Standard care *Format*: Individual, face-to-face during dialysis *Delivered by*: Exercise physiologist *Duration*: 3 times a week for 12 weeks	cant improvement in depression in the intervention group compared with control	vement in role physical (p=0.035), social functioning (p=0.029) and role emotional (p<0.001) subscale of HRQoL in the intervention group compared with control
Cukor *et al.* (2014) United States	Randomised control trial	65	Age: NR Male:27.3 DD: 50.6(31)	*Intervention*: CBI *Control:* Intervention waitlist *Format*: Individual, face-to-face during dialysis *Delivered by*: Psychologist *Duration*:	*Depression* • Significant decrease in BDI scores in the intervention group compared with the intervention	• Significant improvement in overall HRQoL in the intervention group compared with partic

					60 minutes weekly for 3 months	waitlist condition (p=0.03)	ipants intervention waitlist condition (p=0.04)
Duarte *et al.* (2009) Brazil	Randomised control trial	74	*Intervention group* Age: 52.4±15.9 Male:36.6 DD: 23(42.5)	*Control group* Age: 54.0±12.7 Male:45.5 DD:25.5(47.5)	*Intervention*: CBI *Control*: Standard care *Format*: Group, face-to-face, non-dialysis day *Delivered by*: Psychologist *Duration*: 3 months	*Depression* • Significant reduction in the total BDI score after 9 months of intervention (p<0.001) and the change was significant in the intervention group compared with control (p=0.002)	• A significant change in the mental health of HRQoL in the intervention group compared with control (p=0.004)
Frih *et al.* (2017a) Tuni	Randomised control trial	41	*Intervention group* Age:	*Control group* Age:	*Intervention*: Combined aerobic and resistance exercise	*Anxiety and depression* • Signifi	• Significant increa

sia			64.2±3.4 Male:100 DD: 72.7±12.7	65.2±3.1 Male:100 DD:73.6±13.4	training *Control*: Standard care *Format*: Individual, face-to-face, non-dialysis day *Delivered by*: Physiotherapist *Duration*: 4 times/ week for 4 months	cant decrease in the anxiety and depression score of HADS (p<0.001, p<0.001, respectively) in the intervention group compared with control	se in physical and mental component of HRQoL in the intervention group compared with control (p=0.003, p<0.001 respectively)
Frih *et al.* (2017b) Tunisia	Randomised control trial	53	*Intervention group* Age: 65.4±3.2 Male:100 DD: 75.7±11.4	*Control group* Age: 64.5±4.2 Male:100 DD:76.7±13.2	*Intervention*: Listening to the Holy Quran in combination with resistance training *Control:* Resistance training *Format*: Individual, through the headphone, during dialysis *Delivered*	*Anxiety and depression* • Significant reduction in anxiety, depression in the final measurement in the intervention group compared	• Significant improvement in the mental wellbeing of HRQoL in the intervention group compared with the

					by: Reader *Duration*: 3 times a week for 24 weeks	with the control group (p<0.05)	control group (p<0.05)
Giannaki *et al.* (2013) Greece	Randomised control trial	29	*Intervention group* Age: 56.4± 12.5 Male: 73.33 DD: 46.8± 15.6	*Comparator group 1* Age: 55.7±10.4 Male:57.14 DD: 48±20.4	*Comparator group 2* Age: 56.8± 16.5 Male: 71.4 DD: 43.2± 18	*Intervention*: Intradialytic exercise *Comparator:* 1. Dopamine agonist (DA) intervention 2. Placebo *Format*: Individual, face-to-face, during dialysis *Delivered by*: NR *Duration*: 3 times a week for 6 months	*RLS, sleep, depression* • Significant reduction in RLS (p=0.012) and depressive symptoms (p=0.003) in exercise and DA intervention group compared with placebo • Significant improvement in sleep (p=0.016) in DA intervention compared to	• Improvement in the physical health of HRQoL in exercise (p<0.001) and DA intervention (p=0.003) group • Improvement in the mental health of HRQoL in DA intervention (p=0.004) compared with exercise and placebo

							exercise and placebo	
Henson *et al.* (2010) Australia	Pre-Post test design	13	Age: 54±21.6 Male:75 DD: NR			*Intervention*: Intradialytic exercise *Control:* NA *Format*: Individual, face-to-face, during dialysis *Delivered by*: Physiotherapist *Duration*: 3 times a week for 16 weeks	*Fatigue* • No significant improvement in any fatigue component after exercise intervention (p=0.11)	• Among 8 participants, 4 showed improvement, 2 reported no change and 2 demonstrated decreased in HRQoL • Significance testing not done
Hernandez *et al.* (2018) United States	Pre-Post test design	12	Age: 57.43±12.12 Male:50 DD: 43.2±35.8			*Intervention*: Psychological intervention *Control:* NA *Format*: Individual, web-based, during	*Depression* • Significant reduction in depressive symptoms with an averag	• Improvement in the overall, mental and physical health of

					dialysis *Delivered:* Online *Duration*: 3 times a week, 20-30 minutes per session for 16 weeks	e 4-point drop in the overall score (p=0.04) after the intervention	HRQoL not reported
Hudson *et al.* (2017) UK	Randomised control trial	23	*Intervention group* Age: 49±11.4 Male:56 DD: 23.72±30.14	*Control group* Age: 47±14.2 Male:71 DD:33.70±26.80	*Intervention*: CBT with therapist supported *Control:* CBT only *Format*: Individual, online during dialysis *Delivered:* Psychological wellbeing practitioner *Duration*: 60 minutes for 6 weeks	*Anxiety and depression* • Minimal changes in anxiety and depression score between the intervention and control group. • Significance testing not performed	• Greater improvement in five domains (mood, mobility, pain, self-care and usual activities) of HRQOL in the intervention group compared with control. • Significance testing not

							perfor med
Lerm a *et al.* (201 7) Unite d State s	Rando mised contro l trial	49	*Interventio n group* Age: 41.8±14.7 Male:48.4 DD: 12.1±10.6	*Control group* Age: 41.7±15.1 Male:44.4 DD:13.0±9.2	*Intervention*: CBT *Control:* Standard care *Format*: Group, face-to-face on non-dialysis day *Delivered:* Therapist *Duration*: 5 Weeks	*Anxiety and depressi on* • Reduc tion in the depres sive sympt oms by 77% in the interve ntion group and by 44% in the contro l group with a relativ e risk of 1.7 betwe en groups (p=0.0 07). • Reduc tion in the sympt oms of anxiet y by 71% in the interve ntion group compa red with	• Signif icant impro veme nt in overal l HRQ oL in the interv ention group comp ared with contr ol group s after 9 weeks of interv ention (p=0. 004).

						28% in the control group with a relative risk of 2.6 between groups (p=0.003).	
Moraes *et al.* (2015) Brazil	Quasi-experimental design	52	*Intervention group* Age:44.98 ±12.80 Male:56.75 DD: 57(183)	*Control group* Age: 49.8±10.5 Male:66.66 DD:57(142)	*Intervention*: Resistance exercise training *Control:* Standard care *Format*: Individual, face-to-face, during dialysis *Delivered by*: Physical educator *Duration*: 3 times/week for 6 months	*Appetite* • Significant decrease in obestatin level and increase in acyl-ghrelin level, which control appetite in the intervention group (p<0.05) • Between-group comparison not reported	• Significant improvement in the physical role of HRQoL in the intervention group (p<0.05) compared with control

Pellizzaro *et al.* (2013) Brazil	Randomised control trial	39	*Intervention group* Age: 43±13.8 Male: 73 DD: 60(108)	*Control group (1)* Age: 48.9±10.1 Male:50 DD: 54(109.3)	*Control group (2)* Age: 51.9± 11.6 Male: 57 DD: 54(66)	*Intervention*: Respiratory Muscle training *Control:* 1. Peripheral muscle training 2. Standard care *Format*: Individual, face-to-face, during dialysis *Delivered by*: NR *Duration*: 3 times a week for 10 Weeks	• Significant improvement in fatigue (p=0.002), sleep (p<0.001), pain (p<0.001) and list of symptoms/problems (p=0.014) in intervention group compared with control. • Authors did not report the physical and mental health dimension of HRQoL.	
Rambod *et al.* (2014) Iran	Randomised control trial	81	*Intervention group* Age: 49.07±13.31 Male:67.4 DD: 36.53±36.05	*Control group* Age: 50.72±11.68 Male:55.8 DD:47.67±40.42		*Intervention*: Benson's relaxation technique *Control:* Standard care *Format*: Individual, face-to-face during dialysis *Delivered by*: Interventionist	*Pain* • Significant decrease in pain in the intervention group compared with control (F= 6.03, p=0.01).	• Significant improvement in overall HRQoL in the intervention group compared with the control

					Duration: 8 Weeks		group (F=10.20, *p*=0.002)
Shen *et al.* (2017) Australia	Randomised control trial	40	*Intervention group* Age: 58.6±11.9 Male:71.4 DD: 46(88)	*Control group* Age: 51.6±17.9 Male:55 DD:21.5(43.5)	*Intervention*: Acupressure *Control:* Sham acupressure *Format*: Individual, face-to-face during dialysis *Delivered by*: Traditional Chinese medicine health practitioner *Duration*: 4 Weeks	*Sleep* • No significances between the intervention and control group in sleep	• No significances in terms of HRQoL in the intervention and control group
Tsai *et al.* (2015) Taiwan	Randomised control trial	57	*Intervention group* Age: 64.94±9.51 Male:50 DD: 68.6± 66.6	*Control group* Age: 61.08±11.18 Male:48 DD:75.36 ± 61.2	*Intervention*: Breathing program *Control:* Standard care *Format*: Individual, face-to-face during dialysis *Delivered by:* Dialysis	*Depression and sleep* • Significant decrease in depression scores in the intervention group compared	• Significant increase in role–emotional subscale (F=7.41, *p*=0.009) and

					Nurse *Duration*:10 minutes, 2 times a week for 4 weeks	with the control group (F= 6.97, *p*=0.01). • No significant changes in sleep after intervention in both groups	the mental health of HRQoL (F=6.33, *p*=0.02) in the intervention group compared with the control group

NA: Not applicable; NR: Not reported; HRQoL: Health-related quality of life, CBT: Cognitive Behavioural Therapy; CBI: Cognitive behavioural intervention

Table 2: Symptoms targeted, and interventions used to relieve symptoms

Symptom	**Behavioural Interventions**		**Study Authors**
	Active Intervention	**Passive Intervention**	
Fatigue	Aerobic exercise, muscle training		Henson *et al.* (2010); Pellizzaro *et al.* (2013)
Pain	Muscle training	Relaxation technique, Listening to music	Pellizzaro *et al.* (2013); Rambod *et al.* (2014); Burrai *et al.* (2019)

Sleep disturbance	Aerobic exercise, muscle training	Acupressure, listening to music, Breathing Program	Arab *et al.* (2016); Burrai *et al.* (2019); Giannaki *et al.* (2013); Pellizzaro *et al.* (2013); Shen *et al.* (2017); Tsai *et al.* (2015)
Restless leg syndrome	Aerobic exercise		Giannaki *et al.* (2013)
Anorexia	Resistance exercise training		Moraes *et al.* (2015)
Cramps		Listening to music	Burrai *et al.* (2019)
Itching		Listening to music	Burrai *et al.* (2019)
Anxiety	Exercise (aerobic and resistance)	Listening to music and holy Qur'an, CBT/CBI	Burrai *et al.* (2019); Frih *et al.* (2017a); Frih *et al.* (2017b); Hudson *et al.* (2017); Lerma *et al.* (2017)
Depression	Aerobic exercise, Progressive resistance training	Listening to music and holy Qur'an, CBT/psychological intervention, breathing program	Burrai *et al.* (2019); Chan *et al.* (2016); Cukor *et al.* (2014); Duarte *et al.* (2009); Frih *et al.* (2017a); Frih *et al.* (2017b); Giannaki *et al.* (2013); Hernandez *et al.* (2018); Hudson *et al.* (2017); Lerma *et al.* (2017); Tsai *et al.* (2015)