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Interventions for improving sleep quality in people with chronic kidney disease (Review)

Natale P, Ruospo M, Saglimbene VM, Palmer SC, Strippoli GFM

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[Intervention Review]

Interventions for improving sleep quality in people with chronic kidney disease

Patrizia Natale^{1,2}, Marinella Ruospo¹, Valeria M Saglimbene^{1,3}, Suetonia C Palmer⁴, Giovanni FM Strippoli^{1,2,3,5,6}

¹Medical Scientific Office, Diaverum, Lund, Sweden. ²Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy. ³Sydney School of Public Health, The University of Sydney, Sydney, Australia. ⁴Department of Medicine, University of Otago Christchurch, Christchurch, New Zealand. ⁵Diaverum Academy, Bari, Italy. ⁶Cochrane Kidney and Transplant, Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, Australia

Contact address: Giovanni FM Strippoli, Cochrane Kidney and Transplant, Centre for Kidney Research, The Children's Hospital at Westmead, Westmead, NSW, 2145, Australia. giovanni.strippoli@uniba.it, gfmstrippoli@gmail.com.

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ABSTRACT

Background

Sleep disorders are commonly experienced by people with chronic kidney disease (CKD). Several approaches for improving sleep quality are used in clinical practice including relaxation techniques, exercise, acupuncture, and medication.

Objectives

To assess the effectiveness and associated adverse events of interventions designed to improve sleep quality among adults and children with CKD including people with end-stage kidney disease (ESKD) treated with dialysis or kidney transplantation.

Search methods

We searched the Cochrane Kidney and Transplant Register of Studies up to 8 October 2018 with the Information Specialist using search terms relevant to this review. Studies in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE, conference proceedings, the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Selection criteria

We included randomised controlled trials (RCTs) or quasi-randomised RCTs of any intervention in which investigators reported effects on sleep quality. Two authors independently screened titles and abstracts of identified records.

Data collection and analysis

Two review authors independently extracted data and assessed the risk of bias for included studies. The primary outcomes were sleep quality, sleep onset latency, sleep duration, sleep interruption, and sleep efficiency. Risks of bias were assessed using the Cochrane tool. Evidence certainty was assessed using the GRADE approach. We calculated treatment estimates as risk ratios (RR) for dichotomous outcomes or mean difference (MD) or standardised MD (SMD) for continuous outcomes to account for heterogeneity in measures of sleep quality.

Main results

Sixty-seven studies involving 3427 participants met the eligibility criteria. Thirty-six studies involving 2239 participants were included in meta-analyses. Follow-up for clinical outcomes ranged between 0.3 and 52.8 weeks (median 5 weeks). Interventions included relaxation techniques, exercise, acupuncture, cognitive-behavioural therapy (CBT), educational interventions, benzodiazepine treatment,

dopaminergic agonists, telephone support, melatonin, reflexology, light therapy, different forms of peritoneal dialysis, music, aromatherapy, and massage. Incomplete reporting of key methodological details resulted in uncertain risk of bias in many studies.

In very low certainty evidence relaxation techniques had uncertain effects on sleep quality and duration, health-related quality of life (HRQoL), depression, anxiety, and fatigue. Studies were not designed to evaluate the effects of relaxation on sleep latency or hospitalisation. Exercise had uncertain effects on sleep quality (SMD -1.10, 95% CI -2.26 to 0.05; $I^2 = 90\%$; 5 studies, 165 participants; very low certainty evidence). Exercise probably decreased depression (MD -9.05, 95% CI -13.72 to -4.39; $I^2 = 0\%$; 2 studies, 46 participants; moderate certainty evidence) and fatigue (SMD -0.68, 95% CI -1.07 to -0.29; $I^2 = 0\%$; 2 studies, 107 participants; moderate certainty evidence). Compared with no acupressure, acupressure had uncertain effects on sleep quality (Pittsburgh Sleep Quality Index (PSQI) scale 0 - 21) (MD -1.27, 95% CI -2.13 to -0.40; $I^2 = 89\%$; 6 studies, 367 participants; very low certainty evidence). Acupressure probably slightly improved sleep latency (scale 0 - 3) (MD -0.59, 95% CI -0.92 to -0.27; $I^2 = 0\%$; 3 studies, 173 participants; moderate certainty evidence) and sleep time (scale 0 - 3) (MD -0.60, 95% CI -1.12 to -0.09; $I^2 = 68\%$; 3 studies, 173 participants; moderate certainty evidence), although effects on sleep disturbance were uncertain as the evidence certainty was very low (scale 0 - 3) (MD -0.49, 95% CI -1.16 to 0.19; $I^2 = 97\%$). In moderate certainty evidence, acupressure probably decrease fatigue (MD -1.07, 95% CI -1.67 to -0.48; $I^2 = 0\%$; 2 studies, 137 participants). Acupressure had uncertain effects on depression (MD -3.65, 95% CI -7.63 to 0.33; $I^2 = 27\%$; 2 studies, 137 participants; very low certainty evidence) while studies were not designed to evaluate the effect of acupressure on HRQoL, anxiety, or hospitalisation. It was uncertain whether acupressure compared with sham acupressure improved sleep quality (PSQI scale 0 to 21) because the certainty of the evidence was very low (MD -2.25, 95% CI -6.33 to 1.82; $I^2 = 96\%$; 2 studies, 129 participants), but total sleep time may have been improved (SMD -0.34, 95% CI -0.73 to 0.04; $I^2 = 0\%$; 2 studies, 107 participants; low certainty evidence). ^{2 = 2} There were no studies designed to directly examine and/or correlate efficacy of any interventions aimed at improving sleep that may have been attempted for the spectrum of sleep disordered breathing. No studies reported treatment effects for children. Adverse effects of therapies were very uncertain.

Authors' conclusions

The evidence base for improving sleep quality and related outcomes for adults and children with CKD is sparse. Relaxation techniques and exercise had uncertain effects on sleep outcomes. Acupressure may improve sleep latency and duration, although these findings are based on few studies. The effects of acupressure were not confirmed in studies in which sham acupressure was used as the control. Given the very low certainty evidence, future research will very likely change the evidence base. Based on the importance of symptom management to patients, caregivers and clinicians, future studies of sleep interventions among people with CKD should be a priority.

PLAIN LANGUAGE SUMMARY

Interventions to improve sleep in adults and children with kidney disease

What is the issue?

People with kidney disease can have severe sleep problems related to use of medications, depression, anxiety, pain, and itch that impact on the quality of sleep itself, including the time it takes to get to sleep, staying asleep, and the total time spent sleeping. Kidney disease is linked to sleep disordered breathing that can decrease sleep quality. We looked at whether treatment could help improve the quality of sleep for people who have kidney disease. We looked for studies that included children and adults with kidney disease, including those who were treated with dialysis or a kidney transplant.

What did we do?

We looked at electronic databases to find research studies of any treatment that was designed to help with sleep problems. Studies needed to be randomised (in other words, patients needed to have an equal chance that they might receive one of the treatments in the study). We collected information from the studies and combined this to identify whether treatment was helpful or if there were important side-effects. We looked at how certain we could be that the treatments had any effects based on how well the studies were conducted (quality). The information in this review is up to date as of October 2018.

What did we find?

We found 67 studies that involved 3427 adults. We found no studies for children. The treatments for sleep included relaxation, exercise, medicines, education, psychological support, acupressure, music, aromatherapy, and massage. Generally, the studies were small and most did not tell us about the benefits and safety of the treatments. We did not find good information about relaxation, exercise, or medicines. We found that acupressure may reduce the amount of time it takes to get to sleep and may increase the time spent asleep. But these effects on sleep were not seen when acupressure was compared against "pretend" or "sham" acupressure. There was not enough information to learn about side-effects of treatments, or to know about treatments that are designed to help improve breathing when asleep.

Conclusions

Information about ways to help improve sleep for people with kidney disease is not ready to help patients directly. New research is very likely to change our knowledge about treatments for sleep among people with kidney disease.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Summary of findings: relaxation versus control for sleep outcomes in people with chronic kidney disease (CKD)

Relaxation versus control for sleep outcomes in people with CKD

Patient or population: people with CKD

Intervention: relaxation¹

Comparison: without relaxation technique/training

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Without relaxation training/technique	Relaxation training/technique				
Sleep quality PSQI (median follow-up: 8 weeks)	The mean sleep quality index score ranged across control groups from 1.53 to 11.09	The mean sleep quality index score in the intervention groups was 1.62 lower (95% CI -5.03 to 1.79) A lower score is indicative of higher sleep quality	MD -1.62 (95% CI -5.03 to 1.79)	259 (4)	⊕⊕⊕⊕ Very low ^{2 3 4}	It is very uncertain whether relaxation makes any difference to sleep quality
Sleep latency PSQI (median follow-up: 8 weeks)	Only one study reported sleep latency	Not estimable as only a single study reported this measure	Not estimable.	Insufficient data observations	Not estimable	Studies were not designed to measure effects of relaxation on sleep latency
Quality of life Quality of Life Index - dialysis version and Medical Outcome Studies 36-Item Short Form Health Survey (median follow-up: 6 weeks)	The mean quality of life index score ranged across control groups from 17.73 to 43.08	The mean quality of life index score in the intervention groups was 0.47 higher (95% CI -0.09 to 1.04) A higher score is indicative of higher perceived quality of life	SMD 0.47 (95% CI -0.09 to 1.04)	138 (2)	⊕⊕⊕⊕ Low ^{4 5}	It is uncertain whether relaxation makes any difference to quality of life

Depression Center for Epidemiologic Studies Depression Scale and The Beck Depression Inventory II (median follow-up: 6 weeks)	The mean depression index score ranged across control groups from 9.1 to 9.56	The mean depression index score in the intervention groups was 0.04 higher (95% -1.27 to 1.35) A higher score is indicative of more depressive symptoms	SMD 0.04 (95% CI -1.27 to 1.35)	108 (2)	⊕⊕⊕⊕ Very low ^{4 6}	It is very uncertain whether relaxation makes any difference to depressive symptoms
Anxiety Beck Anxiety Inventory and Spielberger State-Trait Anxiety Inventory (median follow-up: 8 weeks)	The mean anxiety index score ranged across control groups from 31.61 to 34.9	The mean anxiety index score in the intervention groups was 0.11 higher (95% CI -0.55 to 0.77) A higher score is indicative of more anxiety symptoms	SMD 0.11 (95% CI -0.55 to 0.77)	119 (2)	⊕⊕⊕⊕ Very low ^{4 5 7}	It is very uncertain whether relaxation makes any difference to anxiety
Fatigue PROMIS-Fatigue Short Form 1.0 and Rhoten and Piper fatigue (median follow-up: 8 weeks)	The mean fatigue score ranged across control groups from 55.5 to 81.17	The mean fatigue score in the intervention groups was 0.61 lower (95% CI -2.09 to 0.87) A higher score is indicative of worse fatigue	SMD -0.61 (95% CI -2.09 to 0.87)	119 (2)	⊕⊕⊕⊕ Very low ^{4 6}	It is very uncertain whether relaxation makes any difference to fatigue
Hospitalisation (median follow-up: 4 weeks)	Not estimable ⁸	Not estimable	Not estimable.	Insufficient data observations	Not estimable	Studies were not designed to measure effects of relaxation on hospitalisation

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **MD:** mean difference; **SMD:** standardised mean difference; **PSQI:** Pittsburgh Sleep Quality Index

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Relaxation techniques included progressive muscle relaxation, nurse-led breathing training, mindfulness, and the Benson relaxation technique.

² Three out of four studies had high or unclear risks of bias for allocation concealment, blinding of participants or investigators, and blinding of outcome assessment.

³ There was substantial heterogeneity in the findings of available studies that appeared related to a single study (Amini 2016).

- 4 The certainty in the evidence was downgraded due to imprecision in the treatment estimates, consistent with benefit or harm.
 5 There was moderate heterogeneity in the findings of available studies.
 6 There was substantial heterogeneity in the findings of available studies (two downgrades).
 7 Risks of bias for the included studies were high for allocation concealment.
 8 The estimated risk of hospitalisation was not estimable as a single study reported this outcome.

Summary of findings 2. Summary of findings: exercise versus control

Exercise compared to control for sleep outcomes in people with chronic kidney disease (CKD)

Patient or population: people with CKD

Settings: CKD

Intervention: exercise¹

Comparison: without exercise

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Without exercise	Exercise				
Sleep quality PSQI, ESS and tri-axial accelerometer (median follow-up: 26.4 weeks)	The mean sleep quality score ranged across control groups from 8.85 to 43.6	The mean sleep quality index score in the intervention groups was 1.10 lower (95% CI -2.26 to 0.05). A lower score is indicative of higher sleep quality	SMD -1.10 (95% CI -2.26 to 0.05)	165 (5)	⊕⊕⊕⊕ Very low ^{2 3 4}	It is very uncertain whether exercise makes any difference to sleep quality
Sleep latency	No data observations	Not estimable	No observations	Insufficient data observations	Not estimable	Studies were not designed to measure effects of exercise on sleep latency
Quality of life	No data observations	Not estimable	No observations	Insufficient data observations	Not estimable	Studies were not designed to measure effects of exercise on quality of life

Depression Zung Self-Rating Depression Scale (ZUNG) (median follow-up: 26.4 weeks)	The mean depression index score ranged across control groups from 43.7 to 43.71	The mean depression index score in the intervention groups was 9.05 lower (95% CI -13.72 to -4.39) A higher score is indicative of worse depressive symptoms	MD -9.05 (95% CI -13.72 to -4.39)	46 (2)	⊕⊕⊕⊖ Moderate ⁵	Exercise probably decreases depressive symptoms
Anxiety Beck Anxiety Inventory (BECK) (median follow-up: 8 weeks)	Only one study reported anxiety.	Not estimable as only a single study reported this measure	Not estimable.	Insufficient data observation	Not estimable	Studies were not designed to measure effects of exercise on anxiety
Fatigue PIPER Fatigue Scale (PFS) and Visual Analogue Scale (VAS) (median follow-up: 13.2 weeks)	The mean fatigue index score ranged across control groups from 6.9 to 81.17	The mean fatigue index score in the intervention groups was 0.68 lower (95% CI -1.07 to -0.29). A higher score is indicative of worse fatigue	SMD -0.68 (95% CI -1.07 to -0.29)	107 (2)	⊕⊕⊕⊖ Moderate ⁶	Exercise probably improves fatigue
Hospitalisation	No data observations	Not estimable	No observations.	Insufficient data observations	Not estimable	Studies were not designed to measure effects of exercise on hospitalisation

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI**: Confidence interval; **SMD**: standardised mean difference; **MD**: mean difference

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change the certainty in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on the certainty in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on the certainty in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Exercise interventions were aerobic exercise daily, exercise during HD, and yoga-based exercise

² All studies in this analysis had unclear methods for allocation concealment, and outcomes were not clearly blinded in two of three studies

³ The certainty in the evidence was downgraded due to imprecision in the treatment estimates, leading to a treatment estimate consistent with benefit or harm

⁴ There was substantial heterogeneity in the findings of available studies (two downgrades)

⁵ None of the available studies reported low risk methods for allocation concealment

⁶ None of the available studies reported low risk methods for allocation concealment or blinding of outcome measures

Summary of findings 3. Summary of findings: acupressure versus control

Acupressure versus control for sleep outcomes in people with chronic kidney disease (CKD)

Patient or population: people with CKD

Settings: CKD

Intervention: acupressure

Comparison: without acupressure (no treatment)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Without acupressure	Acupressure				
Sleep quality PSQI (median follow-up: 4 weeks)	The mean sleep quality index score ranged across control groups from 1.29 to 11	The mean sleep quality index score in the intervention groups was 1.27 lower (95% CI -2.13 to -0.40) A lower score is indicative of higher sleep quality	MD -1.27 (95% CI -2.13 to -0.40)	367 (6)	⊕⊕⊕⊕ Very low ^{1 2}	It is very uncertain whether acupressure makes any difference to sleep quality
Sleep latency PSQI (median follow-up: 4 weeks)	The mean sleep latency index score ranged across control groups from 1.74 to 2.4	The mean sleep latency index score in the intervention groups was 0.59 lower (95% CI -0.92 to -0.27) A lower score is indicative of shorter sleep latency	MD -0.59 (95% CI -0.92 to -0.27)	173 (3)	⊕⊕⊕⊖ Moderate ¹	Acupressure may shorten sleep latency
Quality of life	No data observations.	Not estimable	No observations	Insufficient data observations	Not estimable.	Studies were not designed to measure effects of acupressure on quality of life
Depression	The mean depression index score ranged across control groups from 18.88 to 21.61	The mean depression index score in the intervention groups was 3.65 lower (95% CI -7.63 to 0.33)	MD -3.65 (95% CI -7.63 to 0.33)	137 (2)	⊕⊕⊕⊖ Very low ^{3 4 5}	It is very uncertain whether acupressure makes any difference to depressive symptoms

Beck Depression Inventory (BECK) (median follow-up: 4 weeks)		A higher score is indicative of worse depressive symptoms.				
Anxiety	No data observations	Not estimable	No observations	Insufficient data observations	Not estimable.	Studies were not designed to measure effects of acupressure on anxiety
Fatigue PIPER Fatigue Scale (PSF) (median follow-up: 4 weeks)	The mean fatigue index score ranged across control groups from 5.7 to 5.71	The mean fatigue index score in the intervention groups was 1.07 lower (95% CI -1.67 to -0.48) A higher score is indicative of worse fatigue	MD -1.07 (95% CI -1.67 to -0.48)	137 (2)	⊕⊕⊕⊖ Moderate ³	Accupressure may reduce fatigue
Hospitalisation	No data observations	Not estimable	No observations	Insufficient data observations	Not estimable	Studies were not designed to measure effects of acupressure on hospitalisation

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI**: Confidence interval; **SMD**: standardised mean difference; **MD**: mean difference

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ None of the studies reported low risk methods for allocation concealment but one was unblinded for participants and investigators

² There was substantial heterogeneity in the findings of available studies (2 downgrades)

³ None of the studies reported low risk methods for allocation concealment or was blinded for participants and investigators

⁴ The certainty in the evidence was downgraded due to imprecision in the treatment estimates, leading to a treatment estimate consistent with benefit or harm

⁵ There was moderate heterogeneity in the findings of available studies

BACKGROUND

Description of the condition

Sleep duration and quality is commonly decreased in people with chronic kidney disease (CKD) and sleep disorders are often present even in the early stages of CKD. The prevalence rate of any sleep disorder in CKD ranges from 45% to 80% in adults with end-stage kidney disease (ESKD) and affects approximately half of patients with earlier stages of CKD (Iliescu 2004). The true prevalence is uncertain due to heterogeneous definitions of sleep quality including problems initiating or maintaining sleep, early or difficulty waking, restlessness, tiredness on waking, and daytime sleepiness (Murtagh 2010). Risk factors of sleep disturbance in the general population such as older age, male gender, obesity, smoking, increased neck circumference and diabetes are also prevalent in the CKD population (Roumelioti 2011). Dialysis treatment modality may impact sleep dysfunction. People treated with automated peritoneal dialysis (PD) appear to have less severe sleep-related breathing disorders (SBD) compared to continuous ambulatory PD patients (Roumelioti 2016). Kidney transplantation is associated with a low rate of sleep disorders (Mavanur 2010).

Among people with CKD, sleep disorders have been associated with impaired neurocognition, including inattention, lower performance at school or productivity at work, and driving related accidents (Ezzat 2015; Stabouli 2016). CKD is associated with sleep apnoea (central and obstructive), in part due to altered ventilatory control and upper airway obstruction (Markou 2006; Sim 2009). Poor sleep quality is a source of patient stress and is linked to lower health-related quality of life (HRQoL) (Iliescu 2003), depression and greater use of antidepressants, narcotics and hypnotic medications, and worse life expectancy in people with a range of kidney function (Elder 2008; Kumar 2010; Unruh 2006). Overall, impaired sleep is experienced by patients as changes in their sleep-wake cycle (insomnia, excessive sleepiness or both) and sleep-disordered breathing (Young 2004). Contributing factors include restless legs syndrome (RLS) or periodic leg movement, night-time dialysis care, depressed mood and anxiety, increased prescribing of neuroactive medications and analgesia, pain and itch, and altered sleep hygiene including napping during the day (Ogna 2016). Sleep disorders have been associated with increased cardiovascular risk and may contribute to the morbidity and mortality of people with advanced (stages 4 to 5) CKD and those treated with dialysis (Roumelioti 2011). Some studies have shown that sleep disturbances are associated with increased cardiovascular risk and arterial hypertension (Gonçalves 2007), subclinical atherosclerosis (Drager 2009), coronary heart disease (Hung 1990), heart failure (Hedner 1990), arrhythmias (Hoffstein 1994), cerebrovascular disease (Munoz 2006), type 2 diabetes mellitus and dysglycaemia (Botros 2009; Shpirer 2011), metabolic syndrome and its components (Assoumou 2012; Kono 2007) and dyslipidaemia (Assoumou 2012; Drager 2010). The major causes for a disordered sleep in CKD derive from biological, psychological, and environmental factors (Ahmad 2013; Ezzat 2015). Putative determinants of sleep disorders in people with ESKD include serum concentrations of creatinine, urea, phosphorus, parathyroid hormone (PTH), anaemia, nocturnal hypoxaemia, blood pressure, disease intrusiveness, time on dialysis, and comorbidity. Psychological factors and treatment-related factors (such as nocturnal dialysis) may cause alterations in sleep and insomnia in CKD patients (De Santo 2008).

Description of the intervention

Due to the variable causes of altered sleep quality in people with CKD, a range of interventions are used including behavioural therapy with or without medication. A suggested approach to management of sleep has been to identify and treat any specific cause including disordered breathing, restless leg syndrome, pruritus, depression and anxiety, or pain (Murtagh 2010). General approaches to sleep management include a range of behavioural therapies such as sleep hygiene, stimulus control, and avoidance of caffeine, alcohol, and daytime sleeping, short-term hypnotics to re-establish sleep patterns, exercise, and complementary therapies (Jespersen 2015). CKD may constrain the use of neuroactive medications, which can lead to dependence if used in the longer-term.

How the intervention might work

Numerous interventions including behavioural therapy, exercise, pharmacological agents and complementary therapy in addition to specific treatments for conditions associated with sleep impairment have individual mechanisms of action. In general, the effectiveness and safety of treatments may differ in people with CKD due to the frequency of additional severe symptoms including fatigue, pain, and depression, inactivity and frailty, and the altered metabolism of commonly-used medications that may cause over-sedation or lead to interactions with other treatments.

Why it is important to do this review

People with CKD have identified the importance of research focused on developing better treatments to reduce symptoms of CKD (Manns 2014; Tong 2008). In this review, we aimed to summarise the current evidence for treatments to improve sleep quality in CKD. This review is required given the range of causes of impaired sleep, the heterogeneity in available treatments and their potential for adverse effects, the impact of sleep changes on quality of life and prognosis, and the relative priority placed on research to manage symptoms by patients and caregivers.

OBJECTIVES

To assess the effectiveness and associated adverse events of interventions designed to improve sleep quality among adults and children with CKD.

METHODS

Criteria for considering studies for this review

Types of studies

Eligible studies were randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at interventions for improving sleep quality in adults and children with CKD. We excluded studies which did not report sleep outcomes. We included eligible cross-over studies in the review as we deemed them a common method for assessing the effects of interventions to increase sleep quality.

Types of participants

Inclusion criteria

Adults and children with CKD (as defined by Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for evaluation and management of CKD ([KDIGO 2013](#)) including all stages of CKD. We included people treated with dialysis, those who had ESKD treated without dialysis, recipients of a kidney transplant, and those with earlier stages (1-4) of CKD.

Exclusion criteria

None.

Types of interventions

We considered any educational, physical, psychological, behavioural, or pharmacological intervention including:

- Behavioural intervention: sleep hygiene education, stimulus control, relaxation, sleep restriction, cognitive therapy, and cognitive-behavioural therapy (CBT)
- Pharmacological treatments: benzodiazepines, non-benzodiazepine hypnotics, antidepressants, melatonin agonists, orexin receptor antagonists
- Interventions for disordered breathing: patient education, weight loss, exercise, physiotherapy, sleep positioning, positive airway pressure, oral appliances, upper airway surgery, dialysis management
- Exercise and other complementary interventions including music therapy, relaxation therapy, meditation, and hypnotherapy
- Optimisation of renal replacement therapy (dialysis).

We considered any mode, frequency, and duration of therapy and interventions administered in any clinical setting.

Types of outcome measures

Primary outcomes

1. Sleep quality as measured by a sleep-specific quality of life measure
2. Sleep onset latency
3. Total sleep time
4. Sleep interruption: number of awakenings and waking after sleep onset
5. Sleep efficiency: percent of time spent in bed asleep.

Secondary outcomes

1. Depression
2. Anxiety
3. HRQoL
4. Fatigue
5. Daytime sleepiness
6. Death
7. Hospital admission
8. Major cardiovascular event
9. Adverse events (as reported by investigators).

We included studies that measured outcomes using standardised questionnaires with established reliability and validity (e.g.

Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Short-Form 36 (SF-36)). We extracted endpoints as post-intervention mean or change scores, together with standard deviations (SD), or the number of participants experiencing one or more events.

We considered the study period and follow-up as described in the included studies. When assessing outcomes in relation to time points we grouped the data as (when possible): immediate post-intervention, short-term (post-intervention to one month), medium-term (between one and three months follow-up), and long-term (more than three months follow-up) effects.

Due to the heterogeneity of sleep disorders, interventions and clinical outcomes, we categorised sleep disorders according to aetiology. We aimed to group results by outcomes (so that all information for each category of sleep disorder and associated interventions was grouped by the impact of the intervention on outcomes).

To maximize clinical utility, we aimed to separate studies according to clinical setting (CKD/dialysis/transplant and for adults and children). However, insufficient data observations precluded subgroup analysis.

Search methods for identification of studies

Electronic searches

We searched the [Cochrane Kidney and Transplant Register of Studies](#) up to 8 October 2018 through contact with the Information Specialist using search terms relevant to this review. The Register contains studies identified from the following sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of kidney-related journals and the proceedings of major kidney conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected kidney and transplant journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE based on the scope of Cochrane Kidney and Transplant. Details of search strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the *Specialised Register* section of information about [Cochrane Kidney and Transplant](#).

See [Appendix 1](#) for search terms used in strategies for this review.

Searching other resources

1. Reference lists of review articles, relevant studies and clinical practice guidelines.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Data collection and analysis

Selection of studies

The search strategy described was used to obtain titles and abstracts of studies that may be relevant to the review. The titles and abstracts were screened independently by two review authors, who discarded studies that were not applicable. Studies and reviews that might have included relevant data or information on studies were retained initially. Two review authors independently assessed retrieved abstracts and, if necessary the full text, of these studies to determine which studies met the review inclusion criteria.

Data extraction and management

Data extraction was carried out independently by two authors using standard data extraction forms. Studies reported in non-English language journals were translated before assessment. Where more than one publication of one study existed, reports were grouped together and the publication with the most complete data was used in the analyses. Where relevant outcomes were only published in earlier versions, these data were used. Any discrepancy between published versions was highlighted. From each study, review authors extracted the following information.

1. General information: author, year of publication, title, publication source, country, language
2. Study design: design (e.g. parallel or cross-over), method of randomisation and concealment, nature of the control group, blinding of study assessments, washout period in cross-over design, inclusion criteria exclusion criteria
3. Participants: total sample size, number in experimental group, number in control group, age, gender, stage of CKD, ethnicity, diagnosis, comorbidity, sleep quality and reason for impaired sleep, duration of sleep impairment, previous or additional treatments
4. Intervention: type of treatment employed, provider, setting, length and frequency of treatment, duration of intervention, implementation
5. Outcomes: methods of assessment, primary and secondary outcome measures, pre-test means and post-test means or change scores and SD for all groups for all outcomes specified, numbers of participants experiencing one or more event, number of participants at risk, follow-up duration

We will report the results of our findings separately focusing on sleep disorder categories and based on different stages of CKD.

Assessment of risk of bias in included studies

The following items were independently assessed by two review authors using the risk of bias assessment tool ([Higgins 2011](#)) (see [Appendix 2](#)).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
 - * Participants and personnel (performance bias)
 - * Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?

- Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
- Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

For dichotomous outcomes (adverse events, death, major adverse cardiovascular event, fatigue, depression, anxiety) results were expressed as risk ratio (RR) with 95% confidence intervals (CI). Where continuous scales of measurement were used to assess the effects of treatment (sleep assessments, HRQoL, daytime sleepiness, depression, anxiety, fatigue), the mean difference (MD) was used, or the standardised mean difference (SMD) if different scales were used.

Unit of analysis issues

Cluster-randomised studies

We anticipated that studies using clustered randomisation would have controlled for clustering effects. In case of doubt, we planned to contact the authors to ask for individual participant data to calculate an estimate of the intra cluster correlation coefficient (ICC). If this was not possible, we planned to obtain external estimates of the ICC from a similar study or from a study of a similar population as described in the Cochrane Handbook for Systematic Reviews of Interventions ([Higgins 2011](#)). When the ICC was established, we planned to re-analyse the study data. If ICCs from other sources were used, we planned to report this and to conduct sensitivity analyses to investigate the effect of variation in the ICC.

Cross-over studies

Cross-over studies were analysed using combined data from all study periods, or using first period data if combined data was not available.

Studies with more than two treatment arms

If more than one of the interventions was a sleep intervention, and there was sufficient information in the study to assess the similarity of the interventions, we planned to combine similar interventions to allow for a single pair-wise comparison.

Dealing with missing data

Any further information required from the original authors was requested by written correspondence (e.g. emailing corresponding author) and any relevant information obtained in this manner was included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population was carefully performed. Attrition rates, for example drop-outs, losses to follow-up and withdrawals were investigated. Issues of missing data and imputation methods (for example, last-observation-carried-forward) were critically appraised ([Higgins 2011](#)).

Assessment of heterogeneity

We assessed for evidence of statistical heterogeneity by visual inspection of the forest plot. We quantified statistical heterogeneity using the I^2 statistic, which describes the percentage of total variation across studies that is due to heterogeneity rather than

sampling error (Higgins 2003). A guide to the interpretation of I^2 values was as follows.

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity.

The importance of the observed value of I^2 depends on the magnitude and direction of treatment effects and the strength of evidence for heterogeneity (e.g. P-value from the χ^2 test, or a confidence interval for I^2) (Higgins 2011).

Assessment of reporting biases

If possible, funnel plots were planned to assess for the potential existence of small study effects (Higgins 2011).

Data synthesis

We assessed study outcomes using a variety of assessment tools and reported in various metrics. We calculated mean differences (MD) when all studies reported the same sleep outcome measure. We calculated standardised mean differences (SMD) to account for variable outcome measures) for each comparison, using the generic inverse variance method in a random-effect meta-analysis model. We selected end of treatment values for inclusion in meta-analysis, to maximise the number of studies that could be pooled.

We calculated treatment effects were using random-effects meta-analysis. We planned to explore treatment effects using a fixed-effect model to ensure robustness of the model chosen and susceptibility to outliers. Adverse effects were tabulated and assessed with descriptive techniques, as they were likely to be different for the various interventions used.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis were planned a priori to explore possible sources of heterogeneity (e.g. participants, interventions and study quality such as age, stage of CKD, country, duration of treatment or follow-up, study quality). As the range of sleep disorders is complex and the pathobiologies of each are sufficiently different, we planned a framework for sleep disorder categories to be used as a framework for analysis.

We planned the following sleep disorder categories to construct the review and analyse data.

1. Insomnias: insomnia and short sleeper
2. Hypersomnias: narcolepsy; idiopathic hypersomnia; insufficient sleep syndrome; long sleeper; excessive daytime sleepiness
3. SBD: mild-moderate-severe obstructive sleep apnoea; central sleep apnoea; child sleep apnoea; snoring
4. Circadian rhythm sleep-wake disorders: irregular sleep-wake rhythm; delayed sleep-wake phase; advanced sleep-wake phase
5. Parasomnias: confusional arousals; sleep walking; sleep terrors; nightmares; sleep eating disorder; sleep talking; night awakening
6. Sleep movement disorders: RLS; periodic limb movements; sleep leg cramps; bruxism; rapid eye movement behaviour disorders; limb pains; pruritus; itch.

However, there were few data available in included studies, and reporting of the results by this framework was not possible. We planned to report the treatment comparisons by sleep disorder and as a total including all studies when there was no evidence of substantial heterogeneity between groups. We planned a priori to report the results of our findings separately for people with earlier stages of CKD, those with ESKD and recipients of a kidney transplant. However, there were too few data to enable these subgroup analyses to be conducted.

Sensitivity analysis

Where possible, we planned sensitivity analyses to explore the influence of the following factors on effect size.

- Repeating the analysis excluding unpublished studies
- Repeating the analysis taking account of risk of bias, as specified
- Repeating the analysis excluding any very long or large studies to establish how much they dominate the results
- Repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), and country.

'Summary of Findings' tables

We presented the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the main outcomes (Schünemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (GRADE 2008; GRADE 2011). The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. We used methods and recommendations described in Section 8.5 and Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011), using GRADEpro software (grade.pro.org/). The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schünemann 2011b). We justified all decisions to downgrade the quality of studies using footnotes, and made comments to aid the reader's understanding of the review where necessary. Two review authors, working independently, judged the quality of the evidence, with disagreements resolved by discussion or by involving a third review author (SP). We justified, documented and incorporated the judgements into the reporting of results for each outcome. We extracted study data, formatted our comparisons in data tables, and prepared a 'Summary of findings' table before writing the results and conclusions of our review.

We presented the following outcomes in the 'Summary of findings' tables.

- Sleep quality
- Sleep latency
- HRQoL
- Depression
- Anxiety

- Fatigue
- Hospitalisation

We have produced three 'Summary of Findings' tables, one for each of the following treatment comparisons.

1. Relaxation techniques compared to no intervention control
2. Exercise interventions compared to no intervention control
3. Acupressure compared to no intervention control.

RESULTS

Description of studies

[Characteristics of included studies](#); [Characteristics of excluded studies](#); [Characteristics of studies awaiting classification](#); [Characteristics of ongoing studies](#)

Figure 1. Study flow diagram.

Included studies

Sixty-seven studies (3427 participants) reported in 92 publications were included in the systematic review ([Afshar 2011](#); [Amini 2016](#); [Aoike 2018](#); [Arab 2016](#); [Bro 1999](#); [Burkhalter 2015](#); [Champagne 2008](#); [Chen 2008a](#); [Chen 2011a](#); [Cho 2018](#); [Chow 2010](#); [Dai 2007a](#); [Dashti-Khavidaki 2011](#); [Dauvilliers 2016](#); [Duarte 2009](#); [Edalat-Nejad 2013](#); [EMSCAP 2009](#); [Farrokian 2016](#); [Ghavami 2016](#); [Giannaki 2013](#); [Giannaki 2013a](#); [Hanna 2013](#); [Hou 2014](#); [IRCT2013021212448N1](#); [IRCT2014061717237N3](#); [IRCT2015051122218N1](#); [Jean 1995](#); [Kolner 1989](#); [Li 2014b](#); [MELODY](#)

Results of the search

The electronic search strategy of the Cochrane Kidney and Transplant Specialised Register (8 October 2018) identified 127 records ([Figure 1](#)). After duplicates were removed we screened the titles and abstracts and 10 records were excluded (not RCTs). The full text of the remaining 114 records was evaluated. We included 67 studies (92 records) and excluded 3 studies (10 records). We also identified 11 ongoing studies and one study is completed but with no published results - these studies will be assessed in a future update of this review.

[2013](#); [Micozkadioglu 2004](#); [Momennasab 2018](#); [Muz 2017](#); [Nasiri 2011](#); [Natarajan 2003](#); [NCT02825589](#); [Parker 2007](#); [Pellecchia 2004](#); [Pellizzaro 2013](#); [Pieta 1998](#); [Pooranfar 2014](#); [Rambod 2013](#); [Razazian 2015](#); [Reilly-Spong 2015](#); [Ren 2017a](#); [Sabbatini 2003](#); [Saeedi 2014](#); [Shariati 2012](#); [SIESTA 2017](#); [Silva 2017](#); [Sklar 1998](#); [Solak 2012](#); [Soleimani 2016](#); [Soreide 1991](#); [Sun 2017](#); [Tol 2010](#); [Trenkwalder 1995](#); [Tsai 2015](#); [Tsay 2003a](#); [Tsay 2004](#); [Turk 2010](#); [Unal 2016](#); [Walker 1996](#); [Williams 2017](#); [Yurtkuran 2007](#); [Zhao 2011](#); [Zou 2015](#)). Thirty-six studies involving 2239 participants were included in meta-analysis. Thirty-one studies were not included in meta-analyses as outcome data were not reported in a format

that could be extracted for analysis (Aoike 2018; Champagne 2008; Chen 2008a; Edalat-Nejad 2013; EMSCAP 2009; Ghavami 2016; Hanna 2013; IRCT2013021212448N1; IRCT2014061717237N3; IRCT2015051122218N1; Jean 1995; Kolner 1989; Micozkadioglu 2004; Nasiri 2011; NCT02825589; Parker 2007; Pellecchia 2004; Pellizzaro 2013; Pieta 1998; Pooranfar 2014; Ren 2017a; Sabbatini 2003; Silva 2017; Sklar 1998; Solak 2012; Soreide 1991; Tol 2010; Trenkwalder 1995; Turk 2010; Walker 1996; Williams 2017).

Studies were published between 1989 and 2018. Thirty-seven studies received funding from governmental or healthcare organisations, and thirty studies did not report a funding source. Sixty-one studies enrolled 3201 people treated with long-term dialysis. Of these, 57 studies involved participants on haemodialysis and four studies involved participants treated with peritoneal dialysis (Bro 1999; Chen 2008a; Chow 2010; Li 2014b). One study reported 14 patients treated with either haemodialysis and peritoneal dialysis (Pieta 1998), one study involved 63 kidney transplant candidates who were treated with haemodialysis, or peritoneal dialysis or who were pre-dialysis (Reilly-Spong 2015). Three studies enrolled 104 kidney transplant recipients (Burkhalter 2015; Hanna 2013; Pooranfar 2014) and one study enrolled 45 people with CKD stages 3 and 4 (Aoike 2018).

Studies were conducted in Australia (SIESTA 2017), Brazil (Aoike 2018; Duarte 2009; Pellizzaro 2013; Silva 2017), Canada (Champagne 2008; Pieta 1998; Walker 1996), China (Chow 2010; Dai 2007a; Hou 2014; Li 2014b; Ren 2017a; Sun 2017; Zhao 2011; Zou 2015), Denmark (Bro 1999), France (Jean 1995), Germany (Trenkwalder 1995), Greece (Giannaki 2013; Giannaki 2013a), Iran (Afshar 2011; Amini 2016; Arab 2016; Dashti-Khavidaki 2011; Edalat-Nejad 2013; Farrokian 2016; Ghavami 2016; IRCT2013021212448N1; IRCT2014061717237N3; IRCT2015051122218N1; Momennasab 2018; Nasiri 2011; Pooranfar 2014; Rambod 2013; Razazian 2015; Saeedi 2014; Shariati 2012; Soleimani 2016), Italy (Pellecchia 2004; Sabbatini 2003), Korea (Cho 2018), Slovakia (Tol 2010), Switzerland (Burkhalter 2015; Hanna 2013), Taiwan (Chen 2008a; Chen 2011a; Tsai 2015; Tsay 2003a; Tsay 2004), Thailand (NCT02825589), The Netherlands (EMSCAP 2009; MELODY 2013; Parker 2007), Turkey (Micozkadioglu 2004; Muz 2017; Solak 2012; Turk 2010; Unal 2016; Yurtkuran 2007), and the USA (Kolner 1989; Natarajan 2003; Reilly-Spong 2015; Sklar 1998; Soreide 1991; Williams 2017). One study was conducted both in the USA and Europe (Dauvilliers 2016).

The mean age of participants in the 36 studies contributing outcome data was 54.3 years. Follow-up for clinical outcomes ranged between 0.3 and 52.8 weeks (median 5 weeks).

Sleep interventions

The methods for implementation, tailoring, and measurement of adherence of interventions are provided in Table 1 using a TIDieR

(Template for Intervention Description and Replication) checklist (Hoffmann 2014).

Among studies included in the meta-analyses, interventions included relaxation techniques (progressive muscle relaxation, nurse-led breathing training, mindfulness, and the Benson relaxation technique) in four studies (Amini 2016; Rambod 2013; Reilly-Spong 2015; Tsai 2015) (291 participants), exercise in four studies (Afshar 2011; Cho 2018; Giannaki 2013a; Yurtkuran 2007) (138 participants), acupressure in eight studies (493 participants) (Arab 2016; Dai 2007a; Shariati 2012; SIESTA 2017; Tsay 2003a; Tsay 2004; Zhao 2011; Zou 2015), cognitive-behavioural therapy (CBT) in three studies (255 participants) (Chen 2011a; Duarte 2009; Hou 2014), sleep hygiene education in three studies (Chow 2010; Saeedi 2014; Soleimani 2016) (220 participants), benzodiazepine medication in Dashti-Khavidaki 2011 (23 participants), dopaminergic agonists in three studies (Giannaki 2013; Razazian 2015; Dauvilliers 2016) (136 participants), telephone support in Li 2014b (135 participants), melatonin in two studies (MELODY 2013; Natarajan 2003) (75 participants), reflexology in two studies (Farrokian 2016; Unal 2016) (167 participants), light therapy in Burkhalter 2015 (28 participants), different forms of peritoneal dialysis in Bro 1999 (34 participants), music in Momennasab 2018 (102 participants), aromatherapy in Muz 2017 (62 participants), and massage in Sun 2017 (80 participants).

Seven studies reported three treatment groups. In Amini 2016, relaxation techniques were compared with exercise or no treatment control. In Arab 2016 and Tsay 2003a, acupressure was compared with sham acupressure or no treatment control. In Tsay 2004 acupressure was compared with Transcutaneous Electrical Acupoint Stimulation (TEAS) or no treatment control. In Giannaki 2013, exercise was compared with a dopamine agonist (ropinirole) or placebo. In Momennasab 2018 music during haemodialysis was compared with music at bedtime or no treatment control. In Unal 2016, reflexology was compared with massage or no treatment control. Cho 2018 reported four treatment groups in which aerobic exercise was compared with resistance exercise, combination exercise or no treatment control.

See Characteristics of included studies.

Excluded studies

After full-text review we excluded three studies. Cooper 2004 enrolled patients with uncontrolled hypertension while ACTIVE Dialysis 2015 and Deng 2017 did not report sleep outcomes (see Characteristics of excluded studies).

Risk of bias in included studies

See Figure 2; Figure 3 for summary of 'Risk of bias' assessments. Reporting of study methodology was incomplete for most studies. The summary risks of bias are shown in Figure 2 and risk of bias in each individual study is shown in Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Afshar 2011	?	?	-	-	?	+	?
Amini 2016	?	?	+	?	?	+	?
Aoike 2018	?	?	-	-	-	+	+
Arab 2016	?	?	-	+	-	+	+
Bro 1999	?	?	-	-	-	+	+
Burkhalter 2015	?	+	-	?	+	+	+
Champagne 2008	?	?	-	?	-	?	-
Chen 2008a	+	-	-	-	+	+	+
Chen 2011a	+	?	-	-	+	+	+
Cho 2018	?	?	-	+	-	+	+
Chow 2010	+	?	-	-	+	+	+
Dai 2007a	?	?	-	-	?	+	+
Dashti-Khavidaki 2011	?	?	?	?	+	+	?
Dauwilliers 2016	+	+	+	+	-	+	-
Duarte 2009	-	?	-	-	-	+	+
Edalat-Nejad 2013	?	?	+	+	?	-	?
EMSCAP 2009	?	?	+	+	?	-	?
Farrokian 2016	+	?	-	-	+	+	+
Ghavami 2016	?	?	-	-	?	-	?
Giannaki 2013	?	?	+	+	-	+	+

Figure 3. (Continued)

Giannaki 2013	?	?	+	+	-	+	+
Giannaki 2013a	?	?	-	-	+	+	+
Hanna 2013	?	?	-	+	?	?	?
Hou 2014	?	?	-	-	-	+	+
IRCT2013021212448N1	?	?	-	-	?	?	+
IRCT2014061717237N3	?	?	+	?	?	?	?
IRCT2015051122218N1	?	?	+	?	?	?	?
Jean 1995	?	?	?	+	?	-	?
Kolner 1989	?	?	+	?	?	?	?
Li 2014b	+	?	-	?	+	+	+
MELODY 2013	?	?	+	+	-	+	+
Micozkadioglu 2004	?	?	-	-	-	-	?
Momennasab 2018	?	?	-	-	+	+	+
Muz 2017	?	?	-	-	-	+	+
Nasiri 2011	?	?	-	-	?	-	+
Natarajan 2003	?	?	+	+	+	?	?
NCT02825589	?	?	-	-	?	?	?
Parker 2007	?	?	-	+	?	-	?
Pellecchia 2004	+	?	-	-	-	-	?
Pellizzaro 2013	?	?	-	?	-	-	+
Pieta 1998	?	?	+	-	-	-	?
Pooranfar 2014	?	?	-	-	?	-	?
Rambod 2013	+	?	-	-	+	+	+
Razazian 2015	?	?	+	?	-	+	+
Reilly-Spong 2015	+	?	-	+	-	+	+
Ren 2017a	?	?	-	-	?	-	?
Sabbatini 2003	?	?	-	?	-	-	?
Saeedi 2014	?	?	-	-	+	+	+
Shariati 2012	?	?	-	?	?	+	+
SIESTA 2017	+	+	-	+	+	-	-
Silva 2017	?	?	-	-	-	-	?

Figure 3. (Continued)

Silva 2017	?	?	-	-	-	-	?
Sklar 1998	?	?	-	-	-	-	?
Solak 2012	+	?	-	-	+	-	?
Soleimani 2016	?	?	-	-	+	+	?
Soreide 1991	?	?	+	+	+	-	?
Sun 2017	?	?	-	-	?	+	?
Tol 2010	?	?	?	-	+	-	?
Trenkwalder 1995	?	?	+	-	+	-	?
Tsai 2015	+	+	-	-	-	+	+
Tsay 2003a	?	?	-	+	-	+	+
Tsay 2004	?	?	-	+	+	+	+
Turk 2010	+	+	-	-	?	-	?
Unal 2016	?	?	-	-	+	+	+
Walker 1996	?	?	+	-	-	-	-
Williams 2017	?	?	-	-	?	-	+
Yurtkuran 2007	+	?	-	-	+	+	+
Zhao 2011	?	?	-	?	?	?	+
Zou 2015	+	?	+	+	-	+	+

Allocation

Random sequence generation

Fifteen studies reported low risk methods for random sequence generation (Chen 2008a; Chen 2011a; Chow 2010; Farrokian 2016; Li 2014b; Pellecchia 2004; Rambod 2013; Reilly-Spong 2015; Dauvilliers 2016; SIESTA 2017; Solak 2012; Tsai 2015; Turk 2010; Yurtkuran 2007; Zou 2015). One study reported inadequate (high risk) random sequence generation (Duarte 2009). The risk of bias from random sequence generation methods was unclear in the remaining 51 studies.

Allocation concealment

Five studies reported low risk methods for allocation concealment (Burkhalter 2015; Dauvilliers 2016; SIESTA 2017; Tsai 2015; Turk 2010). In one study (Chen 2008a) allocation concealment methods were at high risk of bias. Risk of bias from allocation concealment was unclear in the remaining 61 studies.

Blinding

Performance bias

Sixteen studies reported low risk methods for performance bias (Amini 2016; Edalat-Nejad 2013; Giannaki 2013; EMSCAP

2009; Kolner 1989; IRCT2014061717237N3; MELODY 2013; IRCT2015051122218N1; Natarajan 2003; Pieta 1998; Razazian 2015; Dauvilliers 2016; Soreide 1991; Trenkwalder 1995; Walker 1996; Zou 2015). Performance bias was judged as high risk in 48 studies (Afshar 2011; Aoike 2018; Arab 2016; Bro 1999; Burkhalter 2015; Champagne 2008; Chen 2008a; Chen 2011a; Cho 2018; Chow 2010; Dai 2007a; Duarte 2009; Farrokian 2016; Ghavami 2016; Giannaki 2013a; Hanna 2013; Hou 2014; IRCT2013021212448N1; Li 2014b; Micozkadioglu 2004; Momennasab 2018; Muz 2017; Nasiri 2011; Parker 2007; Pellecchia 2004; Pellizzaro 2013; Pooranfar 2014; Rambod 2013; Reilly-Spong 2015; Ren 2017a; Sabbatini 2003; Saeedi 2014; NCT02825589; Shariati 2012; SIESTA 2017; Silva 2017; Sklar 1998; Solak 2012; Soleimani 2016; Sun 2017; Tsai 2015; Tsay 2003a; Tsay 2004; Turk 2010; Unal 2016; Williams 2017; Yurtkuran 2007; Zhao 2011). Risks from performance bias was unclear in the remaining three studies.

Detection bias

Detection bias was judged to be low risk in 17 studies (Arab 2016; Cho 2018; Edalat-Nejad 2013; Giannaki 2013; Hanna 2013; Jean 1995; EMSCAP 2009; MELODY 2013; Natarajan 2003; Parker 2007; Reilly-Spong 2015; Dauvilliers 2016; SIESTA 2017; Soreide 1991; Tsay 2003a; Tsay 2004; Zou 2015) and high risk in 37 (Afshar 2011; Aoike 2018; Bro 1999; Chen 2008a; Chen 2011a;

Chow 2010; Dai 2007a; Duarte 2009; Farrokian 2016; Ghavami 2016; Giannaki 2013a; Hou 2014; IRCT2013021212448N1; Micozkadioglu 2004; Momennasab 2018; Muz 2017; Nasiri 2011; Pellecchia 2004; Pieta 1998; Pooranfar 2014; Rambod 2013; Ren 2017a; Saeedi 2014; NCT02825589; Silva 2017; Sklar 1998; Solak 2012; Soleimani 2016; Sun 2017; Tol 2010; Trenkwalder 1995; Tsai 2015; Turk 2010; Unal 2016; Walker 1996; Williams 2017; Yurtkuran 2007). Risk of detection bias was unclear in the remaining 13 studies.

Incomplete outcome data

Attrition bias was low risk in 21 studies (Burkhalter 2015; Chen 2008a; Chen 2011a; Chow 2010; Dashti-Khavidaki 2011; Farrokian 2016; Giannaki 2013a; Li 2014b; Momennasab 2018; Natarajan 2003; Rambod 2013; Saeedi 2014; SIESTA 2017; Solak 2012; Soleimani 2016; Soreide 1991; Tol 2010; Trenkwalder 1995; Tsay 2004; Unal 2016; Yurtkuran 2007) and high risk in 24 studies (Aoike 2018; Arab 2016; Bro 1999; Champagne 2008; Cho 2018; Duarte 2009; Giannaki 2013; Hou 2014; MELODY 2013; Micozkadioglu 2004; Muz 2017; Pellecchia 2004; Pellizzaro 2013; Pieta 1998; Razazian 2015; Reilly-Spong 2015; Dauvilliers 2016; Sabbatini 2003; Silva 2017; Sklar 1998; Tsay 2003a; Tsai 2015; Walker 1996; Zou 2015). Risks from attrition bias were unclear in the remaining 22 studies.

Selective reporting

Thirty-five studies were at low risk of reporting bias (Afshar 2011; Amini 2016; Aoike 2018; Arab 2016; Bro 1999; Burkhalter 2015; Chen 2008a; Chen 2011a; Cho 2018; Chow 2010; Dai 2007a; Dashti-Khavidaki 2011; Dauvilliers 2016; Duarte 2009; Farrokian 2016; Giannaki 2013; Giannaki 2013a; Hou 2014; Li 2014b; MELODY 2013; Momennasab 2018; Muz 2017; Rambod 2013; Razazian 2015; Reilly-Spong 2015; Saeedi 2014; Shariati 2012; Soleimani 2016; Sun 2017; Tsai 2015; Tsay 2003a; Tsay 2004; Unal 2016; Yurtkuran 2007; Zou 2015), and high risk in 23 studies (Edalat-Nejad 2013; Ghavami 2016; Jean 1995; EMSCAP 2009; Micozkadioglu 2004; Nasiri 2011; Parker 2007; Pellecchia 2004; Pellizzaro 2013; Pieta 1998; Pooranfar 2014; Ren 2017a; Sabbatini 2003; SIESTA 2017; Silva 2017; Sklar 1998; Solak 2012; Soreide 1991; Tol 2010; Trenkwalder 1995; Turk 2010; Walker 1996; Williams 2017). The remaining nine studies were at unclear risk of reporting bias.

Other potential sources of bias

Thirty-four studies were judged to be at low risk of other potential biases (Aoike 2018; Arab 2016; Bro 1999; Burkhalter 2015; Chen 2008a; Chen 2011a; Cho 2018; Chow 2010; Dai 2007a; Duarte 2009; Farrokian 2016; Giannaki 2013; Giannaki 2013a; Hou 2014; IRCT2013021212448N1; Li 2014b; MELODY 2013; Momennasab 2018; Muz 2017; Nasiri 2011; Pellizzaro 2013; Rambod 2013; Razazian 2015; Reilly-Spong 2015; Saeedi 2014; Shariati 2012; Tsai 2015; Tsay 2003a; Tsay 2004; Unal 2016; Williams 2017; Yurtkuran 2007; Zhao 2011; Zou 2015), four studies were judged to be high risk of bias (Champagne 2008; Dauvilliers 2016; SIESTA 2017; Walker 1996), and risks of bias were unclear in the remaining 29 studies.

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings: relaxation versus control for sleep outcomes in people with chronic kidney disease (CKD); **Summary of findings 2** Summary of findings: exercise versus control; **Summary of findings 3** Summary of findings: acupressure versus control

There were no studies designed to directly examine and/or correlate efficacy of any interventions aimed at improving sleep that may have been attempted for the spectrum of sleep disordered breathing.

Relaxation versus control

Four studies (Amini 2016; Rambod 2013; Reilly-Spong 2015; Tsai 2015) (259 participants) compared relaxation techniques with no treatment intervention. Interventions included progressive muscle relaxation, nurse-led breathing, mindfulness, and the Benson relaxation technique. The median follow-up in these studies was eight weeks. The certainty of the evidence was graded as low or very low for all outcomes (**Summary of findings for the main comparison**) and several analyses showed evidence of moderate to substantial statistical heterogeneity.

Relaxation techniques had uncertain effects on the global Pittsburgh Sleep Quality Index (PSQI) score (scale 0 - 21) (**Analysis 1.1** (4 studies, 259 participants): MD -1.62, 95% CI -5.03 to 1.79; $I^2 = 97\%$; very low certainty evidence). Single studies reported no difference between relaxation and control for sleep latency (**Analysis 1.2**), total sleep time (**Analysis 1.3**), and hospitalisation (**Analysis 1.5**), and improved sleep disturbance with relaxation (**Analysis 1.4**); however meta-analyses were not possible leading to very low certainty about the effects of relaxation on these outcomes. Relaxation techniques had very uncertain effects on anxiety (**Analysis 1.6** (2 studies; 119 participants): SMD 0.11, 95% CI -0.55 to 0.77; $I^2 = 69\%$; very low certainty evidence). Relaxation techniques had uncertain effects on pain (**Analysis 1.7** (3 studies, 189 participants): SMD -0.26, 95% CI -0.67 to 0.15; $I^2 = 49\%$; low certainty evidence), fatigue (**Analysis 1.8** (2 studies, 119 participants): SMD -0.61, 95% CI -2.09 to 0.87; $I^2 = 93\%$; very low certainty evidence), quality of life (**Analysis 1.9** (2 studies, 138 participants): SMD 0.47, 95% CI -0.09 to 1.04; $I^2 = 62\%$; low certainty evidence), and depressive symptoms (**Analysis 1.10** (2 studies, 108 participants): SMD 0.04, 95% CI -1.27 to 1.35; $I^2 = 91\%$; very low certainty evidence). Studies were not designed to measure the effects of relaxation on death. Adverse events of relaxation techniques were rarely reported (**Table 2**).

Exercise versus control

Six studies (Afshar 2011; Amini 2016; Cho 2018; Giannaki 2013; Giannaki 2013a; Yurtkuran 2007) (205 participants) compared exercise with a no treatment control. Exercise interventions included daily aerobic exercise, exercise during haemodialysis, and yoga-based exercise. The median follow-up was 26.4 weeks. The certainty of the evidence was moderate or very low for all outcomes (**Summary of findings 2**). One meta-analysis (sleep quality) showed evidence of substantial statistical heterogeneity.

Exercise interventions had very uncertain effects on sleep quality (**Analysis 2.1** (5 studies, 165 participants): SMD -1.10, 95% CI -2.26 to 0.05; $I^2 = 90\%$; very low certainty evidence). Single studies reported no differences in total sleep time (**Analysis 2.2**), sleep efficiency (**Analysis 2.3**), sleep disturbance (**Analysis 2.4**), anxiety (**Analysis 2.5**), or pain (**Analysis 2.6**) between exercise and control; however meta-analyses were not possible. Exercise probably decreased fatigue (**Analysis 2.7** (2 studies, 107 participants): SMD -0.68, 95% CI -1.07 to -0.29; $I^2 = 0\%$; moderate certainty evidence). Exercise probably decreased depressive symptoms (**Analysis 2.8** (2 studies, 46 participants): MD -9.05, 95% CI -13.72 to -4.39; $I^2 = 0\%$; moderate

certainty evidence). Studies were not designed to measure the effects of exercise on sleep latency, quality of life, death, or hospitalisation. Adverse events related to exercise interventions were rarely reported (Table 2).

Exercise versus dopaminergic agonist (ropinirole)

Giannaki 2013 (22 participants) reported no differences between exercise intervention and dopaminergic agonist (ropinirole) on sleep quality (Analysis 3.1) or depression (Analysis 3.2); meta-analysis was not conducted.

Aerobic versus resistance exercise

Cho 2018 (21 participants) reported no differences between aerobic and resistance exercise on sleep quality (Analysis 4.1), total sleep time (Analysis 4.2), or sleep efficiency (Analysis 4.3). As only a single study was available, meta-analysis was not conducted.

Acupressure versus no intervention

Six studies (Arab 2016; Shariati 2012; Tsay 2003a; Tsay 2004; Zhao 2011; Zou 2015) involving 304 participants compared acupressure with no intervention. The median follow-up was four weeks. The certainty of the evidence is shown in the Summary of findings 3 and one analysis (on sleep quality) showed evidence of substantial statistical heterogeneity.

It is uncertain whether acupressure improved the PSQI score (scale 0 to 21) because the certainty of the evidence was very low (Analysis 5.1 (6 studies, 367 participants): MD -1.27, 95% CI -2.13 to -0.40; $I^2 = 89\%$). Acupressure probably slightly improved sleep latency (scale 0 to 3) (Analysis 5.2 (3 studies, 173 participants): MD -0.59, 95% CI -0.92 to -0.27; $I^2 = 0\%$; moderate certainty evidence) and may have slightly increased total sleep time (scale 0 to 3) (Analysis 5.3 (3 studies, 173 participants): MD -0.60, 95% CI -1.12 to -0.09; $I^2 = 68\%$; low certainty evidence). It was uncertain whether acupressure decreased sleep disturbance because the certainty of the evidence was very low (scale 0 to 3) (Analysis 5.4 (3 studies, 173 participants): MD -0.49, 95% CI -1.16 to 0.19; $I^2 = 97\%$; very low certainty evidence). Acupressure probably leads to slightly better sleep efficiency (scale 0 to 3) (Analysis 5.6 (2 studies, 107 participants): MD -0.18, 95% CI -0.39 to 0.03; $I^2 = 0\%$; moderate certainty evidence). Acupressure probably improved fatigue (Analysis 5.8 (2 studies, 137 participants): MD -1.07, 95% CI -1.67 to -0.48; $I^2 = 0\%$; moderate certainty evidence). It was uncertain whether acupressure decreased depressive symptoms (Analysis 5.9 (2 studies, 137 participants): MD -3.65, 95% CI -7.63 to 0.33; $I^2 = 27\%$; very low certainty evidence). Studies were not designed to measure the effects of acupressure on quality of life, anxiety, or hospitalisation. Adverse events related to acupressure interventions were rarely reported (Table 2).

Single studies reported no differences in sleep interruption (Analysis 5.5) or death (all causes) (Analysis 5.7); meta-analyses were not possible.

Acupressure versus sham acupressure control

Three studies (Arab 2016; SIESTA 2017; Tsay 2003a) involving 107 participants compared acupressure with sham acupressure. The median follow-up was 4 weeks. Compared with sham acupressure, it is uncertain whether acupressure improves sleep quality because the certainty of the evidence is very low (Analysis 6.1 (2 studies,

129 participants): MD -2.25, 95% CI -6.33 to 1.82; $I^2 = 96\%$). One study reported the effects of acupressure or sham acupressure on sleep latency (Analysis 6.2) and sleep interruption (Analysis 6.3). Acupressure probably improve total sleep time (Analysis 6.4 (2 studies, 107 participants): SMD -0.34, 95% CI -0.73 to 0.04; $I^2 = 0\%$; moderate certainty evidence) compared with sham acupressure.

Single studies reported no differences in sleep disturbance (Analysis 6.5), hospitalisation (Analysis 6.6), fatigue (Analysis 6.7), or depressive symptoms (Analysis 6.8); meta-analyses were not possible.

Acupressure versus transcutaneous electrical acupoint stimulation

Tsay 2004 (70 participants) compared acupressure with another form of acupressure, Transcutaneous Electrical Acupoint Stimulation (TEAS). This study reported no differences in sleep quality (Analysis 7.1), fatigue (Analysis 7.2), or depression (Analysis 7.3); meta-analyses were not performed.

Acupressure versus benzodiazepine

Dai 2007a (82 participants) reported sleep quality was improved with acupressure compared to benzodiazepine therapy (Analysis 8.1); meta-analysis was not conducted.

Cognitive-behavioural therapy versus control

Two studies (Duarte 2009; Hou 2014) involving 183 participants compared CBT with no intervention. The median follow-up was 13.2 weeks. Duarte 2009 used KDOL-SR (higher score is better); we have multiplied the mean values by -1 to account for the different direction of the scale. Compared with no intervention, CBT may improve sleep quality however the certainty of the evidence was very low (Analysis 9.1 (2 studies, 183 participants): SMD -0.65, 95% CI -1.03 to -0.26; $I^2 = 39\%$). Single studies reported improvement in sleep latency (Analysis 9.2), total sleep time (Analysis 9.3), sleep efficiency (Analysis 9.4), anxiety (Analysis 9.6), and quality of life (Analysis 9.7), and no differences in death (all causes) (Analysis 9.5); meta-analyses were not performed. CBT probably improved depressive symptoms (Analysis 9.8 (2 studies, 183 participants): SMD -0.76, 95% CI -1.06 to -0.46; $I^2 = 0\%$; moderate certainty evidence) compared with no intervention.

Cognitive-behavioural therapy versus education

Chen 2011a (72 participants) compared CBT with education. This study reported possible improvement in sleep quality with CBT (Analysis 10.1), no differences in sleep latency (Analysis 10.2), or total sleep time (Analysis 10.3); possible improvement in sleep efficiency with education (Analysis 10.4), and no differences in depression (Analysis 10.5), anxiety (Analysis 10.6), or fatigue (Analysis 10.7). Meta-analyses were not performed.

Education versus control

Three studies (Chow 2010; Saeedi 2014; Soleimani 2016) involving 220 participants compared sleep hygiene or health behaviour education with no treatment intervention. Chow 2010 used KDOL-SR (higher score is better); we have multiplied the mean values by -1 to account for the different direction of the scale.

The median follow-up was 4 weeks. Compared with no intervention, education may improve sleep quality however the

certainty of the evidence was very low ([Analysis 11.1](#) (3 studies, 220 participants): SMD -0.50, 95% CI -0.77 to -0.23; $I^2 = 0\%$). Education probably improved sleep latency ([Analysis 11.2](#) (2 studies, 135 participants): MD -0.50, 95% CI -0.76 to -0.23; $I^2 = 0\%$; moderate certainty evidence), total sleep time ([Analysis 11.3](#) (2 studies, 135 participants): MD -0.27, 95% CI -0.59 to 0.05; $I^2 = 0\%$; moderate certainty evidence), sleep efficiency ([Analysis 11.4](#) (2 studies, 135 participants): MD -0.30, 95% CI -0.66 to 0.06; $I^2 = 0\%$; moderate certainty evidence), and sleep disturbance ([Analysis 11.5](#) (2 studies, 135 participants): MD -0.38, 95% CI -0.52 to -0.24; $I^2 = 0\%$; moderate certainty evidence) compared with no intervention. [Chow 2010](#) reported no differences between education or no intervention on pain ([Analysis 11.6](#)), fatigue ([Analysis 11.7](#)), and quality of life ([Analysis 11.8](#)); meta-analyses were not performed.

Benzodiazepine 1 versus benzodiazepine 2

[Dashti-Khavidaki 2011](#) (23 participants) compared benzodiazepine (zolpidem) with treatment using another benzodiazepine (clonazepam). This study reported no difference in sleep quality ([Analysis 12.1](#)); meta-analysis was not performed.

Dopaminergic agonist versus control

Two studies ([Dauvilliers 2016](#); [Giannaki 2013](#)) involving 39 participants compared dopaminergic agonist (rotigotine or ropinirole) with no intervention. The median follow-up was 16.2 weeks. [Giannaki 2013](#) reported no difference in sleep quality ([Analysis 13.1](#)). [Dauvilliers 2016](#) reported no differences in sleep latency ([Analysis 13.2](#)), or quality of life ([Analysis 13.5](#)), and possible improvement in total sleep time ([Analysis 13.3](#)), sleep efficiency ([Analysis 13.4](#)) with rotigotine; meta-analyses were not performed.

Telephone support versus control

[Li 2014b](#) (135 participants) reported telephone support may improve sleep quality compared to no intervention ([Analysis 14.1](#)), but no differences in pain ([Analysis 14.2](#)), fatigue ([Analysis 14.3](#)), or quality of life ([Analysis 14.4](#)); meta-analyses were not performed.

Melatonin versus control

Two studies ([Natarajan 2003](#); [MELODY 2013](#)) involving 75 participants compared melatonin with no intervention. The median follow-up was 30.9 weeks. [Natarajan 2003](#) reported sleep quality improved from baseline with melatonin ([Analysis 15.1](#)) and [MELODY 2013](#) reported no difference in the number of deaths ([Analysis 15.2](#)); meta-analyses were not performed.

Reflexology versus control

Two studies ([Farrokian 2016](#); [Unal 2016](#)) involving 132 participants compared reflexology with no intervention. The median follow-up was 4 weeks. Compared with no intervention, reflexology probably slightly improves sleep quality ([Analysis 16.1](#) (2 studies, 132 participants): MD -5.90, 95% CI -6.56 to -5.23; $I^2 = 0\%$; moderate certainty evidence). [Unal 2016](#) reported reflexology probably improved fatigue ([Analysis 16.2](#)); meta-analysis was not performed.

Reflexology versus massage

[Unal 2016](#) (70 participants) compared reflexology with back massage. This study reported reflexology improved sleep quality ([Analysis 17.1](#)) and fatigue ([Analysis 17.2](#)); meta-analyses were not performed.

Light therapy versus control

[Burkhalter 2015](#) (28 participants) compared light therapy with no intervention. This study reported sleep latency improved from baseline with light therapy ([Analysis 18.1](#)), and no differences in sleep efficiency ([Analysis 18.2](#)) or depressive symptoms ([Analysis 18.3](#)); meta-analyses were not performed.

Gabapentin versus dopaminergic agonist

[Razanian 2015](#) (82 participants) compared gabapentin with treatment using a dopaminergic agonist (levodopa/carbidopa). This study reported sleep latency ([Analysis 19.1](#)) and sleep disturbance ([Analysis 19.3](#)) improved with gabapentin, and there were no differences in total sleep time ([Analysis 19.2](#)) or cardiovascular death ([Analysis 19.4](#)); meta-analyses were not performed.

Continuous ambulatory peritoneal dialysis (CAPD) versus automated peritoneal dialysis (APD)

[Bro 1999](#) (34 participants) compared CAPD with APD. This study reported no differences in sleep quality ([Analysis 20.1](#)); meta-analysis was not performed.

Music during haemodialysis versus control

[Momennasab 2018](#) (69 participants) compared music during haemodialysis with no intervention. This study reported music improved sleep quality ([Analysis 21.1](#)), sleep latency ([Analysis 21.2](#)), total sleep time ([Analysis 21.3](#)) and sleep disturbance ([Analysis 21.4](#)); meta-analyses were not performed.

Music during haemodialysis versus music at bedtime

[Momennasab 2018](#) (67 participants) compared music during haemodialysis with music at bedtime. This study reported music at bedtime improved sleep quality ([Analysis 22.1](#)), sleep latency ([Analysis 22.2](#)), total sleep time ([Analysis 22.3](#)) and sleep disturbance ([Analysis 22.4](#)); meta-analyses were not performed.

Aromatherapy versus control

[Muz 2017](#) compared aromatherapy with no intervention. This study reported aromatherapy improved sleep quality ([Analysis 23.1](#)), sleep latency ([Analysis 23.2](#)), total sleep time ([Analysis 23.3](#)), sleep efficiency ([Analysis 23.4](#)), and sleep disturbance ([Analysis 23.5](#)); meta-analyses were not performed.

Massage versus control

[Sun 2017](#) (80 participants) compared abdominal massage with no intervention. This study reported massage improved sleep quality ([Analysis 24.1](#)), pain ([Analysis 24.2](#)), and quality of life ([Analysis 24.3](#)); meta-analyses were not performed.

Subgroup and sensitivity analysis

Overall, the planned subgroup and sensitivity analyses to explore for sources of heterogeneity were not possible due to the lack of data observations. However, we were not able to determine if [Afshar 2011](#) was eligible for our review because the study design was not clearly defined. We provided a sensitivity analysis for the comparator education versus control and explored data removing this study from our analysis. In this additional analysis, exercise interventions had very uncertain effects on sleep quality (4 studies,

137 participants: SMD -0.97, 95% CI -2.42 to 0.48; $I^2 = 92\%$; very low certainty evidence).

DISCUSSION

Summary of main results

This review summarises 67 studies involving 3427 participants with CKD that reported the effects of a variety of therapies on sleep quality and related outcomes. All studies were in adults; no studies were identified that evaluated therapy for children with CKD. Nearly all studies involved patients with ESKD treated with dialysis, while a small number included people with milder stages of kidney disease, and recipients of a kidney transplant. Sleep interventions were evaluated during very short-term follow-up. Studies continued for a median of 5 weeks. The most common interventions were relaxation techniques, exercise, acupressure, CBT, and sleep hygiene or health behaviour education. Other therapies included benzodiazepines, dopaminergic agonist therapy, telephone support, melatonin, reflexology, light therapy, different forms of peritoneal dialysis, music, aromatherapy and massage. Risks of bias in the included studies were often high or unclear, and these risks combined with imprecision in effect estimates led frequently to very low certainty evidence. The effect of sleep management on sleep quality, sleep latency, total sleep time, depression and fatigue were documented often using different outcome measures which limited our ability to combine studies.

In general, relaxation techniques and exercise had uncertain effects on sleep quality. In moderate quality evidence, acupressure may increase total sleep duration, but had uncertain effects on other aspects of sleep quality when compared with no treatment control. Sleep hygiene education may decrease the time taken to sleep, increases sleep duration, and may reduce sleep disturbance. There were no studies designed to directly examine and/or correlate efficacy of any interventions aimed at improving sleep that may have been attempted for the spectrum of sleep disordered breathing. Adverse event reporting was sparse. Insufficient evidence was available to determine the long-term effectiveness and safety of all approaches.

Overall, this review suggests that current evidence for sleep interventions in people with CKD is insufficient to guide clinical practice. Due to limitations in the evidence because of inconsistent treatment effects measured by different studies, and limitations in studies based on the reporting of methods, the confidence in the evidence for most outcomes was downgraded from high confidence, meaning that future studies might have different results and lead to changing in our knowledge about the impact of sleep intervention in people with CKD. Possible beneficial effects of sleep interventions such as sleep hygiene education and acupressure suggest that research in this field may have an important impact on clinical outcomes.

Overall completeness and applicability of evidence

This review found that studies specifically designed to evaluate interventions for sleep disorders in CKD were generally sparse and infrequent. Notably, most studies focused on care for people with ESKD, reflecting the burden of symptoms for this group of patients. There were no studies among children, who may be considerably impacted by sleep disorders, including impaired social and

educational attainment and neurocognitive development and reduced quality of life (Mitchell 2006). Studies generally did not routinely report or were not designed to evaluate unintended adverse effects of therapy. The limited number of relevant studies identified for inclusion also prevented examination of the impact of interventions within specific clinical settings such as gender, stage of kidney disease, or duration or intensity of treatment. Some interventions (such as CBT) included different techniques and approaches to manage sleep disorders. The lack of sufficient studies and differences in outcome measures precluded analyses that combined these treatments. The external validity of the review may be limited as most of the studies were not specifically designed to examine interventions in patients with a prespecified diagnosis of sleep impairment, were conducted in higher income countries, and were short-term. Although sleep related outcomes and HRQoL were reported using validated tools for CKD, there was a lack of consistency in estimating outcomes among the current studies. In the future research studies, standardised outcome measures of sleep quality would enhance our ability to compare different treatments.

Quality of the evidence

We assessed the quality of study evidence using standard risks of bias domains within the Cochrane tool and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (GRADE 2011), which considers study limitations, imprecision, indirectness, inconsistency and publication bias. Overall, most studies had unclear risks of bias for sequence generation and allocation concealment, which may have led to over-estimated treatment effects (Page 2016). We rated the certainty of the evidence for relaxation techniques as low or very low, downgraded for unexplained heterogeneity, methodological limitations, and imprecision in summary effects. We assessed the certainty of the evidence for exercise on sleep quality as very low due to an imprecise treatment effect, study risk of bias, and unexplained statistical heterogeneity. The limited number of studies prevented exploration of potential sources of heterogeneity in the analyses. We rated the certainty of the evidence for acupressure interventions on sleep quality as very low, similarly due to methodological limitations in available studies, and marked unexplained heterogeneity. Such assessments suggest that the true effects of relaxation techniques, exercise, and acupressure may be substantially different from the intervention effects reported in the review, with future research very likely to change the treatment estimates observed in this review.

Potential biases in the review process

This review was conducted according to a pre-specified protocol, used a highly sensitive search strategy, was conducted by two independent review authors, and considered evidence certainty in interpretation of the results. However, the study has limitations which need to be noted when interpreting the results. First, we excluded studies in which sleep disorders were not reported as a clinical outcome. This restriction may have led to low power in analyses for adverse effects of the included interventions. Second, we only included studies targeting interventions for sleep outcomes. Other interventions that may be less amenable to a randomised study design, such as home based dialysis therapies, could not be included. Third, we used only end of treatment values for sleep outcomes to maximise data for inclusion in meta-analysis. We did not include change in sleep scores from baseline to end of

treatment, that may have provided further insights into treatment effects. Fourth, we pooled data from a range of clinical settings including stage of kidney disease; due to insufficient studies, we were not able to evaluate whether treatments had different benefits or harms for different clinical settings. We included other outcomes not directly related to sleep endpoints in the review and summary of findings tables. Fifth, as our search strategy and eligibility criteria did not aim to include all studies reporting these outcomes, we could not include all available studies in the literature for these endpoints; the results of these meta-analyses may not reflect the overall evidence. Finally, we did not grade the certainty of all evidence for all outcomes. However, it is likely, due to the very small number of studies in the meta-analyses, that evidence certainty was low or very low for many of these ungraded outcomes.

Agreements and disagreements with other studies or reviews

The findings in this review are more cautious compared with those from a review of non-pharmacological interventions for improving sleep quality in patients treated with dialysis published in 2015 (Yang 2015). In that review of 12 RCTs and one cohort study, the authors concluded that CBT, physical training, and acupressure could improve sleep quality, measured using the PSQI. Differences between the Yang 2015 review and the present Cochrane review included use of change in sleep quality scores, meta-analysis of single studies, inclusion of non-randomised data, and limited consideration of evidence certainty when drawing conclusions about treatment effects. In a recently published Cochrane review (Kim 2016), Kim and colleagues evaluated acupressure and related interventions among patients with CKD and included sleep outcomes. As reported in the present review, the review authors documented very low certainty evidence that manual acupressure improved sleep quality (PSQI decrease of 2.46 on average) at four weeks. Similarly, there was no evidence that manual acupressure made any difference to sleep quality compared with sham acupressure. In a recent Cochrane review of interventions for restless legs syndrome amongst patients on dialysis (Gopaluni 2016), meta-analyses of studies evaluating gabapentin, levodopa, vitamin C and E, iron dextran, or ropinirole were not possible.

AUTHORS' CONCLUSIONS

Implications for practice

Evidence is lacking about certain interventions (such as relaxation techniques, exercise, acupressure, CBT, educational interventions,

benzodiazepine treatment, dopaminergic agonists, telephone support, melatonin, reflexology, light therapy, different forms of peritoneal dialysis, music, aromatherapy and massage) in improving sleep quality among adults and children with CKD. There is insufficient evidence to provide direction to health policy makers and practitioners. Very low quality evidence suggests acupressure may have small effects, but this is not confirmed in sham studies. All findings should be interpreted with caution as very few studies could be included in meta-analysis. Information for people with milder stages of CKD and for children are especially sparse, including information about schooling attainment and neurocognitive development. The potential adverse effects of treatment are largely unknown. There were no studies designed to directly examine and/or correlate efficacy of any interventions aimed at improving sleep that may have been attempted for the spectrum of sleep disordered breathing.

Implications for research

Despite a large number of studies, there is a lack of high-certainty research for sleep disorders in people with CKD. Given the high symptom burden experienced by people with CKD, together with the prioritisation of research informing symptom management, new research initiatives for improving sleep disorders would address an important clinical uncertainty. This review identified a number of opportunities for future intervention research specifically targeting sleep including:

1. Studies of interventions for improving sleep in children with CKD
2. Studies of interventions for sleep-disordered breathing and obstructive sleep apnoea
3. Investigation of longer term treatment with extended periods of follow-up
4. Studies of promising interventions sufficiently powered to examine effects on patient-centred outcomes such as next day function and quality of life for adults and educational and social functioning and neurocognitive development in children
5. Exploration of the adverse effects of treatment
6. Larger studies comparing acupressure with sham acupressure.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Afshar 2011

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: 2009 Duration of follow-up: 8 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre People on maintenance HD for > 3 months, aged > 20 years, and good compliance with dialysis treatment (not missing more than 2 dialysis sessions in the prior month) and had sleep problems (in regular sleeping time at night) Number: treatment group (14); control group (14) Mean age $\pm$ SD (years): treatment group (21.06 $\pm$ 50.71); control group (19.40 $\pm$ 53.00) Sex (M/F): all males Exclusion criteria: active infection or inflammation; autoimmune disorders; malignancy; psychiatric diseases; severe musculoskeletal disorders; poor controlled diabetes; uncontrolled heart failure or pulmonary diseases; hospitalisation during the prior month; using drugs that influence serum cytokines levels; vascular access in the lower extremity; BMI > 25 kg/m²
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Aerobic training: 5 minutes of warm-up and 10 to 30 minutes of stationary cycling, 3 times/week <p>Control group</p> <ul style="list-style-type: none"> Not reported
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI)
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported Quoting from the paper: "This is a descriptive cross-sectional case control study that was performed in a haemodialysis unit in Tehran, Iran, in 2009." However, both in the abstract and in the main body the study was reporting as the following "The participants were randomly divided into the training group and the control group (n = 14 in each group)." It was not completely clear if the study should be included: we contacted the author to ask clarification about this issue. We will perform sensitivity analysis with and without this study

Afshar 2011 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were randomly assigned into control and training groups." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The Pittsburgh Sleep Quality Index and the Baecke questionnaire on physical activity were filled out for all participants." Comment: Sleep quality was assessed using the PSQI which was self-administered by participants who could be aware of treatment assignment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Low risk	Quote: "The global Pittsburgh Sleep Quality Index (PSQI) score was calculated at baseline and at the end of the study (after the 8th week)." Comment: Sleep outcomes was measured by PSQI questionnaire in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Unclear risk	Quote: "The participants' characteristics are shown in Table 1." Comment: The baseline characteristics and the co-interventions were not provided in sufficient detail to perform assess comparability between groups, the study funding source was not described. There was insufficient information to permit judgement

Amini 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: 2016 Duration of follow-up: 8 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre Signing the informed consent form to participate in the study; history of undergoing regular HD for at least 12 months; lack of suffering from severe neuromuscular diseases; depression; severe and unmanaged underlying diseases; lack of taking antidepressants and anti-anxiety and hypnotic medicines; lack of participating in exercise or non-pharmacological programs within the past 6 months; being able to perform interventional exercises Number: treatment group 1 (32); treatment group 2 (32); control group (35) Mean age (years): treatment group 1 (56.12); treatment group 2 (54.31); control group (55.22) Sex (M/F): treatment group 1 (22/11); treatment group 2 (21/11); control group (21/14)

Amini 2016 (Continued)

- Exclusion criteria: not reported

Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> • Progressive muscle relaxation: daily for 60 days <p>Treatment group 2</p> <ul style="list-style-type: none"> • Aerobic exercise: daily for 60 days <p>Control group</p> <ul style="list-style-type: none"> • Not reported
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Anxiety (Beck) • Fatigue (Piper)
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "In this double-blind clinical trial, 100 haemodialysis patients were randomly assigned to three groups: Progressive Muscle Relaxation (PMR), aerobic exercise, and control."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "In this double-blind clinical trial, 100 haemodialysis patients were randomly assigned to three groups: Progressive Muscle Relaxation (PMR), aerobic exercise, and control."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Sleep quality was assessed using PSQI questionnaire. Investigators did not report the method for outcome measurement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Low risk	Sleep reported according to prespecified analysis at baseline and at end of treatment using the PSQI scale. Data for meta-analysis were available for sleep quality
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Aoike 2018

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT
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Interventions for improving sleep quality in people with chronic kidney disease (Review)

Aoike 2018 (Continued)

	<ul style="list-style-type: none"> Duration of study: not reported Duration of follow-up: 24 weeks
Participants	<ul style="list-style-type: none"> Country: Brazil Setting: Single centre Patients 18 to 70 years with CKD stages 3 and 4; BMI > 25 kg/m²; SBP < 180 mmHg and DBP < 100 mmHg; serum Hb > 11 g/dL; HbA1c < 8%; absence of chronic obstructive pulmonary disease, congestive heart failure or active coronary disease Number (randomised/analysed): treatment group 1 (14/12); treatment group 2 (16/13); control group (15/15) Mean age ± SD (years): treatment group 1 (56 ± 8.3); treatment group 2 (56.3 ± 7.9); control group (54.3 ± 8.7) Sex (M/F): treatment group 1 (8/4); treatment group 2 (9/4); control group (10/5) Exclusion criteria: use of beta-blockers or EPO; arrhythmia or myocardial ischemias detected by cardiovascular stress testing
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Home-based exercise group: training was performed for 30 min with increments of 10 min in duration every 4 weeks until week 8 <p>Treatment group 2</p> <ul style="list-style-type: none"> Centre-based exercise group: training was performed for 30 min with increments of 10 min in duration every 4 weeks until week 8 <p>Control group</p> <ul style="list-style-type: none"> Not reported <p>Co-interventions</p> <ul style="list-style-type: none"> Renal-specific diet containing approximately 30 kcal/kg/day and 0.6 to 0.8 g/kg/day of protein
Outcomes	<ul style="list-style-type: none"> PSQI score and SF-36 total score (data not extractable) No adverse events were observed
Notes	<ul style="list-style-type: none"> Funding source: Sao Paulo Research Foundation (FAPESP) (2009/14786-0), Coordination for the Improvement of Higher Education Personnel (CAPES), Oswaldo Ramos Foundation, Psychobiology and Exercise Study Centre (CEPE) and the Research Incentive Fund Association (AFIP). NCT02379533

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The patients were assigned to exercise or control groups after a blocked randomisation procedure using a random block of 6 participants."</p> <p>Comment: Not reported sufficient information for the adjudication. Participants were randomised using block randomisation (random block of 6 participants), but method for sequence generation was not described</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "The patients were assigned to exercise or control groups after a blocked randomisation procedure using a random block of 6 participants."</p> <p>Comment: Not reported sufficient information to permit judgement. Participants were randomised using block randomisation (random block of 6 participants), but allocation concealment was not described</p>

Aoike 2018 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The patients assigned to the exercise group were allowed to choose their preferred mode of exercise between home- and centre-based." Comment: Treatment characteristics were sufficiently different that blinding of treatment allocation was not possible
Blinding of outcome assessment (detection bias) All outcomes	High risk	Sleep quality was assessed using PSQI. All questionnaires were individually administered by the same observer in a quiet room with the patient rested. It is not clear whether the observer was blinded to treatment allocation. Participant was aware of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "As shown in Fig. 1, 50 patients agreed to participate in the study. Before randomisation, five patients were excluded: three were due to an eGFR below 15 mL/min, and two withdrew their consent. Therefore, 45 patients were randomised. Five patients were lost during the follow-up due to social and financial issues. Thus, the present study was completed with a total of 40 patients." Comment: > 10% loss of participants. 3/16 in the allocation exercise centre-based group and 2/14 in the allocation exercise home-based group and 0/15 in control group were lost to follow-up for reasons that appeared unrelated to treatment
Selective reporting (reporting bias)	Low risk	Sleep quality was assessed at all study time points using PSQI. Data were reported as mean and 95% confidence interval at each time point (in figure format)
Other bias	Low risk	Baseline and non-randomised co-intervention characteristics were similar between groups. This study was supported by Sao Paulo Research Foundation (FAPESP). The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Arab 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: 2011 Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: multicentre Patients aged 18 to 70 years; a 6-month history of HD 3 times/week, 4 hours/session; a PSQI ≥ 5; having complete consciousness, hearing and speaking ability; no diagnosed psychological disorder requiring daily medication; no history of cancer, lupus, skin disease, advanced cardiac failure, insulin-dependent diabetes or stroke; no limb amputation or scar in the pressure points; at least basic formal education Number (randomised/analysed): treatment group 1 (36/32); control group 1 (36/30); control group 2 (36/31) Mean age $\pm$ SD (years): not reported Sex (M/F): treatment group 1 (17/15); control group 1 (17/13); control group 2 (16/15) Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> Acupressure: 3 times/week during dialysis

Arab 2016 (Continued)

Control group 1

- Placebo acupressure: 3 times/week during dialysis

Control group 2

- No treatment

Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep interruption (PSQI) • HRQoL (SF-36)
Notes	<ul style="list-style-type: none"> • Funding source: Golestan University of Medical Sciences grant. IRCT201106145864N2

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "The randomisation process was concealed by using sealed envelopes, and the person responsible for enrolment did not know which group the patients would be allocated to."</p> <p>Comment: Unclear if envelopes were opaque and were sequentially numbered</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were assigned to acupressure or sham. A single-blind study is considered as high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants completed the PSQI questionnaire at baseline and end of study. Participants were unaware of treatment assignment. The assessor and statistician were blind to the study groups
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "During the study period 15 participants (four, six, and five from the acupressure, placebo acupressure, and no treatment groups, respectively) were withdrawn for different reasons such as transplantation, absence for travel, hospitalisation, major stress due to a close relative's death, and unwillingness to continue in the study."</p> <p>Comment: > 10% loss of participants. 4/36 in the acupressure group and 6/36 in the sham acupressure group and 5/36 in control group were lost to follow-up for reasons that appear unrelated to treatment</p>
Selective reporting (reporting bias)	Low risk	Sleep quality was assessed using PSQI among all study participant groups at all time points. Data were available for inclusion in meta-analysis
Other bias	Low risk	Baseline and non-randomised co-intervention characteristics were similar between groups. This study was supported by The Golestan University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Bro 1999

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT
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Bro 1999 (Continued)

	<ul style="list-style-type: none"> Duration of study: not reported Duration of follow-up: 26.4 weeks
Participants	<ul style="list-style-type: none"> Country: Denmark Setting: multicentre (3 sites) Aged ≥ 18 years, minimum of 1 month of CAPD treatment; consideration by staff that patient would be able to learn to use the APD machine; a recent (within 3 months) PET showing high or high-average peritoneal transport characteristics; $Kt/V \geq 1.70/\text{week}$ and a total $\text{CrCl} \geq 50 \text{ L/week}/1.73 \text{ m}^2$ Number (randomised/analysed): treatment group (17/12); control group (17/13) Mean age $\pm$ SD (years): treatment group (50.2 ± 18.97); control group (54.2 ± 17.32) Men: treatment group (66.7%); control group (61.5%) Exclusion criteria: < 18 years; pregnancy; lactation; mental retardation or dementia; psychiatric illness; inability to speak Danish; any major medical or surgical event in the previous 3 months; malignancy; a recent (within 3 months) PET showing low or low-average peritoneal transport characteristics; $Kt/V < 1.70/\text{week}$ and/or $\text{CrCl} < 50 \text{ L/week}/1.73 \text{ m}^2$; ultrafiltration failure despite optimised CAPD treatment
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> APD <p>Control group</p> <ul style="list-style-type: none"> CAPD
Outcomes	<ul style="list-style-type: none"> Sleep quality HRQoL (SF-36) Adverse events
Notes	<ul style="list-style-type: none"> Funding source: Danish Society of Nephrology Research Foundation Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "Sealed envelopes containing the treatment allocation were arranged in groups of 10 and used for the randomisation procedure, which took place at the main centre (Rigshospitalet in Copenhagen)."</p> <p>Comment: uncertain if envelopes were opaque or sequentially numbered</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	This paper was an open blind study. An open blind study is considered as high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Sleep quality was assessed using the SF-36 which was self-administered by participants who were aware of treatment assignment
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "From the CAPD arm, four patients terminated prematurely: 1 received a kidney transplant after 12 days; 2 were changed to haemodialysis after 2 months, 1 because of edema of the scrotum, the other because of peritoneal catheter dysfunction and sepsis. The fourth patient never started the study"

Bro 1999 (Continued)

because of a sudden deterioration of the general health status. From the APD arm, 5 patients dropped out before the end of the study: 1 received a kidney transplant after 2 months, 1 wished to stop APD treatment after 14 days because of psychosocial factors, 1 stopped after 2 months because of a subjective feeling of inadequate dialysis, 1 stopped APD treatment after 15 days due to inability to handle the cycle. The fifth patient never started the study because of a sudden impairment of visual acuity."

Comment: > 10% loss of participants. 4/17 in CAPD group and 5/17 in APD group were lost to follow-up for reasons that appear unrelated to treatment

Selective reporting (reporting bias)	Low risk	Sleep quality was measured by Self-administered Short-Form (SF-36) questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Baseline and non-randomised co-intervention characteristics were similar between groups. This study was supported by The Danish Society of Nephrology Research Foundation. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Burkhalter 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 3 weeks
Participants	<ul style="list-style-type: none"> Country: Switzerland Setting: Multicentre (3 sites) Adult kidney transplant recipients more than 1 year post-transplant and diagnosed with sleep-wake disturbance (sleep assessment interview in the preceding study); German speaking; on stable immunosuppressive drugs; no signs of acute rejection; and normal ocular function (by self-report and by chart review) Number: treatment group (15); control group (15) Mean age $\pm$ SD (years): treatment group (60.72 ± 10.33); control group (58.54 ± 14.91) Men (%): treatment group (8/7); control group (7/8) Exclusion criteria: acute illness or hospitalisation
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Bright light therapy: 30 min daily for 3 weeks <p>Control group</p> <ul style="list-style-type: none"> Usual care
Outcomes	<ul style="list-style-type: none"> Sleep quality Sleep onset latency (Actimeter) Sleep efficiency (Actimeter) Depression (DASS 21)
Notes	<ul style="list-style-type: none"> Funding source: Swiss Renal Foundation. NCT01256983

Risk of bias

Bias	Authors' judgement	Support for judgement
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Burkhalter 2015 (Continued)

Random sequence generation (selection bias)	Unclear risk	<p>Quote: "This pilot randomised multicentre wait-list controlled trial included 30 home-dwelling RTX randomly assigned 1:1 to either 3 weeks of BLT or a wait-list control group."</p> <p>Comment: Not reported sufficient information to permit judgement. This pilot study used a multicentre randomised wait-list controlled design with a 1:1 randomisation sequence (Fig. 2), so that everybody benefits from the intervention that is staggered over time</p>
Allocation concealment (selection bias)	Low risk	<p>Quote: "A computerized random allocation sequence was generated by an external research assistant. Sequentially numbered opaque envelopes containing the allocation information. Until each participant opened his or her assignment package, the research team had no knowledge of allocations."</p> <p>Comment: Investigators could not foresee assignment and it could be considered as low risk of bias</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were aware on the group assigned. Treatment characteristics were sufficiently different that blinding of treatment allocation was not possible: Light Energy HF 3304 was installed in each participant's home in the intervention group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up was similar into the two groups and < 10%. 1/15 in bright light therapy and 1/15 in usual care group were lost to follow-up. One patient from each group found the study too burdensome
Selective reporting (reporting bias)	Low risk	Sleep outcomes were measured by PSQI among all study participant groups. Data about the end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Baseline and non-randomised co-intervention characteristics were similar between groups. This study was supported by The Swiss Renal Foundation. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Champagne 2008

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 13.2 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Canada Setting: not reported HD patients with moderate sleep apnoea Number: 15 Mean age $\pm$ SD: 58 $\pm$ 14 years Sex (M/F): 8/1 had completed protocol Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> HDF

Champagne 2008 (Continued)

	Control group
	<ul style="list-style-type: none"> • HD
Outcomes	<ul style="list-style-type: none"> • Sleep apnoea (polysomnogram) • 24 hour BP • Sleep-related QoL (SF-36; FOSQ; Quebec Sleep Questionnaire) • ESS
Notes	<ul style="list-style-type: none"> • Abstract-only publication • Outcome data could not be meta-analysed • Funding source: Gambro. NCT0038084

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not reported. However, patients were randomised to HD or HDF. As these treatments are physically different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	High risk	> 10% loss of participants: overall 6/15 have completed the protocol to date. However, it was not clear whether there was a differential rate loss to follow-up between the two study groups
Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	High risk	Cross-over study in which investigators did not report outcome measures appropriately for the crossover study design. Sponsor could be involved into the analysis

Chen 2008a

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Duration of study: not reported • Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> • Country: Taiwan • Setting: single centre • All patients ≥ 18 years who had been undergoing maintenance PD for longer than 3 months using conventional glucose-based lactate buffer PD solutions; history of sleep disturbance for more than 3 months (insomnia); without active medical or unstable psychiatric condition and other documented symptoms of OSA and periodic limb movement disorders, such as RLS

Chen 2008a (Continued)

- Number: treatment group (13); control group (13)
- Mean age $\pm$ SD (years): treatment group (51.9 ± 8.6); control group (48.7 ± 14.6)
- Sex (M/F): treatment group (8/5); control group (7/6)
- Exclusion criteria: not reported

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • CBT and sleep hygiene education: 1 hour/week <p>Control group</p> <ul style="list-style-type: none"> • Sleep hygiene education: 1 hour/week
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep latency (PSQI) • Total sleep time (PSQI) • Sleep efficiency (PSQI) • Fatigue (FSS) • Adverse events
Notes	<ul style="list-style-type: none"> • Funding source: Ta-Tung Kidney Foundation and Mrs Hsin-Chin Lee Kidney Research Fund. NCT00155441

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "We randomly assigned participants by using computer-generated randomised numbers with an allocation ratio of 1:1; i.e., to either the CBT group (N 13) or the control group (N 13). No stratification or blocking factors were used."</p> <p>Comment: Computer-generation is considered method at low risk of bias</p>
Allocation concealment (selection bias)	High risk	<p>Quote: "The generation of allocation sequence and assignment of participants was performed by the project director."</p> <p>Comment: The investigators enrolling participants could possibly foresee assignments</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This pilot study did not use a double-blind design, and participants were informed of their allocation sequence by telephone. The sequence was concealed until the interventions were assigned."</p> <p>Comment: As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Patients were randomised to or sleep hygiene education. As primary outcome was surveys completed by unblinded participants, the outcome assessment was carried out by patients who were aware of treatment assignment</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>< 10% loss of participants, as reported in the flow chart. 0/13 in the CBT + sleep hygiene group did not receive intervention and 2/13 in the sleep hygiene group did not receive intervention. All participants were included in analysis</p>
Selective reporting (reporting bias)	Low risk	<p>Quote: "Primary outcomes were the effects of the 4-week cognitive-behavioral therapy (CBT) on quality of sleep and severity of fatigue. [...] Primary outcomes with respect to efficacy of cognitive-behavioral therapy (CBT) were assessed by means of 2 instruments: the Pittsburgh Sleep Quality Index (PSQI) and the</p>

Chen 2008a (Continued)

Fatigue Severity Scale (FSS). [...] The 2 measurements were completed before and after the 4-week trial by all participants in both groups."

Comment: Sleep outcomes was measured by PSQI questionnaire in all participants at end of treatment in a format that was extractable for meta-analysis

Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Ta-Tung Kidney Foundation and Mrs Hsin-Chin Lee Kidney Research Fund. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent
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Chen 2011a

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 6 weeks
Participants	<ul style="list-style-type: none"> Country: Taiwan Setting: Single centre Patients ≥ 18 years undergoing maintenance HD who had chronic sleep disturbances; PSQI score of > 5 during screening of enrolment; history of sleep disturbance for > 6 months; patients without active medical and psychiatric conditions and other documented symptoms of OSA (defined as ESS > 10 or typical symptoms) and periodic limb movement disorders, such as RLS Number (randomised/analysed): treatment group (40/37); control group (40/35) Mean age $\pm$ SD (years): treatment group (57 ± 9) control group (59 ± 11) Men (%): treatment group (17/20) control group (13/22) Exclusion criteria: PSQI ≤ 5; history of sleep disturbance for < 6 months; active medical conditions; active psychiatric conditions; documented symptoms of OSA and RLS
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> CBT and sleep hygiene education: 30 minutes, 3 times/week <p>Control group</p> <ul style="list-style-type: none"> Sleep hygiene education
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep duration Sleep latency Sleep efficiency Fatigue (FSS) Depression (Beck) Anxiety (BAI)
Notes	<ul style="list-style-type: none"> Funding source: supported by grants from the Far Eastern Memorial Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
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Chen 2011a (Continued)

Random sequence generation (selection bias)	Low risk	<p>Quote: "We randomised participants by computer-generated random numbers with an allocation ratio of 1:1; that is, either to the cognitive-behavioral therapy (CBT) group or to the control group."</p> <p>Comment: Computer-generation is considered method at low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "Participants were informed of their allocation sequence by the nursing staff, and the sequence was concealed until the interventions were assigned. The generation of allocation sequence and assignment of participants was performed by the project director."</p> <p>Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement.</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This study was an open-labelled design."</p> <p>Comment: An open-label study is considered as high risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Participants were informed of their allocation sequence by the nursing staff."</p> <p>Comment: Participants completed the PSQI questionnaire at baseline and end of study. Participants were aware of treatment assignment. Outcome assessment was unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Quote: "After randomisation, three participants in the cognitive-behavioral therapy (CBT) group and five participants in the control group refused to participate and withdrew their informed consent because of personal considerations. Therefore, a total of 72 subjects (37 in the cognitive-behavioral therapy (CBT) group and 35 in the control group) participated."</p> <p>Comment: 8 patients (3/40 in the CBT group and 5/40 in the sleep hygiene group) refused to participate after randomisation and withdrew their informed consent. However, as reported in flow chart, in both groups there were no lost to follow-up in people who received the intervention</p>
Selective reporting (reporting bias)	Low risk	<p>Quote: "The primary outcomes with respect to efficacy of cognitive-behavioral therapy (CBT) were assessed with the Pittsburgh Sleep Quality Index (PSQI)."</p> <p>Comment: Sleep outcomes were measured by PSQI questionnaire in all participants at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Far Eastern Memorial. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent</p>

Cho 2018

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: December 2014 to March 2015 Duration of follow-up: 12 weeks
Participants	<ul style="list-style-type: none"> Country: Korea Setting: not reported

Cho 2018 (Continued)

- Age ≥ 20 years; HD ≥ 6 months; HD treatment thrice weekly; no hospitalisations during the previous 3 months, except for vascular access repair; no amputations or prostheses in upper and lower extremities; cognitive capacity sufficient for communication; able to ambulate and wear the physical activity monitor for 7 days; and good compliance with the study protocol
- Number (randomised/analysed): treatment group 1 (15/11); treatment group 2 (14/10); treatment group 3 (15/12); control group (13/13)
- Mean age $\pm$ SD (years): treatment group 1 (55.2 ± 11.9); treatment group 2 (52.9 ± 8.8); treatment group 3 (50.0 ± 14.3); control group (59.4 ± 10.8)
- Sex (M/F): treatment group 1 (2/9); treatment group 2 (6/4); treatment group 3 (8/4); control group (7/6)
- Exclusion criteria: any acute infectious or other inflammatory illnesses; current malignancy except basal cell carcinoma; acute myocardial infarction or unstable angina within the past 12 months; current heart or lung failure or severe liver disease; severe uncontrolled diabetes; severe retinal diseases, such as proliferative diabetic retinopathy and vitreous haemorrhage; orthopaedic disorders exacerbated by activity

Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> • Aerobic exercise: 30 min of intradialytic aerobic exercise 3 times/week, which consisted of stationary cycling <p>Treatment group 2</p> <ul style="list-style-type: none"> • Resistance exercise: programmed session of intradialytic resistance exercise 3 times/week using elastic resistive bands and soft weights <p>Treatment group 3</p> <ul style="list-style-type: none"> • Combination exercise: both intradialytic aerobic exercise and resistance exercise, 3 times/week <p>Control group</p> <ul style="list-style-type: none"> • No intradialytic exercise but patients received warm-up stretches only
Outcomes	<ul style="list-style-type: none"> • Sleep quality (ActiLife) • Total sleep time • Sleep efficiency • Hospitalisation • Cardiovascular events • Adverse events
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "This 12-week study was a randomised parallel design investigating the effects of different exercise regimes on changes in daily physical activity (DPA) and sleep quality (SQ)."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement

Cho 2018 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Allocation was concealed at the time of participant consent; however, participants and the researcher were made aware of their group at the commencement of the intervention. Due to the nature of the intervention, blinding of intervention groups to the researcher and dialysis patients was not possible." Comment: As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Sleep quality were measured with a triaxial accelerometer (wActiSleep-BT; ActiGraph, Pensacola, FL) during a continuous 7-day wear period." Comment: Although these treatments were different, and participants were aware of treatment assignment, the outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	As reported in the flow chart, 4/15 in the aerobic exercise group, 4/14 in the resistance exercise group, 3/15 in the combination exercise group and 0/13 in the control group were lost to follow-up for reasons that appear unrelated to treatment. There was a differential rate loss to follow-up between the study groups
Selective reporting (reporting bias)	Low risk	Sleep outcomes was measured by accelerometer in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent

Chow 2010

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: 2005 Duration of follow-up: 6 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: multicentre Inclusion criteria: PD patients who were able to access a telephone after discharge from the hospital Number (randomised/analysed): treatment group (50/43); control group (50/42) Education program: 50 Control: 50 Mean age $\pm$ SD (years): treatment group (59.4 $\pm$ 13.97); control group (54.5 $\pm$ 12.8) Sex (M/F): treatment group (28/15); control group (24/18) Exclusion criteria: intermittent PD or HD and those with planned admissions for special treatment procedures; Tenckhoff catheters in situ for < 3 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Education program: 20 to 30 minutes <p>Control group</p> <ul style="list-style-type: none"> Routine discharge care
Outcomes	<ul style="list-style-type: none"> Sleep quality (KDQOL-SF) HRQoL

Chow 2010 (Continued)

- Pain
- Fatigue

Notes

- Funding source: Research Grants Council of Hong Kong
- Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from Wong 2010 (secondary publication): "This is a randomised controlled trial. 120 sets of computer-generated random numbers were used, and patients who fitted the criteria were randomised to the study or control group." Comment: In Chow 2010 sequence generation methods were not reported in sufficient detail to make an adjudication. However, in Wong 2010 "computer-generation" was considered a method at low risk of bias
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The data were collected in 2005 at three time intervals using a structured self-report questionnaire." Comment: Patients were randomised to lower educational program or control group. As these treatments were different, and participants were aware of treatment assignment when they completed self-reported questionnaires, outcome assessment were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	As reported in flow chart, 4/50 patients in the intervention group and 5/50 in the control group were lost to follow-up: these were small numbers and there was not a differential loss between groups. Moreover, 3/50 participants in the intervention discontinued for death, renal transplantation and change of treatment regimen; 3/50 participants in the control group discontinued because they declined to be interviewed due to the change of treatment regimen. In the end, 43 participants in the intervention group and 42 in the control group were analysed. There was no evidence of differential loss to follow-up that may have been related to the intervention
Selective reporting (reporting bias)	Low risk	Quote: "To determine the attribution of time effects from the two groups, repeated measures were conducted separately for the groups at the three time intervals." Comment: Sleep outcomes was measured by the Kidney Disease Quality of Life Short Form (KDQOL-SF) at end of treatment in all participants in a format that was extractable for meta-analysis.
Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The authors had a Research Grants Council of Hong Kong. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Dai 2007a

Methods	<ul style="list-style-type: none"> Study design: parallel, open-label RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: single centre Patients with ESKD (NKF-K/DOQI diagnostic criteria) with sleep disturbance and having ≥ 23 points in the Self-Rating Scale of Sleep and no mental disorder; willingness to participate in the study Number: treatment group 1 (42); treatment group 2 (40) Mean age $\pm$ SD (years): treatment group 1 (53.0 ± 15.1); treatment group 2 (60.4 ± 18.2) Men: 47.6% Exclusion criteria: not reported
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Lower extremity point massage (manual acupressure): once/day, and 20 to 30 seconds each time <p>Treatment group 2</p> <ul style="list-style-type: none"> Estazolam (oral): 1 mg/day
Outcomes	<ul style="list-style-type: none"> Sleep quality Adverse events
Notes	<ul style="list-style-type: none"> Not English Trial number registration: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "82 cases of patients with End Stage Kidney Disease with sleep disorders were randomly divided into observation group and control group."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to make an adjudication</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	The study was an open-label study. An open-label study is considered as high risk of bias, Both participants and therapists were aware of the treatments assignment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported. However, patients were randomised to lower extremity point massage or Estrazolam. As these treatments are physically different, blinding of participants and investigators to treatment assignment was unlikely
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Low risk	Quote: "Self-Rating Scale of Sleep (SRSS) was used to evaluate sleep conditions."

Dai 2007a (Continued)

Comment: Sleep outcomes was measured by the Self-Rating Scale of Sleep at end of treatment in all participants in a format that was extractable for meta-analysis

Other bias	Low risk	Study appears free of other biases
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Dashti-Khavidaki 2011

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 2 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre Inclusion criteria: HD patients Number: treatment group 1 (12); treatment group 2 (11) Mean age $\pm$ SD: 60 $\pm$ 14 years Overall: 60 (14) Sex (M/F): 16/7 Exclusion criteria: suffer from any concurrent situations that may affect sleep quality including cancer, congestive heart failure, connective tissue disease, and psychiatric disorders
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Zolpidem (oral): 5 to 10 mg/day <p>Treatment group 2</p> <ul style="list-style-type: none"> Clonazepam (oral): 1 mg/day
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Adverse events
Notes	<ul style="list-style-type: none"> Funding source: Tehran University of Medical Sciences Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "Permuted block randomisation with a block size of 4 was used to randomised patients to receive zolpidem (10 mg for patients younger than 60 years old and 5 mg for older participants) or clonazepam (1 mg), nightly for the 1st two weeks."</p> <p>Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	<p>Quote: "Patients were blinded to the drug administered in each group."</p> <p>Comment: Not reported whether investigators were blinded. Method of blinding participants not discussed (identical medication? placebo)</p>

Dashti-Khavidaki 2011 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Sleep quality was assessed using PSQI questionnaire which were filled out by one of the researchers. Unclear whether the researchers and/or participants were unaware of treatment assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 23 randomised participants provided outcome data at the end of the first period of randomisation
Selective reporting (reporting bias)	Low risk	Outcomes were reported in a method that was appropriate for study design (crossover trial) or allowed data extraction for meta-analysis. The PSQI was assessed at baseline, and after each treatment phase in all participants
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Dauvilliers 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: April 2012 to October 2013 Duration of follow-up: 6 weeks
Participants	<ul style="list-style-type: none"> Country: USA and Europe Setting: multicentre (12 sites) Adult patients aged 18 and 85 years with ESKD requiring HD (regular dialysis schedule of 3 times/week for at least 3 months) with diagnosis of RLS based on the RLSSG criteria (RLS-diagnostic index score ≥ 11 points), moderate to severe RLS symptoms (score ≥ 15), CGI-1 (severity of illness) score ≥ 4, and PLMI ≥ 15 PLM/h in bed (assessed by baseline polysomnography); BMI of 18 to ≤ 40 kg/m²; Hb ≥ 8 g/dL (≥ 4.97 mmol/L), and ferritin concentration ≥ 100 ng/mL at screening (visit 1) Number: treatment group (20); control group (10) Mean age $\pm$ SD (years): treatment group (57.2 ± 12.6); control group (50.7 ± 16.3) Sex (M/F): treatment group (13/7); control group (7/3) Exclusion criteria: previous treatment with rotigotine; symptomatic orthostatic hypotension, or clinically relevant cardiovascular, venous, or arterial peripheral diseases; narcolepsy or other disorders of central hypersomnia; clinically relevant polyneuropathy or verticospasms, or additional clinically relevant concomitant diseases; evidence of an impulse control disorder according to the modified Minnesota Impulsive Disorders Interview at screening (visit 1); a lifetime history of suicide attempt or suicidal ideation in the past 6 months; a history of psychotic episodes; or a history of chronic alcohol or drug abuse within the prior 12 months; any medical or psychiatric condition that in the opinion of the investigator could have jeopardized or compromised the patient's well-being or ability to participate in the study; a medical history indicating intolerance to dopaminergic therapy (if pretreated) or augmentation of RLS symptoms during previous treatment with any dopaminergic agent; known hypersensitivity to any of the components of the study medication, such as a history of significant skin hypersensitivity to adhesives, known hypersensitivity to other transdermal medications, or unresolved contact dermatitis
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Rotigotine (transdermal patch): 1 to 3 mg/day <p>Control group</p> <ul style="list-style-type: none"> Placebo (transdermal patch)
Outcomes	<ul style="list-style-type: none"> Sleep onset latency Total sleep time Sleep efficiency

Dauvilliers 2016 (Continued)

- HRQoL
- Adverse events

Notes

- Funding source: UCB Pharma. NCT01537042.
- Scales used: RLS-QoL; PLMI; SF-36; IRLS sum score; CGI-1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was carried out by an interactive web response system (ICON Clinical Research L.P.), with strata defined by region". Comment: IWRS indicates automated random sequence
Allocation concealment (selection bias)	Low risk	Quote: "Randomization was carried out by an interactive web response system (ICON Clinical Research L.P.), with strata defined by region". Comment: IWRS indicates centrally allocated treatment assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The RENALYS trial was a double-blind, randomised trial". "Study treatment was administered by a transdermal patch; active and placebo patches were matched in size and appearance." Comment: A double-blind study is considered as low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Recordings from the second night were used for analysis. Polysomnography recordings were transferred to a central reader and scored by trained personnel according to the American Academy of Sleep Medicine Guidelines." Comment: Outcome assessment of the primary outcome was conducted centrally
Incomplete outcome data (attrition bias) All outcomes	High risk	30 patients were randomly assigned: 25 patients completed the study and were included in the efficacy analyses. All patients who were excluded were all receiving rotigotine Imbalance of loss to follow-up between treatment groups
Selective reporting (reporting bias)	Low risk	A full range of expected sleep measures was done at standard time points involving all randomly assigned patients who had at least 1 patch applied during the treatment period and who evaluable data at baseline and end of maintenance treatment. No imputation of missing values
Other bias	High risk	Imbalance at baseline of time since first symptoms of RLS and time diagnosis between treatment groups. The sponsor was involved in the design of the study, analysis and interpretation of data, writing the report, and the decision to submit the manuscript for the publication

Duarte 2009

Methods

- Study design: parallel RCT
- Duration of study: not reported
- Duration of follow-up: 13.2 weeks

Participants

- Country: Brazil
- Setting: multicentre (2 sites)

Duarte 2009 (Continued)

- Patients 18 to 80 years with ESKD receiving outpatient HD treatment (average of 4 hours/session, 3 times/week) for at last 3 months; diagnosis of a major depressive disorder according to the MINI43 criteria; patients with anxiety symptoms were not excluded from the study
- Number (randomised/analysed: treatment group (46/41); control group (44/41)
- Mean age $\pm$ SD (years): treatment group (52.4 $\pm$ 15.9); control group (54 $\pm$ 12.7)
- Sex (M/F): treatment group (15/26); control group (20/24)
- Exclusion criteria: living-donor kidney transplant scheduled within the next several months; current hospitalisation; psychiatric comorbidity (axis I of the DSM-IV) diagnosed by the MINI (anxiety disorders (panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, generalized anxiety disorder, social phobia), psychotic syndrome, and anti-social personality disorder, cognitive impairment (deficiency of memory or unable to understand the questionnaires) or mental retardation; current substance abuse; unstable clinical condition

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • CBT: 12 weekly sessions, 1 hour and 30 minutes <p>Control group</p> <ul style="list-style-type: none"> • Usual care: sessions of 30 to 50 minutes
Outcomes	<ul style="list-style-type: none"> • Sleep quality (KDQOL-SF) • Depression (BDI) • HRQoL (KDQOL-SR) • Death (all causes)
Notes	<ul style="list-style-type: none"> • Funding source: Fundac , a Estado de Sa • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	<p>Quote: "A randomisation list was prepared according to blocks, and sealed envelopes were used, containing the patient's allocation group according to the following sequence of combinations: AABB/ABAB/ABBA/BBAA/BABA/BAAB."</p> <p>Comment: Investigators described a non-random component in the sequence generation</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "The list for patient allocation was prepared by the research coordination centre following a concealed randomisation procedure. The envelopes with the treatment code were sealed and kept at the study site and were consecutively opened when a new patient was selected for inclusion."</p> <p>Comment: It was not clear if envelopes were opaque and sequentially numbers</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	Personnel should be aware of the treatments allocations
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The questionnaires were administered and rated by a trained psychologist who was blinded to the treatment group allocation."</p> <p>Comment: Patients were randomised to CBT or usual care. As these treatments are physically different, blinding of participants and investigators to treatment assignment was unlikely</p>

Duarte 2009 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "During the first 3 months, five patients were lost in the intervention group because of consent withdrawal (n=2), transplantation (n=2), and exclusion due to psychotic symptoms (n=1). None of the patients in the intervention group were discontinued because of a cognitive-behavioral therapy (CBT) adverse effect." Comment: In the first 3 months participant discontinued in the intervention group. At the end of the study, as reported in the flow chart, > 10% loss of participants both in intervention (10/46) and in control group (6/44)
Selective reporting (reporting bias)	Low risk	Sleep outcomes were measure by the KDQOL-SF questionnaire in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "The groups were homogeneous to most socia-demographic, clinical, and laboratory data (Table 1). However, the intervention group had a lower percentage of married patients, of those dwelling with family members, and of individuals with cerebrovascular disease." Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Fundac , a Estado de Sa but it seems that it not influenced data. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Edalat-Nejad 2013

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 6 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Iran Setting: not reported Aged > 18 years; ability to give informed consent; duration of HD > 3 months, PSQI score ≥ 5 and adherence to regular and steady dialysis program or medication that interfere with melatonin secretion (such as beta adrenoreceptors blocking drug) Number (randomised/analysed): 68/82 Mean age $\pm$ SD: 58 ± 14 years Sex (M/F): not reported Exclusion criteria: known major illness (malignancy, active infection and uncontrolled heart failure); pregnancy; iron deficiency anaemia, poor control diabetes mellitus ($HbA1c > 7.5$); current use of melatonin or known allergy of melatonin; acute medical or surgical condition that required hospitalisation or operation throughout the study and dementia or psychotic disorder as diagnosed by researchers that interferes with patient's participation in this study
Interventions	Treatment group <ul style="list-style-type: none"> Melatonin (oral): 3 mg/day Control group <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Death (all causes)
Notes	<ul style="list-style-type: none"> Funding source: Arak University of Medical Sciences. IRCT201108077253N1

Edalat-Nejad 2013 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Eighty-two consenting patients randomly took placebo or melatonin." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to placebo or melatonin for 6 weeks. Melatonin (Melatonin Plus) and placebo were packaged in identical 3-mg tablets." Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "In a 6-week randomised, double-blind cross-over clinical trial." Comment: A double-blind study is considered as low risk of bias. The intervention and comparison were packaged as identical 3-mg tablets
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "In this study, patients completed this questionnaire by themselves or received assistance from research nurses during HD. Patients completed the Pittsburgh Sleep Quality Index (PSQI) questionnaire at the beginning of study and after the 6 weeks treatment by drug or placebo." Comment: Participants completed the PSQI questionnaire at baseline and end of study. Participants were unaware of treatment assignment because Melatonin and placebo had the same packaging. Treatment outcome assessment was blinded for sleep outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "During the course of the study, a total of 14 patients were withdrawn for reasons explained in Table 1." Comment: Overall, 14/82 participants were lost to follow-up (> 10%). However, it was not clear whether there was a differential rate loss to follow-up between the two study groups
Selective reporting (reporting bias)	High risk	Quote: "Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI)." The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. Arak University of Medical Sciences provided the financial and logistical resources. There was insufficient information to permit judgement

EMSCAP 2009

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 6 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: The Netherlands Setting: single centre

Interventions for improving sleep quality in people with chronic kidney disease (Review)

EMSCAP 2009 (Continued)

- Patients aged 18 and 85 years and on stable HD (> 3 months on HD with adequate dialysis efficacy) were included
- Number: 24
- Mean age $\pm$ SD: 71 $\pm$ 14.3 years
- Sex (M/F): 18/6
- Exclusion criteria: prior use of melatonin; use of hypnotics that could not be stopped during the study, and severe psychological or neurological disease

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Melatonin (oral): 3 mg/day <p>Control group</p> <ul style="list-style-type: none"> • Placebo
Outcomes	<ul style="list-style-type: none"> • Sleep onset latency (Actigraphy) • Total sleep time • Sleep efficiency • Death (all causes)
Notes	<ul style="list-style-type: none"> • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "The study design is a randomised, double-blind, placebo-controlled, cross-over study."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "At baseline, daytime haemodialysis patients were asked to fill out a sleep questionnaire and to wear an actometer for seven consecutive days."</p> <p>Comment: The outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<p>Quote: "At baseline 24 patients were included in the study. From this group, two patients died, one terminated his dialysis in our hospital and one was excluded due to noncompliance. Twenty patients (14 male, six female) completed the 18-week investigation period."</p> <p>Comment: Overall, 4/24 participants were lost to follow-up (> 10%). However, it was not clear whether there was a differential rate loss to follow-up between the two study groups</p>
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes was not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	Quote: "The general characteristics of the patients, shown in Table 1, were similar to the main characteristics of the general Dutch dialysis population."

EMSCAP 2009 (Continued)

Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Farrokian 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: single centre HD patients Number: treatment group (31); control group (31) Mean age $\pm$ SD (years): treatment group (57.87 ± 13.36); control group (55.19 ± 15.06) Sex (M/F): treatment group (18/13); control group (19/12) Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Foot reflexology: three days/week (from 6 am to 8 pm) <p>Control group</p> <ul style="list-style-type: none"> Not reported
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI)
Notes	<ul style="list-style-type: none"> Not English Funding source: Qazvin University of Medical Sciences. IRCT2015122125642N1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "In this study randomisation was conducted using a random numbers table."</p> <p>Comment: Random numbers table as considered as low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	This was a non-blinded study. A non-blinded study is considered as high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not reported. However, as these treatments were different, and participants were aware of treatment assignment when they completed the self-reported questionnaires PSQI, outcome assessment were not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	As reported in the flow chart, all participants were included in analysis. There was no evidence of differential loss to follow-up that may have been related to the intervention

Farrokian 2016 (Continued)

Selective reporting (reporting bias)	Low risk	Quote: "Before the intervention, Pittsburgh Sleep Quality Index (PSQI) questionnaire for all patients in both groups was completed. [...] After the intervention, the Pittsburgh Sleep Quality Index (PSQI) was completed by the patients, again." Comment: Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Table 1 showed the demographic characteristics of study participants in the two groups: there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Qazvin University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Ghavami 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: not reported
Participants	<ul style="list-style-type: none"> Country: Iran Setting: not reported Inclusion criteria: HD patients Number: 60 Mean age $\pm$ SD (years): not reported Sex (M/F): not reported Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> Hot stone massage therapy: for 12 sessions Control group <ul style="list-style-type: none"> Routine health care
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI)
Notes	<ul style="list-style-type: none"> Abstract-only publication Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This is a randomised clinical trial. The Study samples were 60 haemodialysis patients that were divided randomly into two groups: control group and intervention group." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement

Ghavami 2016 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Data were obtained from the patients information form and Pittsburgh Sleep Quality Index (PSQI)." Comment: Patients were randomised to hot stone massage therapy or routine health care. As these treatments are physically different, blinding of participants and investigators to treatment assignment was unlikely. As patients provided information about the outcome of sleep quality directly and were aware of treatment allocation, outcome assessment was not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	High risk	Quote: "Sleep quality score of patients measured by Pittsburgh Sleep Quality Index (PSQI)." Sleep quality was assessed before intervention and after 12 sessions (hot stone massage therapy on standard care). it was unclear whether this was done for all participants at all time points. Data were not reported in a way that could be included in meta-analysis
Other bias	Unclear risk	Quote: "No baseline differences existed between the two groups for the mean of Pittsburgh Sleep Quality Index (PSQI) score." Comment: The baseline characteristics and the co-interventions were not provided in sufficient detail to perform assess comparability between groups, the study funding source(s) were not described. There was insufficient information to permit judgement

Giannaki 2013

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: September 2007 to October 2009 Duration of follow-up: 26.4 weeks
Participants	<ul style="list-style-type: none"> Country: Greece Setting: single centre RLS diagnosis; on HD therapy for at least 3 months with adequate dialysis delivery Number (randomised/analysed): treatment group 1 (16/15); treatment group 2 (8/7); control group (8/7) Mean age $\pm$ SD (years): treatment group 1 (56.4 ± 12.5); treatment group 2 (55.7 ± 10.4); control group (56.8 ± 16.5) Sex (M/F): treatment group 1 (4/11); treatment group 2 (3/4); control group (2/5) Exclusion criteria: diagnosed neuropathies, or reasons for being in a catabolic state within 3 months prior to the start of the study; or with CRP blood levels > 3.0 mg/L, unable to exercise; or refuse to participate for personal reasons
Interventions	Treatment group 1 <ul style="list-style-type: none"> Exercise training: 3 times/week during the HD session

Giannaki 2013 (Continued)

Treatment group 2

- Ropinirole (oral): 0.25 mg/day

Control group

- Placebo

Outcomes	<ul style="list-style-type: none"> • Sleep quality (ESS) • Depression (Zung scale) • QoL (SF-36) • Adverse events
Notes	<ul style="list-style-type: none"> • Funding source: Community Funds of the Greek Ministry of Development-General Secretariat of Research and Technology and by the European Social Fund

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "In this randomised, partially double blind, placebo controlled trial, thirty two haemodialysis patients with restless legs syndrome were randomly assigned into three groups."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "Both the patients and the investigators were blinded to the type of the medication used in the second and third group (double-blind design). [...] The Dopamine Agonist used was ropinirole (Adartrel, GlaxoSmithKline, UK). It was powdered and inserted in an empty capsule (the rest was filled with plain flour), in a 0.25 mg/dose, which was maintained stable until the end of the study. We consciously decided not to perform a dose titration in order to minimize any augmentation phenomena that could affect the study outcomes. Placebo was made by plain flour filled in the same type of capsules. Patients were instructed to receive their capsules once daily, 2 hours before bedtime. Both the ropinirole and the placebo capsules were made at the UHL pharmacy and their packaging was identical."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "All questionnaires were completed with the interview method, by experienced personnel. [...] The Epworth Sleepiness Scale (ESS) was used to assess the daily sleepiness level of the patients. [...] Finally, a weekly sleep diary was used to evaluate the patient's quality of sleep."</p> <p>Comment: Participants and investigators were unaware of treatment assignment. Treatment outcome assessment was blinded for sleep outcomes</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Three patients dropped out for reasons unrelated to the study during the follow-up period making those who completed the study twenty nine. [...] The study's flow chart is presented in Figure 1. Briefly a total of forty-five patients were screened while thirty-two patients enrolled in the study and were randomly assigned in one of the three groups. Three patients dropped out for reasons unrelated to the study during the follow-up period making those who completed the study twenty nine."</p>

Giannaki 2013 (Continued)

Comment: As reported in the flow chart, 1/16 in the exercise training group, 1/8 in the dopamine agonist group and 1/8 in placebo group were lost to follow-up for reasons that appeared unrelated to treatment (> 10% loss to follow-up)

Selective reporting (reporting bias)	Low risk	Sleep outcomes were measure by ESS in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	<p>Quote: "The patient's characteristics are presented in Table 1. [...] The baseline score in the IRLS severity scale, Zung depression scale, sleep diary, daily sleepiness status and overall QoL score did not differ between the three groups."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by The Community Funds of the Greek Ministry of Development-General Secretariat of Research and Technology and by the European Social Fund. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent</p>

Giannaki 2013a

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 26.4 weeks
Participants	<ul style="list-style-type: none"> Country: Greece Setting: multicentre (2 sites) Dialysis for at least ≥ 3 months with adequate dialysis delivery (Kt/V) and with stable clinical condition with RLS Number: treatment group (12); control group (12) Mean age $\pm$ SD (years): treatment group (59.2 ± 11.8); control group (58 ± 10.7) Sex (M/F): treatment group (9/3); control group (8/4) Exclusion criteria: diagnosed neuropathies or reasons for being in a catabolic state within 3 months prior to the start of the study; unable to exercise
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Progressive exercise training group: 45 min during the HD session 3 times/week <p>Control group</p> <ul style="list-style-type: none"> No-resistance exercise
Outcomes	<ul style="list-style-type: none"> Sleep quality (sleep diary; ESS) Depression (Zung scale) Adverse events
Notes	<ul style="list-style-type: none"> Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The randomisation procedure was completed using customized randomisation software."

Giannaki 2013a (Continued)

		Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "Patients were randomised separately based on the host hospital (Hospital 1, n = 12, Hospital 2, n = 12)."</p> <p>Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote from the title: "A single-blind randomised controlled trial."</p> <p>Comment: A single-blind study is considered as a high risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The patient's subjective sleep quality levels were assessed by using a weekly sleep diary. [...] The HD patient's daily sleepiness status was assessed by using the Epworth Sleepiness Scale (ESS)."</p> <p>Comment: Participant could be aware of treatment allocation. Outcome assessment was unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All of the patients successfully completed the 6-month intervention programme with no adverse effects and no augmentation phenomena to report."
Selective reporting (reporting bias)	Low risk	Sleep outcomes was measured by ESS questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	<p>Quote: "No significant differences in the patients' basic characteristics were found between the two groups ($P > 0.05$). [...] At baseline, no significant differences were observed between the two groups in sleep quality, daily sleepiness status, depression score and IRLS score ($P > 0.05$)."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent</p>

Hanna 2013

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 3 weeks
Participants	<ul style="list-style-type: none"> Country: Switzerland Setting: not reported Kidney transplant recipients Number: 30 Mean age $\pm$ SD: 59.6 $\pm$ 12.6 years Sex (M/F): not reported Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Morning light bright therapy: 30 minutes daily <p>Control group</p>

Hanna 2013 (Continued)

- Usual care

Outcomes	<ul style="list-style-type: none"> • Sleep onset latency (Actimeter) • Sleep efficiency
Notes	<ul style="list-style-type: none"> • Abstract-only publication • Trial registration number: not reported.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This was a non-blinded, 1:1 randomised controlled wait-listed pilot trial."</p> <p>Comment: Participant could be aware of treatment allocation. Outcome assessment was unlikely to be blinded</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "The rest-activity cycle was monitored throughout the whole period with a wrist actimeter".</p> <p>Comment: The outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Unclear risk	<p>Quote: "The rest-activity cycle was monitored throughout the whole period with a wrist actimeter."</p> <p>Comment: Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis</p>
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Hou 2014

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Duration of study: December 2005 to April 2006 • Duration of follow-up: 13.2 weeks
Participants	<ul style="list-style-type: none"> • Country: China • Setting: single centre • Patients with ESKD, who underwent HD for at least 3 months, with stable condition with sleep impairment • Number (randomised/analysed): treatment group (52/51); control group (51/47) • Mean age $\pm$ SD (years): treatment group (54.5 $\pm$ 13.8); control group (52.4 $\pm$ 14.5) • Sex (M/F): treatment group (20/31); control group (22/25)

Hou 2014 (Continued)

- Exclusion criteria: not reported

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • CBT and conventional HD: 20 minutes to relax every 2 days three times week <p>Control group</p> <ul style="list-style-type: none"> • Conventional HD
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep onset latency • Total sleep time • Sleep efficiency • Depression (SCL-90) • Anxiety • Sleep disturbance
Notes	<ul style="list-style-type: none"> • Funding source: The Science and Technology Development Program of Zhanjiang • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The patients were numbered and randomly assigned to treatment (n = 52) and control (n = 51) groups."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "The treatment group was treated with cognitive-behavioral therapy in addition to conventional haemodialysis. the intervention methods, theory, effects and notes were not told to the patients and their families."</p> <p>Comment: Although the intervention was not told to the patients the methods of intervention and control treatment were physically different, and therefore masking of treatment allocation for patients and investigators was unlikely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Pittsburgh Sleep Quality Index (PSQI) was used to assess quality of sleep of patients in the latest 1 month. [...] The evaluation was performed by professional physicians. The subjects should ask questions independently. If they did not understand the question, the physicians should explain, but not give a hint."</p> <p>Comment: Patients and investigators completed sleep assessment and were aware of treatment assignment</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "During the study (investigation), five subjects withdrew, including one in treatment group and four in control group."</p> <p>Comment: 5/103 patients were lost to follow-up: while these were small numbers, there was differential loss between groups</p>
Selective reporting (reporting bias)	Low risk	<p>Quote: "Two groups were assessed using the questionnaires before and 2, 4, 6, 8, 10, and 12 weeks after treatment."</p>

Hou 2014 (Continued)

Comment: Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis

Other bias	Low risk	Baseline and non-randomised co-intervention characteristics were similar between groups. This study was supported by The Science and Technology Development Program of Zhanjiang. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent
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IRCT2013021212448N1

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 12 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: not reported Age 18 to 60 years; HD patients suffering from fatigue Number: treatment group (26); control group (26) Mean age $\pm$ SD (years): 45 years (SD not reported) Sex (M/F): treatment group (14/12); control group (16/10) Exclusion criteria: chronic disease or severe physical illness, inability to communicate and questions
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Collaborative care model (Motivation, Readying, Involvement and Evaluation): 2 hours/day for 2 months <p>Control group</p> <ul style="list-style-type: none"> No treatment
Outcomes	<ul style="list-style-type: none"> Fatigue (FSS)
Notes	<ul style="list-style-type: none"> Not in English Funding source: Ahvaz Jundishapur University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "In this controlled clinical trial study, 52 patients undergoing maintenance haemodialysis were purposively selected and randomly divided into two groups of test and control."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely

IRCT2013021212448N1 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The findings were analysed by the researchers and then the results were discussed with the patients." Comment: Patients were randomised to collaborative care model or control group. As these treatments were different, and participants and investigators could be aware of treatment assignment, outcome assessment could not be blinded. The primary outcome was fatigue and it was assessed by the Fatigue Severity Scale
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	Low risk	Table 1 showed the demographic characteristics of study participants in the two groups: there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Ahvaz Jundishapur University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

IRCT2014061717237N3

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre HD patients aged 18 to 65 years; at least 6 months history of HD (3 times/week, 4 hours/session); PSQI ≥ 5; complete alertness, hearing and speech ability; having the ability to read and write; not having developing a psychiatric disorder which lead to consumption of psychiatric drugs; cancer; lupus erythematosus; dermatological disease; advanced heart failure; stroke; amputation; sore, infection or fistula in acupoints; carpal tunnel syndrome Number: 74 Mean age $\pm$ SD (years): not reported Sex (M/F): not reported Exclusion criteria: hospitalisation in ICU; consumption of psychiatric drugs and distortion in mental status; death during intervention; the incidence of severe stressful event such as the death of someone close; not wanting to continue participation; travel; surgery; transplant
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Acupressure: 3 times/week <p>Control group 1</p> <ul style="list-style-type: none"> Massage on pseudo-points: 3 times/week <p>Control group 2</p> <ul style="list-style-type: none"> No Intervention
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI)

IRCT2014061717237N3 (Continued)

- Anxiety (STAI)
- Death (all causes)
- Sudden death
- Cardiovascular death

- Notes
- Not English
 - Funding source: Golestan University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from the Iranian Registry of Clinical Trial: "Randomization strategies: Considering sleep quality level, patients were allocated to three matched intervention, placebo and control groups. Allocation will be achieved using stratified random allocation." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	As reported in the Iranian Registry of Clinical Trial, this was a double-blind study. A double-blind study is considered as low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The data was collected by Pittsburgh Sleep Quality Index (PSQI) and State-Trait Anxiety Inventory (STAI)." Comment: Not reported with sufficient information to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis.
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

IRCT2015051122218N1

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Duration of study: • Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> • Country: Iran • Setting: not reported • HD patients aged 18 to 65 years; PSQI ≥ 5; HD for at least 6 months dialysis experiences; full awakeness and audio visual ability for learning Chamomile consumption • Number: 110 • Mean age $\pm$ SD (years): not reported • Sex (M/F): not reported

IRCT2015051122218N1 (Continued)

- Exclusion criteria: no tendency to continue the study; suffering from important diseases during the study; reaction to Chamomile consumption; kidney transplant; pregnancy and breast feeding; taking chamomile for at least 3 days; moving to other place or hospital

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Chamomile (oral): 400 mg/day, taken between 21:00 and 22:00 <p>Control group</p> <ul style="list-style-type: none"> • Placebo (oral): taken between 21:00 and 22:00
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Death (all causes) • Sudden death • Cardiovascular death • Hospital admissions
Notes	<ul style="list-style-type: none"> • Not English • Funding source: Arak University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "This is a randomised clinical trial. 110 haemodialysis patients were selected by convenience sampling and randomly allocated in two groups."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	As reported in the Iranian Registry of Clinical Trial, this was a double-blind study. A double-blind study is considered as low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<p>Quote: "Data was gathered with demographic questionnaire and Pittsburgh Sleep Quality Index (PSQI)."</p> <p>Comment: Not reported with sufficient information to permit judgement</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Jean 1995

Methods	<ul style="list-style-type: none"> • Study design: cross-over study • Duration of study: not reported
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Interventions for improving sleep quality in people with chronic kidney disease (Review)

Jean 1995 (Continued)

	<ul style="list-style-type: none"> Duration of follow-up: 6 sessions (first phase)
Participants	<ul style="list-style-type: none"> Country: France Setting: not reported HD patients on dialysis for 15 hours/week Number: 10 Age range: 35 to 7 years Sex (M/F): 8/2 Exclusion criteria: patients with risk factor of SAS (obesity, hypothyroidism, alcohol abuse, use of hypnotics, obvious airway narrowing)
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Acetate <p>Treatment group 2</p> <ul style="list-style-type: none"> Bicarbonate
Outcomes	<ul style="list-style-type: none"> Sleeping time (data not extractable) (polysomnography)
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Were randomly assigned first to acetate or bicarbonate. then to the other form of treatment."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	The two interventions were acetate and bicarbonate dialysis. While these are physically similar, it was not stated whether patients and/or investigators were unaware of treatment assignment
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "Polysomnography was carried out using standard techniques and provided measures of sleep architecture and disordered respiration."</p> <p>Comment: Sleep measures were based on polysomnography which were performed and analysed using PC software. As the outcome was an objective measure, it was unlikely to be biased by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of patients who were lost to follow-up or who were not included in analysis was not reported
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis

Jean 1995 (Continued)

Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement
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Kolner 1989

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 1 week
Participants	<ul style="list-style-type: none"> Country: USA Setting: not reported HD patients Number: treatment group (6); control group (6) Mean age $\pm$ SD (years): not reported Sex (M/F): not reported Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Triazolam (oral): 7 days <p>Control group</p> <ul style="list-style-type: none"> Placebo: 7 days
Outcomes	<ul style="list-style-type: none"> Sleep improvement Adverse effects
Notes	<ul style="list-style-type: none"> Abstract-only publication Funding source: not reported Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "Haemodialysis patients with sleep disorder who were not already taking a hypnotic were selected for a double-blind, placebo-controlled trial of Triazolam."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Incomplete outcome data (attrition bias)	Unclear risk	Not reported in sufficient detail to permit judgement

Kolner 1989 (Continued)

All outcomes

Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Li 2014b

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: 2010 to 2012 Duration of follow-up: 12 weeks 	
Participants	<ul style="list-style-type: none"> Country: China Setting: multicentre (2 sites) PD patients who were Mandarin-speaking; able to communicate and access a telephone after discharge and agreed to participate Number: treatment group (80/69); control group (80/66) Mean age $\pm$ SD (years): treatment group (57.4 $\pm$ 12.8); control group (55.2 $\pm$ 11.9) Sex (M/F): treatment group (42/27); control group (37/29) Exclusion criteria: receiving intermittent PD or HD and those with planned admissions for special treatment procedures; Tenckhoff catheters in situ for < 3 months; psychosis or dementia; dying or unable to communicate; and those who have been transferred to another unit during their stay in hospital 	
Interventions	Treatment group <ul style="list-style-type: none"> Post-discharge nurse-led telephone support Control group <ul style="list-style-type: none"> Routine hospital discharge care 	
Outcomes	<ul style="list-style-type: none"> Sleep quality (KDQOL-SF) HRQoL Pain Fatigue 	
Notes	<ul style="list-style-type: none"> Funding source: Guangdong Province and the Guangdong Natural Science Foundation Trial registration number: not reported 	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were assigned to the study or control group using fifty sets of computer-generated random numbers." Comment: Computer-generation is considered method at low risk of bias
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement

Li 2014b (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The participants were identified by codes, which were not associated with their names." Comment: Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Sleep quality was assessed using the KDQOL-SF. Investigators did not report the method for outcome measurement
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "During the data collection period, 186 patients met the eligibility criteria and were assessed by the hospital nurse for recruitment into the study. Twenty-six patients who failed to meet the inclusion criteria were excluded. Of these, 16 were transferred to haemodialysis before discharge. Of the remaining ten, six refused to participate, while four were unable due to their physical condition. The 160 patients who joined the study were randomly assigned to either the study or control group. There were 80 patients in each of the treatment arms. At week 12, 69 of the 80 (86.3%) study patients and 66 of the 80 (82.5%) controls had completed the follow-up questionnaires. A total of 135 patients completed the protocol and were included in the analysis (Figure 1)." Comment: As reported in the flow chart, 5/80 in the Post-discharge nurse-led telephone support group, 6/80 in the Routine hospital discharge care group were lost to follow-up for reasons that appeared unrelated to treatment (<10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	Low risk	As reported in Table 3, sleep outcomes were reported in different points of time. Sleep quality was measured by the Kidney Disease Quality of Life Short Form at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "Table 1 and Table 2 display the comparison of baseline demographic data and clinical data between the control and study groups respectively." Comment: there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Guangdong Province and the Guangdong Natural Science Foundation. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

MELODY 2013

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: April 2007 to March 2009 Duration of follow-up: 52.8 week
Participants	<ul style="list-style-type: none"> Country: The Netherlands Setting: Multicentre Stable HD patients aged 18 to 85 years with a HD history of at least 3 months and adequate dialysis efficacy; patients could participate when they suffered from subjective sleep problems at baseline according to the ESS questionnaire and their mean sleep onset latency measured by means of atriography was longer than 15 min Number: treatment group (33); control group (34) Mean age $\pm$ SD (years): treatment group (65.5 $\pm$ 11.7); control group (64.4 $\pm$ 12) Sex (M/F): treatment group (19/14); control group (22/12)

MELODY 2013 (Continued)

- Exclusion criteria: current melatonin use known hypersensitivity to melatonin; severe psychological or neurological disease; unstable angina pectoris NYHA class IV heart failure, pregnancy, participation in another clinical study 1 month prior to the start of this study

Interventions	Treatment group <ul style="list-style-type: none"> • Melatonin (oral): 3 mg/day Control group <ul style="list-style-type: none"> • Placebo
Outcomes	<ul style="list-style-type: none"> • HRQoL (Actigraphy) • Death (all causes)
Notes	<ul style="list-style-type: none"> • Funding source: Dutch Kidney Foundation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Random allocation of 68 study medication kits was made in block sizes of four." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "In this randomised double-blind placebo-controlled trial haemodialysis patients suffering from subjective sleep problems received melatonin 3mg day-1 vs. placebo during 12 months." Comment: A double-blind study is considered as low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Sleep parameters were investigated by means of actigraphy." Comment: Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Reasons for loss to follow-up are shown in Figure 2." Comment: As reported in the flow chart, 11/33 in the Melatonin group and 14/34 in the placebo group were lost to follow-up for reasons that appeared unrelated to treatment (>10% loss to follow-up, there was a differential loss between groups)
Selective reporting (reporting bias)	Low risk	As reported in Figure 3, sleep outcomes were reported in different points of time. Sleep quality was measured by actigraphy at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "Clinical characteristics between the melatonin and placebo group at baseline did not differ (Table 2). Some baseline values of quality of life and sleep parameters differed between the melatonin and placebo group and, therefore, we corrected for baseline values in our analyses." Comment: there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was sup-

MELODY 2013 (Continued)

ported by Dutch Kidney Foundation. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Micozkadioglu 2004

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 4 (first phase)
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: single centre Patients on HD with RLS Number: 15 Mean age $\pm$ SD: 45.8 $\pm$ 15.3 Sex (M/F): 10/5 Exclusion criteria: not reported
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Levodopa (oral): 125 mg/day <p>Treatment group 2</p> <ul style="list-style-type: none"> Gabapentin (oral): 200 mg after HD
Outcomes	<ul style="list-style-type: none"> Quality of life (PSQI) Quality of sleep Pain
Notes	<ul style="list-style-type: none"> Funding source: There was no pharmaceutical industry support of this study Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Subjects were randomised and there was a washout period of two weeks between two medications."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote from the title: "An open-label study."</p> <p>Comment: An open-label study is considered as a high risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Patients with Restless Legs Syndrome (RLS) answered three questionnaires (RLS rating scale proposed by IRLSSG, the Short Form (SF)-36 and the Pittsburgh Sleep Quality Index)."</p> <p>Comment: Sleep quality was assessed using PSQI questionnaire. Investigators did not report the method for outcome measurement. However, participant</p>

Micozkadioglu 2004 (Continued)

		could be aware of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "One of the patients had severe gabapentin-related side effects at the beginning and dropped out of the study." Comment: 1/15 of the overall population (only in gabapentin group) was lost to follow-up for reasons that appeared related to treatment. There was a differential loss between groups
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. There was insufficient information to permit judgement

Momennasab 2018

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: May to December 2016 Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: multicentre (3 sites) HD patients aged 18 and 60 years; a history of HD for at least 6 months, with at least 2 and a maximum of 3 dialysis sessions/week; no history of severe sleep disturbances; no history of hearing disturbances or being partially deaf, mental illnesses, or advanced cardiopulmonary disease; and no drug addiction Number (randomised/analysed): treatment group 1 (35/34); treatment group 2 (35/33); control group (35/35) Mean age $\pm$ SD (years): treatment group 1 (48.83 ± 11.11); treatment group 2 (50.86 ± 10.73); control group (49.89 ± 11.53) Sex (M/F): treatment group 1 (20/14); treatment group 2 (20/13); control group (16/19) Exclusion criteria: major physical or mental events during the study and not listening to music more than 2 times in a week for the second intervention group (listening to music at bedtime)
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Listening to music during HD: to listen to the music 1 hour after beginning HD <p>Treatment group 2</p> <ul style="list-style-type: none"> Listening to music before sleep: to listen to the music after their routine preparation for sleep every night <p>Control group</p> <ul style="list-style-type: none"> Routine care without any intervention
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep latency Total sleep time Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: Vice-Chancellor for Research Affairs, Shiraz University of Medical Sciences, Iran

Momennasab 2018 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This study was a randomised, controlled clinical trial with a pre-post-test design." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "At first, all participants signed the informed consent and completed the Pittsburgh Sleep Quality Index (PSQI) and a demographic information questionnaire simultaneously." Comment: Sleep quality was assessed by the PSQI. Participant could be aware of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	As reported in the flow chart, 0/35 in the music during haemodialysis group, 0/35 in the music at bedtime group and 0/35 in the control group were lost to follow-up. There was not a differential rate loss to follow-up between the study groups
Selective reporting (reporting bias)	Low risk	Quote: "Sleep quality was measured by the Pittsburgh Sleep Quality Index (PSQI) during two stages (before and one week after the intervention)." Comment: Sleep outcomes was measured by the PSQI in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "There was no significant difference between the three groups regarding age, gender, marital status, job status, and educational level ($p > 0.05$). [...] The sponsor had no involvement in the conducting the study and publication of the article." Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Vice-Chancellor for Research Affairs of the Shiraz University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Muz 2017

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: multicentre (5 sites) Patients aged 18 and above, no eye or hearing disabilities, voluntary participation in the study, to undergo haemodialysis for 3 months, to continue dialysis in the same unit/centre, to undergo

Interventions for improving sleep quality in people with chronic kidney disease (Review)

Muz 2017 (Continued)

haemodialysis treatment for three sessions in one week, not to take any sleeping pill before aromatherapy and during the course of the study, to have average or severe fatigue symptoms (Visual Analogue Scale (VAS) fatigue score should be 3 or more) to have a score of 5 or more from the PSQI, to speak Turkish

- Number (randomised/analysed): treatment group (41/27); control group (39/35)
- Mean age $\pm$ SD (years): treatment group (52.26 $\pm$ 14.5); control group (59.26 $\pm$ 12.43)
- Sex (M/F): treatment group (18/9); control group (16/19)
- Exclusion criteria: respiratory system disease; allergy to essential oils used, any obstacle to smell; use of other integrative medicine applications during treatment

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Aromatherapy: sweet orange and lavender oil, applied by inhalation <p>Control group</p> <ul style="list-style-type: none"> • Routine care
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep latency • Total sleep time • Sleep efficiency • Sleep disturbance • Fatigue (data was not extractable)
Notes	<ul style="list-style-type: none"> • Funding source: This study was supported, in part, by a grant from the Erciyes University Scientific Research Projects Unit • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "This randomised controlled study was conducted with five haemodialysis units in two cities in Turkey."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "During the initial follow-up of patients, the information form, Visual Analog Scale (VAS) score, Piper Fatigue Scale (PFS), and Pittsburgh Sleep Quality Index (PSQI) were determined via face-to-face interview and patient documents."</p> <p>Comment: Sleep quality was assessed by the PSQI. Participant and investigators could be aware of treatment allocation. Outcome assessment was unlikely to be blinded</p>

Muz 2017 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	As reported in the Figure 1, 14/41 in the aromatherapy group and 4/39 in the control group were lost to follow-up. There was a differential rate loss to follow-up between the two study groups
Selective reporting (reporting bias)	Low risk	Quote: "All of the forms were performed at baseline and at follow-up at the end of the four weeks (baseline and last follow-up)." Comment: Sleep outcomes was measured by the PSQI in all participants at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "The authors are grateful to Associate Professor Ahmet Ozturk (Department of Biostatistics at Erciyes University) for supporting statistical analysis." Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by the Erciyes University Scientific Research Projects Unit. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Nasiri 2011

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: single centre Patients with kidney failure by patient's medical records, capable to participate in study; undergoing HD for 3 times/week, at least 3 months have a history of HD, age >18 years and have low quality of sleep with score of more than 5 by means of PSQI Number: 62 Mean age $\pm$ SD (years): treatment group (48.68 $\pm$ 13.49); control group (47.81 $\pm$ 11.55) Sex (M/F): "Gender distribution in experimental and control groups were 61.3 and 58.1% respectively." Exclusion criteria: diabetes; cancer; cerebral infarction; skin disease
Interventions	Treatment group <ul style="list-style-type: none"> Acupressure: 3 days/week, one hour after starting and after telling readiness by patients Control group <ul style="list-style-type: none"> No treatment
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: Guilan University of Medical Science

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This study was a randomised clinical trial."

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Nasiri 2011 (Continued)

		Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Sleep quality was assessed using PSQI and sleep log. It is not clear whether the observer was blinded to treatment allocation. However, patients were randomised to acupuncture or control. As these treatments are physically different, participant could be aware of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	High risk	Quote: "Sleep quality was measured using Pittsburgh Sleep Quality Index (PSQI) before and after treatments". Comment: Sleep quality was measured by PSQI at end of treatment in a format that was not extractable for meta-analysis (number of patients per group was not provided)
Other bias	Low risk	Quote: "The mean age of subject was 48.68 ± 13.49 in experimental group and 47.81 ± 11.55 in control group; the gender distribution in experimental group and control groups were 61.3% and 58.1%, respectively. Moreover, 77.4% in experimental and 80.6% in control group were married. 35.5% from experimental and 32.3% from control group were graduated from primary school. Less than half percent (45.2) of participants in experimental group were unemployed, this was 51.6% in control group. The received salary for nearly all patients (90.3%) in both group were under 250, dollars per month. The majority of participants had a private sleep room (90.3% in experimental and 87.1% in control group), regarding treatments shifts, most of patients were under treatment in both morning and night shift in both groups. The mean of duration of dialysis treatment was 4.65 ± 3.29 years in experimental group and 4.94 ± 3.73 years in control group. Regarding effective drinks on sleep consisting tea, milk and coffee, the highest rank were assigned to consumption of tea with mean of 2 cup per day. The cigarette smoking was 16.1% in both groups; the mean cigarette was 1.17 and 1.09 in experimental and control groups; respectively. Approximately most patients were lived in city (74.2% in experimental and 71% in control group) and do not exercise (only 25.8% in experimental group and 29% in control group do exercise). No statistically difference between two groups were seen on demographic variables. Table 1 shows the result of sleep quality by Pittsburgh Sleep Quality Index (PSQI) before intervention." Comment: there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Guilan University of Medical Science. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Natarajan 2003

Methods

- Study design: cross-over study

Interventions for improving sleep quality in people with chronic kidney disease (Review)

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Natarajan 2003 (Continued)

	<ul style="list-style-type: none"> Duration of study: not reported Duration of follow-up: 4 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: USA Setting: not reported HD patients Number: 8 Mean age $\pm$ SD: 50.81 $\pm$ 6.21 years Sex (M/F): 1/7 Exclusion criteria: patients with HCT < 30%, serum ferritin $\leq$ 100 mg/dL, iPTH > 350 pg/mL; prior history of Parkinson's disease or seizure disorders
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Melatonin (oral): 3 mg/day, 1 hour before bed <p>Control group</p> <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Sleep quality (actigraphy)
Notes	<ul style="list-style-type: none"> Abstract-only publication Funding source: not reported Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "In a prospective, randomised, double blind, placebo-controlled, cross-over study, patients were enrolled to receive either melatonin or placebo."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "Wrist actigraphy (IM System) was used to monitor sleep quality (actigraphy counts per 30 second epoch) over three nights each at baseline and two treatment periods"</p> <p>Comment: Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Quote: "8 patients completed the study."</p> <p>Comment: All participants were included in analysis</p>
Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

NCT02825589

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: start date July 2016 Duration of follow-up: not reported
Participants	<ul style="list-style-type: none"> Country: Thailand Setting: not reported HD patients with subclinical hypervolaemia; defined as euvolemic status on physical examination despite the ratio of extracellular water to total body water more than 0.4 on BIA, who were poor sleeper PSQI >5 to either BIA-guided group or standard clinical-guided dry weight group Number: 19 Mean age $\pm$ SD: 63.53 $\pm$ 11.12 years Males: 42.11% Exclusion criteria: bed ridden status; alteration of consciousness; unstable haemodynamics
Interventions	Treatment group <ul style="list-style-type: none"> BIA-guided dry weight target Control group <ul style="list-style-type: none"> Clinical evaluation of dry weight
Outcomes	<ul style="list-style-type: none"> Sleep duration and efficiency (PSQI)
Notes	<ul style="list-style-type: none"> Abstract-only publication Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "We randomly assigned 19 chronic haemodialysis patients with sub-clinical hypervolaemia." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The outcomes were changes in Pittsburgh Sleep Quality Index (PSQI) score, and sleep duration and efficiency (by actigraphy) at 1 month and 3 months." Comment: The Sleep duration and efficiency used an objective measure which was unlikely to be influenced by knowledge of treatment allocation. However, the PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias)	Unclear risk	Not reported in sufficient detail to permit judgement

NCT02825589 (Continued)

All outcomes

Selective reporting (reporting bias)	Unclear risk	Unclear whether outcome was assessed for both intervention and control groups. Data were not extractable for the meta-analysis
Other bias	Unclear risk	Not reported in sufficient detail to permit judgement

Parker 2007

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: not reported
Participants	<ul style="list-style-type: none"> Country: The Netherlands Setting: single centre Clinically stable, well-dialysed HD patients Number: 7 Mean age $\pm$ SD: 46.1 $\pm$ 11.1 years Sex (M/F): 3/4 Exclusion criteria: major chronic conditions associated with changes in sleep or body temperature, such as chronic infections, heart failure, chronic lung disease, arthritis, organic brain disease, drug/alcohol abuse, or past psychiatric disorders requiring treatment; routinely taking medications known to modulate central nervous system state (beta-blockers, other antihypertensives such as clonidine and methyldopa, antidepressants, sedatives, activating agents, or pain medications) or alter body temperature (non-steroidal anti-inflammatory drugs and acetaminophen)
Interventions	Treatment group 1 <ul style="list-style-type: none"> HD in warm condition (dialysate 37°C) Treatment group 2 <ul style="list-style-type: none"> HD in cool condition (dialysate 35°C)
Outcomes	<ul style="list-style-type: none"> Sleep onset latency (polysomnography) Total sleep time Sleep efficiency
Notes	<ul style="list-style-type: none"> Funding source: Funded by the National Institute of Health Trial registration number: NCT00218790 & NCT00460863 - these studies have the same study population, intervention and outcomes data Author published it in two different papers. In this review we considered these two citations as a single study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The three-phase study was conducted using a randomised, single-blinded (KPP), crossover design." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement

Parker 2007 (Continued)

Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The three-phase study was conducted using a randomised, single-blinded (KPP), crossover design." Comment: Study personnel connected patients, and therefore masking of treatment allocation for investigators was unlikely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Polysomnography measures of nocturnal sleep as recorded by the Oxford Ambulatory Polysomnographic Equipment (MR95 recorder)." Comment: Polysomnography was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The study was supported by the National Institute of Health. There was insufficient information to permit judgement

Pellecchia 2004

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 6 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Italy Setting: Single centre HD patients with RLS Number: 11 Mean age $\pm$ SD: 56.2 $\pm$ 8.7 years Sex (M/F): 7/4 Exclusion criteria: clinically significant orthostatic hypotension or an unstable medical condition including serious cardiovascular, pulmonary, hepatic, or psychiatric disease and with concurrent or past diagnosis of malignant melanoma
Interventions	Treatment group 1 <ul style="list-style-type: none"> Levodopa (oral, slow release levodopa/carbidopa): 100 to 200 mg/d Treatment group 2 <ul style="list-style-type: none"> Ropinirole (oral): 0.25 to 2 mg/d
Outcomes	<ul style="list-style-type: none"> Sleep quality and total sleep time (data not extractable) (sleep diary) Adverse events
Notes	<ul style="list-style-type: none"> Funding source: not reported

Pellecchia 2004 (Continued)

- Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The allocation to the 2 treatment sequences was randomised using a computer random number generator." Comment: Computer-generation is considered method at low risk of bias
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Patients were given evening doses of ropinirole or levodopa, 2 hours before bedtime." Comment: As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "To measure the effects of treatment on sleep quality, all patients were asked to fill in a 7-night sleep diary during the screening period, the washout week, and the last week of each treatment period." Comment: The sleep diary was a subjective measure which was likely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "One patient, while under treatment with levodopa, withdrew his consent to continue the study because of severe vomiting." Comment: 1/11 of the overall population (only in levodopa group) was lost to follow-up for reasons that appeared related to treatment. There was a differential loss between groups
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Pellizzaro 2013

Methods	<ul style="list-style-type: none"> • Study design: parallel RCT • Duration of study: June to September 2009 • Duration of follow-up: 10 weeks
Participants	<ul style="list-style-type: none"> • Country: Brazil • Setting: single centre • Patients aged 18 and 70 years on dialysis for more than 3 months, and to agree to participate by signing an informed consent form • Number (randomised/analysed): treatment group 1 (15/11); treatment group 2 (15/14); control group (15/14) • Mean age $\pm$ SD (years): treatment group 1 (43 ± 13.8); treatment group 2 (48.9 ± 10.1); control group (51.9 ± 11.6) • Sex (M/F): treatment group 1 (8/3); treatment group 2 7/7(); control group (8/6)

Pellizzaro 2013 (Continued)

- Exclusion criteria: unstable angina, uncontrolled cardiac arrhythmia, decompensated heart failure, SBP > 200 mmHg, DBP > 120 mmHg, acute pericarditis or myocarditis; decompensated diabetes mellitus (fasting serum glucose > 300 mg/dL); severe untreated mitral or aortic insufficiency/stenosis; severe lung conditions; acute systemic infection; severe bone disease; patients with lower limb amputations; patients with cognitive disorders; unable to perform the proposed tests due to disabling musculoskeletal, bone, or joint disorders

Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> • Respiratory muscle training: patients performed 3 sets of 15 inspirations at the equipment mouth piece and rested for 60 seconds <p>Treatment group 2</p> <ul style="list-style-type: none"> • Peripheral muscle training: patients performed 3 sets of 15 inspirations at the equipment mouth piece and rested for 60 seconds <p>Control group</p> <ul style="list-style-type: none"> • No treatment
Outcomes	<ul style="list-style-type: none"> • No outcomes of interest reported
Notes	<ul style="list-style-type: none"> • Funding source: Hospital de Clínicas de Porto Alegre (FIPE/HCPA). Protocol number: 3087/09

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "This is a randomised controlled clinical trial aiming to study respiratory and peripheral muscle training, and having as endpoints changes in functional, biochemical, and inflammatory parameters."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Outcome was assessed using the Kidney Disease Quality of Life Short Form (KDQOL-SF). Investigators did not report the method for outcome measurement
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Of the 45 patients initially included, six did not complete the study protocol due to non-compliance (n = 5) or death (n = 1) and were not included in the analysis."</p> <p>Comment: 4/15 in the Respiratory Muscle Training (RMT) group, 1/15 in the Peripheral Muscle Training (PMT) and 1/15 in control group were lost to follow-up for reasons that appeared unrelated to treatment (there was a differential loss between groups)</p>
Selective reporting (reporting bias)	High risk	Outcome was measured by the Kidney Disease Quality of Life Short Form (KDQOL-SF) at end of treatment in a format that was not extractable for meta-analysis

Pellizzaro 2013 (Continued)

Other bias	Low risk	<p>Quote: "The number of comorbidity and the median time on HD did not differ among the three groups, as shown in Table 1."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Hospital de Clínicas de Porto Alegre. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent</p>
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Pieta 1998

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: Duration of follow-up: 1.5 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Canada Setting: multicentre Sleep apnoea patients undergoing HD and PD Number: 14 Mean age $\pm$ SD: 42.5 years (SD not reported) Sex (M/F): 3/5 Exclusion criteria: pregnant patients or those to expecting to become pregnant; uncontrolled hypertension; unstable angina, or cardiac arrhythmia
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Pergolide (oral): 0.05 to 0.25 mg/day <p>Control group</p> <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Adverse events
Notes	<ul style="list-style-type: none"> Funding source: Kidney foundation of Canada Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Eight patients on chronic haemodialysis and continuous peritoneal dialysis completed a double-blind placebo-controlled crossover study."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "The study was designed as a double-blind randomised crossover trial comparing placebo to pergolide."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>

Pieta 1998 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The primary outcome measures included leg movements (using actigraphy, polysomnography and questionnaire) and sleep quality (using polysomnography and questionnaire)."</p> <p>Comment: Polysomnography was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation. However, the sleep questionnaire was a subjective measure which was likely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Fourteen patients were initially selected for the study and were randomised, but six withdrew during the study, two because of side effects, two because they found not taking hypnotics and L-dopa/carbidopa to be intolerable, one because she received a renal transplant while the study was in progress, and one because of noncompliance."</p> <p>Comment: Overall, 6/14 were lost to the follow-up for reasons that appeared unrelated to treatment (> 10% loss to follow-up, it was not clear if there was a differential loss between groups)</p>
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a cross-over study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The study was supported by the Kidney foundation of Canada. There was insufficient information to permit judgement

Pooranfar 2014

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 10 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre Patients aged between 20 and 50 years, who received transplants 2 to 3 years beforehand; no history of consumption of alcohol and caffeine; no regular exercise activities Number: treatment group (29); control group (15) Mean age $\pm$ SD: 36.2 $\pm$ 2.2 years Sex (M/F): not reported Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Exercise training: cumulative exercise program, 3 days/week <p>Control group</p> <ul style="list-style-type: none"> Did not participate in any regular exercise activity during this period
Outcomes	<ul style="list-style-type: none"> Sleep quality, total sleep time (data not extractable) (PSQI)
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported

Risk of bias

Pooranfar 2014 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "44 renal transplant recipients were selected to participate in the study and randomised into exercise (n=29) and control (n=15) groups." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Sleep quality of the subjects was evaluated using Pittsburgh Sleep Quality Index (PSQI) questionnaire; the sleep quantity was assessed by recording the duration of convenient nocturnal sleep of the subjects." Comment: Sleep quality was assessed by the PSQI. Participant and investigators could be aware of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	High risk	Quote: "Sleep quality and quantity questionnaire was completed before and after the research." Comment: Sleep outcomes was measured by the PSQI in all participants at end of treatment in a format that was not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Rambod 2013

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: February 2011 to January 2012 Duration of follow-up: 8 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: single centre Patients ≥ 18 years old; HD twice a week or more for at least the 3 previous months; alert and oriented; literate; willing to participate in the study Number: treatment group (43); control group (43) Mean age $\pm$ SD (years): treatment group (49.07 ± 13.31); control group (50.72 ± 11.68) Sex (M/F): treatment group (29/14); control group (24/19) Exclusion criteria: unstable hypertension, arrhythmia, cardiac angina, congestive heart failure, acute cerebrovascular accident; hepatic failure; Presence of physical limitations to learning prior to the training or during the relaxation therapy; patients with emotional turmoil during the previous month
Interventions	Treatment group

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Rambod 2013 (Continued)

- Benson's relaxation technique: twice a day each time for 20 minutes

Control group

- Routine care

Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep onset latency • Total sleep time • HRQoL • Pain • Sleep disturbance • Adverse events
Notes	<ul style="list-style-type: none"> • Funding source: Shiraz University of Medical Sciences • IRCT2013061613690N1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "Simple randomisation procedure was performed by a table of random numbers from the list of HD patients. Then, in order to allocate the participants into the study groups, a block randomisation procedure with a random sequence of 2 or 4 block sizes was used to provide balance between the groups and prevent selection bias. Therefore, all the patients were randomly allocated into either the intervention (43) or the control group (43) through block randomisation."</p> <p>Comment: Random numbers table as considered as low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "In this study, the HD nurses and physicians remained blind to the outcome measures and allocation of the subjects to the intervention and control groups. Moreover, the interventionist who taught the Benson's relaxation technique was masked of the aim of the study. The researcher assistant who collected the data was also blind to the study groups and the intervention. In addition, the statistician who performed the data analysis was kept blinded to the allocation, as well."</p> <p>Comment: Blinding of participants was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The participants completed a structured questionnaire including the demographic characteristics and the Pittsburgh Sleep Quality Index (PSQI). Demographic information included the subjects' age, gender, level of education, marital status, and length of time on HD (month). The required data were recorded by the subjects while the assistant researcher was in their bedside."</p> <p>Comment: Sleep quality was assessed using PSQI, a self-reported questionnaire. The PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded</p>
Incomplete outcome data (attrition bias)	Low risk	<p>Quote: "During the study, two patients in the control group were withdrawn because of kidney transplantation and lack of interest to continue their coop-</p>

Rambod 2013 (Continued)

All outcomes

eration. One subject in the intervention group was also excluded due to kidney trans-plantation. Therefore, forty two HD patients in the Benson's relaxation technique group participated in the eight week intervention, while 41 subjects in the control group just received the routine care and the study was pursued by 83 patients (Figure 1)."

Comment: As reported in the flow chart, 1/43 in the Benson's relaxation technique group and 2/43 in the routine care group were lost to follow-up for reasons that appeared unrelated to treatment (< 10% loss to follow-up, there was not a differential loss between groups)

Selective reporting (reporting bias)	Low risk	Sleep quality was measured by PSQI at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Shiraz University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Razazian 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: April 2011 to June 2012 Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: single centre Presence of all four characteristics with a minimum score of 10, minimum time of haemodialysis of three months, age more than 15 years and no evidence of other cause on neurological examination Number (randomised/analysed): treatment group 1 (44/42); treatment group 2 (43/40) Mean age $\pm$ SD (years): treatment group 1 (57.8 ± 13.7); treatment group 2 (52.6 ± 11.5) Sex (M/F): treatment group 1 (24/18); treatment group 2 (22/18) Exclusion criteria: treatment with psychotropic agents during the recent 4 weeks; presence of another neurological disease comorbid with ESKD; iron deficiency; pregnancy
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Gabapentin (oral): 200 mg/day <p>Treatment group 2</p> <ul style="list-style-type: none"> Levodopa/carbidopa (oral): 110 mg/day
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI, ESS, IRLS) Sleep onset latency Total sleep time Sleep disturbance Cardiovascular death Adverse events
Notes	<ul style="list-style-type: none"> Funding source: not reported IRCT201112078323N1

Risk of bias

Razazian 2015 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "We conducted a randomised clinical trial using four weeks of gabapentin or levodopa-c therapy to treat RLS symptoms in haemodialysis patients." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The research team performing the measurements and patients were masked to treatment assignment." Comment: A double-blind study is considered as low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The evaluation tools included the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS). The Pittsburgh Sleep Quality Index (PSQI) assesses sleep quality by measuring subjective sleep quality in the preceding one-month period." Comment: Sleep quality was assessed using PSQI questionnaire. Investigators did not report the method for outcome measurement
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "During the course of the study period, two patients dropped out during the study secondary to somnolence and lethargy. These patients were administered gabapentin when the symptoms developed. One patient died because of myocardial infarction. One patient failed to follow-up due to migration. One of the patients had allergy to levodopa-c during the first week and dropped out of the study. Despite these lapses in compliance, 82 patients continued to participate. Figure 1 summarizes the trial profile." Comment: As reported in the flow chart, 1/44 in Gabapentin group and 3/43 in Levodopa/Carbidopa group were lost to follow-up for reasons that appeared unrelated to treatment. Although these were small numbers, there was a differential loss between groups
Selective reporting (reporting bias)	Low risk	Sleep quality was measured by PSQI at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "Patient demographics are listed in Table 1. Baseline characteristics of the study participants, including sex, age and duration of dialysis, were similar between the study treatment groups. Laboratory assessments including Hb, ferritin, iron and TIBC were also similar between the study groups (Table 1). Baseline IRLS scores and sleep parameters were comparable between treatment groups (Table 2)." Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent

Reilly-Spong 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: January 2010 to March 2012 Duration of follow-up: 8 weeks
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Reilly-Spong 2015 (Continued)

Participants	<ul style="list-style-type: none"> Country: USA Setting: multicentre (recruited through transplant centre; dialysis clinics; community organisations and Internet sites) Aged ≥ 18 years; evaluated as eligible for kidney transplant (HD, PH, predialysis); no previous transplants; English-speaking, literate and mentally intact; interested in attending two in-person workshops; reachable by telephone and able to use their phone for 6 weekly teleconferences Number: treatment group 1 (31); treatment group 2 (32) Mean age $\pm$ SD (years): treatment group 1 (51.7 ± 12.1); treatment group 2 (53.8 ± 11.4) Sex (M/F): treatment group 1 (9/22); treatment group 2 (18/14) Exclusion criteria: medically unstable or not receiving standard medical care; expected to receive a transplant in the next 3 months, serious mental health issues (suicidal, psychotic disorder, delirium), previous MBSR class or regularly practicing mindfulness meditation
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Telephone-based MBSR: telephone-based MBSR workshops were scheduled on Sundays when dialysis clinics are closed <p>Treatment group 2</p> <ul style="list-style-type: none"> Telephone support: telephone support workshops were scheduled on Sundays when dialysis clinics are closed
Outcomes	<ul style="list-style-type: none"> Sleep quality (actigraphy) Depression (Center for Epidemiologic Studies – Depression) Anxiety (STAI) Pain Fatigue (PROMIS-Fatigue Short Form) HRQoL (SF-12)
Notes	<ul style="list-style-type: none"> Funding source: National Institute of Diabetes and Digestive and Kidney Diseases and National Center for Advancing Translational Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "Randomisation schedules were computer-generated using SAS, and designed using small randomly permuted blocks to promote balance within strata across treatment arms. The randomisation schedule was generated by the study statistician who was masked with respect to variables other than stratification variables."</p> <p>Comment: Computer-generation is considered method at low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote from Gross 2017: "Random assignments were concealed from staff and patients until after baseline assessment when the statistician emailed assignments to staff."</p> <p>Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "Participants completed baseline assessments prior to randomisation and returned materials prior to attending their assigned intervention. This is a single-blind study."</p> <p>Comment: A single-blind study is considered as high risk of bias</p>

Reilly-Spong 2015 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "This is a single-blind study with blinded endpoints for physiological parameters: actigraphy-derived sleep values and salivary cortisol levels." Comment: Actigraphy was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote from Gross 2017: "Participant flow diagram. The flow of patients into the trial from initial contact through follow-up is detailed by treatment group. Of 63 patients randomised, 8 patients withdrew prior to attending their assigned intervention. The remaining patients (n = 55) comprised the analysis sample, and of these, 51 had 2-month pre-transplant outcomes, and 42 had 6-month pre-transplant outcomes." Comment: As reported in the flow chart in Gross 2017, 4/32 in telephone-based MBSR group and 4/31 in telephone support group were lost to follow-up for reasons that appeared unrelated to treatment (> 10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	Low risk	As reported in Gross 2017, sleep quality was measured by actigraphy at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by National Institute of Diabetes and Digestive and Kidney Diseases and National Center for Advancing Translational Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Ren 2017a

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: multicentre (2 sites) Inclusion criteria: <ul style="list-style-type: none"> Patients aged 18 and 75 years; period of HD over 3 months and no surgical operation and change in HD method are performed within 3 months; secondly, patient is in stable condition during the experiment; thirdly, patient is voluntary to participate the study with consent, understanding and cooperation; according to scoring method of PSQI, HD patient with over 7 total points was regarded as positive standard of screening Number: 142 Mean age $\pm$ SD (years): not reported Sex (M/F): not reported Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> Herb foot-bath: 30 g agastache rugosus, 15 g herba eupatorii, 10 g safflower carthamus, 30 g radix rehmanniae recen, 20 g angelica sinensis and 30 g radix paeoniae alba Control group <ul style="list-style-type: none"> No treatment

Ren 2017a (Continued)

Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep latency • Total sleep time • Sleep efficiency
Notes	<ul style="list-style-type: none"> • Funding source: National Science Foundation of China and the Fundamental Research Funds for the Central Universities of Central South University • Trial registration number: not reported • We contacted the author for clarifications but we do not receive answers

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Haemodialysis patients in accordance with inclusive criteria were randomly divided into control and intervention group."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Pittsburgh Sleep Quality Index (PSQI) and Dialysis Symptom Index (DSI) were applied to quantify sleep quality and symptom distress of haemodialysis patients."</p> <p>Comment: Sleep quality was assessed using PSQI questionnaire, a subjective measure which was likely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	High risk	<p>Quote: "Comparison of Pittsburgh Sleep Quality Index (PSQI) scores between pre- and post-intervention."</p> <p>Comment: Sleep quality was measured by PSQI at end of treatment in a format that was not extractable for meta-analysis</p>
Other bias	Unclear risk	The baseline characteristics of the patients were not reported. The study was supported by the National Science Foundation of China and the Fundamental Research Funds for the Central Universities of Central South University. There was insufficient information to permit judgement

Sabbatini 2003

Methods	<ul style="list-style-type: none"> • Study design: cross-over study • Duration of study: not reported
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Sabbatini 2003 (Continued)

- Duration of follow-up: 2 week (first phase)

Participants	<ul style="list-style-type: none"> • Country: Italy • Setting: multicentre (number of sites not reported) • Time on HD ranging between 6 and 60 months; aged < 70 years; iPTH < 400 ng/mL; abstinence from hypnotics during the last 3 months; all patients had insomnia • Number: 14 • Mean age $\pm$ SD: 54.7 $\pm$ 11.3 years • Sex (M/F): 9/4 • Exclusion criteria: presence of concurrent affections (cancer, congestive heart failure, connective tissue disease, diabetes); psychiatric disorders
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Zaleplon (oral): 5 to 10 mg/day <p>Control group</p> <ul style="list-style-type: none"> • Placebo
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Adverse events
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This was a randomised, double-blind, placebo-controlled crossover study."</p> <p>Comment: Although the authors declared that the study was double-blind, the investigators who were assigning participants to 2 different treatments, did not provide an identical treatment to each group (pill size and colour). The investigators did not clearly state these details, then even though they declared the study is double blinded, the treatments were physically different</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<p>Quote: "The sleep quality was determined by the Pittsburgh Sleep Quality Index (PSQI) score, a score derived by a self-rated questionnaire."</p> <p>Comment: Sleep quality was assessed using PSQI questionnaire. Investigators did not report the method for outcome measurement</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Four patients (3 males and 1 female) left the study during the first experimental period (3 on placebo and 1 on Zaleplon); the causes of their dropping out were absence of any positive result (2 males, both on placebo), tachycardia and flushing (1 male, on Zaleplon), and family doctor advised in the absence of any disturbance (1 female, on placebo)."</p>

Sabbatini 2003 (Continued)

Comment: Overall, 4/14 were lost to the follow-up for reasons that appeared related to treatment (> 10% loss to follow-up, it was not clear if there was a differential loss between groups)

Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Saeedi 2014

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: multicentre Aged 18 to 65 years; having a history of HD for at least 6 months, having undergone HD 2 or 3 times/week; having acceptable ability to learn sleep hygiene program Number (randomised/analysed): treatment group (41/38); control group (41/38) Mean age $\pm$ SD (years): treatment group (52.27 $\pm$ 17.32); control group (57.87 $\pm$ 13.95) Sex (M/F): treatment group (15/23); control group (20/18) Exclusion criteria: unwilling to continue to participate in the study; suffering from known mental diseases including deep anxiety and depression (according to patient answer and his/her medical history); having cognitive impairment; experiencing an unpredictable crisis or disease during the study period; severe physical crisis (acute illness, hospitalisation, and extensive surgery); psychological crisis (bereavement, divorce) in the past 6 months
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Sleep hygiene education: 6 weekly sessions of half-hour sleep hygiene training program <p>Control group</p> <ul style="list-style-type: none"> No treatment
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Sleep efficiency Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: Arak University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This randomised controlled trial was conducted on patients undergoing maintenance haemodialysis in haemodialysis centres of Arak Valiasr Hospital. Eighty-two patients with sleep problem were randomly selected."

Saeedi 2014 (Continued)

		Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI), which is a standard self-report questionnaire for determining the quality of sleep during the past month." Comment: Sleep quality was assessed using the PSQI, a self-reported questionnaire. The PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Six of 82 patients (3 in the intervention group and 3 in the control group) were excluded from the study and data of 76 patients were analysed." Comment: 3/41 in Sleep hygiene education group and 3/41 in control group were lost to follow-up (<10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	Low risk	Quote: "Sleep quality was assessed by the Pittsburgh Sleep Quality Index (PSQI) before and after the intervention." Comment: As reported in table 2, sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	Quote: "The two groups did not have any significant differences in terms of age, sex distribution, educational level, marital status, daily activity, duration and frequency of haemodialysis, and use of sleep medications, identified through self-report (Table 1). [...] The mean global scores and component scores of sleep quality were not significantly different between the two groups before the intervention." Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. This study was supported by Arak University of Medical Sciences. The funding agency did not appear to be involved in study conduct. No other sources of bias were apparent

Shariati 2012

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Iran Setting: multicentre ESKD diagnosis confirmed by a nephrologist, routinely receiving 4 hour afternoon maintenance HD 3 times/week, for at least 3 months, aged > 18 years; PSQI 35 scores of five points or over; good mental

Shariati 2012 (Continued)

health status; no dementia, ability to communicate in Persian; no limb amputation; agreement to participate in the study

- Number: treatment group (22); control group (22)
- Mean age $\pm$ SD (years): treatment group (53.5 ± 12.5); control group (55.5 ± 10.6)
- Sex (M/F): treatment group (12/10); control group (11/11)
- Exclusion criteria: major chronic illness such as insulin-dependent diabetes (diabetic neuropathy), cancer, or lupus erythematosus; transfer to ICU with any reason; surgery; infection; bleeding during research period; dialysis complications needing immediate medical intervention; disabling mental or physical diseases affecting answering to the questions; current skin problems (e.g. ulcer, rash) in the acupressure areas

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Acupressure: 15 min <p>Control group</p> <ul style="list-style-type: none"> • No treatment
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Sleep onset latency • Total sleep time • Sleep efficiency • Sleep disturbance
Notes	<ul style="list-style-type: none"> • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The study was a randomised control trial."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This was a double-blind study; the interviewer and care providers, did not know what types of treatment patients received."</p> <p>Comment: Although the authors declared that the study was double-blind, blinding of participants was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely</p>
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	<p>Sleep quality was assessed using PSQI questionnaire. Investigators did not report the method for outcome measurement</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<p>Quote: "Four subjects dropped out of the study for different reasons; including death, transfer to another ward in order to transplantation, transfer to ICU, and disagreement with participation."</p> <p>Comment: Overall, 4/44 were lost to the follow-up for reasons that appeared unrelated to treatment (although <10% loss to follow-up, it was not clear if there was a differential loss between groups)</p>

Shariati 2012 (Continued)

Selective reporting (reporting bias)	Low risk	<p>Quote: "Table 2 presents sleep quality scores before and after acupressure in two groups."</p> <p>Comment: As reported in table 2, sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "Characteristics of participants in each group are presented in Table 1. [...] There was no significant difference in the data pertaining to age distribution ($p = 0.72$), age mean ($p = 0.72$), gender ($p = 0.55$), educational status ($p = 0.76$), work status ($p = 0.18$), marital status ($p = 0.48$), haemodialysis duration distribution ($p = 0.22$), mean haemodialysis duration ($p = 0.48$), mean blood urea, creatinine, and haemoglobin ($p > 0.2$). These data indicated homogeneity of demographic data of subjects across groups. Moreover, advance in kidney disease leads to decrease in sleep quality⁴⁰; however, there were no differences in mean blood urea, creatinine, and haemoglobin between the groups at baseline. [...] These data indicates homogeneity of sleep quality indices in subjects in two groups at baseline and shows that changes of these items in subjects across groups after intervention were absent before acupressure which helps to evaluate the effectiveness of the intervention."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent</p>

SIESTA 2017

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Australia Setting: multicentre (2 sites) Aged > 18 years with ESKD and self-reported poor sleep quality who were receiving thrice weekly HD or HDF for at least 3 months prior to study enrolment and had no plans to change their RRT within the study period Number (randomised/analysed): treatment group (21/21); control group (21/20) Mean age $\pm$ SD (years): treatment group (58.6 ± 11.9); control group (51.6 ± 17.9) Sex (M/F): treatment group (14/6); control group (11/9) Exclusion criteria: history of amputation (precluding ability to apply acupressure treatment on limbs); serious skin diseases (e.g. dermatitis and burn) near the location of acupoints; previous knowledge of the Traditional Chinese Medicine to minimize the risk of participants being able to distinguish the real acupoints from the sham or the nonspecific acupoint
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Real acupressure therapy <p>Control group</p> <ul style="list-style-type: none"> Sham acupressure therapy
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Sleep efficiency

SIESTA 2017 (Continued)

- HRQoL (SF-8)
- Pain
- Sleep disturbance
- Hospital admissions
- Adverse events

Notes

- Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer-generated randomisation schedule was kept." Comment: Computer-generation is considered method at low risk of bias
Allocation concealment (selection bias)	Low risk	Quote: "To ensure adequate concealment of allocation, a computer-generated randomisation schedule was kept in sequentially numbered, sealed opaque envelopes." Comment: Investigators could not foresee assignment and it could be considered as low risk of bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "The Study Investigating the Efficacy, Safety, and Tolerability of Acupressure (SIESTA) versus sham therapy for improving sleep quality in patients with end-stage kidney disease on haemodialysis] study was an investigator initiated, multicenter, prospective, 1:1 randomised, single-blind, sham-controlled, parallel design trial." Comment: A single-blind study is considered as a high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Study participants, care providers working in the dialysis units, an outcome assessor, and study statistician were blinded to the participant's allocation to minimize the potential for performance bias." Comment: Sleep quality was assessed using PSQI questionnaire. Investigators reported that the outcome assessor was blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Forty-two patients were randomly assigned to receive either real acupressure therapy (n = 21) or sham acupressure therapy (control: n = 21; Figure 1). One participant declined to participate after randomisation but prior to receiving any treatment." Comment: 0/21 in Real acupressure therapy group and 1/21 in Sham acupressure therapy group were lost to follow-up (< 10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	High risk	Sleep outcome was measured by PSQI at end of treatment in a format that was not extractable for meta-analysis (SD not reported). Dichotomous outcomes (hospitalisation) at end of treatment in a format that was extractable for meta-analysis
Other bias	High risk	Quote: "Overall, the groups were comparable on baseline characteristics except for significantly longer dialysis duration (46 months versus 21.5 months, p = 0.04) and duration of each dialysis session (5.2 ± 0.5 versus 4.7 ± 0.6 hours, p = 0.01) in the intervention group (Table 1). At baseline, the intervention group patients reported a significantly higher frequency of experiencing days with no chance of daytime somnolence compared to the control group (median 4.5 versus 0.5, p = 0.03; Supplementary Table S1). Other parameters reported in the sleep diary were comparable between the two groups (i.e., sleep duration,

SIESTA 2017 (Continued)

ability to fall asleep, mood, exercise, frequency of daytime naps, and alcohol or caffeine consumption)."

Comment: There was evidence of some different baseline characteristics, or different non- randomised co-interventions between groups. The sources of funding were not reported

Silva 2017

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: January to December 2015 Duration of follow-up: 1 week (first phase)
Participants	<ul style="list-style-type: none"> Country: Brazil Setting: Single centre Dialysis vintage of at least 6 months; age between 18 and 70 years; diagnosis of OSA by overnight PSG; and residual diuresis lower than 500 ml/day Number (randomised/analysed): treatment group 1 (9/7); treatment group 2 (8/7) Mean age $\pm$ SD: 53 $\pm$ 9 years Sex (M/F): 8/6 Exclusion criteria: diagnosed heart failure, atrial fibrillation, chronic obstructive pulmonary disease or neoplasia; inferior limbs prosthesis or amputation; current CPAP treatment; negative screening by the Berlin scale; thrombosis of superior vena cava; presence of ascites or pleural effusion
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> CPAP <p>Treatment group 2</p> <ul style="list-style-type: none"> Compression stockings
Outcomes	<ul style="list-style-type: none"> Sleep onset latency (polysomnography) Total sleep time Sleep efficiency
Notes	<ul style="list-style-type: none"> Funding source: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Patients were randomly assigned for another polysomnography either for Continuous Positive Airway Pressure (CPAP) titration or after wearing Compression Stockings (CS) for 1 week during daytime and then crossed over to the other treatment. Randomization was done by block, with two possibilities: baseline-CS-CPAP or baseline-CPAP-CS. Patients had not been previously treated with Continuous Positive Airway Pressure (CPAP) or Compression Stockings (CS) before study entry."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement

Silva 2017 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "All sleep studies were scored by the same physician, who was blinded to the use of Compression Stockings (CS) or baseline and to the measurements of leg fluid volume and NC."</p> <p>Comment: Patients were randomised to CPAP or compression stockings. As these treatments are physically different, blinding of participants to treatment assignment was unlikely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The primary outcome was the overnight fluid redistribution assessed in the three polysomnographs exams. Secondary outcomes were variation of NC and change in AHI in polysomnographs exam after Continuous Positive Airway Pressure (CPAP) titration and after wearing Compression Stockings (CS) in comparison to baseline. [...] Epworth Sleepiness Scale (ESS) was applied before polysomnograph exam in two moments: at baseline and after wearing Compression Stockings (ES) for 1 week."</p> <p>Comment: Polysomnography was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation. However, the ESS was a subjective measure which was likely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	As reported in the flow chart (Figure 1), in the first phase of randomisation 2/9 in CPAP group and 1/8 in compression stockings group were lost to follow-up (> 10% loss to follow-up, there was a differential loss between groups)
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a cross-over study design and were not extractable for meta-analysis
Other bias	Unclear risk	<p>Quote: "The baseline characteristics of the studied population are described in Table 1."</p> <p>Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). There was insufficient information to permit judgement</p>

Sklar 1998

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 1 week (first phase)
Participants	<ul style="list-style-type: none"> Country: USA Setting: single centre HD patients with fatigue index greater than 4 Number (randomised/analysed): 21/16 Mean age $\pm$ SD: 61 $\pm$ 3 years Sex (M/F): 9/7 Exclusion criteria: not reported
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Dialyzer with cuprophane membrane: each patients was dialysed 3 times/week <p>Treatment group 2</p>

Sklar 1998 (Continued)

- Low flux dialyzer with polymethyl methacrylate membrane: each patients was dialyzed 3 times/week

Outcomes	<ul style="list-style-type: none"> • Fatigue score (log sheets)
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "We conducted a crossover study with random assignment to ascertain whether a biocompatible membrane might attenuate the increase of TNF-α and severity of PDF."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "Patients were blinded with respect to the type of membrane used during all dialysis treatments throughout the study."</p> <p>Comment: Although the intervention was not told to the patients the methods of intervention and control treatment were physically different, and therefore masking of treatment allocation for patients and investigators was unlikely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Levels of PDF were determined by analysis of 6-hour logs of sleep and perception of fatigue recorded by patients after each of these dialysis treatments. At the completion of the study, the patients submitted their log sheets to one of the investigators."</p> <p>Comment: The sleep log was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcomes assessment were unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Five patients were not included in the data analysis because they were individuals who destabilized medically (n=2) or submitted incomplete log sheets (n=3)."</p> <p>Comment: Overall, 5/21 were lost to the follow-up for reasons that appeared unrelated to treatment (> 10% loss to follow-up, it was not clear if there was a differential loss between groups)</p>
Selective reporting (reporting bias)	High risk	<p>The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis</p>
Other bias	Unclear risk	<p>Quote: "The remaining 16 patients had a mean age of 61$\pm$3 years and included 9 men and 7 women. Causes of renal failure included diabetes mellitus (n=7), hypertension (n=3), chronic glomerulonephritis (n=4), polycystic kidney disease (n=1), and analgesic abuse (n=1)."</p> <p>Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement</p>

Solak 2012

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 6 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: single centre Patients age > 18 years with neuropathic pain regardless of pruritus symptoms with prior diagnosis of peripheral neuropathy or being on drug treatment for peripheral neuropathy for at least 3 months; minimum 40 mm pain score in the Short Form of McGill Pain Questionnaire; undergoing HD for at least 6 months, achievement of dialysis adequacy (Kt/V > 1.2) Number (randomised/analysed): 50/40 Mean age $\pm$ SD (years): 58.2 $\pm$ 13.7 years Sex (M/F): 12/28 Exclusion criteria: the presence of hepatic, cardiopulmonary and uncontrolled psychiatric disease; pain syndromes other than peripheral neuropathy; specific dermatologic disease; which may cause pain and/or pruritus; abnormal blood counts (white blood cells < 2500/mm³ and platelet count < 10 x 10³/mm³); presence of active malignancy; untreated hypothyroidism and patients with extremity amputation
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Gabapentin (oral): 150 mg/day <p>Treatment group 2</p> <ul style="list-style-type: none"> Pregabalin (oral): 75 mg/day
Outcomes	<ul style="list-style-type: none"> Sleep quality (SF-MPQ) Depression HRQoL (SF-36) Pain Adverse events
Notes	<ul style="list-style-type: none"> Funding source: no sources of funding Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "Patients were randomised into either Gabapentin (25 patients) or Pregabalin (25 patients) treatment arms using computer generated random numbers."</p> <p>Comment: Computer-generation is considered method at low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "This is a 14 week long, open-label, prospective, randomised crossover study that was conducted at a private haemodialysis centre."</p> <p>Comment: An open-label study is considered as high risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "All patients were instructed to complete the Short Form of McGill Pain Questionnaire (SF-MPQ) for assessment of pain and Visual Analogue Scale</p>

Solak 2012 (Continued)

		(VAS) for assessment of pruritus at the baseline evaluation. The same questionnaires were repeated after each treatment phase."
		Comment: Outcomes were assessed using the Short Form of McGill Pain Questionnaire (SF-MPQ) and Visual Analogue Scale (VAS), self-reported questionnaires. These questionnaires were subjective measures which were likely to be influenced by knowledge of treatment allocation. Outcomes assessment were unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Fifty patients who fulfilled inclusion criteria and agreed to participate in the study were enrolled. Forty out of 50 patients completed the entire study period. Ten patients were dropped because of various reasons (Figure 1)." Comment: As reported in the flow chart (Figure 1), in the first phase of randomisation 1/25 in Gabapentin group and 1/25 in Pregabalin group were lost to follow-up (<10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a cross-over study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Soleimani 2016

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: not reported
Participants	<ul style="list-style-type: none"> Country: Iran Setting: Single centre HD patients ≥ 18 years; having at least six-month history of HD, full consciousness and adequate auditory and verbal ability to respond to questions. Number: treatment group (30); control group (30) Mean age $\pm$ SD (years): Not reported Sex (M/F): treatment group (16/14); control group (17/13) Exclusion criteria: history of confirmed psychiatric disorder, alcoholism, physical and mental retardation and drug addiction
Interventions	Treatment group <ul style="list-style-type: none"> Sleep hygiene education Control group <ul style="list-style-type: none"> No treatment
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Sleep efficiency Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: Research and Technology Deputy of Shahid Beheshti University of Medical Sciences

Soleimani 2016 (Continued)

- Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This study is a randomised controlled clinical trial." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The participants were assessed individually through questionnaire interviewing before the intervention. [...] The instrument of data gathering was a questionnaire administered during dialysis and recovery of overall conditions of the patients. If a patient was literate, he/she was given the questionnaire to fill out and if the patient was illiterate, the questions were asked and his/her responses were ticked by the interviewer." Comment: Sleep quality was assessed using PSQI, a self-reported questionnaire. The PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "After sampling was completed, the patients were assigned to two groups, one intervention and one case, of 30 each and in the intervention group, one patient was excluded because of declining to continue participation." Comment: As reported in the flow chart, 1/30 in Sleep hygiene education group and 0/30 in control group were lost to follow-up for reasons that appeared unrelated to treatment (<10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	Low risk	Quote: "Sleep quality of participants was measured before and after the intervention by Pittsburgh Sleep Quality Index (PSQI)." Comment: As reported in table 4, sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Unclear risk	Quote: "The demographic data of all the patients were gathered by a questionnaire." Comment: The baseline characteristics for the patients were not reported in sufficient detail to permit judgement (Table 3). The study was supported by Research and Technology Deputy of Shahid Beheshti University of Medical Sciences. There was insufficient information to permit judgement

Soreide 1991

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 0.3 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: USA Setting: single centre HD patients who reported remarkable sleep disturbances (several awakenings during the night, difficulties in falling asleep, daily drowsiness, etc.) were considered for the study Number: 7 Median age (interquartile range): 43 years (36 to 48) Sex (M/F): 4/3 Exclusion criteria: not reported
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Branch-chain amino acid <p>Control group</p> <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Sleep efficiency (polysomnography) Sleep latency
Notes	<ul style="list-style-type: none"> Funding source: Unger Vetlesen Medical Foundation Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "They were subsequently randomised, in double-blind, cross over fashion, to receive either Branch-chain amino acid (BSAA) (60 mg/kg/hr = 1.4 ml/kg/hr. corresponding to 100 ml/hr in a 70 kg person) or saline, intravenously, for seven hours on the two study nights."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "They were subsequently randomised, in double-blind, cross over fashion, to receive either Branch-chain amino acid (BSAA) (60 mg/kg/hr = 1.4 ml/kg/hr. corresponding to 100 ml/hr in a 70 kg person) or saline, intravenously, for seven hours on the two study nights."</p> <p>Comment: A double-blind study is considered as low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "The polysomnograms were scored for sleep stages and incidence, length and severity of apneas/hypopnoeas by a registered polysomnographic technologist unfamiliar with the premises of the study."</p> <p>Comment: Polysomnography was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation</p>

Soreide 1991 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients completed the study
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	<p>Quote: "Six of the patients were on antihypertensive medications, including beta blockers. The polysomnographic investigation revealed that only one patient had severe sleep apnoea. This patient was very different from the rest both with respect to sleep and respiratory pattern, and he is therefore presented separately. Table 1 shows patient characteristics of the six non-apneic patients."</p> <p>Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The study was supported by Unger Vetlesen Medical Foundation. There was insufficient information to permit judgement</p>

Sun 2017

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: single centre Meet the diagnostic criteria, including two or more of the following: 1) at least 25% of defecation was hard; 2) at least 25% of defecation was blocked or hard stool; 3) at least 25% of defecation was considered as defecation insufficiency; 4) at least 25% of defecation caused an obstruction of the anorectum; 5) at least 25% of defecation needs manual assistance; 6) bowel movement less than 3 times per week. Long-term maintenance HD treatment; aged 32 to 68 years old; the patient or family member has signed the informed consent form; good adherence to this study Number: treatment group (40); control group (40) Mean age $\pm$ SD (years): treatment group (47.9 ± 9.3); control group (45.2 ± 8.6) Sex (M/F): treatment group (24/16); control group (26/14) Exclusion criteria: non-uraemic constipation; not maintenance HD; recently taken constipation drugs therapists; other intestinal diseases or organic constipation; skin diseases around the umbilicus; failure to comply with the study programme
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Nursing intervention: abdominal massage, patient's education and training exercise <p>Control group</p> <ul style="list-style-type: none"> Conventional nursing care
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Quality of life Pain
Notes	<ul style="list-style-type: none"> Not English Funding source: not reported Trial registration number: not reported

Sun 2017 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "Sleep quality was assessed using Pittsburgh Sleep Quality Index (PSQI)." Comment: Sleep quality was assessed using PSQI, a self-reported questionnaire. The PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (reporting bias)	Low risk	As reported in table 3, sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients were not reported in sufficient detail to permit judgement. The sources of funding were not reported. There was insufficient information to permit judgement

Tol 2010

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 8 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Slovakia Setting: single centre HD patients with pruritus Number: 14 Mean age $\pm$ SD: 59.7 $\pm$ 17.2 years Sex (M/F): 7/7 Exclusion criteria: < 18 years, pregnant and lactating women
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Gabapentin (oral): 300 mg/day <p>Control group</p> <ul style="list-style-type: none"> Placebo

Tol 2010 (Continued)

Outcomes	<ul style="list-style-type: none"> Depression (PSI; SF-36) Adverse events
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported
Risk of bias	
Bias	Authors' judgement Support for judgement
Random sequence generation (selection bias)	<p>Unclear risk</p> <p>Quote: "On a random and blinded basis, patients were assigned to receive eight weeks of Gabapentin therapy. There was a 1-week washout period between the sequential treatment phases."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	<p>Unclear risk</p> <p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	<p>Unclear risk</p> <p>Quote: "On a random and blinded basis, patients were assigned to receive eight weeks of Gabapentin therapy."</p> <p>Comment: The blinding was not reported in sufficient detail to permit judgement</p>
Blinding of outcome assessment (detection bias) All outcomes	<p>High risk</p> <p>Quote: "A questionnaire with a set of clinical variables, as well as a modified Post-Sleep Inventory (PSI), was applied to all patients."</p> <p>Comment: Sleep quality was assessed using the PSI, a self-reported questionnaire. The PSI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	<p>Low risk</p> <p>All patients completed the study</p>
Selective reporting (reporting bias)	<p>High risk</p> <p>The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis</p>
Other bias	<p>Unclear risk</p> <p>Quote: "The characteristics of cases with pruritus are shown in Table 1."</p> <p>Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement</p>

Trenkwalder 1995

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 4 (first phase)
Participants	<ul style="list-style-type: none"> Country: Germany Setting: Single centre Inclusion criteria:

Trenkwalder 1995 (Continued)

- HD patients were included if they exhibited RLS symptoms such as 1) paraesthesias or other sensory complaints of the lower limbs; 2) an irresistible urge to move the legs; 3) appearance of their symptoms only at rest; 4) increased severity in the evening or at night and 5) stable symptoms during the previous 2 weeks. After rating clinical symptoms at baseline, patients were referred to polysomnography without any treatment. Patients were included if they had more than 5 PLM-arousals/hour of sleep, a sleep latency of more than 25 minutes and/or a sleep efficiency index of less than 85%
- Number: 11
- Overall: 11
- Mean age $\pm$ SD: 49 $\pm$ 11 years
- Sex (M/F): 6/5
- Exclusion criteria: signs of any other sleep disorder on polysomnography, especially narcolepsy and sleep apnoea syndrome; receiving neuroleptic or antidepressant medications or with any severe additional illness or history of drug abuse; pregnant or lactating women and women without safe contraceptive methods were not allowed to participate in this study

Interventions	Treatment group <ul style="list-style-type: none"> • L-dopa + benserazide (oral): 200 mg + 50 mg/day Control group <ul style="list-style-type: none"> • Placebo
Outcomes	<ul style="list-style-type: none"> • Sleep onset latency (actigraphy; polysomnography)
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Following a 2-week baseline period, all patients were treated first with either L-dopa and then placebo or vice versa for 4 weeks in a randomised, controlled, double-blind crossover trial." Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Seventeen patients with idiopathic and 11 with uraemic (on continuous haemodialysis) RLS were evaluated comparatively by polysomnography, actigraphy and subjective ratings in a randomised, controlled and double-blind crossover trial with L-dopa and placebo for 4 weeks each." Comment: A double-blind study is considered as a low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "At baseline and at the end of both treatment periods, polysomnography recordings of each patient were made for one night. [...] In parallel to the polysomnography and for two additional nights, PLM were recorded by an Actigraph during each period. [...] At baseline and at the end of each treatment period, patients rated their quality of life, concerning well being and complaints during the previous week, using modified 50-mm Hamburger Visual Analogue Scales (VAS)." Comment: Polysomnography and actigraphy were used to assess the outcomes. Outcomes used objective measures which was unlikely to be influenced by knowledge of treatment allocation. However, the Hamburger Visual

Trenkwalder 1995 (Continued)

		Analogue Scales was a subjective measure which was likely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	All patients completed the study
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	Quote: "The characteristics of the valid patients are reported in Table 1." Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Tsai 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Taiwan Setting: single centre Patients with CKD aged ≥ 18 years or older and without hearing impairment receiving HD in 2 or 3 3-hour sessions weekly and to have been undergoing regular maintenance HD for more than 3 months Number: treatment group (32); control group (32) Mean age $\pm$ SD (years): treatment group (64.94 ± 9.51); control group (61.08 ± 11.18) Sex (M/F): treatment group (16/16); control group (15/17) Exclusion criteria: patients with CKD who were bedridden or hospitalised; those with psychiatric disorders confirmed by medical records
Interventions	Treatment group <ul style="list-style-type: none"> Nurse-led breathing training group: 8 sessions, twice weekly Control group <ul style="list-style-type: none"> No intervention
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Depression (BDI) HRQoL (SF-36) Pain Hospital admissions
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The random allocation sequence was generated using free online software providing randomly permuted blocks and random block sizes."

Tsai 2015 (Continued)

<p>Comment: Investigators describes a random component in the sequence generation that could be considered as low risk of bias</p>		
Allocation concealment (selection bias)	Low risk	<p>Quote: "Another independent research assistant who did not participate in participant enrolment, data collection, or data analyses generated the allocation sequence. The allocation sequence was concealed in sequentially numbered, opaque, sealed envelopes that were safeguarded by the primary investigator (one of us, P-ST) until it was time to assign the participants to groups. The dialysis nurse who delivered the intervention ensured that each envelope was still sealed, wrote a participant's name."</p> <p>Comment: Investigators could not foresee assignment and it could be considered as low risk of bias</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "This was an outcome assessor-blind, randomisation controlled trial. [...] An independent research assistant (one of us, S-HT) who was not involved in implementing the intervention and who was blinded to participants' group allocation performed the outcome assessment."</p> <p>Comment: Although the authors reported that the outcome assessor was unaware of the treatments assigned, participants completed the Beck Depression Inventory II (BDI-II), the PSQI, and the SF-36 that were self-reported questionnaires. Participants were aware of the treatment assigned</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Sixty-four participants were randomised equally to either the intervention or the control group. Three participants in the control group subsequently withdrew because of hospitalisation; and four participants in the control group refused to complete post-test questionnaires at Week 6. Only the 57 participants who completed the posttest questionnaires were included in the data analysis. (See Figure 1 for the flow of participants through the study)."</p> <p>Comment: As reported in the flow chart, 0/32 in Nurse-led breathing training group and 7/32 in control group were lost to follow-up (> 10% loss to follow-up, there was a differential loss between groups)</p>
Selective reporting (reporting bias)	Low risk	<p>Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "Demographic data for the two groups were comparable, except that average body mass index was significantly lower in the control group. No differences were observed in sleeping pill use, comorbidity, characteristics of dialysis treatments, or parameters of dialysis treatment adequacy.[...] No significant between-group differences were observed in baseline Pittsburgh Sleep Quality Index (PSQI) scores."</p> <p>Comment: As reported in Table 2, overall there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent</p>

Tsay 2003a

Methods • Study design: parallel RCT

Tsay 2003a (Continued)

	<ul style="list-style-type: none"> Duration of study: not reported Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Taiwan Setting: multicentre (number of sites not reported) Patients with ESKD who complain of sleep disturbance; aged 18 to 65 years; clear mental status with no dementia; able to communicate; and afternoon dialysis subjects. Number (randomised/analysed): treatment group (35/35); control group 1 (35/32); control group 2 (35/31) Mean age $\pm$ SD: 55.52 $\pm$ 12.98 years Sex (M/F): treatment group (17/18.35); control group 1 (10/22); control group 2 (15/16) Exclusion criteria: DSM IV psychiatric disorders; major chronic illness such as insulin-dependent diabetes; cancer; lupus erythematosus
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Acupressure group and usual care: received acupressure massage 3 times/week for 4 weeks <p>Control group 1</p> <ul style="list-style-type: none"> Sham acupressure and usual care: received acupressure massage 3 times/week for 4 weeks <p>Control group 2</p> <ul style="list-style-type: none"> Usual care
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Depression Fatigue Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: National Science Counsel of Taiwan Trial registration number: not reported The second report of this study was retracted as it was a duplicate publication. We have retained both studies in this review as they met the review eligibility criteria. We have ensured that the results of this study are only included once throughout

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The study is a randomised controlled trial. Adult patients undergoing haemodialysis routinely for End Stage Renal Disease were randomised into experimental (receiving an acupressure plus usual care), placebo (receiving sham acupressure plus usual care), or control groups (receiving usual care)."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "After consenting to participate, 105 subjects were stratified by gender and age, and then blind randomised to acupressure treatment plus usual care, sham acupressure plus usual care, or routine care groups. A total of 98 patients finished this study. Only the researcher and the acupressure nurse

Tsay 2003a (Continued)

		<p>were aware of which treatment the patients were receiving. The patients care providers (physicians, nurses, dieticians, social workers), and two trained research assistants, who collected all the data, were uninformed as to the participants' treatment group."</p> <p>Comment: Investigators were aware of the treatment allocation</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "Quality of sleep was measured by using the Pittsburgh Sleep Quality Index (PSQI) that was developed to screen patients with sleep quality and disturbance. [...] A sleep log was used to monitor sleep daily. Participants recorded when they woke up and the frequency of their nocturnal awakenings. Sleep log is widely used in clinical and research settings. Although reliability and validity of the daily log are rarely reported, researches have compared the daily log with polysomnographic monitoring, and found that objective data and subjective data were highly agreeable ($\kappa=0.87$), and that sensitivity and specificity were also high (92.3% and 95.6%) in narcoleptic subjects and control subjects. Researchers concluded that the log could provide accurate information about sleep/wake patterns."</p> <p>Comment: Sleep quality was assess using PSQI questionnaire. Outcome assessment was by patient-reported questionnaires, and patients were blinded to treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote from Tsay 2003 (secondary study): "Each group had 35 subjects in the study. However, three patients in the sham group and four in the control group were dropped from the study: one was hospitalised and patients were transferred to other dialysis centres."</p> <p>Comment: 0/35 in Acupressure group, 3/35 in sham group and 4/35 in control group were lost to follow-up (there was a differential loss between groups)</p>
Selective reporting (reporting bias)	Low risk	<p>Quote: "The main outcomes measured were the Pittsburgh Sleep Quality Index (PSQI) and the sleep log. Data were collected at pretreatment and following treatment. [...] Results of the means and standard deviations of pretest and posttest on quality of sleep across groups are presented in Table 1."</p> <p>Comment: Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "The typical participants were 55.52 years old ($SD=12.98$), female (54.8%), married (82.7%), and retired or unemployed (88.7%). Most had graduated from elementary school (38.8%) and high school (36.7%); and were religious (76.5%). The mean renal disease severity was moderately severe ($mean=6.89$, $SD=2.08$, $range=1-10$), and the mean length of dialysis was 60.25 months ($SD=55.84$). No statistically significant differences in gender, age, education levels, consumption of milk, tea, and coffee or smoking, current use of medication, number of chronic diseases, and length of being on dialysis were seen among the acupressure, sham acupressure, or control groups ($p > 0.05$). The data indicates homogeneity of subjects across the groups."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The study was supported by The National Science Counsel of Taiwan. No other sources of bias were apparent</p>

Tsay 2004

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported
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Tsay 2004 (Continued)

	<ul style="list-style-type: none"> Duration of follow-up: 4 weeks
Participants	<ul style="list-style-type: none"> Country: Taiwan Setting: multicentre (number of sites not reported) Aged ≥ 18 years diagnosed with ESKD treated with HD for at least 3 months; complaints of fatigue symptoms; PSQI scores of at least 5 points; BDI scores ≥ 10 points Number (randomised/analysed): treatment group 1 (36/35); control group 1 (36/35); control group 2 (36/36) Mean age $\pm$ SD (years): treatment group 1 (57.23 ± 10.93); control group 1 (60.49 ± 12.21); control group 2 (56.81 ± 13.30) Sex (M/F): (36/70) Exclusion criteria: with lower-extremity amputations; co-morbid diagnoses of psychiatric disorders; congestive heart failure; chronic obstructive pulmonary disease; insulin-dependent diabetes; neuro-muscular disease; SLE; rheumatoid arthritis; cancer; regular steroid therapy; use of anti-hypertension medications
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Acupressure: 15 minutes of treatment 3 times/week for 1 month <p>Control group 1</p> <ul style="list-style-type: none"> TEAS: 15 minutes of treatment 3 times/week for 1 month <p>Control group 2</p> <ul style="list-style-type: none"> Massage at locations with no acupoints
Outcomes	<ul style="list-style-type: none"> Sleep quality Depression Fatigue
Notes	<ul style="list-style-type: none"> Funding source: National Science Counsel of Taiwan Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The study was a randomised controlled trial; qualified patients were randomly assigned to acupressure, Transcutaneous Electrical Acupoint Stimulation (TEAS) or control groups."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Sleep quality was assessed using PSQI questionnaire. Outcome assessment was by patient-reported questionnaires, and patients were blinded to treatment allocation

Tsay 2004 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Quote: "108 patients agreed and consented to the study. One hundred and six patients completed the study. Two patients were dropped over the 1-month intervention: 1 in the acupuncture group and 1 in the control group. One patient was lost for medical reasons, while the other patient relocated."</p> <p>Comment: 1/36 in Acupuncture group, 1/36 in TEAS group and 0/36 in control group were lost to follow-up (< 10% loss to follow-up, there was not a differential loss between groups)</p>
Selective reporting (reporting bias)	Low risk	<p>Quote: "Methods of measurement included the revised Piper Fatigue Scale (PFS), the Pittsburgh Sleep Quality Index (PSQI) and the Beck Depression Inventory (BDI-II). Data were collected at baseline, during the intervention and post-treatment."</p> <p>Comment: Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "There were no differences in the clinical and demographic characteristics of the patients between the groups ($p > 0.05$)."</p> <p>Comment: As reported in Table 1 in Tsay 2004a, there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The study was supported by The National Science Council of Taiwan. No other sources of bias were apparent</p>

Turk 2010

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 4 weeks (first phase)
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: not reported Males aged 20 and 70 years of age who were undergoing maintenance HD and were in a stable heterosexual relationship for the previous 6 months with a clinical diagnosis of erectile dysfunction ≥ 6 months were considered for inclusion in the study Number: 16 Mean age $\pm$ SD: 47.2 ± 10.8 years Sex (M/F): all male Exclusion criteria: current treatment of erectile dysfunction regardless of drug or method; alcohol or drug abuse; inability to follow study instructions; major haematologic or hepatic abnormalities; myocardial infarction in the preceding 6 months and concomitant treatment with nitrate or derivatives; uncontrolled hypertension or symptomatic hypotension; penile anatomical deformity; bleeding diathesis and active peptic ulcer disease; scheduled for kidney transplant or alternate surgical procedure
Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> Sildenafil (oral): 50 mg/day <p>Treatment group 2</p> <ul style="list-style-type: none"> Vardenafil (oral): 10 mg/day
Outcomes	<ul style="list-style-type: none"> Total sleep time (PSI) Depression (BDI)

Turk 2010 (Continued)

- HRQoL (SF-36)
- Adverse events

- Notes
- Funding source: not reported
 - Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Thirty-two patients were randomised into either sildenafil or varde-nafil groups by opening pre-numbered sealed opaque envelopes containing a computer-generated randomisation sequence." Comment: A computer-generated sequence is considered as low risk of bias
Allocation concealment (selection bias)	Low risk	Quote: "Thirty-two patients were randomised into either sildenafil or varde-nafil groups by opening pre-numbered sealed opaque envelopes containing a computer-generated randomisation sequence." Comment: Investigators could not foresee assignment and it could be consid-ered as low risk of bias
Blinding of participants and personnel (perfor-mance bias) All outcomes	High risk	Quote: "This was an open-label, prospective, randomised crossover study." Comment: An open-label study is considered as high risk of bias
Blinding of outcome as-sessment (detection bias) All outcomes	High risk	Quote: "The patients in each group were instructed to complete the Interna-tional Index of Erectile Function (IIEF-5) and 36-item Short-Form Health (SF-36) surveys at baseline." Comment: Outcome was assessed using the Short-Form Health (SF-36), a self-reported questionnaire. The Short-Form Health (SF-36) was a subjective mea-sure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Selective reporting (re-ported bias)	High risk	The methods for reporting outcomes were not appropriate for a crossover study design and were not extractable for meta-analysis
Other bias	Unclear risk	The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The sources of funding were not reported. There was insufficient information to permit judgement

Unal 2016

- Methods
- Study design: parallel RCT
 - Duration of study: January 2014 to February 2015
 - Duration of follow-up: 4 weeks
- Participants
- Country: Turkey
 - Setting: Single centre

Unal 2016 (Continued)

- Patients aged 18 to 60 years who received HD therapy twice/week, who did not have any communication problems
- Number: treatment group 1 (36); treatment group 2 (37); control group (37)
- Mean age $\pm$ SD (years): treatment group 1 (51.74 ± 12.29); treatment group 2 (53.89 ± 13.18); control group (57.37 ± 13.12)
- Sex (M/F): treatment group 1 (19/16); treatment group 2 (16/19); control group (20/15)
- Exclusion criteria: skin lesions; open foot wounds; malignant diseases; thrombosis or bleeding disorders

Interventions	<p>Treatment group 1</p> <ul style="list-style-type: none"> • Foot reflexology: 2 times/week for 8 sessions <p>Treatment group 2</p> <ul style="list-style-type: none"> • Back massage: 2 times/week for 8 sessions <p>Control group</p> <ul style="list-style-type: none"> • No treatment
Outcomes	<ul style="list-style-type: none"> • Sleep quality (PSQI) • Fatigue (VASF)
Notes	<ul style="list-style-type: none"> • This research was approved as a doctoral thesis of Kevser Sevgi Unal by Ataturk University Institute of Health Sciences and presented at the ENDA & WANS Congress held in Hannover, Germany • Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "The data for this randomised, controlled, experimental study were collected between January 2014 and February 2015."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of participants and investigators was not reported in sufficient detail to permit judgement. However, due to physical differences between interventions, awareness of treatment allocation was likely
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "The Visual Analogue Scale for Fatigue (VASF) and the Pittsburgh Sleep Quality Index (PSQI) were administered to the patients as a pretest immediately before they were taken to haemodialysis."</p> <p>Comment: Sleep quality was assessed using PSQI, a self-reported questionnaire. The PSQI was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcome assessment was unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The patients were randomly assigned to three groups: the foot reflexology group (n = 36), the back massage group (n = 37) and the control group (n = 37). From the 110 patients, a total of 105 patients (35 patients per group) reached the end of the study, with one patient in the foot reflexology group

Unal 2016 (Continued)

		and two patients in the back massage group having withdrawn from the study, and two patients in the control group having left the dialysis centre."
		Comment: As reported in the flow chart, 1/36 in Foot reflexology group, 2/37 in Back massage group and 2/37 in control group were lost to follow-up (<10% loss to follow-up, there was not a differential loss between groups)
Selective reporting (reporting bias)	Low risk	Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis
Other bias	Low risk	As reported in Table 1, there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The study was approved as a doctoral thesis of Kevser Sevgi Unal by Ataturk University Institute of Health Sciences. No other sources of bias were apparent

Walker 1996

Methods	<ul style="list-style-type: none"> Study design: cross-over study Duration of study: not reported Duration of follow-up: 1 week (first phase)
Participants	<ul style="list-style-type: none"> Country: Canada Setting: single centre HD patients with RLS not being treated with levodopa and no current medical history of uncontrolled hypertension, untreated angina or cardiac arrhythmia Number (randomised/analysed): 8/5 Mean age $\pm$ SD: 68.2 years (SD not reported) Sex (M/F): 1/4 Exclusion criteria: not reported
Interventions	Treatment group <ul style="list-style-type: none"> L-dopa/carbidopa (oral): 100 mg/25 mg per day Control group <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Sleep latency (polysomnography) Sleep efficiency Total sleep time (data not extractable)
Notes	<ul style="list-style-type: none"> Funding source: Kidney Foundation of Canada and Baxter Healthcare Corporation Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomised by a research pharmacist and issued medication or placebo for 1 week followed by a questionnaire and an overnight polysomnographic (PSG) assessment. After a 1-week washout period, the patients crossed over to the alternate medication and followed the same procedure for a subsequent week."

Walker 1996 (Continued)

		Comment: Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The study was designed as a double-blind, randomised, crossover trial comparing placebo to a controlled release formulation of levodopa/carbidopa at a dose of 100/125 mg nightly taken 1 hour prior to bedtime." Comment: A double-blind study is considered as a low risk of bias
Blinding of outcome assessment (detection bias) All outcomes	High risk	Quote: "The questionnaire was completed during the seventh night of medication at the time of polysomnography. It involved questions pertaining to assessment of the previous week's experience on medication and required rating that experience. Objective data were obtained by overnight polysomnography following the supervised ingestion of study medication on the seventh night." Comment: Polysomnography was used to assess the outcome. Outcome used an objective measure which was unlikely to be influenced by knowledge of treatment allocation. However, the sleep questionnaire was a subjective measure which was likely to be influenced by knowledge of treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Eight patients were randomised but three withdrew prior to starting the protocol, two because of intercurrent illness and one due to personal reasons. Five patients completed the study protocol and were compliant with medication." Comment: Overall, 3/8 were lost to the follow-up for reasons that appeared unrelated to treatment (> 10% loss to follow-up, it was not clear if there was a differential loss between groups)
Selective reporting (reporting bias)	High risk	The methods for reporting outcomes were not appropriate for a cross-over study design and were not extractable for meta-analysis
Other bias	High risk	Quote: "There were four females and one male. The mean age was 68.2 years and mean weight was 75.2 kg. Four patients were taking sedatives but stopped the medication during the week of active drug. Three patients stopped their sedatives while on placebo, but one patient continued sedative use during the week of placebo because of distress due to the inability to sleep." Comment: The baseline characteristics for the patients in the first phase of randomised treatment were not reported. The study was supported by Kidney Foundation of Canada and Baxter Healthcare Corporation. Sponsor could be involved into the analysis

Williams 2017

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: February 2016 to August 2016 Duration of follow-up: 5 weeks
Participants	<ul style="list-style-type: none"> Country: USA Setting: multicentre (2 sites) Patients aged 18 to 75 years who performed HD 3 times/week, on HD for > 3 months were required to have the ability to walk without assistance or assistive devices to ensure that the device is able to track activity

Williams 2017 (Continued)

- Number: treatment group (15); control group (14)
- Mean age $\pm$ SD (years): treatment group (56 ± 13); control group (48 ± 15)
- Sex (M/F): treatment group (9/6); control group (3/11)
- Exclusion criteria: unstable health (e.g. acute infections, congestive heart failure (CHF) NYHA class 4 and/or unstable angina); hospitalised within 3 months before enrolment for non-access-related reasons; cognitively impaired; patients with a known nickel allergy previously worn activity tracking devices

Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Feedback group of activity level: patients received a report of activity and sleep data in the week leading to the date of each HD treatment <p>Control group</p> <ul style="list-style-type: none"> • No feedback on activity level
Outcomes	<ul style="list-style-type: none"> • Sleep quality (Fitbit flex) • Sleep efficiency • Death (all causes) <p>(data not extractable)</p>
Notes	<ul style="list-style-type: none"> • Funding source: not reported • Peter Kotanko holds stock in Fresenius Medical Care • Protocol number: 20152105

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	<p>Quote: "Participants were randomly assigned to 2 groups after enrolment."</p> <p>Comment: Sequence generation methods were not reported in sufficient detail to permit judgement</p>
Allocation concealment (selection bias)	Unclear risk	<p>Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "The 'feedback' group (n = 15) received a report of activity and sleep data in the week leading to the date of each HD treatment, while the control group (n = 14) did not."</p> <p>Comment: As these treatments are different, blinding of participants and investigators to treatment assignment was unlikely</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Quote: "Activity and sleep parameters were measured using a commercially available activity tracker in 29 haemodialysis patients. [...] Participants were asked to keep a daily sleep log, in which they recorded the times they went to bed and the times they woke up."</p> <p>Comment: Sleep quality and efficiency used an objective measure which was unlikely to be influenced by knowledge of treatment allocation. However, the sleep log was a subjective measure which was likely to be influenced by knowledge of treatment allocation</p>
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	<p>Quote: "Thirty one participants were enrolled in the study. Two of them died during the study period; their data were not included in the analysis."</p>

Williams 2017 (Continued)

		Comment: Although <10% loss to follow-up, it was not clear if there was a differential loss between groups
Selective reporting (reporting bias)	High risk	Quote: "Based on their average daily step counts, participants were separated into 3 categories." Comment: Sleep quality was measured by activity tracker at end of treatment in a format that was not extractable for meta-analysis
Other bias	Low risk	As reported in Table 1, there was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported: however, Peter Kotanko holds stock in Fresenius Medical Care. The remaining authors declared no competing interest. No other sources of bias were apparent

Yurtkuran 2007

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 13.2 weeks
Participants	<ul style="list-style-type: none"> Country: Turkey Setting: single centre Dialysis for at least 6 months (4 h/day, 3 times/week); no unstable hypertension, arrhythmia or cardiac angina after 10 min of fast pedaling; no use of analgesic or NSAID; average musculoskeletal pain score of at least 2 on a scale of 0–10 (VAS) in the previous month Number: treatment group (20); control group (20) Mean age $\pm$ SD (years): treatment group (38 ± 14.2); control group (41 ± 9.97) Sex (M/F): treatment group (9/11); control group (7/13) Exclusion criteria: Ischaemic cardiac pain, arrhythmia or unstable hypertension after 10 min fast pedaling; unstable angina, congestive heart failure (grade II), significant cardiac valve disease and conduction abnormalities according to the screening electrocardiogram; cerebrovascular disease; electrolyte imbalance; persistent hyperkalaemia before dialysis; diabetes mellitus; active liver disease; arthritic or orthopaedic problems limiting exercise; peripheral vascular disease; undisciplined patients
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Yoga-based exercise program: The duration was 15 min/session at the beginning, gradually increasing to 30 min/session till the end of the first month <p>Control group</p> <ul style="list-style-type: none"> No treatment
Outcomes	<ul style="list-style-type: none"> Pain Fatigue Sleep disturbance
Notes	<ul style="list-style-type: none"> Funding source: not reported Trial registration number: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
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Yurtkuran 2007 (Continued)

Random sequence generation (selection bias)	Low risk	<p>Quote: "In the single-blind study, simple randomisation was done by a physician using a computer-generated table of random numbers, and 40 participants were allocated to two groups. The procedure was concealed from the evaluating physician."</p> <p>Comment: A computer-generated table of random numbers is considered as low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	<p>Quote: "In the single-blind study, simple randomisation was done by a physician using a computer-generated table of random numbers, and 40 participants were allocated to two groups. The procedure was concealed from the evaluating physician."</p> <p>Comment: Method of allocation concealment was not reported in sufficient detail to permit judgement</p>
Blinding of participants and personnel (performance bias) All outcomes	High risk	<p>Quote: "In the single-blind study, simple randomisation was done by a physician using a computer-generated table of random numbers, and 40 participants were allocated to two groups. The procedure was concealed from the evaluating physician."</p> <p>Comment: A single-blind study is considered as high risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	High risk	<p>Outcomes were assessed using Visual Analogue Scale (VAS), a self-reported questionnaire. This questionnaire was a subjective measure which was likely to be influenced by knowledge of treatment allocation. Outcomes assessment were unlikely to be blinded</p>
Incomplete outcome data (attrition bias) All outcomes	Low risk	<p>Quote: "Three of the 40 patients who met the inclusion criteria were dropped, as they missed three sessions in a 3-month-period and adhered poorly to the exercise instructions. Thus, 19 patients in the exercise group and 18 patients in the control group were left (Figure 1)."</p> <p>Comment: As reported in Figure 1, 1/20 in Yoga-based exercise program group and 2/20 in control group were lost to follow-up for reasons that appeared unrelated to treatment (< 10% loss to follow-up, there was not a differential loss between groups)</p>
Selective reporting (reporting bias)	Low risk	<p>Outcomes were measured by Visual Analogue Scale (VAS) questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "The baseline values in the treatment and control groups were statistically similar (Table 1)."</p> <p>Comment: There was not evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported</p>

Zhao 2011

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: not reported Duration of follow-up: 8 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: single centre

Zhao 2011 (Continued)

- Aged 18 to 80 years; ESKD (CrCl < 10 mL/min or SCr ≥ 8.0 mg/dL); impaired sleep quality (PSQI ≥ 7); sleep disturbance diagnosed by the China Classification and Diagnostic Criteria of Mental Disorders, 3rd edition; maintenance HD for at least 3 months; no changes of HD methods and no surgery in recent 3 months; no fever or inflammation in recent week; no use of medication which might affect sleep quality in recent 2 weeks; expected stable condition during the study; written informed consent
- Number: treatment group (30); control group (30)
- Mean age ± SD (years): treatment group (52.30 ± 9.45); control group (52.53 ± 8.77)
- Sex (M/F): 16/14
- Exclusion criteria: history of severe impaired sleep quality before the initiation of HD; other systemic comorbidity that might affect the sleep quality; major comorbidity such as acute heart failure, cardiovascular diseases, severe infection; use of treatments other than the study interventions for the relief of sleep disturbance; skin irritability or infection on auricles

Interventions	Treatment group <ul style="list-style-type: none"> • Ear acupressure using magnetic bead plaster Control group <ul style="list-style-type: none"> • Routine care
Outcomes	<ul style="list-style-type: none"> • Sleep quality
Notes	<ul style="list-style-type: none"> • Chinese dissertation • Funding source: not reported

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Detailed randomisation method was not reported (only 'randomly divided'). Sequence generation methods were not reported in sufficient detail to permit judgement
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement
Blinding of participants and personnel (performance bias) All outcomes	High risk	An open-label study is considered as high risk of bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported in sufficient detail to permit judgement
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The number of patients at post-treatment was not reported. Not reported sufficient information to permit judgement
Selective reporting (reporting bias)	Unclear risk	Not reported in sufficient detail to permit judgement. Study protocol was not available
Other bias	Low risk	There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The sources of funding were not reported. No other sources of bias were apparent

Zou 2015

Methods	<ul style="list-style-type: none"> Study design: parallel RCT Duration of study: September to November 2012 Duration of follow-up: 8 weeks
Participants	<ul style="list-style-type: none"> Country: China Setting: single centre Patients aged 19 to 75 years under regular maintain HD treatment (weekly treatment ≥ 10 hours) for 12 to 120 months; chronic primary insomnia diagnosed according to DSM-IV-TR; global score of PSQI > 7; free of hypnotics use or using a minimum maintaining dose of estazolam (≤ 1 mg/d) during the past three months; informed consent provided Number: treatment group (32); control group (31) Mean age $\pm$ SD (years): treatment group (53.28 ± 12.68); control group (58.55 ± 10) Sex (M/F): treatment group (17/15); control group (11/20) Exclusion criteria: presence of co-morbidities including cancer, congestive heart failure, connective tissue disease and hematologic diseases; inadequately dialysed, indicating by $Kt/V < 1.20$; presence of severe physical symptoms such as bone pain, itchy skin, sleep apnoea and restless legs which are obviously causative for insomnia; fatigue caused by severe anaemia ($Hb < 60$ g/L) or malnutrition (serum albumin < 30 g/L)
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Auricular acupressure <p>Control group</p> <ul style="list-style-type: none"> Placebo
Outcomes	<ul style="list-style-type: none"> Sleep quality (PSQI) Sleep onset latency Total sleep time Sleep efficiency Sleep disturbance Death (all causes) Adverse events (none reported)
Notes	<ul style="list-style-type: none"> Funding source: Project of Research Studio of Famous Old TCM Practitioners Experience Heritage, State Administration of Traditional Chinese Medicine; and Research Project for Practice Development of National TCM Clinical Research Bases, P.R. China. CHICTR-TRC-12002272

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	<p>Quote: "A random sequence generated by Microsoft Excel software 2003, was produced by an investigator not involved in running the trial. The random sequence was kept by him and the assignment was unaware to other research staffs."</p> <p>Comment: The sequence generation is made by Microsoft Excel software 2003 and it is considered as low risk of bias</p>
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not reported in sufficient detail to permit judgement

Zou 2015 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	<p>Quote: "This pilot study was designed to be a two-arm (allocation ratio 1:1), double-blind, sham-controlled, randomised trial, and registered on Chinese Clinical Trial Registry. [...] Both the participants and the research nurse were blinded to the treatment protocol. Because acupoint names in Chinese often reflect the effects of the point (e.g. Shen men refers to tranquillization), all points used in the study were given a code to avoid breaking the blinding (e.g. 1A, 1B, see Fig 2). The nurse selected for this study did not have previous AA training or experience. He was made aware that the study was going to compare two different AA protocols, and was asked not to read the AA chart during the study. He was trained to apply both treatment protocols, and instructed not to discuss the difference of treatments with the participants. To avoid the Hawthorne and Rosenthal effects, he was required to limit the interaction with the participants. He would not ask participants whether they felt sore when placing the seeds on the acupoints (a common practice for confirming the accuracy of point location). The participants would not ask him any question about the manipulation and report any results to him. Any question regarding manipulation was directed to another investigator (X.Q.Wu) whom was responsible for teaching the participants how to apply the squeezing method. All results were reported to the investigator (Y.C. Wu) whom was responsible for recording results in a clinical interview. Another investigator, who conducted the statistical analysis, did not know the group assignment until the analyses completed."</p> <p>Comment: A double-blind study is considered as a low risk of bias</p>
Blinding of outcome assessment (detection bias) All outcomes	Low risk	<p>Quote: "All results were reported to the investigator (Y.C. Wu) whom was responsible for recording results in a clinical interview. Another investigator, who conducted the statistical analysis, did not know the group assignment until the analyses completed."</p> <p>Comment: The PSQI questionnaire was assessed at baseline, 4, 8 weeks after randomisation and 4, 8, 12 weeks post-treatment. Participants were unaware of treatment assignment. The assessor and statistician were blind to the study groups</p>
Incomplete outcome data (attrition bias) All outcomes	High risk	<p>Quote: "Eventually, 63 (30.3%) patients were included, with 32 randomly assigned to receive AA on specific acupoints and 31 on sham acupoints (Fig 1). Five participants (7.9%) withdrew during the study. Three participants in SAA group and one in AA group withdrew at four weeks after treatments, due to complaining of lacking in effect. One participant in AA group discontinued due to transferring to another haemodialysis unit (Figure 1)."</p> <p>Comment: As reported in the flow chart, 5/32 in Auricular acupressure group and 3/31 in placebo group were lost to follow-up (>10% loss to follow-up, there was a differential loss between groups)</p>
Selective reporting (reporting bias)	Low risk	<p>Sleep quality was measured by PSQI questionnaire at end of treatment in a format that was extractable for meta-analysis</p>
Other bias	Low risk	<p>Quote: "No significant difference was found between two groups on baseline demographic and clinical characteristics, including age, gender, co-morbidities, sleep medication intake, and dialysis adequacy (Table 1). [...] The founders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript."</p> <p>Comment: There was no evidence of different baseline characteristics, or different non-randomised co-interventions between groups. The study was supported by The Project of Research Studio of Famous Old TCM Practitioners Experience Heritage and The Research Project for Practice Development of National. No other sources of bias were apparent</p>

APD - automated peritoneal dialysis; BDI - Beck Depression Inventory; BIA - bioelectrical impedance analysis; BMI - body mass index; BP - blood pressure; CAPD - continuous ambulatory peritoneal dialysis; CGI - clinical global impression; CBT - cognitive-behavioural therapy; CKD - chronic kidney disease; CrCl - creatinine clearance; CPAP - continuous positive airway pressure; CRP - C-reactive protein; DBP - diastolic BP; DSM-IV-TR - Diagnostic and Statistical Manual of Mental Disorders fourth edition- Text Revision; EPO - erythropoietin; ESKD - end-stage kidney disease; ESS - Epworth Sleepiness Scale; Hb - haemoglobin; HbA1c - glycated haemoglobin; HD - haemodialysis; HDF - haemodiafiltration; HCT - hematocrit; HRQoL - health-related quality of life; ICU - intensive care unit; iPTH - intact parathyroid hormone; RLSSG - International RLS Study Group; Kt/V - dialyser urea clearance adequacy; KDQOL-SF - Kidney Disease and Quality of Life-Short Form; MBSR - mindfulness-based stress reduction; M/F - male/female; NYHA - New York Heart Association; NSAID - nonsteroidal anti-inflammatory drug/s; OSA - obstructive sleep apnoea; PD - peritoneal dialysis; PET - peritoneal equilibration test; PSI - post-sleep inventory; PSQI - Pittsburgh Sleep Quality Index; PLMI - periodic limb movements index; RCT - randomised controlled trial; RLS - restless legs syndrome; RRT - renal replacement therapy; SBP - systolic BP; SCr - serum creatinine; SD - standard deviation; SF-36 - Self-administered Short-Form; SLE - systemic lupus erythematosus; TEAS - transcutaneous electrical acupoint stimulation; VAS - visual analogue scale

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
ACTIVE Dialysis 2015	Outcomes of interest not reported: extended weekly HD hours (≥ 24 hours) versus standard hours HD (12 to 15 hours); sleep quality was not a reported outcome
Cooper 2004	Wrong population: nasal CPAP or usual care among people with uncontrolled hypertension (not stated whether patients had CKD)
Deng 2017	Outcomes of interest not reported: iron sucrose versus normal saline for RLS; sleep quality was not a reported outcome

CKD - chronic kidney disease; CPAP - continuous positive airway pressure; HD - haemodialysis; RLS - restless legs syndrome

Characteristics of studies awaiting assessment [ordered by study ID]

So 2007

Methods	As reported in the abstract "This study was designed for a nonequivalent control group repeated measures quasi-experimental study." Comment: Not clear if the study is a RCT
Participants	43 HD patients, 21 for the experimental group and 22 for the control group
Interventions	2 weeks pruritus intervention program was given to the experimental group only
Outcomes	Not reported
Notes	Not in English

HD - haemodialysis; RCT- randomised controlled trial

Characteristics of ongoing studies [ordered by study ID]

CTRI/2016/04/006870

Trial name or title	Effectiveness of self care management support intervention on medication adherence, pruritus severity, sleep quality and quality of life in patients with chronic kidney disease associated pruritus
Methods	<ul style="list-style-type: none"> RCT evaluating the effectiveness of a self-care management support intervention on medication adherence, pruritus severity, sleep quality, and quality of life in patients with CKD-associated pruritus

CTRI/2016/04/006870 (Continued)

	<ul style="list-style-type: none"> • Sample size: 210 • Phase 4 • Estimated duration: 12 months • Status: not yet recruiting
Participants	<ul style="list-style-type: none"> • Country: India • Male and female patients with CKD; aged 18 to 70 years • Inclusion criteria <ul style="list-style-type: none"> * 1. Have mild, moderate and severe pruritus * 2. Are expected to continue treatment as out patient * 3. Can read and comprehend Tamil, English, and Hindi * 4. Give consent to participate in the study • Exclusion criteria: cognitive, hearing and speech disabilities; serious illness and unable to follow the instructions; undergoing HD; history of dermatologic diseases such as psoriasis, various form of dermatitis, lichen simplex and dermatophytosis; unwilling to comply with the study protocol, mode of administration and duration of treatment; sick during the study period
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> • Self-care management support intervention <p>Control group</p> <ul style="list-style-type: none"> • Standard care
Outcomes	<ul style="list-style-type: none"> • Increase in medication adherence • Reduction of pruritus severity • Increase in sleep quality • Improve in QoL
Starting date	02/01/2017. Described on the Clinical Trials Registry - India as "not recruiting". The trial registration record has not been updated since 27 January 2016. Emailed investigator (Professor Anandha Ruby) at the College of Nursing, Christian Medical College, Vellore to request an update on the trial status on 17 April 2018. Reply not received.
Contact information	rubyrejoicy@yahoo.co.in
Notes	Funding source: Research institution and hospital

Dos Reis Santos 2013

Trial name or title	Cardiovascular risk and mortality in end-stage renal disease patients undergoing dialysis: sleep study, pulmonary function, respiratory mechanics, upper airway collapsibility, autonomic nervous activity, depression, anxiety, stress and quality of life: a prospective, double blind, randomised controlled clinical trial
Methods	<ul style="list-style-type: none"> • RCT • Sample size: 57 • Phase 4 • Estimated duration: not reported • Status of study: not yet recruiting
Participants	<ul style="list-style-type: none"> • Setting: Brazil

Dos Reis Santos 2013 (Continued)

	<ul style="list-style-type: none"> Male or female patients aged 18 to 80 years; CKD; candidate for kidney transplant with indication for dialysis; cognitive level sufficient for understanding the procedures and following the instructions; and agreement to participate by signing a statement of informed consent Exclusion criteria: craniofacial abnormalities; undergoing active treatment of sleep apnoea; active malignancy; active alcohol and/or drug abuse; and dementia or treatment-refractory psychiatric diseases leading to an inability to provide informed consent
Interventions	<ul style="list-style-type: none"> Diurnal HD Nocturnal HD Control group
Outcomes	<ul style="list-style-type: none"> Sleep parameters Pulmonary function Respiratory mechanics Upper airway collapsibility Autonomic nervous activity Depression Anxiety Stress QoL
Starting date	2 April 2012
Contact information	oliveira.lvf@uninove.br. Contacted the investigator by email on 17 April 2018 to request an update on the trial status. Update not received. The trial is reported as having commenced on 2 April 2012. Protocol published in 2013. No results found
Notes	Funding source: The Sleep Laboratory receives funding from the Nove de Julho University (Brazil) and research projects approved by the Brazilian fostering agencies Fundação de Amparo a Pesquisa do Estado de São Paulo (local acronym FAPESP; protocol no. 2003/01810-4) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (local acronym CNPq; Research Productivity modality; process no. 307618/2010-2)

IRCT2016060228219N1

Trial name or title	Effects of cool dialysate on sleep quality in patients undergoing haemodialysis
Methods	As reported in the study protocol: "The study was a randomised single blind controlled clinical trial, done in the before and after treatment method"
Participants	<ul style="list-style-type: none"> Country: Iran The study will be done on 13 patients in the intervention group and 13 patients in the control group. Male and female patients; consent for participation in the study; age older than 18 years and maximum 75 years; suffering from vision, hearing loss; not suffering from clear mental disorders and severe emotional mood disorders, which prevent effective communication; patients with CKD (patients who 6 months have passed since their dialysis); patients receiving dialysis treatment three times a week and each session for 4 hours; not suffering from endocrine disorders (such as hypothyroidism, hyperparathyroidism); patients who have received score higher than 5 PSQI; patients with haemoglobin levels are greater than 8 mg/dl; lack of debilitating diseases and disorders such as severe chronic heart, respiratory, hepatic, history of seizures and severe neuropathy based on medical records and patient history; lack of psychiatric disorders (schizophrenia, anxiety, depression) or dementia or stay in psychiatric wards because of the items listed; no history of kidney transplant

IRCT2016060228219N1 (Continued)

- Exclusion criteria: develop acute complications during HD (disequilibrium syndrome, embolism, dysrhythmia, cardiac, respiratory arrest, coma); discontinued dialysis for any reason; referred for kidney transplants (patients who get kidney transplantation during the study); death; cannot tolerate cold dialysis; unwillingness to continue to participate in the study

Interventions	Treatment group <ul style="list-style-type: none"> • HD with cold dialysis solution with temperature (35.5°C) for 4 weeks control group <ul style="list-style-type: none"> • HD with dialysis solution with standard temperature (37°C), for 4 weeks
Outcomes	Not reported
Starting date	22 September 2016 (expected recruitment end date 21 November 2016)
Contact information	ghanbarabadi93@medsab.ac.ir
Notes	Contacted author team (ghanbarabadi93@medsab.ac.ir) to request an update on the trial status. Emailed 16 April 2018. No reply received

IRCT2017020311885N8

Trial name or title	Effects of transcranial direct-current stimulation (tDCS) on the treatment of depressive and anxiety symptoms and improve quality of sleep in patients with chronic renal diseases on dialysis- a randomised double-blind placebo controlled trial
Methods	RCT
Participants	<ul style="list-style-type: none"> • Country: Iran • Males and females of two "anxiety-depression" and "sleep disorders" in HD • Exclusion criteria: history of head trauma in patient; history of epilepsy in patients or their families; past history of bipolar or psychotic disease; acute suicidal ideas; consumption of neuroleptics during the study; addiction to drugs or alcohol; pregnancy; having metal prosthesis or implant; severe anorexia; past history of neurologic dx., serious medical illness
Interventions	<ul style="list-style-type: none"> • tDCS.F3-Fp2 protocol • Placebo
Outcomes	<ul style="list-style-type: none"> • Anxiety • Depression • Sleep quality
Starting date	20-03-2015
Contact information	sfarnia@mazums.ac.ir
Notes	Funding source: Mazandaran Research Center of Psychiatry and Behavioral Sciences

NCT01620580

Trial name or title	Symptom management program for haemodialysis patients
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NCT01620580 (Continued)

Methods	RCT
Participants	<ul style="list-style-type: none"> Country: USA Males and females on HD; aged ≥ 18 years; on HD 3 times/week; received HD for ≥ 6 months; read and write English; have telephone service Exclusion criteria: history of dementia; AIDS; active cancer; inability to give informed consent
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Self-management strategies <p>Control group</p> <ul style="list-style-type: none"> Dietary information
Outcomes	<ul style="list-style-type: none"> Decrease symptom burden The study aims are: to compare the differences between the self-management intervention and control group on the following outcomes: decreased symptoms: itching, tiredness, numbness, sleep disturbance (difficulty falling asleep & difficulty staying asleep); adherence to treatment diary Improved social functioning, physical functioning and emotional status Feasibility of implementing self-management intervention To evaluate the feasibility of implementing the self-management intervention for a larger randomised controlled study treatment delivered (number of interventions sessions delivered and strategies used); treatment receipts (understanding of strategies); and treatment enactment (reported perception of usefulness of the strategies)
Starting date	September 2011
Contact information	Francess Danquah, The University of Texas Health Science Center, Houston
Notes	Funding source: The University of Texas Health Science Center, Houston

NCT01922999

Trial name or title	A randomised, prospective, double blind, placebo-controlled trial of two different doses of oral melatonin supplements in chronic kidney disease (CKD)-associated sleep disorders
Methods	RCT
Participants	<ul style="list-style-type: none"> Country: USA Males and females aged 18 to 85 years with CKD or SKD with eGFR < 30 mL/min; receiving HD for > 3 months; normal healthy controls must be without a known history of CKD and be willing to have formal polysomnography test and plasma melatonin measurements Exclusion criteria: outpatient HD for < 3 months; eGFR > 30 mL/min; receiving beta blocker therapy within one month of randomisation; receiving nifedipine therapy within one month randomisation; on PD; chronic home oxygen supplementation; receiving chronic home CPAP therapy; actively receiving outpatient sleep medications; diabetic gastroparesis unresponsive to medication; known pregnancy or unwilling to use contraception during the course of the study; functioning kidney allograft; currently receiving long-term immunosuppressive therapy; receiving low dose prednisone (≤ 10 mg/day); unable to give informed consent
Interventions	<p>Treatment group</p> <ul style="list-style-type: none"> Melatonin (1mg or 3 mg daily) <p>Control group</p>

NCT01922999 (Continued)

- Placebo

Outcomes	2 groups will be compared to see who group achieved a 25% reduction in sleep latency or 25% increase in total sleep time at the end of 60 days. Using the PSQI questionnaire as the index to measure quality of sleep and sleep patterns
Starting date	December 2012
Contact information	Southeast Renal Research Institute
Notes	Funding source: Southeast Renal Research Institute

NCT02361268

Trial name or title	End-stage renal disease intra-dialysis lifestyle education study
Methods	RCT
Participants	<ul style="list-style-type: none"> • Country: USA • Males and females aged ≥ 18 years on maintenance HD for ≥ 3 months; adequately dialysed (Kt/V ≥ 1.2 measured within last 3 months); expected to remain in present HD shift for next 4 months and expected to remain on HD for at least 6 months • Exclusion criteria: acute or chronic medical conditions that would make intra-dialysis yoga potentially hazardous; unstable cardiac disease e.g. angina, life threatening arrhythmia; chronic lung disease that prevents gentle exercise or deep breathing exercises; active cerebrovascular disease; major depression; chronic symptoms of nausea, vomiting, or diarrhoea; current participation in exercise or mind body program/practice; cognitive impairment (MMSE ≤ 24) measured at baseline testing visit
Interventions	<ul style="list-style-type: none"> • Intradialysis-yoga • Educational program
Outcomes	<ul style="list-style-type: none"> • QoL • Fatigue • Emotional states • Depression • Patient satisfaction • Sleep quality • Self-efficacy for self-management • Physical performance • Blood pressure • Endothelial function • Arterial stiffness • Cardiovagal and sympathoneural functioning including baroreflex and heart rate variability
Starting date	July 2015
Contact information	Gurjeet Birdee, Vanderbilt University Medical Center
Notes	Funding source. Vanderbilt University Medical Center

NCT02420184

Trial name or title	Treatment of obstructive sleep apnoea in chronic kidney disease
Methods	RCT
Participants	<ul style="list-style-type: none"> Country: Canada Males and females with CKD stage 3 or 4; OSA (RDI > 15) and nocturnal hypoxaemia (SaO₂ < 90% for > 12% of night) Exclusion criteria: failure to meet inclusion criteria; current therapy with CPAP or supplemental oxygen; severe daytime sleepiness reflected by an ESS > 15; any driver who holds a commercial drivers' license or who reports a recent history (past 6 months) of a road traffic accident; severe nocturnal hypoxaemia reflected by mean SaO₂ < 80% during level 3 sleep testing; daytime hypoxaemia reflected by partial pressure of PaO₂ < 60 mmHg during wakefulness; hypoventilation reflected by PaCO₂ > 45 mmHg during wakefulness; central sleep apnoea that accounts for > 50% of the estimated RDI; unable to provide informed consent
Interventions	<ul style="list-style-type: none"> CPAP therapy Placebo
Outcomes	<ul style="list-style-type: none"> eGFR ACR
Starting date	June 2015
Contact information	Patrick Hanly, University of Calgary
Notes	Funding source: University of Calgary

NCT02816762

Trial name or title	Effect of continuous positive airway pressure on albuminuria in patients with diabetic nephropathy and obstructive sleep apnoea
Methods	RCT
Participants	<ul style="list-style-type: none"> Country: Spain Males and females aged 18 to 80 years; Overweight or obesity (BMI ≥ 25 kg/m²); previous diagnosis of type 2 diabetes, fulfilling at least one of the following criteria: 1) current treatment with oral antidiabetic drugs and/or insulin; 2) a fasting glucose value above 126 mg/dl on at least 2 occasions; 3) blood glucose level at 2 hours after an oral glucose tolerance test is equal to or more than 200 mg/dL; or 4) a HbA1c level > 6.5%; clinical diagnosis of diabetic kidney disease, with a urinary ACR > 30 mg/g and an eGFR > 20 mL/min/1.73 m²; treatment with stable doses of ACEi, ARB or anti-aldosterone agents in the last 4 weeks Exclusion criteria: nondiabetic kidney disease (confirmed by biopsy); dialysis for AKI within the 6 previous months; evidence in the clinic history of relevant bilateral stenosis of renal artery (> 75%); Urinary ACR > 3000 mg/g, at the baseline visit; SBP ≥ 180 mmHg or DBP ≥ 110 mmHg at the baseline visit; stroke, transient Ischaemic attack, acute coronary syndrome, or hospitalisation for heart failure worsening, within the previous 30 days; professional drivers, risk profession or respiratory failure; severe daytime sleepiness (ESS > 18); concomitant treatment with high doses of acetylsalicylic acid (> 500 mg/day) or continuous treatment with NSAIDs; previous treatment with CPAP; participation in another clinical study within the 30 days prior to randomisation
Interventions	<ul style="list-style-type: none"> CPAP therapy Pharmacological treatment

NCT02816762 (Continued)

Outcomes	<ul style="list-style-type: none"> Albuminuria levels HbA1c HOMA index QUICKI index Cholesterol levels (total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides) C-reactive protein HRQoL assessed by the SF-12 questionnaire HRQoL assessed by the EuroQoL questionnaire Physical activity of patients with diabetic kidney disease and OSA Plasma levels of biomarker of inflammation (interleukin (IL)-1beta, IL-6, IL-8 and tumour necrosis factor-alpha) Plasma levels of 8-isoprostane Plasma levels of endothelin, intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 Plasma levels of appetite-regulating hormones (leptin and adiponectin) Identify the CPAP-responder subgroup of OSA patients with diabetic kidney disease in those the CPAP treatment achieve an albuminuria reduction > 20% from baseline
Starting date	June 2016
Contact information	Francisco Garcia-Rio, Hospital Universitario La Paz
Notes	Funding source: Hospital Universitario La Paz

NCT02939586

Trial name or title	A cross-sectional, randomised-controlled study to investigate the effect of HDF in sleep apnoea
Methods	Cross-over study
Participants	<ul style="list-style-type: none"> Males and females aged ≥ 18 years receiving maintenance HD for > 3 months; able to provide informed consent; satisfactory written and spoken English language skills Exclusion criteria: acute dialysis or acutely unwell patients; home dialysis patients; unable to participate in the study in the opinion of the participant's primary Nephrologist or due to language barrier or cognitive impairment; already on treatment for sleep-disordered breathing
Interventions	<ul style="list-style-type: none"> HD HDF
Outcomes	<ul style="list-style-type: none"> Objective sleep quality (total sleep time, sleep efficiency, types of sleep (% of non-rapid eye movement (NREM) and rapid eye movement (REM)), arousal (episodes/hr), apnoea-hypopnoea index (AHI), and oxygen saturation) Subjective sleep quality (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction) Overall QoL (physical and social functioning, physical and emotional role limitations, physical pain, mental health, vitality, general health perceptions plus the burden of kidney disease, and symptoms/problems commonly associated with kidney disease) The different concentration of inflammatory biomarker (CRP, $\beta 2M$, TNF-α, IL-6 and IL-8)
Starting date	October 2016
Contact information	Ginger Chu, John Hunter Hospital

NCT02939586 (Continued)

Notes

Funding source: John Hunter Hospital

Wu 2018

Trial name or title	Auricular acupressure for insomnia in haemodialysis patients: study protocol for a randomised controlled trial
Methods	RCT
Participants	<ul style="list-style-type: none"> Patients receiving regular HD treatment for more than 3 months and less than 10 years; gender: both; country: China Inclusion criteria: <ul style="list-style-type: none"> 1. Males and females aged 18 to 75 years on regular HD (two or three sessions every week, 4 h each session, total weekly dialysis period ≥ 10 h) for between 3 months and 10 years; insomnia diagnosed according to DSM-5; baseline global PSQI score > 7; informed consent provided Exclusion criteria: presence of comorbidities including cancer, congestive heart failure, connective tissue disease and haematological diseases; inadequately dialyzed, indicated by $Kt/V < 1.20$; presence of severe physical symptoms, such as bone pain, itchy skin, sleep apnoea and restless legs, which are obviously causative of insomnia; and exhaustion caused by severe anaemia ($Hb < 60$ g/L) or malnutrition (serum albumin < 30 g/L)
Interventions	<ul style="list-style-type: none"> Auricular acupressure on either active points Control points (points irrelevant to insomnia management)
Outcomes	<ul style="list-style-type: none"> Sleep quality Changes in PSQI scores (including global score and scores of each of the seven domains) at the end of treatment and at each follow-up visit compared with baseline
Starting date	December 2016
Contact information	doctorzc541888@126.com; linqizhan656635@163.com.
Notes	TCM Research Project of Guangdong Provincial Hospital of Chinese Medicine (YN2015MS25), and supported by MOST/SATCM of the People's Republic of China grant 2013BAI02B04 and the State Administration of Traditional Chinese Medicine, P.R. China (No. 201007005). The sponsor will not have a role in the design, conduct or interpretation of the study, or in any decision to submit the manuscript for publication. NCT03015766

ACEi - angiotensin-converting enzyme inhibitors; ACR - albumin/creatinine ratio; AIDS - acquired immunodeficiency syndrome; AKI - acute kidney injury; ARB - angiotensin II receptor blockers; CKD - chronic kidney disease; DBP - diastolic blood pressure; DM-5 - Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; ESKD - end-stage kidney disease; (e)GRF - (estimated) glomerular filtration rate; Hb - haemoglobin; HbA1c - glycated haemoglobin; HRQoL - health-related quality of life; Kt/V - dialyser urea clearance adequacy; MMSE - mini-mental state examination; NSAIDs - nonsteroidal anti-inflammatory drugs; OSA - obstructive sleep apnoea; PD - peritoneal dialysis; PSQI - Pittsburgh Sleep Quality Index; QoL - quality of life; RCT - randomised controlled trial; SBP - systolic blood pressure

DATA AND ANALYSES

Comparison 1. Relaxation versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	4	259	Mean Difference (IV, Random, 95% CI)	-1.62 [-5.03, 1.79]
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Hospitalisation	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
6 Anxiety	2	119	Std. Mean Difference (IV, Random, 95% CI)	0.11 [-0.55, 0.77]
7 Pain	3	189	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.67, 0.15]
8 Fatigue	2	119	Std. Mean Difference (IV, Random, 95% CI)	-0.61 [-2.09, 0.87]
9 Quality of life	2	138	Std. Mean Difference (IV, Random, 95% CI)	0.47 [-0.09, 1.04]
10 Depression	2	108	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-1.27, 1.35]

Analysis 1.1. Comparison 1 Relaxation versus control, Outcome 1 Sleep quality.

Analysis 1.2. Comparison 1 Relaxation versus control, Outcome 2 Sleep latency.

Analysis 1.3. Comparison 1 Relaxation versus control, Outcome 3 Total sleep time.

Study or subgroup	Relaxation		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Rambod 2013	42	5.8 (2.1)	41	5.1 (2)		0.71[-0.17,1.59]
					Favours relaxation Favours control	

Analysis 1.4. Comparison 1 Relaxation versus control, Outcome 4 Sleep disturbance.

Study or subgroup	Relaxation		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Rambod 2013	42	5.5 (3.8)	41	10.6 (6.6)		-5.05[-7.37,-2.73]
					Favours relaxation Favours control	

Analysis 1.5. Comparison 1 Relaxation versus control, Outcome 5 Hospitalisation.

Study or subgroup	Relaxation		Control		Risk Ratio	Risk Ratio
	n/N		n/N		IV, Random, 95% CI	IV, Random, 95% CI
Tsai 2015	0/32		3/32			0.14[0.01,2.66]
					Favours relaxation Favours control	

Analysis 1.6. Comparison 1 Relaxation versus control, Outcome 6 Anxiety.

Study or subgroup	Relaxation		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Reilly-Spong 2015	24	40.8 (14.7)	27	34.9 (10.1)		47.59%	0.47[-0.09,1.02]
Amini 2016	33	30.2 (5.6)	35	31.6 (7.6)		52.41%	-0.21[-0.68,0.27]
Total ***	57		62			100%	0.11[-0.55,0.77]
Heterogeneity: Tau ² =0.16; Chi ² =3.23, df=1(P=0.07); I ² =69.05%							
Test for overall effect: Z=0.34(P=0.74)							
					Favours relaxation Favours control		

Analysis 1.7. Comparison 1 Relaxation versus control, Outcome 7 Pain.

Study or subgroup	Relaxation		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Reilly-Spong 2015	24	43.9 (12.6)	27	46.1 (11.1)		30.35%	-0.18[-0.73,0.37]
Tsai 2015	32	76.5 (20.5)	25	74.8 (24.4)		32.1%	0.07[-0.45,0.6]
Rambod 2013	41	3.9 (2.7)	40	5.6 (2.8)		37.55%	-0.6[-1.05,-0.16]
Total ***	97		92			100%	-0.26[-0.67,0.15]
Heterogeneity: Tau ² =0.06; Chi ² =3.91, df=2(P=0.14); I ² =48.84%							
Test for overall effect: Z=1.24(P=0.21)							
					Favours relaxation Favours control		

Analysis 1.8. Comparison 1 Relaxation versus control, Outcome 8 Fatigue.

Analysis 1.9. Comparison 1 Relaxation versus control, Outcome 9 Quality of life.

Analysis 1.10. Comparison 1 Relaxation versus control, Outcome 10 Depression.

Comparison 2. Exercise versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	5	165	Std. Mean Difference (IV, Random, 95% CI)	-1.10 [-2.26, 0.05]
2 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
4 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Anxiety	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Fatigue	2	107	Std. Mean Difference (IV, Random, 95% CI)	-0.68 [-1.07, -0.29]
8 Depression	2	46	Mean Difference (IV, Random, 95% CI)	-9.05 [-13.72, -4.39]

Analysis 2.1. Comparison 2 Exercise versus control, Outcome 1 Sleep quality.

Analysis 2.2. Comparison 2 Exercise versus control, Outcome 2 Total sleep time.

Analysis 2.3. Comparison 2 Exercise versus control, Outcome 3 Sleep efficiency.

Analysis 2.4. Comparison 2 Exercise versus control, Outcome 4 Sleep disturbance.

Study or subgroup	Exercise		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Yurtkuran 2007	20	3.4 (5.2)	20	4.3 (8.2)		-0.9[-5.16,3.36]
					Favours exercise -10 -5 0 5 10 Favours control	

Analysis 2.5. Comparison 2 Exercise versus control, Outcome 5 Anxiety.

Study or subgroup	Exercise		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Amini 2016	32	31.7 (13.2)	35	31.6 (7.6)		0.12[-5.09,5.33]
					Favours exercise -10 -5 0 5 10 Favours control	

Analysis 2.6. Comparison 2 Exercise versus control, Outcome 6 Pain.

Study or subgroup	Exercise		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Yurtkuran 2007	20	3.1 (7.2)	20	4.2 (5.4)		-1.1[-5.04,2.84]
					Favours exercise -10 -5 0 5 10 Favours control	

Analysis 2.7. Comparison 2 Exercise versus control, Outcome 7 Fatigue.

Study or subgroup	Exercise		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Yurtkuran 2007	20	3.3 (1.5)	20	6.9 (7.2)		37.38%	-0.68[-1.32,-0.04]
Amini 2016	32	59.9 (28.9)	35	81.2 (32.6)		62.62%	-0.68[-1.17,-0.19]
Total ***	52		55			100%	-0.68[-1.07,-0.29]
Heterogeneity: Tau ² =0; Chi ² =0, df=1(P=1); I ² =0%							
Test for overall effect: Z=3.41(P=0)							
					Favours exercise -2 -1 0 1 2 Favours control		

Analysis 2.8. Comparison 2 Exercise versus control, Outcome 8 Depression.

Study or subgroup	Exercise		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Giannaki 2013	15	35.8 (6.4)	7	43.7 (11.2)		27.59%	-7.87[-16.75,1.01]
Giannaki 2013a	12	34.2 (7)	12	43.7 (6.7)		72.41%	-9.5[-14.98,-4.02]
Total ***	27		19			100%	-9.05[-13.72,-4.39]
Heterogeneity: Tau ² =0; Chi ² =0.09, df=1(P=0.76); I ² =0%							
Test for overall effect: Z=3.8(P=0)							
					Favours exercise -20 -10 0 10 20 Favours control		

Comparison 3. Exercise versus dopaminergic agonist

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Depression	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 3.1. Comparison 3 Exercise versus dopaminergic agonist, Outcome 1 Sleep quality.

Study or subgroup	Exercise		DA		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Giannaki 2013	15	7.3 (4.1)	7	5.9 (3.7)		1.45[-2.49, 5.39]
					Favours exercise	Favours DA

Analysis 3.2. Comparison 3 Exercise versus dopaminergic agonist, Outcome 2 Depression.

Study or subgroup	Exercise		DA		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Giannaki 2013	15	35.8 (6.4)	7	39.4 (4.4)		-3.58[-8.14, 0.98]
					Favours exercise	Favours DA

Comparison 4. Aerobic versus resistance exercise

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4 Aerobic versus resistance exercise, Outcome 1 Sleep quality.

Study or subgroup	Aerobic		Resistance		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Cho 2018	11	44.5 (9.6)	10	40 (15.4)		4.5[-6.6, 15.6]
					Favours aerobic	Favours resistance

Analysis 4.2. Comparison 4 Aerobic versus resistance exercise, Outcome 2 Total sleep time.

Study or subgroup	Aerobic		Resistance		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Cho 2018	11	405 (131)	10	431 (120)		-26[-133.35,81.35]
Favours aerobic -200 -100 0 100 200 Favours resistance						

Analysis 4.3. Comparison 4 Aerobic versus resistance exercise, Outcome 3 Sleep efficiency.

Study or subgroup	Aerobic		Resistance		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Cho 2018	11	93.3 (2.2)	10	94.1 (3.3)		-0.8[-3.22,1.62]
Favours aerobic -4 -2 0 2 4 Favours resistance						

Comparison 5. Acupressure versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	6	367	Mean Difference (IV, Random, 95% CI)	-1.27 [-2.13, -0.40]
2 Sleep latency	3	173	Mean Difference (IV, Random, 95% CI)	-0.59 [-0.92, -0.27]
3 Total sleep time	3	173	Mean Difference (IV, Random, 95% CI)	-0.60 [-1.12, -0.09]
4 Sleep disturbance	3	173	Mean Difference (IV, Random, 95% CI)	-0.49 [-1.16, 0.19]
5 Sleep interruption	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6 Sleep efficiency	2	107	Mean Difference (IV, Random, 95% CI)	-0.18 [-0.39, 0.03]
7 Death (all causes)	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
8 Fatigue	2	137	Mean Difference (IV, Random, 95% CI)	-1.07 [-1.67, -0.48]
9 Depression	2	137	Mean Difference (IV, Random, 95% CI)	-3.65 [-7.63, 0.33]

Analysis 5.1. Comparison 5 Acupressure versus control, Outcome 1 Sleep quality.

Study or subgroup	Acupressure		Control		Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Zhao 2011	30	7.5 (10)	30	11 (14)		1.82%	-3.5[-9.66,2.66]
Tsay 2004	35	7.8 (4)	36	9.8 (4.7)		10.72%	-1.95[-3.97,0.07]
Arab 2016	32	6.2 (1.9)	31	10.7 (3.9)		14.17%	-4.5[-6.04,-2.96]
Shariati 2012	22	0.9 (0.9)	22	1.9 (0.8)		23.77%	-0.96[-1.46,-0.46]
Tsay 2003a	35	1 (0.8)	31	1.6 (0.9)		24.42%	-0.57[-0.98,-0.16]
Zou 2015	32	1.3 (0.6)	31	1.3 (0.6)		25.09%	0.05[-0.24,0.34]
Favours acupressure -10 -5 0 5 10 Favours control

Analysis 5.2. Comparison 5 Acupressure versus control, Outcome 2 Sleep latency.

Analysis 5.3. Comparison 5 Acupressure versus control, Outcome 3 Total sleep time.

Analysis 5.4. Comparison 5 Acupressure versus control, Outcome 4 Sleep disturbance.

Analysis 5.5. Comparison 5 Acupressure versus control, Outcome 5 Sleep interruption.

Study or subgroup	Acupressure		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Arab 2016	32	2.2 (0.7)	31	2.5 (0.7)		-0.3[-0.65,0.05]
					Favours acupressure -2 -1 0 1 2 Favours control	

Analysis 5.6. Comparison 5 Acupressure versus control, Outcome 6 Sleep efficiency.

Study or subgroup	Acupressure		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Zou 2015	32	1.4 (0.9)	31	1.6 (1.5)		11.48%	-0.17[-0.79,0.45]
Shariati 2012	22	0.1 (0.3)	22	0.3 (0.5)		88.52%	-0.18[-0.4,0.04]
Total ***	54		53			100%	-0.18[-0.39,0.03]
Heterogeneity: Tau ² =0; Chi ² =0, df=1(P=0.98); I ² =0%							
Test for overall effect: Z=1.67(P=0.1)							
					Favours acupressure -2 -1 0 1 2 Favours control		

Analysis 5.7. Comparison 5 Acupressure versus control, Outcome 7 Death (all causes).

Study or subgroup	Acupressure n/N	Control n/N	Risk Ratio IV, Random, 95% CI		Risk Ratio IV, Random, 95% CI
Zou 2015	3/32	0/31			6.79[0.36,126.24]
			Favours acupressure	0.005 0.1 1 10 200	Favours control

Analysis 5.8. Comparison 5 Acupressure versus control, Outcome 8 Fatigue.

Study or subgroup	Acupressure		Control		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Tsay 2003a	35	4.7 (1.8)	31	5.7 (1.8)		47.06%	-1.05[-1.92,-0.18]
Tsay 2004	35	4.6 (1.7)	36	5.7 (1.8)		52.94%	-1.09[-1.91,-0.27]
Total ***	70		67			100%	-1.07[-1.67,-0.48]
Heterogeneity: Tau ² =0; Chi ² =0, df=1(P=0.95); I ² =0%							
Test for overall effect: Z=3.52(P=0)							
					Favours acupressure -2 -1 0 1 2 Favours control		

Analysis 5.9. Comparison 5 Acupressure versus control, Outcome 9 Depression.

Comparison 6. Acupressure versus sham acupressure

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	2	129	Mean Difference (IV, Random, 95% CI)	-2.25 [-6.33, 1.82]
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Sleep interruption	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Total sleep time	2	107	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.73, 0.04]
5 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6 Hospitalisation	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
7 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8 Depression	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Acupressure versus sham acupressure, Outcome 1 Sleep quality.

Analysis 6.2. Comparison 6 Acupressure versus sham acupressure, Outcome 2 Sleep latency.

Study or subgroup	Acupressure		Sham acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2003a	35	1.4 (1.1)	31	2.2 (1.1)		-0.82[-1.34,-0.3]
Favours acupressure Favours sham acupressure						

Analysis 6.3. Comparison 6 Acupressure versus sham acupressure, Outcome 3 Sleep interruption.

Study or subgroup	Acupressure		Sham acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Arab 2016	32	2.2 (0.7)	30	2.7 (1)		-0.5[-0.92,-0.08]
Favours acupressure Favours sham acupressure						

Analysis 6.4. Comparison 6 Acupressure versus sham acupressure, Outcome 4 Total sleep time.

Study or subgroup	Acupressure		Sham acupressure		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
SIESTA 2017	21	6.6 (2.1)	19	7 (1.3)		37.75%	-0.22[-0.84,0.4]
Tsay 2003a	35	1.4 (1)	32	1.9 (1.2)		62.25%	-0.42[-0.9,0.07]
Total ***	56		51			100%	-0.34[-0.73,0.04]
Heterogeneity: Tau ² =0; Chi ² =0.24, df=1(P=0.62); I ² =0%							
Test for overall effect: Z=1.77(P=0.08)							
Favours acupressure Favours sham acupressure							

Analysis 6.5. Comparison 6 Acupressure versus sham acupressure, Outcome 5 Sleep disturbance.

Study or subgroup	Acupressure		Sham acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2003a	35	1 (0.5)	32	1.1 (0.7)		-0.09[-0.37,0.19]
Favours acupressure Favours sham acupressure						

Analysis 6.6. Comparison 6 Acupressure versus sham acupressure, Outcome 6 Hospitalisation.

Study or subgroup	Acupressure		Sham acupressure		Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	n/N		n/N			
SIESTA 2017	2/21		4/20			0.48[0.1,2.32]
Favours acupressure Favours sham acupressure						

Analysis 6.7. Comparison 6 Acupressure versus sham acupressure, Outcome 7 Fatigue.

Study or subgroup	Acupressure		Sham acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2003a	35	4.7 (1.8)	32	4.7 (1.5)		-0.04[-0.83,0.75]
					Favours acupressure	Favours sham acupressure

Analysis 6.8. Comparison 6 Acupressure versus sham acupressure, Outcome 8 Depression.

Study or subgroup	Acupressure		Sham acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2003a	35	20.4 (10.7)	32	18.2 (11.1)		2.17[-3.05,7.39]
					Favours acupressure	Favours sham acupressure

Comparison 7. Acupressure versus transcutaneous electrical acupoint stimulation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Depression	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 7.1. Comparison 7 Acupressure versus transcutaneous electrical acupoint stimulation, Outcome 1 Sleep quality.

Study or subgroup	Acupressure		Acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2004	35	7.8 (4)	35	6.3 (4.6)		1.48[-0.53,3.49]
					Favours acupressure	Favours acupressure

Analysis 7.2. Comparison 7 Acupressure versus transcutaneous electrical acupoint stimulation, Outcome 2 Fatigue.

Study or subgroup	Acupressure		Acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2004	35	4.6 (1.7)	35	4.7 (1.5)		-0.09[-0.85,0.67]
					Favours acupressure	Favours acupressure

Analysis 7.3. Comparison 7 Acupressure versus transcutaneous electrical acupoint stimulation, Outcome 3 Depression.

Study or subgroup	Acupressure		Acupressure		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Tsay 2004	35	13.5 (8.8)	35	12.6 (7.6)		0.9[-2.95,4.75]
					-10 -5 0 5 10	Favours acupressure Favours acupressure

Comparison 8. Acupressure versus benzodiazepine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8 Acupressure versus benzodiazepine, Outcome 1 Sleep quality.

Study or subgroup	Acupressure		Estrazolam		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Dai 2007a	42	23.5 (3.9)	40	30.2 (3)		-6.7[-8.19,-5.21]
					-10 -5 0 5 10	Favours acupressure Favours estrazolam

Comparison 9. Cognitive-behavioural therapy versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	2	183	Std. Mean Difference (IV, Random, 95% CI)	-0.65 [-1.03, -0.26]
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Death (all causes)	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected
6 Anxiety	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8 Depression	2	183	Std. Mean Difference (IV, Random, 95% CI)	-0.76 [-1.06, -0.46]

Analysis 9.1. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 1 Sleep quality.

Analysis 9.2. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 2 Sleep latency.

Analysis 9.3. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 3 Total sleep time.

Analysis 9.4. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 4 Sleep efficiency.

Analysis 9.5. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 5 Death (all causes).

Analysis 9.6. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 6 Anxiety.

Study or subgroup	CBT		Control		Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Mean Difference Random, 95% CI
Hou 2014	51	1.8 (0.3)	47	2.4 (0.3)	+	-0.6[-0.72,-0.48]
					Favours CBT -2 -1 0 1 2 Favours control	

Analysis 9.7. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 7 Quality of life.

Study or subgroup	CBT		Control		Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Mean Difference Random, 95% CI
Duarte 2009	41	63.9 (19.3)	44	55 (19.6)		8.9[0.63,17.17]
					Favours control -20 -10 0 10 20 Favours CBT	

Analysis 9.8. Comparison 9 Cognitive-behavioural therapy versus control, Outcome 8 Depression.

Study or subgroup	CBT		Control		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Duarte 2009	41	14.1 (8.7)	44	21.2 (9.1)		46.2%	-0.79[-1.23,-0.35]
Hou 2014	51	2.3 (0.8)	47	2.8 (0.5)		53.8%	-0.74[-1.15,-0.33]
Total ***	92		91			100%	-0.76[-1.06,-0.46]
Heterogeneity: Tau ² =0; Chi ² =0.03, df=1(P=0.86); I ² =0%							
Test for overall effect: Z=4.96(P<0.0001)							
					Favours CBT -2 -1 0 1 2 Favours control		

Comparison 10. Cognitive-behavioural therapy versus education

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Depression	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6 Anxiety	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 10.1. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 1 Sleep quality.

Analysis 10.2. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 2 Sleep latency.

Analysis 10.3. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 3 Total sleep time.

Analysis 10.4. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 4 Sleep efficiency.

Analysis 10.5. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 5 Depression.

Analysis 10.6. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 6 Anxiety.

Analysis 10.7. Comparison 10 Cognitive-behavioural therapy versus education, Outcome 7 Fatigue.

Study or subgroup	CBT		Education		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Chen 2011a	37	3.9 (1.5)	35	4.2 (1.8)		-0.3 [-1.07, 0.47]
					Favours CBT -2 -1 0 1 2 Favours education	

Comparison 11. Education versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	3	220	Std. Mean Difference (IV, Random, 95% CI)	-0.50 [-0.77, -0.23]
2 Sleep latency	2	135	Mean Difference (IV, Random, 95% CI)	-0.50 [-0.76, -0.23]
3 Total sleep time	2	135	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.59, 0.05]
4 Sleep efficiency	2	135	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.66, 0.06]
5 Sleep disturbance	2	135	Mean Difference (IV, Random, 95% CI)	-0.38 [-0.52, -0.24]
6 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 11.1. Comparison 11 Education versus control, Outcome 1 Sleep quality.

Study or subgroup	Education		Control		Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Soleimani 2016	29	1 (1.1)	30	1.7 (2)		27.15%	-0.43 [-0.95, 0.08]
Saeedi 2014	38	1.7 (1)	38	2.5 (0.9)		33.34%	-0.76 [-1.22, -0.29]
Chow 2010	43	-45.2 (24.9)	42	-37.6 (19.1)		39.51%	-0.34 [-0.77, 0.09]
Total ***	110		110			100%	-0.5 [-0.77, -0.23]
Heterogeneity: Tau ² =0; Chi ² =1.79, df=2(P=0.41); I ² =0%							
Test for overall effect: Z=3.67(P=0)							
					Favours education -2 -1 0 1 2 Favours control		

Analysis 11.2. Comparison 11 Education versus control, Outcome 2 Sleep latency.

Study or subgroup	Education		Control		Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Soleimani 2016	29	1.1 (0.9)	30	1.5 (0.8)		35.56%	-0.4 [-0.84, 0.04]
					Favours education -2 -1 0 1 2 Favours control

Analysis 11.3. Comparison 11 Education versus control, Outcome 3 Total sleep time.

Analysis 11.4. Comparison 11 Education versus control, Outcome 4 Sleep efficiency.

Analysis 11.5. Comparison 11 Education versus control, Outcome 5 Sleep disturbance.

Analysis 11.6. Comparison 11 Education versus control, Outcome 6 Pain.

Study or subgroup	Education		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Chow 2010	43	61.5 (32.9)	42	48.2 (28.5)		13.3[0.22,26.38]

Analysis 11.7. Comparison 11 Education versus control, Outcome 7 Fatigue.

Study or subgroup	Education		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Chow 2010	43	45.1 (20.2)	42	39.4 (19.5)		5.7[-2.74,14.14]

Analysis 11.8. Comparison 11 Education versus control, Outcome 8 Quality of life.

Study or subgroup	Education		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Chow 2010	43	47 (15.1)	42	41.9 (17)		5.1[-1.74,11.94]

Comparison 12. Benzodiazepine versus benzodiazepine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 12.1. Comparison 12 Benzodiazepine versus benzodiazepine, Outcome 1 Sleep quality.

Study or subgroup	BDZ 1		BDZ 2		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Dashti-Khavidaki 2011	12	10.3 (3.1)	11	8.3 (2.4)		2.06[-0.19,4.31]

Comparison 13. Dopaminergic agonist versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 13.1. Comparison 13 Dopaminergic agonist versus control, Outcome 1 Sleep quality.

Study or subgroup	N	DA Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Giannaki 2013	7	5.9 (3.7)	7	8.9 (4.1)		-3[-7.09,1.09]
					Favours DA	Favours control

Analysis 13.2. Comparison 13 Dopaminergic agonist versus control, Outcome 2 Sleep latency.

Study or subgroup	N	DA Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Dauvilliers 2016	15	-18.9 (83.9)	10	12.8 (34.5)		-31.68[-79.19,15.83]
					Favours DA	Favours control

Analysis 13.3. Comparison 13 Dopaminergic agonist versus control, Outcome 3 Total sleep time.

Study or subgroup	N	DA Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Dauvilliers 2016	15	39.3 (58.8)	10	-13 (48.7)		52.35[10.94,93.76]
					Favours control	Favours DA

Analysis 13.4. Comparison 13 Dopaminergic agonist versus control, Outcome 4 Sleep efficiency.

Study or subgroup	N	DA Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Dauvilliers 2016	15	7.7 (12.3)	10	-2.8 (10.4)		10.52[1.57,19.47]
					Favours control	Favours DA

Analysis 13.5. Comparison 13 Dopaminergic agonist versus control, Outcome 5 Quality of life.

Study or subgroup	N	Da Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Dauvilliers 2016	15	-10.7 (10.9)	10	-10.2 (10.8)		-0.5[-9.17,8.17]
					Favours control	Favours DA

Comparison 14. Telephone support versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 14.1. Comparison 14 Telephone support versus control, Outcome 1 Sleep quality.

Study or subgroup	Telephone		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Li 2014b	69	61.1 (20.6)	66	54.3 (18.1)		6.8[0.27,13.33]

Analysis 14.2. Comparison 14 Telephone support versus control, Outcome 2 Pain.

Study or subgroup	Telephone		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Li 2014b	69	64.2 (18.2)	66	59.7 (18.9)		4.5[-1.76,10.76]

Analysis 14.3. Comparison 14 Telephone support versus control, Outcome 3 Fatigue.

Study or subgroup	Telephone		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Li 2014b	69	48.4 (17.7)	66	43.3 (18.9)		5.1[-1.08,11.28]

Analysis 14.4. Comparison 14 Telephone support versus control, Outcome 4 Quality of life.

Study or subgroup	Telephone		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Li 2014b	69	49.2 (19.4)	66	47.2 (19.2)		2[-4.51,8.51]

Comparison 15. Melatonin versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Death (all causes)	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected

Analysis 15.1. Comparison 15 Melatonin versus control, Outcome 1 Sleep quality.

Study or subgroup	Melatonin		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Natarajan 2003	2	15.1 (0.8)	6	13.1 (0.7)		1.99[0.71,3.27]

Favours melatonin -4 -2 0 2 4 Favours control

Analysis 15.2. Comparison 15 Melatonin versus control, Outcome 2 Death (all causes).

Study or subgroup	Melatonin		Control		Risk Ratio IV, Random, 95% CI	Risk Ratio IV, Random, 95% CI
	n/N		n/N			
MELODY 2013	3/33		3/34			1.03[0.22,4.74]

Favours melatonin 0.1 0.2 0.5 1 2 5 10 Favours control

Comparison 16. Reflexology versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	2	132	Mean Difference (IV, Random, 95% CI)	-5.90 [-6.56, -5.23]
2 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 16.1. Comparison 16 Reflexology versus control, Outcome 1 Sleep quality.

Study or subgroup	Reflexology		Control		Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Farrokian 2016	31	9.2 (1.9)	31	14.9 (1.5)		62.32%	-5.68[-6.52,-4.84]
Unal 2016	35	5.5 (2.2)	35	11.8 (2.5)		37.68%	-6.26[-7.34,-5.18]
Total ***	66		66			100%	-5.9[-6.56,-5.23]

Heterogeneity: $\tau^2=0$; $\chi^2=0.68$, $df=1$ ($P=0.41$); $I^2=0\%$
Test for overall effect: $Z=17.36$ ($P<0.0001$)

Favours reflexology -10 -5 0 5 10 Favours control

Analysis 16.2. Comparison 16 Reflexology versus control, Outcome 2 Fatigue.

Study or subgroup	Reflexology		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Unal 2016	35	58.5 (18.8)	35	80.7 (21.1)		-22.23[-31.6,-12.86]
					Favours reflexology	Favours control

Comparison 17. Reflexology versus massage

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Fatigue	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 17.1. Comparison 17 Reflexology versus massage, Outcome 1 Sleep quality.

Study or subgroup	Reflexology		Massage		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Unal 2016	35	5.5 (2.2)	35	8.3 (2.4)		-2.8[-3.87,-1.73]
					Favours reflexology	Favours massage

Analysis 17.2. Comparison 17 Reflexology versus massage, Outcome 2 Fatigue.

Study or subgroup	Reflexology		Massage		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Unal 2016	35	58.5 (18.8)	35	70.8 (16.1)		-12.26[-20.45,-4.07]
					Favours reflexology	Favours massage

Comparison 18. Light therapy versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Depression	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 18.1. Comparison 18 Light therapy versus control, Outcome 1 Sleep latency.

Study or subgroup	N	Light Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Burkhalter 2015	14	49.2 (0.8)	14	34.6 (0.9)		14.54[13.94,15.14]

Analysis 18.2. Comparison 18 Light therapy versus control, Outcome 2 Sleep efficiency.

Study or subgroup	N	Light Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Burkhalter 2015	14	74.7 (12.4)	14	71.8 (17.5)		2.9[-8.32,14.12]

Analysis 18.3. Comparison 18 Light therapy versus control, Outcome 3 Depression.

Study or subgroup	N	Light Mean(SD)	N	Control Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Burkhalter 2015	12	4.1 (3.1)	12	4.8 (5.9)		-0.67[-4.43,3.09]

Comparison 19. Gabapentin versus dopaminergic agonist

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Cardiovascular death	1		Risk Ratio (IV, Random, 95% CI)	Totals not selected

Analysis 19.1. Comparison 19 Gabapentin versus dopaminergic agonist, Outcome 1 Sleep latency.

Study or subgroup	N	Gabapentin Mean(SD)	N	DA Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Razazian 2015	42	20.5 (19.4)	40	45.3 (38.3)		-24.8[-38.04,-11.56]

Analysis 19.2. Comparison 19 Gabapentin versus dopaminergic agonist, Outcome 2 Total sleep time.

Study or subgroup	Gabapentin		DA		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Razazian 2015	42	6.4 (1)	40	6.1 (1.5)		0.3[-0.25,0.85]
					Favours gabapentin	Favours DA

Analysis 19.3. Comparison 19 Gabapentin versus dopaminergic agonist, Outcome 3 Sleep disturbance.

Study or subgroup	Gabapentin		DA		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Razazian 2015	42	4 (3.3)	40	7.3 (3.8)		-3.3[-4.84,-1.76]
					Favours gabapentin	Favours DA

Analysis 19.4. Comparison 19 Gabapentin versus dopaminergic agonist, Outcome 4 Cardiovascular death.

Study or subgroup	Gabapentin		DA		Risk Ratio	Risk Ratio
	n/N		n/N		IV, Random, 95% CI	IV, Random, 95% CI
Razazian 2015	0/44		1/43			0.33[0.01,7.79]
					Favours gabapentin	Favours DA

Comparison 20. CAPD versus APD

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 20.1. Comparison 20 CAPD versus APD, Outcome 1 Sleep quality.

Study or subgroup	CAPD		APD		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Bro 1999	17	1.8 (4.7)	17	2.3 (3.1)		-0.5[-3.18,2.18]
					Favours CAPD	Favours APD

Comparison 21. Music versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 21.1. Comparison 21 Music versus control, Outcome 1 Sleep quality.

Study or subgroup	Music		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Momennasab 2018	34	8.2 (2.7)	35	14.2 (4.7)		-6.02[-7.82,-4.22]

Analysis 21.2. Comparison 21 Music versus control, Outcome 2 Sleep latency.

Study or subgroup	Music		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Momennasab 2018	34	1.2 (0.4)	35	1.6 (0.7)		-0.4[-0.66,-0.14]

Analysis 21.3. Comparison 21 Music versus control, Outcome 3 Total sleep time.

Study or subgroup	Music		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Momennasab 2018	34	1.2 (0.4)	35	1.8 (1.1)		-0.66[-1.04,-0.28]

Analysis 21.4. Comparison 21 Music versus control, Outcome 4 Sleep disturbance.

Study or subgroup	Music		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI	Random, 95% CI
Momennasab 2018	34	1.2 (0.4)	35	2.4 (0.8)		-1.26[-1.55,-0.97]

Comparison 22. Music versus music

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 22.1. Comparison 22 Music versus music, Outcome 1 Sleep quality.

Study or subgroup	HD		Bedtime		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Momennasab 2018	34	8.2 (2.7)	33	6 (3.5)		2.2[0.72,3.68]
					Favours HD	Favours bedtime

Analysis 22.2. Comparison 22 Music versus music, Outcome 2 Sleep latency.

Study or subgroup	HD		Bedtime		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Momennasab 2018	34	1.2 (0.4)	33	0.9 (0.5)		0.31[0.1,0.52]
					Favours HD	Favours bedtime

Analysis 22.3. Comparison 22 Music versus music, Outcome 3 Total sleep time.

Study or subgroup	HD		Bedtime		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Momennasab 2018	34	1.2 (0.4)	33	0.9 (0.5)		0.31[0.1,0.52]
					Favours HD	Favours bedtime

Analysis 22.4. Comparison 22 Music versus music, Outcome 4 Sleep disturbance.

Study or subgroup	Music 1		Music 2		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Momennasab 2018	34	1.2 (0.4)	33	0.9 (0.5)		0.31[0.1,0.52]
					Favours music 1	Favours music 2

Comparison 23. Aromatherapy versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Sleep latency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
3 Total sleep time	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4 Sleep efficiency	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Sleep disturbance	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 23.1. Comparison 23 Aromatherapy versus control, Outcome 1 Sleep quality.

Study or subgroup	Aromatherapy		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Muz 2017	27	4.7 (3.7)	35	15.6 (1.8)		-10.96[-12.47,-9.45]
Favours aromatherapy						Favours control

Analysis 23.2. Comparison 23 Aromatherapy versus control, Outcome 2 Sleep latency.

Study or subgroup	Aromatherapy		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Muz 2017	27	0.8 (1)	35	2.9 (0.2)		-2.13[-2.51,-1.75]
Favours aromatherapy						Favours control

Analysis 23.3. Comparison 23 Aromatherapy versus control, Outcome 3 Total sleep time.

Study or subgroup	Aromatherapy		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Muz 2017	27	0.2 (0.4)	35	2.7 (0.5)		-2.52[-2.75,-2.29]
Favours aromatherapy						Favours control

Analysis 23.4. Comparison 23 Aromatherapy versus control, Outcome 4 Sleep efficiency.

Study or subgroup	Aromatherapy		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Muz 2017	27	0.6 (0.6)	35	2.7 (0.8)		-2.06[-2.41,-1.71]
Favours aromatherapy						Favours control

Analysis 23.5. Comparison 23 Aromatherapy versus control, Outcome 5 Sleep disturbance.

Study or subgroup	Aromatherapy		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Muz 2017	27	1.1 (0.5)	35	2 (0.4)		-0.91[-1.14,-0.68]
Favours aromatherapy						Favours control

Comparison 24. Massage versus control

Outcome or sub-group title	No. of studies	No. of participants	Statistical method	Effect size
1 Sleep quality	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
2 Pain	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Quality of life	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 24.1. Comparison 24 Massage versus control, Outcome 1 Sleep quality.

Study or subgroup	Massage		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Sun 2017	40	10.6 (3.1)	40	12.9 (3.7)		-2.29[-3.78,-0.8]
					Favours control	Favours massage

Analysis 24.2. Comparison 24 Massage versus control, Outcome 2 Pain.

Study or subgroup	Massage		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Sun 2017	40	74.8 (9.5)	40	57.5 (9.3)		17.37[13.25,21.49]
					Favours control	Favours massage

Analysis 24.3. Comparison 24 Massage versus control, Outcome 3 Quality of life.

Study or subgroup	Massage		Control		Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
	N	Mean(SD)	N	Mean(SD)		
Sun 2017	40	74.4 (9.5)	40	61.3 (10.3)		13.18[8.85,17.51]
					Favours control	Favours massage

ADDITIONAL TABLES

Table 1. TIDieR framework of intervention descriptions for included studies

Study ID	Intervention	Control	Materials	Sleep intervention				Adherence	
			Why	What	How	Who provided, where and when	Tailoring/modification	How well: Planned	How well: Actual
Afshar 2011	Exercise	Control	To determine the effects of aerobic training on sleep quality, serum leptin, and inflammatory status	People in the intervention group cycled during the 1st two hours of each dialysis session in a recumbent position	Regular aerobic training which consisted of 5 minutes of warm-up and 10 to 30 minutes of stationary cycling	3 sessions per week, for 3 weeks in the clinic	Patients were asked to cycle at an intensity of 12 to 15 of 20 at the rate of perceived exertion of Borg scale, of an individual's maximal capacity	Blood pressure and heart rate of the participants were monitored each 5 minutes, during the exercise	The number of patients who completed the study interventions was not reported
Amini 2016	Relaxation	Control 1: Exercise Control 2: Control	Investigate aerobic exercise and progressive muscle relaxation on anxiety, fatigue, and sleep disorders	Explained to patients while undergoing HD. Recording about muscle relaxation shown	Recording shown to patients. Patients were corrected on technique. Patients then did exercises at home using recording	There was the supervision of a researcher. The intervention was performed daily in the clinic or at home, for 60 days for 8 weeks	-	Researcher followed up every two weeks to encourage exercise program or exclude patients who did not adhere	The number of patients who completed the study interventions was not reported
Aoike 2018	Exercise	Control 1: Exercise Control 2: Control	To test if home-based aerobic exercise program provides similar benefits as a centre-based program	The patients included in the exercise groups were submitted to a moderate aer-	The home-based performed exercise at home, the others at an exercise centre	A physiologist provided the intervention. Exercises were performed in the centre or at home for 30 min for 8 weeks	The exercise training intensity was prescribed according to	-	40 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

				obic exercise program			each pa- tient's ventilatory threshold		
Arab 2016	Acupres- sure	Control 1: Sham Control 2: Control	To investigate the effect of acupres- sure on the sleep and quality of life	The interven- tion group re- ceived acupres- sure in the bi- lateral Shen- men points. The others received either sham acupressure or no treatment	Acupressure was applied using a circu- lar movement. The sham was performed on points at 0.5 cm from the true points	A trained researcher pro- vided the intervention in the clinic for 8 min- utes, 3 times a week for 8 weeks	-	To estab- lish con- sistency of perfor- mance, the amount of pres- sure ap- plied was measured using a scale; 30 measure- ments were recorded	93 patients completed the study
Bro 1999	CAPD	APD	To test if there should be a differ- ence between the effects of APD com- pared to CAPD on quality of life and clinical outcomes	17 patients were allocated to APD treatment and 17 patients to CAPD treat- ment	CAPD and APD devices	Skilled PD nurses pro- vided the intervention in the clinic. APD and CAPD were delivered for 26.4 weeks	One pa- tient on CAPD needed an additional exchange to achieve the target dialysis dose	During the study, patients were seen at month- ly con- trols in the CAPD unit. Adequacy tests were performed every 3 months	25 patients completed the study
Burkhalter 2015	Light	Control	To evaluate the fea- sibility of the inter- vention and to as- sess its efficacy for improving sleep	To receive the appropriate dosage, at a time deter- mined by indi- vidual chrono- type	The patient sited 30–50 cm from the light box lamp, which pro- duced light at eye level	The principal investiga- tor instructed partici- pants on the light box's use to perform at home, 30 min daily for 3 weeks	We al- lowed for a 1.5 h de- viation from the optimum starting time	-	28 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

Cham-pagne 2008	HDF	HD	To compare sleep apnoea severity in HD and HDF	Polysomnography was used to assess the efficacy of the intervention	After the prescribed period, these treatments were inverted	Thrice-weekly schedules for 13.2 weeks (first phase) in the clinic	-	-	At the end of phases II, 6 patients completed the study
Chen 2008a	CBT	Education	To investigate the effectiveness of intervention in patients with insomnia and to investigated the association with cytokine levels	To assist participants in identifying, challenging, and changing misconceptions about sleep	Participants were instructed to relieve muscular tension and perform rhythmic breathing	Research staff (psychiatrist, nephrologist, nurse) provided the intervention at home, 1 hour weekly for 4 weeks	-	-	24 patients completed the study
Chen 2011a	CBT	Education	To validate the efficacy of intervention for sleep disorders and fatigue, depression and anxiety	To assist participants in identifying, challenging, and changing the misconceptions about sleep	The intervention included a psychiatrist-oriented, video assisted program and group discussion and education	2 psychiatrists and a psychologist provided the intervention in the clinic, 30-min tri-weekly for 6 weeks	-	-	All patients who received the treatment completed the study
Cho 2018	Exercise (aerobic exercise)	Control 1: Exercise (resistance exercise) Control 2: Exercise (combination exercise) Control 3: Control	To investigate the effect of intra dialytic exercise on daily physical activity and sleep quality, measured by an accelerometer	To perform recumbent stationary cycling or exercises, involving muscles of both the lower and upper body	A stationary bike or Coloured elastic resistive bands and soft weights were used. All the exercises were performed in a supine or a sitting position	A researcher provided the intervention in the clinic: 5-min warm-up and maximum of 30 min for 12 weeks	According to patients' performance, training loads were adjusted	Participants were encouraged to perform each exercise to optimise movement speed and muscle power	46 patients completed the study
Chow 2010	Education	Control	To examine the effectiveness of a	Patients received a comprehensive dis-	All calls focused on health-relat-	A nurse provided the training program of 24 hours in the clin-	Patients could referral to	Realistic action plan and	85 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

			nurse-led case management programme in improving the quality of life	charge planning protocol and a standardized telephone follow-up regimen	ed behaviours and were audio taped for documentation	ic. A nurse contacted patients by telephone weekly for 6 weeks	the community nurse, the renal team or to the emergency department. The duration of follow-up calls varied, depending on patients' specific	participation of family members in discussing to assess the patient's needs	
Dai 2007a	Acupressure	Estazolam	To study the effect of lower extremity point massage for improving quality of sleep	1 mg of estazolam tablets orally half an hour before sleep or acupressure	-	Intervention was performed in the clinic or at home once a day, 20 to 30 seconds each time for 4 weeks	-	-	The number of patients who completed the study was not reported
Dashti-Khavidaki 2011	Benzodiazepine (zolpidem)	Benzodiazepine (clonazepam)	To compare zolpidem with clonazepam in terms of on sleep quality	5 to 10 mg of zolpidem or 1 mg of clonazepam, orally	After the prescribed period these treatments were inverted	Daily for 2 weeks (first phase) at home	-	-	All patients completed the first phase of treatment
Dauvilliers 2016	Dopaminergic agonist (rotigotine)	Control	To investigate the efficacy on periodic legs movement, sleep, RLS and quality of life	Polysomnography was performed on the 2 consecutive nights	-	Trained personnel provided the intervention that was performed at home (1 to 3 mg of rotigotine) for 6 weeks	-	-	25 patients completed the study
Duarte 2009	CBT	Control	To assess the effectiveness of an intervention in patients with a diagnosis of major depression	The patients attended sessions when they were off HD	Educating on kidney disease, dialysis, depression and the therapeutic cognitive model. All sessions	2 psychologists provided the intervention in the clinic: 12 weekly sessions for 13.2 weeks	Individualized psychotherapy session for providing guidelines	-	74 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

					involved home-work		about the treatment and emotional support		
Edalat-Nejad 2013	Melatonin	Control	Melatonin 3 mg	To assess the effect of the intervention on sleep quality	After the prescribed period these treatments were inverted	Melatonin 3 mg orally per day for 6 weeks (first phase) at home	-	Compliance was confirmed by pill count	At the end of phases II, 68 patients completed the study
EMSCAP 2009	Melatonin	Control	To investigate the effects of exogenous melatonin on sleep-wake rhythm	Actigraphy was used to assess the efficacy of the intervention	After the prescribed period these treatments were inverted	3 mg of melatonin orally per day for 6 weeks (first phase)	-	-	At the end of phases II, 20 patients completed the study
Farrokian 2016	Reflexology	Control	To determine the effect of reflexology massage on sleep quality	Massage will be done by nurse of the same sex of the patient	Slow and regular rhythm massage	Trained nurses provided the intervention in the clinic: 12 sessions of 30 minutes, 3 day a week for 4 weeks	The depth of the massage depended on the patient's tolerance	-	All patients completed the study
Ghavami 2016	Massage	Control	To determine the effectiveness of hot stone massage therapy on sleep quality level	Massage compared with routine health care	-	12 sessions	-	-	The number of patients who completed the study was not reported
Giannaki 2013	Exercise	Control 1: Dopaminergic agonist (ropinirole) Control 2: Control	To compare the changes across groups on RLS symptoms to evaluate quality of life	Cycling compared with ropinirole 0.25 mg orally	Exercise consisted of cycling in a recumbent cycle	A specialized neurologist provided exercises in the clinic 3 times per week, ropinirole was delivered 0.25 mg daily for 26.4 weeks	The exercise intensity was readjusted on a monthly base	-	29 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

Giannaki 2013a	Exercise	Control	To investigate the intervention that reduce RLS severity	The exercise session in both groups included intra-dialytic cycling for 45 min at 50 rpm	The exercise included aerobic exercise performed in a recumbent cycle	A neurologist provided the intervention in the clinic for 45 min, 3 times per week for 26.4 weeks	The exercise intensity was readjusted every 4 weeks to account for the patients' improvement	-	-	All patients completed the study
Hanna 2013	Light	Control	To evaluate the efficacy of the intervention in people with sleep-wake disturbance and depressive symptomatology	Morning light was scheduled according to chronotype daily. The rest-activity cycle was monitored with a wrist actimeter	-	30 minutes daily for 3 weeks	-	-	-	The number of patients who completed the study was not reported
Hou 2014	CBT	Control	To verify the effects of sleep-related behaviour modification in combination with progressive muscle relaxation on insomnia	During the interval of training, they did progressive muscle relaxation with a magnetic tape of "self-relaxation"	The physician did the progressive muscle relaxation for the patients and guided the patients	A physician provided the intervention in the clinic for 20 minutes every 2 days, 3 times week. Relaxation was performed daily at home for 30 min for 13.2 weeks	-	-	-	98 patients completed the study
IRC-T201302121244041	Collaborative care model	Control	To determine the effect of collaborative care model on the fatigue	Care model included motivation, preparation, and evaluation	Sessions about the illness and the proper behaviour to deal with	Researchers, doctors and nurses provide the intervention in the clinic, 2 hours per day for 12 weeks	Half-hour meetings were held to deal with specific needed	-	-	The number of patients who completed the study was not reported
IRC-T2015051122218N1	Chamomile	Control	To determine the effect of chamomile	The intervention group will take syrup of chamomile	-	Chamomile 400 mg/day orally for 4 weeks at home	-	-	-	The number of patients who completed the

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

									study was not reported
IRC- T201406171728743	Acupres- sure	Control 1: Sham Control 2: Control	To determine the relationship between anxiety and sleep quality	In intervention group will receive acupres- sure in true acu- point	Acupressure will be done using pressure with the thumb	2 trained practitioners provided the interven- tion in the clinic, 3 times a week for 4 weeks	-	-	The number of patients who completed the study was not reported
Jean 1995	Acetate dialysis	Bicarbon- ate dialy- sis	To assess the influ- ence of buffer, ac- etate or bicarbon- ate, on sleep and ventilation	Polysomnogra- phy was used to assess the effi- cacy of the in- tervention	After the pre- scribed peri- od these treat- ments were in- verted.	The medical team pro- vided the intervention in the clinic	-	-	At the end of phases II, all patients completed the study
Kolner 1989	Benzodi- apine (tri- azolam)	Control	To test the efficacy of Triazolam in HD patients with sleep disorder	-	-	Daily for 1 week at home	-	-	The number of patients who completed the study was not reported
Li 2014b	Telephone support	Control	To develop an origi- nal telephone sup- port model for improving quality of life	Patients re- ceived a stan- dardized nurse- led telephone sup- port	Sessions to op- timise health outcomes. After discharge start- ed telephone call	A nurse provided the in- tervention in the clinic. Telephone- call contact with pa- tients weekly for 12 weeks	The pa- tient's needs were as- sessed with an in- dividual- ized pro- gram	Each tele- phone call was guided by the pro- tocol and were au- dio taped to ensure consis- ten- cy	135 patients had com- pleted the follow-up question- naires
MELODY 2013	Melatonin	Control	To investigate the effects of drug on sleep and quality of life in patients with sleep problems	Actigraphy was used to assess the efficacy of the intervention	The actiwatch was placed on the wrist of the arm without fis- tula	Physicians provided the intervention in the clinic or at home: 3 mg of melatonin daily for 52.4 weeks	-	-	42 patients completed the study
Micozka-dioglu 2004	Levodopa	Gabapentin	To find the effica- cy of gabapentin compared with lev-	125 mg/day of levodopa 2 hours before sleep. 200 mg of	After the pre- scribed peri- od these treat-	4-week management for each drug (first phase) in the clinic or at home	-	-	14 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

			odopa in the treatment of RLS	gabapentin after HD	ments were inverted				
Momen-nasab 2018	Music	Control 1: Music Control 2: Control	To compare the effectiveness of music therapy during HD and at bedtime on sleep quality	The music used was a 6-pieces piano improvisation in new age (relaxation) genre	Participants were exposed to music via an MP3-player using an occlusive headphone or prerecorded music compact disc	Researchers provided the intervention that was performed in the clinic or at home for 4 weeks	The patient could stop or play the music whenever he/she liked or listen to it again	Patients were assessed about fulfilling the intervention by weekly telephone follow-up	102 patients completed the study
Muz 2017	Aromatherapy	Control	To determine the effect of aromatherapy on the sleep quality and fatigue	Aromatherapy group (sweet orange oil and lavender oil) via inhalation	Lavender and sweet orange oils were dropped to a gauze bandage. Patients had to smell the aromatic mixture for 2 min	Researchers provided the intervention that was performed at home for one month for 2 min before sleeping	-	Patients were called to report any problems. Answers were recorded, and support was provided	62 patients completed the study
Nasiri 2011	Acupressure	Control	To evaluate the effectiveness of acupressure on quality of sleep	4 points were pressured: this pressure was continuous with finger circularly for 1-2 second	-	Researcher and his co-operator provided the intervention in the clinic, 12 times for 5 min, 3 days per week for 4 weeks	-	The force of pressure (consistency / reliability) were confirmed by using a scale	The number of patients who completed the study was not reported
Natarajan 2003	Melatonin	Control	To assess the effect of melatonin administration on sleep quality	Actigraphy was used to assess the efficacy of the intervention		Melatonin 3 mg orally per day, for 4 weeks (first phase) at home	-	-	At the end the first phase, all patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

NCT02825589	Bioelectrical impedance	Control	To assess the effect of bioelectrical impedance analysis on sleep	-	-	13.2 weeks	-	-	The number of patients who completed the study was not reported
Parker 2007	Dialysate 37°	Dialysate 35°	To test if cool dialysate would improve blood flow, heat dissipation and sleep	Subjects received HD in warm condition (37°C) or cool condition (35°C)	After the prescribed period these treatments were inverted	Trained nurses and nephrology co-investigator provided the intervention in the clinic	-	The personnel ensured the integrity and proper functioning of the equipment	The number of patients who completed the study was not reported
Pellecchia 2004	Levodopa	Ropinirole	To determine the efficacy and adverse event profile of ropinirole as compared with levodopa	Levodopa dosage was 100 to 200 mg/d and ropinirole dosage was 0.25 to 2 mg/d	After the prescribed period these treatments were inverted	Medications were performed orally for 6 weeks (first phase) in the clinic or at home	Doses could be doubled according to the investigators' and patients' opinions	-	10 patients completed the study
Pellizzaro 2013	Respiratory muscle training	Control 1: Peripheral muscle training Control 2: Control	To assess the effects of interventions on functional parameters, inflammatory state, and quality of life	Spirometry was used to assess the efficacy of the intervention	Patients performed three sets of 15 inspirations and rested for 60 seconds	30 training sessions for 10 weeks in the clinic	The exercise load was changed throughout the training according to 50% of PImax	-	39 patients completed the study
Pieta 1998	Dopaminergic agonist (pergolide)	Control	To test the effect of pergolide on leg movements and sleep disturbance	Polysomnography was used to assess the efficacy of the intervention	After the prescribed period these treatments were inverted	Pergolide from 0.05 to 0.25 for 1.5 weeks (first phase) at home	-	-	At the end of phases II, 8 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

Pooranfar 2014	Exercise	Control	To assess the effect of a period of exercise on sleep quality and quantity	Participants were acquainted with cycling method on bicycle ergometer, treadmill and other exercises	The sessions were divided into pre-warming, main step (aerobic and resistive exercises using ergometer bicycle) and rest	A researcher provided the intervention: 3 days a week for 10 weeks in 60–90 minute exercise sessions	The exercise program was designed in terms of type, intensity, and frequency according to physical status of the patients	-	The number of patients who completed the study was not reported
Rambod 2013	Relaxation	Control	To evaluate the effect of the intervention on the sleep quality	The intervention group listened to the audiotape of Benson's relaxation technique	The patients were instructed and were comfortably at rest in bed in a separate room	An expert provided the intervention that was performed twice a day for twenty minutes for 8 weeks, in the clinic or at home	-	A CD on relaxation technique and research's number was given to the patients. Weekly Were provided reinforcements	83 patients completed the study
Razazian 2015	Gabapentin	Dopaminergic agonist (levodopa/carbidopa)	To compare drugs in reducing symptoms and sleep problems	Gabapentin 200 mg orally compared to levodopa-c 110 mg orally	-	Gabapentin 200 mg (3 times weekly), levodopa-c 110 mg in a single dose for 4 weeks at home	-	-	83 patients completed the study
Reilly-Spong 2015	Relaxation	Control	To reduce symptoms and improve quality of life using a multi-modal telephone-adapted program	Intervention was a bookend program. Actigraphy was used to assess the efficacy of the intervention	Workshops and teleconferences that included discussions, homework and practice	Certified teachers and a psychologist provided the intervention at the University. Teleconferences were held from patients' home for 8 weeks	Teacher ensured that yoga poses could be modified for people with dis-	Teleconferences used standard guidelines and each group had	52 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

							abilities. Emails were also used to document any deviations from checklists	a unique password. Attendance was recorded	
Ren 2017a	Foot-bath	Control	To explore the intervention effect of herb foot-bath therapy to improve sleep quality and symptom distress	Herbs packed by gauze bag were put into a footbath with boiled water	Feet were put above the foot-bath in water vapour. Until the water temperature was cooled to 38-43°C, feet were put in water	A course of treatment was four weeks; the intervention time was 30-40 min before nightly bedtime every day at home	Once uncomfortable and problems occurred, patient should stop the intervention and reported symptoms	-	The number of patients who completed the study was not reported
Sabbatini 2003	Benzodiazepine (zaleplon)	Control	To test the effects of zaleplon on the sleep quality in patients affected by insomnia	5 to 10 mg of zaleplon	After the prescribed period these treatments were inverted	A nephrologist provided the intervention that was performed at home (5 to 10 mg of zaleplon) for 2 weeks (first phase)	-	-	At the end of phases II, 10 patients completed the study
Saeedi 2014	Education	Control	To investigate the effect of the intervention on the sleep quality for improving quality of life and their satisfaction	Patients in the intervention group participated in sessions on sleep hygiene training program	Direct teaching methods, combination of face-to-face methods, lectures and group discussions	A researcher provided the intervention: 6 weekly sessions of half-hour for 4 weeks	-	-	76 patients completed the study
Shariati 2012	Acupressure	Control	To investigate the effects of acupressure on sleep quality	Acupressure applied consistent pressure on the correct acupoints with small rotational	The intervention group received acupressure on hands and feet	The investigators provided the intervention in the clinic: 15 min, 3 times per week for 4 weeks	Three acupoints that could be used to enhance sleep were chosen for	The precision was confirmed if subjects felt sore, numb, heavy, dis-	40 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

							the sub- jects	tended, and/or warm	
SIESTA 2017	Acupres- sure	Sham	To investigate the effect and safety of acupressure on the sleep quality	-	All selected acupoints were stimulated bi- laterally	An accredited practition- er provided the inter- vention in the clinic (3 min, 3 times a week) for 4 weeks	The inten- sity was adjusted according to the patient's level of tolerance	-	41 patients completed the study
Silva 2017	Continu- ous Pos- itive Air- way Pres- sure	Compres- sion stock- ings	To evaluate the short-term im- pact of treatments on the severity of sleep apnoea	Polysomnogra- phy was used to assess the effi- cacy of the in- tervention	After the pre- scribed peri- od these treat- ments were in- verted	A technician provided the intervention in the clinic for 1 week (first phase)	The lowest pressure was initial- ly applied to all pa- tients and increased progres- sively as needed	-	At the end of phases II, 14 patients completed the study
Sklar 1998	Dialyz- er with cupro- phan mem- brane	Dialyzer with poly- methyl- methacry- late mem- brane	To evaluate the role for type of blood-membrane interaction in post- dialysis fatigue	Using two dif- ferent types of membranes and TNF-alfa as a marker of their biocom- patibility	After the pre- scribed peri- od these treat- ments were in- verted	The Medical team pro- vided the intervention in the clinic thrice weekly, for 1 week (first phase)	-	-	At the end of phases II, 16 patients completed the study
Solak 2012	Gabapentin	Pregabalin	To compare the ef- fects of drugs on sleep quality and depression	Electromyogra- phy was used to assess the effi- cacy of the in- tervention	After the pre- scribed peri- od these treat- ments were in- verted	A neurologist provid- ed the intervention that was performed in the clinic or at home (gabapentin 300 mg thrice weekly, prega- balin 75 mg daily), for 6 weeks (first phase)	-	-	At the end of phases II, 48 patients completed the study
Soleimani 2016	Education	Control	To improve sleep quality through face-to-face sleep health education	Sleep hygiene education was performed. in two sections	The materials and a face-to- face session were provided	Researcher provided the intervention. This proto- col was taught within an hour	-	The par- ticipants asked questions	57 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

								and the materials were as-sessed	
Soreide 1991	Branch-chain amino acid	Control	To assess the effect of the branch-chain amino acid on sleep apnoea	Polysomnography was used to assess the efficacy of the intervention	After the prescribed period these treatments were inverted	For 2 study nights (first phase)	-	-	At the end of phases II, all patients completed the study
Sun 2017	Massage	Control	To assess if stimulating gastric activity improves relax and sleep	Abdominal massage, patient's education and training exercise	Massage to improve below contractility	Nurses provided the intervention in the clinic or at home for 4 weeks	-	-	Data were reported for all patients
Tol 2010	Gabapentin	Control	To determine changes on pruritus, quality of life, depression and sleep quality	Gabapentin 300 mg compared with placebo	After the prescribed period these treatments were inverted	Gabapentin 300 mg orally for 8 weeks (first phase) in the clinic or at home	-	-	At the end of phases II, all patients completed the study
Trenkwalder 1995	L-dopa + benserazide	Control	To assess the effects of L-dopa on sleep quality in restless leg syndrome	Polysomnography was used to assess the efficacy of the intervention	After the prescribed period these treatments were inverted	L-dopa + benserazide (200mg + 50mg) orally for 4 weeks (first phase) at home	-	Patients were monitored by phone calls	At the end of phases II, 28 patients completed the study
Tsai 2015	Relaxation	Control	To examine the efficacy of a nurse-led, in-centre breathing training program in reducing depressive symptoms and improving sleep quality and QoL	The dialysis nurse administered the audio device-guided breathing training in a quiet room	Patients listened to prerecorded instructions on breathing technique and then practiced the breathing exercise	A trained nurse provided the intervention in the clinic: 8 sessions, twice weekly for 4 weeks	Each patient received an individual coaching session	The nurse supervised each practice session and evaluated the breathing exercises to ensure that participants performed	57 patients completed the study

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

								them correctly	
Tsay 2003a	Acupres- sure	Control 1: Sham Control 2: Control	To test the effectiveness of acupres- sure on sleep quality and fatigue	The interven- tion group re- ceived acupres- sure. The placebo group received a mas- sage	Four acupoints were used to decrease fa- tigue	Researchers trained pro- vided the intervention: 15 min, 3 times a week for 4 weeks	-	The pre- cision of acupres- sure was confirmed if subjects felt sore, numb, heavy, dis- tended	98 patients completed the study
Tsay 2004	Acupres- sure	Control 1: Acu- pressure (Transcu- taneous Electrical Acupoint Stimula- tion) Control 2: Control	To test the effectiveness of the in- terventions on fa- tigue, sleep quality and depression	Acupressure compare with transcu- taneous electrical acupoint stimu- lation and control group	Four acupoints were used to decrease fa- tigue	Investigators provided the intervention: 15 min- utes of treatment 3 times a week for 4 weeks	-	The reli- ability of the pres- sure was assesses using a protocol that was standard- ized be- fore each treatment	106 patients completed the study
Turk 2010	Phospho- diesterase type 5 (sildenafil)	Phospho- diesterase type 5 (varde- nafil)	To compare the effects of drugs on depression and sleep quality in male with erec- tile dysfunction	Sildenafil 50 mg orally compared with Var- denafil 10 mg orally	After the pre- scribed peri- od these treat- ments were in- verted	The drugs were adminis- tered prior to sexual inter- course once per week for 4 weeks (first phase) at home	-	-	The number of patients who com- pleted the study was not reported
Unal 2016	Reflexology	Control 1: Massage Control 2: Control	To examine the effectiveness the in- terventions on sleep quality and fatigue	Foot reflexology compared with back mas- sage and control group	3 drops of baby oil were applied at room tem- perature to fa- cilitate the mas- sage	A researcher provided the intervention in the clinic: 30 minutes, 2 days a week for 4 weeks	-	-	105 patients completed the study
Walker 1996	L-dopa/ carbidopa	Control	To determine if lev- odopa/carbidopa decreased leg	L-dopa/car- bidopa 100 mg + 25 mg com-	After the pre- scribed peri- od these treat-	L-dopa/carbidopa 100 mg + 25 mg daily for 1	-	-	At the end of phases II, 5 patients

Table 1. TIDieR framework of intervention descriptions for included studies (Continued)

			movements and improved sleep	pared with placebo	ments were inverted	week (first phase) at home			completed the study
Williams 2017	Feedback group	Control	To determine if providing feedback on activity will have an impact on physical activity levels	All participants were equipped with the tracking bracelet. Intervention group received feedback	Patients in the feedback group received their activity and sleep data at each dialysis treatment	Research coordinators provided the intervention in the clinic or at home. All participants wore the tracking bracelet at all times for 5 weeks	-	-	29 patients completed the study
Yurtkuran 2007	Exercise	Control	To assess if yoga exercise can improve pain, fatigue, sleep disorder and biochemical markers	Yoga-based exercises were done in groups	Using some yogic postures and breathing exercises in the rehabilitation of dialysis patients	A yoga teacher provided the intervention. Exercises were performed in the clinic or at home, 30 min/day twice a week for 13.2 weeks	Some modifications to the program were done to increase patient compliance. The exercise has to be stopped if there is severe fatigue or pain	The exercises were explained to each patient until the physiotherapist was satisfied that all of them could do the exercises	37 patients completed the study
Zhao 2011	Acupressure	Control	To assess the efficacy of acupressure	4 auricular magnetic bead plaster points in fixed points	Take the side of each ear, 2 days later using another ear	Patient provided a self-pressure twice daily for 56 days, for 8 weeks (at home)	-	-	The number of patients who completed the study was not reported
Zou 2015	Acupressure	Control	To assess the feasibility and acceptability of acupressure treatment	Participants received acupressure on five active acupoints	Participants were instructed to press the beads until a slight soreness were felt	Trained nurse practitioner provided the intervention in the clinic for 8 weeks	If the plasters or beads detached, the patients came to hospital	Feasibility was assessed by the percentage of recruitment, retention,	58 patients completed the 8 weeks of treatment, 55 completed the 12 weeks of follow-up

atten-
dance and
adherence

Table 1. TIDieR framework of intervention descriptions for included studies *(Continued)*

APD - automated peritoneal dialysis; CAPD continuous ambulatory peritoneal dialysis; CBT - cognitive-behavioural therapy; HD - haemodialysis; HDF - haemodiafiltration; RLS - restless legs syndrome

Table 2. Studies reporting adverse events

Study ID	Treatment	Control	Adverse events in treatment arm	Adverse events in control arm	Comment
Bro 1999	CAPD	APD	Peritonitis (2); exit-site infection (1)	Peritonitis (1); exit-site infection (1); tunnel infection (1); leakage (1); hernia (1); over-hydration (2)	Quote: "No proper statistics could be applied due to the low numbers of patients and events."
Burkhalter 2015	Light	Control	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "No adverse reactions or symptom complaints were registered."
Chen 2011a	CBT	Education	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "No adverse events were reported during the intervention."
Cho 2018	Exercise (aerobic exercise)	Control 1: Exercise (resistance exercise) Control 2: Exercise (combination exercise) Control 3: Control	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "There were no reported adverse events, such as musculoskeletal injuries, hypoglycaemic episodes, cardiovascular events, or hospitalizations, as result of the intervention."
Dai 2007a	Acupressure	Estazolam	No participants experienced an adverse event	No participants experienced an adverse event	This study was not in English Quote from the "Acupuncture and related interventions for symptoms of chronic kidney disease (Review)": "Whether adverse events related to administration of estazolam such as somnolence, dizziness, hypokinesia and abnormal coordination occurred was not reported in the control group. Potential adverse events of estazolam might have been regarded as one of outcomes (complaints of adverse reaction), not as adverse events."
Dashti-Khavidaki 2011	Benzodiazepine (zolpidem)	Benzodiazepine (clonazepam)	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "In this study, zolpidem was not associated with undesirable sleep side effects such as daytime drowsiness, headache, or amnesia, at least during the short-term course of our study. [...] Meanwhile, the pa-

Table 2. Studies reporting adverse events (Continued)

					tients who received zolpidem did not complain of any particular side effects."
Dauvilliers 2016	Dopaminergic agonist (rotigotine)	Control	Application site reaction of mild pruritus(1); anxiety (1); foot fracture (1); abdominal pain (1); chest pain (1); dyspnoea (2); nausea (4); vomiting (3); diarrhoea (1); hypertension (2); headache (2)	Gastrointestinal infection (1); diarrhoea (2)	Quote: "AEs were reported by 12 (60%) patients receiving rotigotine and 5 (50%) patients receiving placebo (Table 4). Two patients had hypertension of moderate intensity while receiving rotigotine. Both patients were receiving medications for this condition prior to study start. One patient reported an application site reaction (MedDRA [Medical Dictionary for Regulatory Activities] high-level term "application and instillation site reactions") of mild pruritus while receiving 2 mg/24 h of rotigotine; no application site reactions were reported for placebo. Serious AEs were reported for 3 patients receiving rotigotine (foot fracture [n = 1]; anxiety, chest pain, and dyspnoea [n = 1]; and abdominal pain [n = 1]) and 1 patient receiving placebo (gastrointestinal infection)."
Duarte 2009	CBT	Control	Death (4)	Death (4)	Quote: "None of the patients in the intervention group were discontinued because of a CBT adverse effect. [...] Most of these losses were due to death, which is somewhat expected for ESRD patients after almost 1 year of follow-up." Comment: Figure 1 showed the number of deaths for each group
Giannaki 2013	Exercise	Control 1: Dopaminergic agonist (ropinirole) Control 2: Control	No participants experienced an adverse event	No participants experienced an adverse event in both control groups	Quote: "Finally, none of the patients reported any drug adverse reactions or augmentation phenomena from the three interventions."
Giannaki 2013a	Exercise	Control	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "All patients completed the exercise programme with no adverse effects."
MELODY 2013	Melatonin	Control	Death (3)	Death (3)	No adverse events were reported. However, Figure 2 showed the number of deaths for each group
Rambod 2013	Relaxation	Control	No participants experienced an adverse event	No participants experienced an adverse event	Quote: "In this study, no one reported any undesirable side effects or unintended harm sign, symptom, or disease related to participation in the study or the relaxation technique."
Razazian 2015	Gabapentin	Dopaminergic agonist (levodopa/carbidopa)	Somnolence and lethargy (2)	Allergy (1); death for myocardial infarction (1)	Quote: "During the course of the study period, two patients dropped out during the study secondary to somnolence and lethargy. These patients were administered gabapentin when the symptoms developed."

Table 2. Studies reporting adverse events (Continued)

					One patient died because of myocardial infarction."
Reilly-Spong 2015	Relaxation	Control	No participants experienced an adverse event	No participants experienced an adverse event	Quote from Gross 2017: "No intervention-related adverse events occurred."
SIESTA 2017	Acupressure	Sham	Fluid overload (1); ocular haemorrhage (1)	Necrotizing fasciitis (1); physical trauma (1); chest muscle pain (1); arteriovenous graft failure (1)	Quote: "There were six adverse events (6 participants) recorded during the study (Table 4), all of which were rated as serious adverse events (SAEs) as they led to hospitalisation. Two SAEs occurred in the intervention group (fluid overload and ocular haemorrhage) and the remaining four SAEs occurred in the control group (necrotizing fasciitis, physical trauma, chest muscle pain, and arteriovenous graft failure). No adverse event was considered by investigators to be causally related to the study intervention. No local skin reaction (e.g., bruise) from repeated acupressure was reported during the study."
Zou 2015	Acupressure	Control	Death (3)	No participants experienced an adverse event	Quote: "Three participants died during the follow-up period. No evidence supported their deaths were related to the AA intervention. No other adverse event was observed."

APD - automated peritoneal dialysis; CAPD - continuous ambulatory peritoneal dialysis; CBT - cognitive-behavioural therapy

APPENDICES

Appendix 1. Electronic search strategies

Database	Search terms
CENTRAL	<ol style="list-style-type: none"> MeSH descriptor: [Sleep] explode all trees MeSH descriptor: [Sleep Disorders] explode all trees MeSH descriptor: [Sleep Apnea Syndromes] explode all trees sleep*:ti,ab,kw (Word variations have been searched) {or #1-#4} MeSH descriptor: [Kidney Diseases] explode all trees MeSH descriptor: [Renal Replacement Therapy] explode all trees MeSH descriptor: [Renal Insufficiency] explode all trees MeSH descriptor: [Renal Insufficiency, Chronic] explode all trees dialysis:ti,ab,kw (Word variations have been searched) haemodialysis or haemodialysis:ti,ab,kw (Word variations have been searched) hemofiltration or haemofiltration:ti,ab,kw (Word variations have been searched) hemodiafiltration or haemodiafiltration:ti,ab,kw (Word variations have been searched) kidney disease* or renal disease* or kidney failure or renal failure:ti,ab,kw (Word variations have been searched) ESRF or ESKF or ESRD or ESKD:ti,ab,kw (Word variations have been searched)

(Continued)

- 16.CKF or CKD or CRF or CRD:ti,ab,kw (Word variations have been searched)
- 17.CAPD or CCPD or APD:ti,ab,kw (Word variations have been searched)
- 18.predialysis or pre-dialysis:ti,ab,kw (Word variations have been searched)
- 19.{or 6-18}
- 20.{and 5, 19}

MEDLINE

1. exp Sleep/
2. exp Sleep Disorders/
3. sleep\$.tw.
4. exp Sleep Apnea Syndromes/
5. or/1-4
6. Kidney Diseases/
7. exp Renal Replacement Therapy/
8. Renal Insufficiency/
9. exp Renal Insufficiency, Chronic/
- 10.dialysis.tw.
- 11.(haemodialysis or haemodialysis).tw.
- 12.(hemofiltration or haemofiltration).tw.
- 13.(hemodiafiltration or haemodiafiltration).tw.
- 14.(kidney disease* or renal disease* or kidney failure or renal failure).tw.
- 15.(ESRF or ESKF or ESRD or ESKD).tw.
- 16.(CKF or CKD or CRF or CRD).tw.
- 17.(CAPD or CCPD or APD).tw.
- 18.(predialysis or pre-dialysis).tw.
- 19.or/6-18
- 20.and/5,19

EMBASE

1. exp sleep disorder/
2. exp sleep/
3. sleep\$.tw.
4. or/1-3
5. exp renal replacement therapy/
6. kidney disease/
7. chronic kidney disease/
8. kidney failure/
9. chronic kidney failure/
- 10.mild renal impairment/
- 11.stage 1 kidney disease/
- 12.moderate renal impairment/
- 13.severe renal impairment/
- 14.end stage renal disease/
- 15.renal replacement therapy-dependent renal disease/
- 16.kidney transplantation/
- 17.(haemodialysis or haemodialysis).tw.
- 18.(hemofiltration or haemofiltration).tw.
- 19.(hemodiafiltration or haemodiafiltration).tw.
- 20.dialysis.tw.
- 21.(CAPD or CCPD or APD).tw.
- 22.(kidney disease* or renal disease* or kidney failure or renal failure).tw.
- 23.(CKF or CKD or CRF or CRD).tw.
- 24.(ESRF or ESKF or ESRD or ESKD).tw.
- 25.(predialysis or pre-dialysis).tw.

(Continued)

26.((kidney or renal) adj (transplant* or graft* or allograft*)).tw.

27.or/5-26

28.and/4,27

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	<p><i>Low risk of bias:</i> Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimisation (minimisation may be implemented without a random element, and this is considered to be equivalent to being random).</p> <p><i>High risk of bias:</i> Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention.</p> <p><i>Unclear:</i> Insufficient information about the sequence generation process to permit judgement.</p>
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	<p><i>Low risk of bias:</i> Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes).</p> <p><i>High risk of bias:</i> Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure.</p> <p><i>Unclear:</i> Randomisation stated but no information on method used is available.</p>
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	<p><i>Low risk of bias:</i> No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.</p> <p><i>High risk of bias:</i> No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors.	<p><i>Low risk of bias:</i> No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.</p> <p><i>High risk of bias:</i> No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.</p> <p><i>Unclear:</i> Insufficient information to permit judgement</p>
Incomplete outcome data	<p><i>Low risk of bias:</i> No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across</p>

(Continued)

Attrition bias due to amount, nature or handling of incomplete outcome data.

groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods.

High risk of bias: Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation.

Unclear: Insufficient information to permit judgement

Selective reporting

Reporting bias due to selective outcome reporting

Low risk of bias: The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).

High risk of bias: Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub-scales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear: Insufficient information to permit judgement

Other bias

Bias due to problems not covered elsewhere in the table

Low risk of bias: The study appears to be free of other sources of bias.

High risk of bias: Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem.

Unclear: Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
8 August 2019	Amended	Typographical error corrected in Plain Language Summary

HISTORY

Protocol first published: Issue 4, 2017

Review first published: Issue 5, 2019

Date	Event	Description
29 May 2019	Amended	PLS title amended

CONTRIBUTIONS OF AUTHORS

1. Coordinate the review: Suetonia Palmer
2. Draft the protocol: Suetonia Palmer
3. Study selection: Patrizia Natale, Marinella Ruospo, Suetonia Palmer
4. Extract data from studies: Patrizia Natale, Marinella Ruospo
5. Enter data into RevMan: Patrizia Natale, Marinella Ruospo
6. Carry out the analysis: Patrizia Natale, Marinella Ruospo, Suetonia Palmer
7. Interpret the analysis: All authors
8. Draft the final review: Patrizia Natale, Suetonia Palmer
9. Keep the review up to date: Suetonia Palmer

DECLARATIONS OF INTEREST

- Patrizia Natale: none known
- Marinella Ruospo: none known
- Valeria M Saglimbene: none known
- Suetonia C Palmer: none known
- Giovanni FM Strippoli: none known

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Adverse events have been moved from primary outcome (in the protocol) to secondary outcomes (in the review). After the release of the study protocol, we decided to consider as primary outcomes the outcomes related to the sleep management such as sleep quality, sleep onset latency, total sleep time, sleep interruption and sleep efficiency. Accordingly, we moved the adverse events from primary to secondary outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

*Renal Insufficiency, Chronic [complications]; Disease Progression; Kidney Failure, Chronic; Renal Dialysis; Sleep [*physiology]; Sleep Wake Disorders [*etiology] [*therapy]

MeSH check words

Humans