Laatst gewijzigd: 2017-03-01 Verantwoording: Richtlijnwerkgroep Palliatieve zorg bij eindstadium nierfalen Versie: 1.0 Type: Landelijke richtlijn

Vraag 3:
3a: Leidt het gebruik van conflict-/communicatietechnieken Bij patiënten met eindstadium nierfalen tot een betere kwaliteit van leven of meer voldoening in de besluitvorming/het beslisproces over het wel of niet doorgaan of het wel of niet starten met dialyse behandeling?

13B: WELKE COMMUNICATIE- EN CONFLICTTECHNIEKEN (CONFLICT MANAGEMENT) WORDEN DAN BESCHREVEN IN DE GEVONDEN STUDIES?

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Song 2009 [1]	· Design: RCT · Funding/CoI: National Institutes of Health; CoI not reported on · Setting: multiple centers, United States · Sample size: N=58 dyads · Duration: Jan 2007-Jun 2008; outcomes assessed at 1 week and 3 months post-intervention	· Eligibility criteria: self-identified African Americans with end-stage renal disease and their chosen surrogate decision makers, on dialysis for at least 3 months · A priori patient characteristics: intervention vs. control o Age, mean: 58 vs. 58 years o Male: 66% vs. 48% o Married/living with partner: 28% vs. 48%	SPIRIT (N=29) vs. Usual care (N=29) SPIRIT: The guiding theory of SPIRIT is the representational approach to patient education. The representational approach is based on Leventhal's common sense model and the conceptual change model. These representations serve as a cognitive framework in which new information is processed. The conceptual change model proposes that the likelihood of learning increases when an opportunity is given to reflect and comment on current ideas and their consequences, when the individual is dissatisfied with current ideas or recognizes the limitations of the ideas, and when alternative information is seen as beneficial. 1-	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Quality of patient-clinician (or interventionist) communication about end-of-life care (mean ±SD, higher scores indicate better communication, range: 4-12): Patient 1 week: 11.18 ± 1.12 vs. 8.83 ± 3.55 (p=0.03) Patient 3 months: 11.30 ± 1.41 vs. 7.52 ± 3.66 (p<0.01) Surrogate 1 week: 11.68 ± 0.55 vs. 6.79 ± 3.57 (p<0.01) Surrogate 3 months: 11.58 ± 0.72 vs. 10.22 ± 2.49 (p=0.03) Quality of interaction with clinician (or interventionist) (mean ±SD, lower scores indicate better interaction): Patient 1 week: 5.56 ± 0.90 vs. 7.29 ± 3.42 (p<0.01) Patient 3 months: 5.68 ± 0.77 vs. 7.29 ± 2.65 (p not reported) Surrogate 1 week: 5.39 ± 0.96 vs. 7.12 ± 3.39 (p=0.08)	Level of evidence: high risk of bias · High risk of selective reporting · At 3 months 2 vs. 2 surrogates dropped out (2 for marital reasons, 1 died, 1 not reported) and 0 vs. 2 patients dropped out (died) leaving 27 vs. 25 dyads · Completers analyses · Selective reporting: p-values not reported for all comparisons; QoL data not reported

			hour, single session, interview with a patient-surrogate dyad, delivered by a trained nurse interventionist who had completed 3.5 days of training. The elements and goals of SPIRIT are described in Table 1 (below) Usual care: A social worker at each dialysis clinic provided written information on advance directives and the patient's right to have an advance directive to every patient on the first day of dialysis treatment. The social worker encouraged patients to complete an advance directive and addressed their individual questions about life-sustaining treatment options. If completed, the advance directive was placed in the medical record. Questions about their medical condition and related end-of-life treatment options were referred to their physicians. Typically, this usual care is a one-time service provided on admission to the dialysis clinic unless the patient expresses his or her desire for a Do-Not-Resuscitate order	Surrogate 3 months: 5.46 ± 0.59 vs. 6.93 ± 3.04 (p not reported) <u>Satisfaction with decision</u>: CRITICAL OUTCOME Patient Decisional Conflict Scale (score ≥2 indicates difficulty in making choices) (mean (SD)): 1 week: 2.12 (0.31) vs. 2.05 (0.44) 3 months: 1.88 (0.37) vs. 1.94 (0.55) <u>Quality of life</u>: CRITICAL OUTCOME Not reported on Psychospiritual well-being (28-item Self-Perception and Relationship Tool) (mean (SD)) Patient 1 week: 1.71 (0.76) vs. 1.67 (0.79) Patient 3 months: 1.68 (1.03) vs. 1.95 (0.81) Surrogate 1 week: 1.51 (0.90) vs. 1.79 (0.97) Surrogate 3 months: 1.65 (0.99) vs. 1.84 (0.98)	
Song 2010 [2]	· Design: RCT · Funding/CoI: University of Pittsburgh Central Research Development	· Eligibility criteria: dialysis patients with a surrogate, on dialysis for at least 3 months	Patient-centered advance care planning (N=11) vs. Usual care (N=8)	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Quality of patient-clinician (or interventionist)	Level of evidence: high risk of bias · 1 dyad who did not receive allocated

Fund; CoI not reported on · Setting: single centre, United States · Sample size: N=19 dyads · Duration: not reported; follow-up 1 week	· A priori patient characteristics (not reported per group): o Age: mean 53 years o Male: 59% o Single: 65%	Patient-centered advance care planning: The guiding theory is the representational approach to patient education. The representational approach is based on Leventhal's common sense model and the conceptual change model. An in-depth interview with the patient–surrogate dyad, delivered by a trained nurse interventionist who had completed 2.5 days of training. The intervention took place over approximately 1 hour in a face-to-face session. During that session, the interventionist addressed the five elements of the representational approach: (a) representational assessment of participants' beliefs about their illness condition along the five dimensions of illness representation; (b) exploration of gaps or misunderstandings regarding chronic kidney disease and its progression and life-sustaining treatment, including dialysis; (c) creation of conditions for conceptual change; (d) introduction of replacement information; and (e) summarization of the discussion Usual care:	communication about end-of-life care (mean ±SD, higher scores (range: 3-12) indicate better communication): Patient 1 week: 10.10 ±2.08 vs. 8.14 ±2.34 (p<0.05) Quality of interaction with clinician (or interventionist)(mean ±SD, lower scores (range: 5-20) indicate better interaction): Patient 1 week: 6.20 ±2.90 vs. 6.29 ±2.56 (ns) Satisfaction with decision: CRITICAL OUTCOME Patient Decisional Conflict Scale (score ≥2 indicates difficulty in making choices) (mean (SD)): 1 week: 1.92 ±0.43 vs. 1.80 ±0.43 Surrogate's decision making confidence (mean (SD): 1 week: 18.40 ±1.84 vs. 18.57 ±2.44 Quality of life: CRITICAL OUTCOME Psychospiritual well-being (28-item Self-Perception and Relationship Tool) (mean ± SD) Patient 1 week: 1.60 ±0.62 vs. 1.08 ±1.74 Surrogate 1 week: 1.56 ±0.87 vs. 1.97 ±1.07	intervention (patient-centered advanced care planning) excluded from analysis · 1 patient from control group lost to follow-up

			Written information on advance directives was provided to every patient by a nurse or social worker who encouraged patients to complete an advance directive and addressed their questions about life-sustaining treatment options. Completed advance directives were placed in the medical record		
Song 2015 [3]	· Design: RCT · Funding/CoI: National Institutes of Health; CoI: none · Setting: multiple centres, United States · Sample size: N=210 dyads · Duration: Mar 2010-Dec 2012; follow-up 12 months, or 6 months after the patient's death for the dyads	· Eligibility criteria: 18 years or older, self-identified African American or white (acceptability of SPIRIT had not been tested with other groups), on dialysis therapy for at least 6 months, Charlson Comorbidity Index score of 6 or higher or Charlson Comorbidity Index score of 5 and hospitalization in the last 6 months · A priori patient characteristics: intervention vs. control o Age 61 vs. 63 years o Male 40% vs. 45% o Married/living with partner: 51% vs. 40%	SPIRIT (N=109 dyads) vs. Usual care (N=101 dyads) SPIRIT: The interventionists had completed a 31/2-day training program. SPIRIT is a psychoeducational intervention designed to assist patients to clarify their end-of-life preferences, help surrogates increase their understanding of the patient's wishes, and prepare surrogates for the role and responsibilities of being a surrogate. The SPIRIT intervention included 2 sessions, and all sessions included both patient and surrogate. During the first session in a private room at the dialysis center, the interventionist assessed cognitive, emotional, and spiritual/religious aspects of the dyad's	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Not reported on <u>Satisfaction with decision</u>: CRITICAL OUTCOME Patient Decisional Conflict Scale (score ≥2 indicates difficulty in making choices) (mean (SD)): Patient 2 months: 1.7 (0.5) vs. 1.7 (0.5) p=0.6 Patient 6 months: 1.6 (0.5) vs. 1.8 (0.4) p=0.007 Patient 12 months: 1.6 (0.4) vs. 1.8 (0.5) p<0.001 Surrogate´s decision making confidence (range 1-4, higher indicating better) (mean (SD): Surrogate 2 months: 3.7 (0.4) vs. 3.6 (0.5) p=0.05 Surrogate 6 months: 3.7 (0.4) vs. 3.6 (0.5) p=0.1 Surrogate 12 months: 3.7 (0.4) vs. 3.7 (0.5) p=0.7 <u>Quality of life</u>: CRITICAL OUTCOME Not reported on	Level of evidence: unclear risk of bias · Unclear sequence generation, not reported whether blinding of patients and personnel took place

representations of the patient's illness, prognosis, and end-of-life care. This allowed the interventionist to provide individualized information about topics such as the effectiveness of life sustaining treatment for people with end-organ failure and assisted the patient in examining his or her values about life-sustaining treatment at the end of life. The interventionist aimed to help the surrogate prepare for being a decision maker and for the emotional burden of end-of-life decision making by actively involving the surrogate in the discussion. A goals-of-care document was completed at the end of the session to indicate the patient's preferences. In a brief second session delivered 2 weeks later at the patient's home (to reduce travel burden), the goals-of-care document and resuscitation preferences were reviewed. If the surrogate was someone out of the order of the hierarchical compensatory model (e.g., a sibling was chosen when the patient had a spouse), the interventionist explored potential family conflicts and encouraged the dyad to talk with

other family members and complete a health care power of attorney. The interventionist then summarized the patient's end-of-life preferences, listed the surrogate's name and relationship to the patient, and indicated whether the patient desired a do-not-resuscitate order or assistance in completing an advance directive. The interventionist communicated this information to dialysis staff (the social worker and nurse manager or the medical director), and the document was placed in the medical record

Usual care: Written information for advance directives was provided to every patient on the first day of dialysis, and a social worker encouraged patients to complete an advance directive and addressed questions about life-sustaining treatments. A nephrologist, physician assistant, or nurse practitioner reviewed resuscitation statements with the patient to determine whether the patient wanted a do-not-resuscitate (DNR) order in the center. If there was no DNR order in the record, a desire for "full code" (receiving

	cardiopulmonary resuscitation) was presumed

Abbreviations: CoI: conflict of interest; ns: not significant; QoL: quality of life; RCT: randomised controlled trial; SD: standard deviation

Table 1 Elements and Goals of the SPIRIT Intervention [1]

Element	Goal
1. Representational assessment	Both patient and surrogate describe illness representations along with the following dimensions: identity, timeline, consequences, controllability, and spiritual and emotional representations. The goal for all parties is to achieve a deeper understanding of patient's illness experience and the surrogate's experience with his/her loved one's illness.
2. Identifying and exploring gaps and concerns	The interventionist identifies and explores gaps and concerns the dyad may have regarding illness progression, life-sustaining treatment and decision making. The goal for each member of the dyad is to exchange own values and concerns about life-sustaining treatment at the end-of-life.
3. Creating conditions for conceptual change	The interventionist encourages the dyad to share their views and ideas about death and dying and end-of-life care. She assists the patient to identify his/her threshold for unacceptable outcomes of life-sustaining treatment. The goal is to gain a good understanding of the dyad's values of treatment outcomes and concerns.
4. Introducing replacement information	The interventionist presents end-of-life scenarios and encourages the patient to clarify goals of care and express concerns. The interventionist assists the surrogate to examine her/his willingness to take the responsibility to act on them and to appreciate surrogate roles.
5. Summary	The interventionist summarizes the value of the discussion and the need for future discussions. She also assesses any additional support they need such as consultation with social worker at the clinic and spiritual advisor.

References

1. Song, M.K., et al., *Randomized controlled trial of SPIRIT: an effective approach to preparing African-American dialysis patients and families for end of life.* Res Nurs Health, 2009. **32**(3): p. 260-73.
2. Song, M.K., et al., *Effects of an intervention to improve communication about end-of-life care among African Americans with chronic kidney disease.* Appl Nurs Res, 2010. **23**(2): p. 65-72.
3. Song, M.K., et al., *Advance Care Planning and End-of-Life Decision Making in Dialysis: A Randomized Controlled Trial Targeting Patients and Their Surrogates.* Am J Kidney Dis, 2015.

Vraag 4a: Bij patiënten met eindstadium nierfalen (ESRD of CKD stadium V of dialyse), leidt advance care planning tot een betere kwaliteit van leven, hogere tevredenheid van de familieleden?

2VRAAG 4B: WAT ZIJN DE KENMERKEN VAN ACP IN DIE STUDIE(S) WAARIN AANGETOOND WERD DAT HET WERKT?

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Luckett 2014 [1]	· SR · Funding/CoI: none; none · Search date: Apr 2013 · Databases: MEDLINE, PsycINFO, Embase, AMED (Allied and Complementary Medicine Database), CINAHL (Cumulative Index to Nursing and Allied Health Literature), and Sociological Abstracts · Study designs: any design · N included studies: 52 (55 articles), of which 8 intervention studies, of which 4 RCTs	· Eligibility criteria: studies on advanced care planning for adults with chronic kidney disease · Patient characteristics: o Not reported on	Advanced care planning	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME The 2 Song studies found a significant effect on both patient-clinician communication and interaction (no quantified/meta-analysed data) <u>Satisfaction with decision</u>: CRITICAL OUTCOME Neither Song study found a significant effect for decisional conflict (no quantified/meta-analysed data) <u>Quality of life</u>: CRITICAL OUTCOME Neither study by Song s found a significant effect on well-being for either patients or surrogates (no quantified/meta-analysed data) <u>Patient choices</u>: IMPORTANT OUTCOME Not reported on	· Systematic review of low quality · Included RCTs: o Perry 2005 o Singer 1995 o Song 2009 o Song 2010 · Perry 2005 is another intervention (peer-mentor–facilitated ACP sessions) and is not described here · No relevant outcomes reported for Singer 1995

Abbreviations: CoI: conflicts of interest; SR: systematic review

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Song 2009 [2]	· Design: RCT · Funding/CoI: National Institutes of Health; CoI not reported on · Setting: multiple centers, United States · Sample size: N=58 dyads	· Eligibility criteria: self-identified African Americans with end-stage renal disease and their chosen surrogate decision makers, on	SPIRIT (N=29) vs. Usual care (N=29) SPIRIT: The guiding theory of SPIRIT is the representational approach to patient education. The	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Quality of patient-clinician (or interventionist) communication about end-of-life care (mean ±SD, higher scores indicate better	Level of evidence: high risk of bias · High risk of selective reporting · At 3 months 2 vs. 2 surrogates dropped out (2 for marital

· Duration: Jan 2007-Jun 2008; outcomes assessed at 1 week and 3 months post-intervention	dialysis for at least 3 months · A priori patient characteristics: intervention vs. control o Age, mean: 58 vs. 58 years o Male: 66% vs. 48% o Married/living with partner: 28% vs. 48%	representational approach is based on Leventhal's common sense model and the conceptual change model. These representations serve as a cognitive framework in which new information is processed. The conceptual change model proposes that the likelihood of learning increases when an opportunity is given to reflect and comment on current ideas and their consequences, when the individual is dissatisfied with current ideas or recognizes the limitations of the ideas, and when alternative information is seen as beneficial. 1-hour, single session, interview with a patient-surrogate dyad, delivered by a trained nurse interventionist who had completed 3.5 days of training. The elements and goals of SPIRIT are described in Table 1 (below) Usual care: A social worker at each dialysis clinic provided written information on advance directives and the patient's right to have an advance directive to every patient on the first day of dialysis treatment. The social worker encouraged patients to complete an advance directive and addressed their	communication, range: 4-12): Patient 1 week: 11.18 ± 1.12 vs. 8.83 ± 3.55 (p=0.03) Patient 3 months: 11.30 ± 1.41 vs. 7.52 ± 3.66 (p<0.01) Surrogate 1 week: 11.68 ± 0.55 vs. 6.79 ± 3.57 (p<0.01) Surrogate 3 months: 11.58 ± 0.72 vs. 10.22 ± 2.49 (p=0.03) Quality of interaction with clinician (or interventionist) (mean ±SD, lower scores indicate better interaction): Patient 1 week: 5.56 ± 0.90 vs. 7.29 ± 3.42 (p<0.01) Patient 3 months: 5.68 ± 0.77 vs. 7.29 ± 2.65 (p not reported) Surrogate 1 week: 5.39 ± 0.96 vs. 7.12 ± 3.39 (p=0.08) Surrogate 3 months: 5.46 ± 0.59 vs. 6.93 ± 3.04 (p not reported) <u>Satisfaction with decision</u>: CRITICAL OUTCOME Patient Decisional Conflict Scale (score ≥2 indicates difficulty in making choices) (mean (SD)): 1 week: 2.12 (0.31) vs. 2.05 (0.44) 3 months: 1.88 (0.37) vs. 1.94 (0.55) <u>Quality of life</u>: CRITICAL OUTCOME Not reported on Psychospiritual well-being (28-item Self-Perception and Relationship Tool) (mean (SD)) Patient 1 week: 1.71 (0.76) vs. 1.67 (0.79) Patient 3 months: 1.68 (1.03) vs. 1.95 (0.81) Surrogate 1 week: 1.51 (0.90) vs. 1.79 (0.97)	reasons, 1 died, 1 not reported) and 0 vs. 2 patients dropped out (died) leaving 27 vs. 25 dyads · Completers analyses · Selective reporting: p-values not reported for all comparisons; QoL data not reported

			individual questions about life-sustaining treatment options. If completed, the advance directive was placed in the medical record. Questions about their medical condition and related end-of-life treatment options were referred to their physicians. Typically, this usual care is a one-time service provided on admission to the dialysis clinic unless the patient expresses his or her desire for a Do-Not-Resuscitate order	Surrogate 3 months: 1.65 (0.99) vs. 1.84 (0.98) <u>Patient choices</u>: IMPORTANT OUTCOME Not reported on	
Song 2010 [3]	· Design: RCT · Funding/CoI: University of Pittsburgh Central Research Development Fund; CoI not reported on · Setting: single centre, United States · Sample size: N=19 dyads · Duration: not reported; follow-up 1 week	· Eligibility criteria: African-American dialysis patients with a surrogate, on dialysis for at least 3 months · A priori patient characteristics (not reported per group): o Age: mean 53 years o Male: 59% o Single: 65%	Patient-centered advance care planning (N=11) vs. Usual care (N=8) Patient-centered advance care planning: The guiding theory is the representational approach to patient education. The representational approach is based on Leventhal's common sense model and the conceptual change model. An in-depth interview with the patient–surrogate dyad, delivered by a trained nurse interventionist who had completed 2.5 days of training. The intervention took place over approximately 1 hour in a face-to-face session. During that session, the interventionist addressed the five	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Quality of patient-clinician (or interventionist) communication about end-of-life care (mean ±SD, higher scores (range: 3-12) indicate better communication): Patient 1 week: 10.10 ±2.08 vs. 8.14 ±2.34 (p<0.05) Quality of interaction with clinician (or interventionist)(mean ±SD, lower scores (range: 5-20) indicate better interaction): Patient 1 week: 6.20 ±2.90 vs. 6.29 ±2.56 (ns) <u>Satisfaction with decision</u>: CRITICAL OUTCOME Patient Decisional Conflict Scale (score ≥2 indicates difficulty in making choices) (mean (SD)): 1 week: 1.92 ±0.43 vs. 1.80 ±0.43	Level of evidence: high risk of bias · 1 dyad who did not receive allocated intervention (patient-centered advanced care planning) excluded from analysis · 1 patient from control group lost to follow-up

			elements of the representational approach: (a) representational assessment of participants' beliefs about their illness condition along the five dimensions of illness representation; (b) exploration of gaps or misunderstandings regarding chronic kidney disease and its progression and life-sustaining treatment, including dialysis; (c) creation of conditions for conceptual change; (d) introduction of replacement information; and (e) summarization of the discussion Usual care: Written information on advance directives was provided to every patient by a nurse or social worker who encouraged patients to complete an advance directive and addressed their questions about life-sustaining treatment options. Completed advance directives were placed in the medical record	Surrogate's decision making confidence (mean (SD)): 1 week: 18.40 ±1.84 vs. 18.57 ±2.44 <u>Quality of life</u>: CRITICAL OUTCOME Psychospiritual well-being (28-item Self-Perception and Relationship Tool) (mean ± SD) Patient 1 week: 1.60 ±0.62 vs. 1.08 ±1.74 Surrogate 1 week: 1.56 ±0.87 vs. 1.97 ±1.07 <u>Patient choices</u>: IMPORTANT OUTCOME Low chance of survival: Continue all treatment: 80% (8/11) vs. 28.6% (2/8) Cardiopulmonal resuscitation: Attempt resuscitation: 90% (9/11) vs. 57% (4/8)	
Song 2015 [4]	· Design: RCT · Funding/CoI: National Institutes of Health; CoI: none · Setting: multiple centres, United States · Sample size: N=210 dyads · Duration: Mar 2010-Dec 2012; follow-up	· Eligibility criteria: 18 years or older, self-identified African American or white (acceptability of SPIRIT had not been tested with other groups), on dialysis therapy for at least 6 months,	SPIRIT (N=109 dyads) vs. Usual care (N=101 dyads) SPIRIT: The interventionists had completed a 31/2-day training program. SPIRIT is a psychoeducational	<u>Satisfaction with decision making process</u>: CRITICAL OUTCOME Not reported on <u>Satisfaction with decision</u>: CRITICAL OUTCOME Patient Decisional Conflict Scale (range 1-5, score ≥2 indicates difficulty in making choices) (mean (SD)):	Level of evidence: unclear risk of bias · Unclear sequence generation, not reported whether blinding of patients and personnel took place

12 months, or 6 months after the patient's death for the dyads	Charlson Comorbidity Index score of 6 or higher or Charlson Comorbidity Index score of 5 and hospitalization in the last 6 months · A priori patient characteristics: intervention vs. control o Age 61 vs. 63 years o Male 40% vs. 45% o Married/living with partner: 51% vs. 40%	intervention designed to assist patients to clarify their end-of-life preferences, help surrogates increase their understanding of the patient's wishes, and prepare surrogates for the role and responsibilities of being a surrogate. The SPIRIT intervention included 2 sessions, and all sessions included both patient and surrogate. During the first session in a private room at the dialysis center, the interventionist assessed cognitive, emotional, and spiritual/religious aspects of the dyad's representations of the patient's illness, prognosis, and end-of-life care. This allowed the interventionist to provide individualized information about topics such as the effectiveness of life sustaining treatment for people with end-organ failure and assisted the patient in examining his or her values about life-sustaining treatment at the end of life. The interventionist aimed to help the surrogate prepare for being a decision maker and for the emotional burden of end-of-life decision making by actively involving the surrogate in the discussion. A goals-of-care document	Patient 2 months: 1.7 (0.5) vs. 1.7 (0.5) p=0.6 Patient 6 months: 1.6 (0.5) vs. 1.8 (0.4) p=0.007 Patient 12 months: 1.6 (0.4) vs. 1.8 (0.5) p<0.001 Surrogate´s decision making confidence (range 1-4, higher indicating better) (mean (SD): Surrogate 2 months: 3.7 (0.4) vs. 3.6 (0.5) p=0.05 Surrogate 6 months: 3.7 (0.4) vs. 3.6 (0.5) p=0.1 Surrogate 12 months: 3.7 (0.4) vs. 3.7 (0.5) p=0.7 <u>Quality of life</u>: CRITICAL OUTCOME Not reported on <u>Patient choices</u>: IMPORTANT OUTCOME Not reported on

was completed at the end of the session to indicate the patient's preferences. In a brief second session delivered 2 weeks later at the patient's home (to reduce travel burden), the goals-of-care document and resuscitation preferences were reviewed. If the surrogate was someone out of the order of the hierarchical compensatory model (e.g., a sibling was chosen when the patient had a spouse), the interventionist explored potential family conflicts and encouraged the dyad to talk with other family members and complete a health care power of attorney. The interventionist then summarized the patient's end-of-life preferences, listed the surrogate's name and relationship to the patient, and indicated whether the patient desired a do-not-resuscitate order or assistance in completing an advance directive. The interventionist communicated this information to dialysis staff (the social worker and nurse manager or the medical director), and the document was placed in the medical record

Usual care:

	Written information for advance directives was provided to every patient on the first day of dialysis, and a social worker encouraged patients to complete an advance directive and addressed questions about life-sustaining treatments. A nephrologist, physician assistant, or nurse practitioner reviewed resuscitation statements with the patient to determine whether the patient wanted a do-not-resuscitate (DNR) order in the center. If there was no DNR order in the record, a desire for “full code” (receiving cardiopulmonary resuscitation) was presumed

Abbreviations: CoI: conflict of interest; ns: not significant; QoL: quality of life; RCT: randomised controlled trial; SD: standard deviation

Table 2 Elements and Goals of the SPIRIT Intervention [2]

Element	Goal
1. Representational assessment	Both patient and surrogate describe illness representations along with the following dimensions: identity, timeline, consequences, controllability, and spiritual and emotional representations. The goal for all parties is to achieve a deeper understanding of patient’s illness experience and the surrogate’s experience with his/her loved one’s illness.
2. Identifying and exploring gaps and concerns	The interventionist identifies and explores gaps and concerns the dyad may have regarding illness progression, life-sustaining treatment and decision making. The goal for each member of the dyad is to exchange own values and concerns about life-sustaining treatment at the end-of-life.
3. Creating conditions for conceptual change	The interventionist encourages the dyad to share their views and ideas about death and dying and end-of-life care. She assists the patient to identify his/her threshold for unacceptable outcomes of life-sustaining treatment. The goal is to gain a good understanding of the dyad’s values of treatment outcomes and concerns.
4. Introducing replacement information	The interventionist presents end-of-life scenarios and encourages the patient to clarify goals of care and express concerns. The interventionist assists the surrogate to examine her/his willingness to take the responsibility to act on them and to appreciate surrogate roles.
5. Summary	The interventionist summarizes the value of the discussion and the need for future discussions. She also assesses any additional support

they need such as consultation with social worker at the clinic and spiritual advisor.

References

1. Luckett, T., et al., *Advance care planning for adults with CKD: a systematic integrative review.* Am J Kidney Dis, 2014. **63**(5): p. 761-70.
2. Song, M.K., et al., *Randomized controlled trial of SPIRIT: an effective approach to preparing African-American dialysis patients and families for end of life.* Res Nurs Health, 2009. **32**(3): p. 260-73.
3. Song, M.K., et al., *Effects of an intervention to improve communication about end-of-life care among African Americans with chronic kidney disease.* Appl Nurs Res, 2010. **23**(2): p. 65-72.
4. Song, M.K., et al., *Advance Care Planning and End-of-Life Decision Making in Dialysis: A Randomized Controlled Trial Targeting Patients and Their Surrogates.* Am J Kidney Dis, 2015.

3VRAAG 5B: SLEEP

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Edalat-Nejad 2013	· Design: cross-over RCT · Funding/CoI:The Vice Chancellor of the Arak University of Medical Sciences · Setting: University hospital, Iran · Sample size: N=82 · Duration: 12 weeks	· Eligibility criteria: Inclusion criteria: age >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; Exclusion: known major illness (malignancy, active infection and uncontrolled heart failure), pregnancy, iron deficiency anemia, poor control diabetes mellitus (hemoglobin A1c >7.5), current use of melatonin or known allergy of	Melatonin 3 mg + Theanine 10 mg Vs Placebo	<u>Sleep quality</u>: CRITICAL OUTCOME PSQI global score at 6 weeks: 6.99 (SD 3.42) vs 8.91 (SD 4.30), p=0.000 Components of PSQI: Sleep duration 1.00 (SD 0.98) vs 1.60 (SD 1.05), p=0.000 Sleep disturbance 1.03 (SD 0.42) vs 1.15 (SD 0.43), p=0.045 Sleep latency 1.46 (SD 0.90) vs 1.24 (SD 0.81), p=0.087 Daytime dysfunction 1.22 (SD 0.79) vs 1.37 (SD 0.79), p=0.167 Sleep efficiency 1.16 (SD 1.19) vs 1.72 (SD 1.08), p=0.005 Subjective sleep quality 0.79 (SD 0.53) vs 1.41 (SD 1.04), p=0.000 Use of sleep medications 0.32	Level of evidence: unclear risk of bias · No information on randomisation procedure; information on blinding limited to description of identical tablets; dropout rate 17%

		melatonin, acute medical or surgical condition that required hospitalization or operation throughout the study and dementia or psychotic disorder as diagnosed by researchers that interferes with patient's participation in this trial · *A priori* patient characteristics: intervention vs. control o Age mean 58y (SD 14y) o Male 53% o Diabetics 43% o Vintage of 6-296 months		(SD 0.68) vs 0.43 (SD 0.61), p=0.289 <u>Quality of life</u>: CRITICAL OUTCOME No information	
Koch 2008 Koch 2009	· Design: cross-over RCT · Funding/CoI: not reported · Setting: not reported, but likely in the Netherlands · Sample size: N=24 · Duration: 18 weeks	· Eligibility criteria: Inclusion criteria: patients between 18 and 85 years and on stable haemodialysis (>3 months on haemodialysis with adequate dialysis efficacy) were included. Exclusion criteria: prior use of melatonin, use of hypnotics that could not be stopped during the study, and severe psychological or neurological disease. · *A priori* patient characteristics: intervention vs. control	Melatonin 3 mg Vs Placebo	<u>Sleep quality</u>: CRITICAL OUTCOME **Based on actometer after 5 or 11 weeks:** (all values are medians and IQR) 1. On day of dialysis: Sleep onset latency (min): 15.5 (27.8) vs 44.5 (43.3), p<0.05 Sleep efficiency (%): 73.1 (27.5) vs 67.3 (30.7), p<0.05 Actual wake time (%): 19.4 (13.6) vs 20.0 (28.6) Actual sleep time (min): 387.5 (155.6) vs 376.7 (118.6), p<0.05 Fragmentation index: 3.1 (0.7) vs 4.5 (1.1), p<0.05 2. On following night:	Level of evidence: unclear risk of bias · No information on randomisation procedure, no information on blinding other than the statement the trial was double blinded, dropout 16%

	o Age median 71 (IQR 14.3) o Male 70% o BMI median 24.5 (IQR 4.7) o Dialysis duration median 19 months (IQR 20)	Sleep onset latency (min): 28.5 (22.6) vs 36.0 (31.9), p<0.10 Sleep efficiency (%): 69.2 (30.6) vs 65.0 (22.1), p<0.1 Actual awake time (%): 28.2 (23.7) vs 24.8 (14.2) Actual sleep time (min): 386.8 (169.7) vs 351.0 (119.7) Fragmentation index: 3.0 (1.2) vs 3.9 (1.3) **Based on sleep questionnaire** (all values are medians and IQR) 1. On day of dialysis Daytime napping (min): 0 (37.5) vs 30.0 (48.8) Sleep onset latency (min): 15.0 (12.5) vs 45.0 (90.0), p<0.05 Wake periods (min): 25.0 (22.5) vs 30.0 (25.0), p<0.05 Sleep time (min): 480 (120.0) vs 345.0 (180.0), p<0.05 2. On following night Daytime napping (min): 22.5 (35) vs 12.5 (30) Sleep onset latency (min): 15.0 (21.2) vs 40.0 (100), p<0.05 Wake periods (min): 30.0 (17.5) vs 30.0 (2.5), p<0.05 Sleep time (min): 435 (86.3) vs 420 (180.0)
		<u>Quality of life</u>: CRITICAL OUTCOME

				No information	
Russcher 2013	· Design: RCT · Funding/CoI: Dutch Kidney Foundation · Setting: 5 large regional hospitals in the Netherlands · Sample size: N=67 · Duration: 12 months	· Eligibility criteria: Inclusion: stable haemodialysis patients aged 18 to 85 years with a haemodialysis history of at least 3 months and adequate dialysis efficacy, suffered from subjective sleep problems at baseline according to the Epworth Sleepiness Scale (ESS) questionnaire and their mean sleep onset latency measured by means of actigraphy was longer than 15 min Exclusion: current melatonin use, known hypersensitivity to melatonin, severe psychological or neurological disease, unstable angina pectoris, NYHA class IV hear failure, pregnancy, participation in another clinical trial 1 month prior to the start of the study · *A priori* patient characteristics: intervention vs. control o Age mean 65.5 (11.7) vs 64.4 (12.0) o Male 58%vs 65%	Melatonin 3 mg Vs Placebo	<u>Sleep quality</u>: CRITICAL OUTCOME **Based on actometer** 1. On day of dialysis Sleep efficiency at 3 months: 7.6% difference (95% CI 0.77-14.4) Actual sleep time at 3 months (min): 49 difference (95% CI 2.1-95.9) 2. On following night: no significant differences At 6, 9 and 12 months: no significant differences <u>Quality of life</u>: CRITICAL OUTCOME **MOS SF-36** Vitality at 12 months: -1.9% difference (95% CI -12.6-8.7) Physical functioning at 12 months: -11.4% difference (95% CI -21.8- -1.1) Mental health at 12 months: 9.3% difference (95% CI -0.1-18.7), p=0.052 Emotional role at 6 months: 14.6% difference (95% CI -0.6-29.8) Emotional role at 12 months: 29.8% difference (95% CI -1.4 -61.0) Physical role at 12 months: -22.2% (95% CI -49.2-4.8) Social functioning, bodily pain, general health, last year's health: no significant differences	Level of evidence: high risk of bias · Block randomisation, unclear allocation concealment, unclear blinding, 37% dropout rate

		o BMI 26.3 (4.4) vs 25.6 (5.4) o Vintage 30.6 (27.3) vs 28.3 (22.5)			

4VRAAG 5B: PAIN

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Atalay 2013 Biyik 2013	· Design: Randomized crossover trial · Funding/CoI: supported by Selcuk Scientific Research Project Coordinating Office Project Nr 08102027/ No competing interests · Setting: Konya, Turkey · Sample size: N=50 · Duration: 14 weeks	· Eligibility criteria: hemodialysis patients with neuropathic pain · *A priori* patient characteristics: intervention vs. control o Age mean: 58.2y o Male 30% o Hemodialysis duration: 55.1m	Gabapentin vs. Pregabalin	<u>Pain</u>: CRITICAL OUTCOME SFMPQ Total: (p<0.001) Gabapentin: before 18.9 ± 4.3, after 9.3 ± 4.3 Pregabalin: before 18.5 ± 3.9, after 9.8 ± 3.6 Change in % (NS): Gabapentin:-8.9 +/- 4.1 Pregabalin: -9.3 +/- 4.0 SFMPQ VAS: (p<0.001) Gabapentin: before 68.8 ± 12.8, after 33.0 ± 15.6 Pregabalin: before 67.0 ± 11.8, after 32.9 ± 12.8 Change in % (NS): Gabapentin:-33.5 +/- 13.2 Pregabalin: -36.3 +/- 12.4 SFMPQ PPI: (p<0.001) Gabapentin: before 2.8 ± 0.8, after 1.4 ± 0.7 Pregabalin: before 2.8 ± 0.8, after 1.4 ± 0.7 Change in % (NS): Grabapentin:-1.3 +/- 0.8 Pregabalin: -1.4 +/- 0.6 <u>Quality of life</u>: CRITICAL OUTCOME PSQI: (p<0.001)	Level of evidence: high risk of bias · Unclear allocation concealment · Open label study · No ITT analysis: 10 dropouts excluded from analysis

				Gabapentin: before 8.7 ± 4.2, after 5.9 ± 3.0 Pregabalin: before 8.8 ± 4.6, after 6.1 ± 4.2 BDI: (p<0.001) Gabapentin: before 15.1 ± 7.6, after 10.9 ± 5.9 Pregabalin: before 13.61 ± 5.9, after 10.9 ± 5.9 SF-36 physical component scale score: (p<0.001) Gabapentin: before 42.6 +/- 18.2, after 57.1+/- 18.9 Pregabalin: before 42.7 +/- 17.9, after 57.3 +/- 17.1 Change in % (NS): Gabapentin: 13.0 +/- 9.2 Pregabalin: 16.1 +/- 11.2 SF-36 mental component scale score: (p<0.001) Gabapentin: before 51.6 +/- 19.5, after 63.2 +/- 18.3 Pregabalin: before 50.5 +/- 18.6, after 63.1 +/- 15.8 Change in % (p=0.043): Gabapentin:9.6 +/- 11.2 Pregabalin: 14.6 +/- 11.6	

5VRAAG 5D: PRURITUS

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Gooding 2010	· SR · Funding/CoI: No Financial disclosures reported	· Eligibility criteria: participants on haemodialysis suffering from pruritus	Topical capsaicin vs. Placebo	Pruritus: CRITICAL OUTCOME No combination of data (meta-analysis) carried out	· Review of good quality · Included RCTs: Breneman (1992), Yu-Li

	· Search date: until April 2008 · Databases: Medline, Embase, Amed, Cinahl and the Cochrane Library · Study designs: RCTs · N included studies: 6 studies			Quality of life: CRITICAL OUTCOME No combination of data (meta-analysis) carried out	Cho (1996), Targ (1996)
Xander 2013	· SR · Funding/CoI: declare no CoI · Search date: August 2012 · Databases: The Cochrane Library, MEDLINE, EMBASE, BIOSIS, CINAHL, PsycINFO · Study designs: Randomised controlled trials · N included studies: 38 studies including 1286 participants	· Eligibility criteria: adult palliative care patients with pruritus	Pharmacological treatments (30 different treatments included) vs. placebo/ not treatment/ alternative treatment	Pruritus: CRITICAL OUTCOME MA results Pruritus on VAS scale: Nalfurafine vs. placebo: SMD=-0.46 ; 95%CI (-0.65; -0.28) Gabapentin vs. placebo: MD=-5.20 ; 95%CI (-6.7; -3.7) Capsaicin vs. placebo: MD=-0.80 ; 95%CI (-1.34 ; -0.25) Other results narratively presented Quality of life: CRITICAL OUTCOME Not reported	· Review of good quality · Included RCTs: Legroux-Crespel (2004), Pauli-Magnus (2000), Peer (1996), Wilkstrom (2005a), Wilkstrom (2005b), Kumagai (2010), Ashmore (2000), Murphy (2003), Ozaykan (2001), Gunal (2004), Naini (2007), Pour-Reza-Gholi (2007), Silverberg (1977), Silva (1994), Nasrollahi (2007), Pederson (1980), Makhlough (2010), Duque (2005)

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Boaz 2009	· Design: Randomized controlled trial · Funding/CoI: Funding from Ahava Dead Sea Laboratories/ 2	· Eligibility criteria: haemodialysis patients with uremic pruritus · *A priori* patient	Dead Sea minerals enriched body lotion (n=25) vs.	Pruritus: CRITICAL OUTCOME Post treatment severity score (5-point Likert) Itching (p=0.44) P1: 0.5 P2: 1	Level of evidence: unclear risk of bias

	authors employees at Ahava Dead Sea Laboratories · Setting: Institute of Nephrology,E. Wolfson Medical Center, Israel · Sample size: N=78 · Duration: 14 days	characteristics: intervention vs. control o Age mean: 67.8 o Male 57% o Diabetes 33.8%	Placebo 1 (identical to treatment, but without dead sea minerals, n=25) vs. Placebo 2 (lotion without active ingredients, n=28)	DS: 1 Tightness (p=0.70) P1: 0 P2: 0 DS: 0 Dryness (p=0.22) P1: 1 P2: 2 DS: 1 Peeling (p=0.51) P1: 0 P2: 0 DS: 0 Change from baseline severity score Itching (p=0.42) P1: 0 P2: 0 DS: 0 Tightness (p=0.81) P1: 0 P2: 0 DS: 0 Dryness (p=0.60) P1: -0.5 P2: 0 DS: -1 Peeling (p=0.24) P1: -0.5 P2: 0 DS: 0 <u>Quality of life</u>: CRITICAL OUTCOME Not reported	· Unclear allocation concealment · Double-blind study
Ko 2011	· Design: Randomized controlled trial · Funding/CoI: Research grant to one author: NTUHYL.97.S011/ no CoIs declared · Setting: Yun-Lin Branch,Taiwan · Sample size: N=21 · Duration: 12 weeks	· Eligibility criteria: patients with chronic kidney disease, refractory uraemic pruritus · *A priori* patient characteristics: intervention vs. control o Age mean: 60 years o Male 52% o Diabetes mellitus: 33%	Narrowband ultraviolet B (NB-UVB) phototherapy (n=11) vs. Long-wave UVA (n=10)	<u>Pruritus</u>: CRITICAL OUTCOME Pruritus VAS (mean change from baseline) Week 3 (between group: p=0.76) NB-UVB: -1.71 (-3.27; -0.14) Control: -1.43 (-2.63; -0.22) Week 6 (between group: p=0.92) NB-UVB: -3.53 (-6.02; -1.03) Control: -3.38 (-5.54; -1.21) Week 9 (between group: p=0.89) NB-UVB: -3.06 (-5.03;-1.08) Control: -3.24 (-5.56; -0.92)	Level of evidence: high risk of bias · Unclear allocation concealment · Single blinded · 3 dropouts, no ITT analysis

				Week 12 (between group: p=0.24) NB-UVB: -3.91 (-6.17;-1.64) Control: -2.24 (-4.25;-0.23) <u>Quality of life</u>: CRITICAL OUTCOME Not reported <u>Pruritus</u>: CRITICAL OUTCOME Scores from Itch Severity Scale: pre-post-test Difference: Group1:3.81 (3.18) Group2:3.11 (2.45) Control :1.04 (2.47) Frequency: Group1: Pre 0.49 (0.22) Post 0.28 (0.19) Group2: Pre 0.54 (0.24) Post 0.33 (0.22) Control : Pre 0.36 (0.16) Post 0.24 (0.16) Sensibility: Group1: Pre 0.34 (0.25) Post 0.09 (0.10) Group2: Pre 0.23 (0.24) Post 0.11 (0.18) Control : Pre 0.08 (0.14) Post 0.08 (0.15) Area: Group1: Pre 0.52 (0.23) Post 0.32 (0.28) Group2: Pre 0.62 (0.27) Post 0.40 (0.30) Control : Pre 0.41 (0.27) Post 0.36 (0.30) Level: Group1: Pre 0.53 (0.20) Post 0.33 (0.17) Group2: Pre 0.51 (0.19) Post 0.32 (0.15) Control : Pre 0.38 (0.17) Post 0.31 (0.18) Emotion: Group1: Pre 0.18 (0.15) Post 0.07 (0.11) Group2: Pre 0.14 (0.16) Post 0.10 (0.14) Control : Pre 0.09 (0.21) Post 0.05 (0.12) Sex: Group1: Pre 0.10 (0.31) Post 0.00 (0.00)	
Lin 2012	· Design: prospective quasi-experimental design · Funding/CoI: Grant No. DOH100-TD-C-111-002/ no CoI · Setting: Taiwan · Sample size: N=93 · Duration: 3 weeks	· Eligibility criteria: Haemodialysis patients with uremic pruritus · *A priori* patient characteristics: intervention vs. control o Age mean: 62years o Male 59% o Mean intensity of uremic pruritus: mild	Chilled baby-oil (n=30) vs. Un-chilled baby-oil (n=31) vs. Control (n=32)		Level of evidence: high risk of bias · Quasi-randomisation

				Group2: Pre 0.06 (0.25) Post 0.00 (0.00) Control : Pre 0.03 (0.18) Post 0.03 (0.18) Sleep: Group1: Pre 0.41 (0.31) Post 0.23 (0.26) Group2: Pre 0.44 (0.24) Post 0.23 (0.27) Control : Pre 0.20 (0.21) Post 0.13 (0.18) <u>Quality of life</u>: CRITICAL OUTCOME Not reported	
Marquez 2012	· Design: Randomized open-label cross-over trial · Funding/CoI: no CoI; funding not reported · Setting: Argentina · Sample size: N=22 · Duration: 60 days	· Eligibility criteria: patients with chronic hemodialysis with uremic pruritus · *A priori* patient characteristics: intervention vs. control o Age mean: 54y o Time on HD: 4.9y	Desloratadine 5 mg, 3x/wk for 3wks vs. Gabapentin 300 mg, 3x/wk for 3 wks	<u>Pruritus</u>: CRITICAL OUTCOME VAS-score for pruritus Baseline: 5.95 Gabapentin: 4.6 (p=0.07) Wash-out: 5.89 Desloratadine:3.44 (p=0.004) Gabapentin vs. Desloratadine: p=0.16 <u>Quality of life</u>: CRITICAL OUTCOME Not reported	Level of evidence: high risk of bias · Unclear randomisation method and allocation concealment · Open-label study · 3 exclusions after randomisation
Solak 2012	· Design: Randomized crossover trial · Funding/CoI: One author received a grant ERA-EDTA/ further no CoI · Setting: Turkey · Sample size: N=50 · Duration: 14 weeks	· Eligibility criteria: maintenance haemodialysis patients with neuropathy and/or neuropathic pain; 72,5% had pruritus · *A priori* patient characteristics: intervention vs. control o Age mean: 58.2 years o Male 30% o diabetic 38%	Gabapentin vs. Pregabalin	<u>Pruritus</u>: CRITICAL OUTCOME Pruritus VAS Score: Gabapentin: before 5.84 +/- 1.38, after 1.43 +/- 2.0 (p<0.001) Pregabalin: before 5.8 +/- 1.4, after 1.36 +/- 2.32 (p<0.001) Improvement in pruritus VAS-score: gabapentin: -4.41 +/- 1.78 (77.9%) pregabalin : -4.43 +/- 2.1 (79.2%) (p=0.844) <u>Quality of life</u>: CRITICAL OUTCOME See Atalay 2013?	Level of evidence: high risk of bias · Unclear allocation concealment · Open-label study · 10 exclusions after randomisation
Razeghi 2009	· Design: Double-blind clinical trial · Funding/CoI: no CoI	· Eligibility criteria: hemodialysis patients with ESRD suffering from pruritus	Gabapentin vs. Placebo	<u>Pruritus</u>: CRITICAL OUTCOME Pruritus score (VAS): Baseline: 100 gabapentin: 6.44 +/- 8.46 (p < 0.001)	Level of evidence: high risk of bias · Cross-over trial, but

	· Setting: 3 hemodialysis centers, Iran · Sample size: N=34 · Duration: 9 weeks	· A priori patient characteristics : intervention vs. control o Age mean: 58.4years o Male 23% o Median dialysis duration: 50 months		wash-out: 15 +/- 11.27 (p < 0.001) placebo : 81.88 +/- 11.06 (p < 0.001) Quality of life: CRITICAL OUTCOME Not reported	not in a randomized way · Double blinded · High drop-out rate, some due to adverse events

6VRAAG 5E: RESTLESS LEGS

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Aurora 2012	· SR · Funding/CoI: no CoI · Search date: June2011 · Databases: MEDLINE · Study designs: RCTs · N included studies: 126 (12 studies on dialysis/ ESRD patients)	· Eligibility criteria: adults diagnosed with restless legs syndrome	Several treatments, both dopaminergic and others vs. Control	Restless legs symptoms: CRITICAL OUTCOME no MA-results for dialysis/ESRD patients Quality of life: CRITICAL OUTCOME no MA-results for dialysis/ESRD patients	· Low quality: Medline only, no explicit reporting of quality appraisal, unclear if two reviewers were used · Included RCTs: Thorp (2001), Micozkadioglu (2004), Sloand (2004), Pellecchia (2004), Miranda (2004), Sakkas (2008), Giannaki (2010), Trenkwalder (1995), Sandyk (1987), Walker (1996), Read (1981), Bennett (1994)
De Oliveira 2010	· SR · Funding/CoI: nothing to disclose · Search date: 31 January 2009 · Databases: Cochrane Library, Medline, Pubmed, Lilacs, Embase, Scielo. · Study designs: Randomized/Quasi	· Eligibility criteria: Patients with ESRD and RLS (N=111 patients) · Patient characteristics: o Age mean:55years o Male: 59%	All therapy-treatments used for uremic RLS vs. Placebo, no intervention, other drugs	Restless legs symptoms: CRITICAL OUTCOME no MA-results Quality of life: CRITICAL OUTCOME no MA-results	· Good quality review · Included RCTs: Walker (1996). Trenkwalder (1995), Ausserwinkler (1989), Pieta (1998), Sloand (2004), Thorp (2001)

Trenkwalder 2008	-randomized controlled trials · N included studies: 6 · SR · Funding/CoI: Several authors have relations to pharmaceutical companies · Search date: until December 2006 · Databases: Medline, Pubmed, Embase, Cochrane Central Register of Controlled Trials · Study designs: All studies · N included studies: ?	· Eligibility criteria: Patients with restless legs syndrome	Pharmaceutically based treatments for RLS	Restless legs symptoms: CRITICAL OUTCOME no MA-results Quality of life: CRITICAL OUTCOME no MA-results	· Low quality: no explicit reporting of quality appraisal, unclear if two reviewers were used · Included RCTs: Sloand (2004), Collado-Seidel (1999), Micozkadioglu (2004),Thorp (2001)

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Giannaki 2013	· Design: randomized controlled trial · Funding/CoI: no competing interests · Setting: Hospital of Larissa, Greece · Sample size: N=32 · Duration: 6 months	· Eligibility criteria: hemodialysis patients with restless leg syndrome · *A priori* patient characteristics: intervention vs. control o Age mean: 56years o Male 69%	Exercise training for 6 months (n=16) vs. Ropinirole 0.25 mg/d (n=8) vs. Placebo (n=8)	Restless legs symptoms: CRITICAL OUTCOME IRLS: Exercise-Baseline: 25.14 +/-9.09 Exercise-6Months: 13.42+/-11.28 Dopamine-Baseline: 24.14+/-5.55 Dopamine-6Months: 11.57+/-7.84 Placebo-Baseline: 19.71+/-7.49 Placebo-6Months: 18.57+/-10.65 Quality of life: CRITICAL OUTCOME SF-36 MCS score: Exercise-Baseline: 61.1+/-22.0 Exercise-6Months: 70.4+/-18.7	Level of evidence: unclear risk of bias · Randomization method and allocation concealment not described · Double blinding for medication groups · 3 patients lost-to-follow-up, and not included in analysis (1 in each group)

				Dopamine-Baseline: 39.1+/-23.8 Dopamine-6Months: 63.0+/-17.0 Placebo-Baseline: 68.1+/-19.1 Placebo-6Months: 65.0+/-21.9 SF-36 PCS score: Exercise-Baseline: 64.9+/-18.6 Exercise-6Months: 76.4+/-15.6 Dopamine-Baseline: 48.7+/-21.0 Dopamine-6Months: 68.8+/-19.2 Placebo-Baseline: 64.4+/-22.5 Placebo-6Months: 70.5+/-26.5	
Razazian 2015	· Design: Randomized clinical trial · Funding/CoI: no CoI · Setting: Kermanshah University, Iran · Sample size: N=82 · Duration: 4 weeks	· Eligibility criteria: Hemodialysis patients with restless legs · *A priori* patient characteristics: intervention vs. control o Age mean: 55.3 years o Male 56 %	Gabapentin (n=42) vs. Levodopa-c (n=40)	<u>Restless legs symptoms</u>: CRITICAL OUTCOME Pre-IRLS Gabapentin: 27.8 +/- 4.6 Levodopa-c: 27.6 +/- 4.4 Post-IRLS Gabapentin: 10.4 +/- 5.7 Levodopa-c: 14.2 +/- 7.6 <u>Quality of life</u>: CRITICAL OUTCOME Not reported	Level of evidence: unclear risk of bias · Randomization method and allocation concealment not described · 5 drop-outs (2 and 3 respectively)

7VRAAG 5G: DEPRESSION

Systematic reviews

Study ID	Method	Patient characteristics	Intervention(s)	Results	Critical appraisal of review quality
Nagler 2012	· SR · Funding/CoI: None declared · Search date: December 2011 · Databases:Cochrane Renal Group Specialised Register, CENTRAL, MEDLINE, EMBASE, PsychINFO, International Pharmaceutical Abstracts , Clinical trial registries · Study designs:RCTs and observational studies · N included studies: 28	· Eligibility criteria: Adults or children with chronic kidney disease stages 3-5	Antidepressant drug treatment	Depression: CRITICAL OUTCOME no MA-results Quality of life: IMPORTANT OUTCOME no MA-results	· Moderate quality: only one reviewer, inclusions and exclusions not transparent · Included RCTs: Pervin (2006), Blumenfield (1997)
Rabindranath 2005a	· SR · Funding/CoI: Funded by National Kidney Fund (UK) · Search date: March 2006 · Databases: Medline, Embase, Psychinfo, The Cochrane Library · Study designs: RCTs · N included studies: 1	· Eligibility criteria: Patients with ESRD on chronic dialysis and older than 18 years · Patient characteristics: o Age range: 18-70 years	Antidepressants vs. placebo or no treatment or a comparison of drugs	Depression: CRITICAL OUTCOME no MA-results Quality of life: IMPORTANT OUTCOME no MA-results	· High quality · Included RCTs: Blumenfield (1997)
Rabindranath 2005b	· SR · Funding/CoI: funded by the National Kidney Research Fund · Search date: October 2003 · Databases: Medline, Embase, PsycInfo, The Cochrane Library · Study designs: RCTs · N included studies: 0	· Eligibility criteria: patients who are dialysed for ESRD older than 18 years diagnosed with depression	Psychosocial interventions vs. control or no intervention	Depression: CRITICAL OUTCOME no MA-results Quality of life: IMPORTANT OUTCOME no MA-results	· High quality · Included RCTs: -

Primaire studies

Study ID	Method	Patient characteristics	Interventions	Results	Critical appraisal of study quality
Cukor 2014	· Design: Randomized crossover trial · Funding/CoI: Supported by National Institute of Health	· Eligibility criteria: Haemodialysis patients with ESRD and with elevated depressive affect	Cognitive behavioural therapy first (n=33) vs.	Depression: CRITICAL OUTCOME BDI-II: Treatment first: baseline 24.7 (9.8), after treatment 11.7 (9.8), after 2nd phase 9.9 (8.5)	Level of evidence: high risk of bias · Randomization method and allocation

(K23DK076980) /none · Setting: 2 dialysis units in Brooklyn, USA · Sample size: N=65 · Duration: 6 months	· *A priori* patient characteristics: intervention vs. control o Male 27% o Mean dialysis treatment: 50 months	Wait-list control first (n=26)	Wait-list first: baseline 21.9 (8.9), after wait-list 14.5 (8.5), after treatment 9.1 (6.5) Model-estimated mean change score during treatment: treatment first -11.7 (SD 1.5; p<0.001), wait-list first -4.8 (SD 1.4; p<0.001) Model-estimated mean change score during wait-list: untreated group -6.7 (1.7; p<0.001) HAM-D: Treatment first: baseline 15.7 (6.8), after treatment 6.5 (6.8), after 2nd phase 6.7 (5.8) Wait-list first: baseline 12.9 (5.3), after wait-list 10.9 (5.4), after treatment 5.0 (4.3) Model-estimated mean change score during treatment: treatment first -9.1 (SD 1.1; p<0.001), wait-list first -5.9 (SD 1.1; p<0.001) Model-estimated mean change score during wait-list: untreated group -1.9 (1.2; p<0.17) SCID: Treatment first: baseline 54, after treatment 5, after 2nd phase 10 Wait-list first: baseline 33, after wait-list 31, after treatment 4 <u>Quality of life</u>: IMPORTANT OUTCOME KDQOL: Treatment first: Baseline: 99.5 (27.9) Treatment: 115.3 (25.5) Follow-up: 118.3 (27.7) Wait-list: Baseline: 105.1 (23.7) Wait-list: 110.6 (25.1) Delay: 119.7 (24.7)	concealment not described · Patients not blinded, but blinded assessors · 6 drop-outs, no ITT analysis

Duarte 2009	· Design: Randomized clinical trial · Funding/CoI: project supported by Fundacao de Amparo a Pesquisa do Estado de Sao Paulo (04/08710-8)./ authors declare no competing interests · Setting: 2 dialysis units in Brasil · Sample size: N=85 · Duration: 9 months	· Eligibility criteria: Patients with ESRD receiving outpatient hemodialysis treatment · *A priori* patient characteristics: intervention vs. control o Age mean: 53 years o Male 41% o Diabetes 34%	Cognitive-behavioural group therapy (n=41) vs. Control (n=44)	Pooled estimated treatment effect: 11.7 (2.0) <u>Depression</u>: CRITICAL OUTCOME BDI Cognitive Subscale Intervention: Baseline : 13.7±7.1 After 3 mths: 7.1±5.9 After 9 mths: 6.3±7.1 Control: Baseline : 16.7±7.9 After 3 mths: 12.1±6.4 After 9 mths: 10.8±7.1 (intervention vs. control at 3 months: p<0.001) BDI Somatic Subscale Intervention: Baseline : 10.6±4.0 After 3 mths: 7.0±3.8 After 9 mths: 6.1±3.2 Control: Baseline : 10.6±4.1 After 3 mths: 9.1±3.8 After 9 mths: 9.5±3.9 (intervention vs. control at 3 months: p=0.012) BDI total Intervention: Baseline : 24.2±9.7 After 3 mths: 14.1±8.7 After 9 mths: 10.8±8.8 Control: Baseline : 27.3±10.7 After 3 mths: 21.2±9.1 After 9 mths: 17.6±11.2 (intervention vs. control at 3 months: p=0.001) Major depression module MINI: Intervention: Baseline : 6.4±1.3 After 3 mths: 1.9±2.8 After 9 mths: 2.0±3.1 Control: Baseline : 6.4±1.2 After 3 mths: 4.3±2.9 After 9 mths: 3.5±2.9 (intervention vs. control at 3 months: p<0.001) Suicide Risk module MINI:	Level of evidence: high risk of bias · Central randomization · Patients not blinded, but blinded assessors · No ITT analysis

Intervention:
Baseline : 2.2±5.1
After 3 mths: 1.2±4.2
After 9 mths: 0.6±1.2

Control:
Baseline : 1.4±3.5
After 3 mths: 0.7±1.9
After 9 mths: 0.6±2.0
(intervention vs. control at 3 months: p=0.433)

Quality of life:
IMPORTANT OUTCOME
Burden of kidney disease:
Intervention:
Baseline : 28.7±22.4
After 3 mths: 43.6±27.1
After 9 mths: 43.2±28.8

Control:
Baseline : 22.9±22.8
After 3 mths: 27.0±27.3
After 9 mths: 27.3±26.8
(intervention vs. control at 3 months: p=0.004)

Cognitive function:
Intervention:
Baseline : 64.4±23.0
After 3 mths: 77.2±25.1
After 9 mths: 81.1±20.5

Control:
Baseline : 69.1±24.7
After 3 mths: 71.4±26.3
After 9 mths: 76.0±23.8
(intervention vs. control at 3 months: p=0.261)

Quality of social interaction:
Intervention:
Baseline : 65.2±23.3
After 3 mths: 81.1±19.3
After 9 mths: 81.7±18.7

Control:
Baseline : 70.0±22.2
After 3 mths: 66.5±22.3
After 9 mths: 71.2±24.4
(intervention vs. control at 3 months: p=0.002)

Sleep:
Intervention:

				Baseline : 58.1±21.5 After 3 mths: 67.6±23.0 After 9 mths: 73.1±19.1 Control: Baseline : 58.4±18.7 After 3 mths: 58.4±17.8 After 9 mths: 62.8±19.3 (intervention vs. control at 3 months: p=0.034) Mental component summary: Intervention: Baseline : 37.4±11.6 After 3 mths: 47.3±12.1 After 9 mths: 46.3±12.3 Control: Baseline : 41.1±11.2 After 3 mths: 39.3±11.9 After 9 mths: 38.6±11.7 (intervention vs. control at 3 months: p=0.002)	
Hosseini 2012	· Design: Randomized controlled trial · Funding/CoI: supported by grant from Mazandaran University of Medical Sciences / none declared · Setting: Imam Khomeini Hospital, Iran · Sample size: N=44 · Duration: 3 months	· Eligibility criteria: Hemodialysis patients with ESRD · *A priori* patient characteristics: intervention vs. control o Age mean: 50.5 years o Male 42%	Citalopram (n=22) vs. psychological training (n=22)	<u>Depression</u>: CRITICAL OUTCOME HADS Depression Psychol. Training: Pretest : 9.58 ± 3.47 Posttest : 7.33 ± 4.80 Citalopram: Pretest : 9.42 ± 3.11 Posttest : 6.26 ± 4.18 <u>Quality of life</u>: IMPORTANT OUTCOME Not reported	Level of evidence: high risk of bias · Randomization method and allocation concealment not described · No blinding · No ITT analysis
Erdley 2014	· Design: Randomized controlled trial · Funding/CoI: without funding/ no CoI · Setting: Geisinger medical center, USA · Sample size: N=36 · Duration: 6 weeks	· Eligibility criteria: haemodialysis patients with age 60 or older · *A priori* patient characteristics: intervention vs. control o Age mean: 74 years o Male 64% o Diabetic 67%	Problem-solving therapy (n=15) vs. Usual care (n=18)	<u>Depression</u>: CRITICAL OUTCOME BDI PS-therapy: Baseline: 15.7 (8.0) 6 weeks : 9.3 (3.1) Usual care : Baseline: 10.7 (6) 6 weeks : 11.3 (7.4) (PS-therapy vs. Usual care, p=0.6) PHQ-9 PS-therapy: Baseline: 10.5 (4.9) 6 weeks : 3.3 (1.9) Usual care : Baseline: 6.1 (4.1)	Level of evidence: high risk of bias · Allocation concealment not described · No blinding

6 weeks : 5.83 (4.2) (PS-therapy vs. Usual care, p=0.1)

Quality of life: IMPORTANT OUTCOME
Not reported

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