Bijlage Evidence tabellen en GRADE profielen

Evidence tabellen en GRADE profielen behorende bij de uitgangsvragen die via de GRADE methodiek zijn uitgewerkt.

Advance care planning

Wat zijn de (on)gunstige effecten van Advance Care Planning ten opzichte van geen Advance Care Planning bij mensen die palliatieve zorg ontvangen?

Patients	Mensen die palliatieve zorg krijgen of zorgverleners die palliatieve zorg verlenen
Intervention	Advance Care Planning
Control	Geen Advance Care Planning
Outcomes	Patiënttevredenheid, kwaliteit van leven, kwaliteit van leven van mantelzorger, belasting van de patiënt (in tijd en ervaring), belasting van de mantelzorger (in tijd en ervaring), belasting van de zorgverlener (in tijd en ervaring), kosten, kwaliteit van sterven

Tabellen karakteristieken geselecteerde studies – Systematische review

Kernick, 2018

Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
A. Wong (2016) B. Rogers (2017) C. Denvir (2016) D. Brännström (2014) E. Schellinger (2011) F. Johnson (2012) G. McAlister (2015) H. Butler (2015)	Type of study: RCTs, quasi-experimental studies, single-arm observational studies Search date: 23 March 2017 Number of included studies: N= 8 Country A. Hong Kong B. US C. UK D. Sweden E. US F. UK G. Canada H. US Source of funding: None Inclusion criteria: - Population: heart failure	N total at baseline: A. 84 B. 150 C. 100 D. 72 E. 1,894 F. 126 G. 8,339 H. 3,592 Age, years (mean): A. 78.3 B. 71 C. 81 D. 81.9 E. 81% > 65 years F. 78 G. 77 H. 63.9 Disease category: A. NHYA III-IV: 89.3% B. NHYA III-IV: 88% C. No NHYA data D. NHYA III-IV: 100% E. No NHYA data F. NHYA II-IV: 100%	A. ACP involves discussion of EOL issues and treatment preferences B. Multicomponent, interdisciplinary intervention including ACP education by nurse practitioner C. Future Care Planning: an initial, one hour semi-structured meeting with the trial cardiologist and the trial nurse, followed by 2 home visits over 12 weeks by the trial nurse D. Integrated interdisciplinary home-based model, APC based on European Society of Cardiology principles E. In-depth planning discussion for patients, their chosen health agent and/or family. F. Assess both services for recognition of advanced heart failure close to death, evidence of end of life care in relation to place of death G. Do Not Resuscitate patients H. Advance directive patients	A. Usual Care B. Usual Care C. Usual Care, delayed FCP D. Usual Care E. Not stated F. National data. G. CPR patients H. No advance directive patients	Length of follow-up: A. 12 weeks B. 4 years C. 24 weeks D. 6 months E. 2 years F. 12 months G. Not reported H. 5 years Loss-to-follow-up: Not reported.	Quality of Life / Symptoms: - ACP improved QOL in multiple studies. Rogers (2017) found a clinically and significantly improved Kansas City Cardiomyopathy Questionnaire score (9.49 points, 95%CI 0.94,18.05, p=0.03). Brännström (2014) found a better QOL summary score in the ACP group (49.5 vs 61.3, p=0.04). Wong (2016) found an improvement favouring ACP in the McGill QOL score (6.16 vs 7.37, p<0.01) and total Chronic Heart Failure Questionnaire (4.47 vs 5.26, p<0.01). - Patient reported symptoms improved in three RCTs; Wong (2016) found improvement in the	The four RCTs were of moderate quality. The quality of the observational studies was reduced by risk of information bias, insufficient follow-up and the impact of potential confounders. NHYA= New York Heart Association

	- Intervention: ACP/directive, living will, medical directive, resuscitation order/plan, end-of-life order/plan, anticipatory care plan, medical treatment plan - Comparator: usual care - Outcome: hospital (re)admissions, health utilisation, place of death, death in preferred location, patient and family satisfaction Exclusion criteria: Studies involving paediatric, cardiac transplant and left ventricular devices	G. NHYA II-IV: 100% H. No NHYA data				Edmonton Symptom Assessment Scale summary score (73% vs 41.4%, p<0.05) and Chronic Heart Failure Questionnaire dyspnoea and mastery domains (dyspnoea 4.89 vs 5.82, p<0.01; mastery 4.64 vs 5.36, p<0.01); Brännström (2014) showed that NYHA class improved by 36% in the ACP group compared to 9% in UC (p=0.015); Rogers (2017) reported improved scores of depression (-1.94, p=0.02), anxiety (-1.83, p=0.048) and spiritual wellbeing (3.98, p=0.027). Patient burdening: - Four studies showed a reduction in hospital admission/readmission, including two of the larger RCTs; mean average readmission in the ACP group at 6 months of 0.42 compared to 1.47 in the control group (p<0.09) (Brännström 2014) and reduced RR of readmission at 12 weeks in the ACP group (0.55, p=0.009) (Wong 2016). - Fewer nights spent in hospital in the intervention group (8.6 vs 11.8, p=0.01) (Denvir 2016). - Increased hospice use in the ACP groups (Denvir 2016; McAlister 2015; Butler 2015). Quality of death: Two studies reported increased deaths in preferred location and	

						increased out-of-hospital deaths with ACP than known baseline estimates (Denvir 2016; Johnson 2012).	

Lim, 2016							
Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
A. Kirchhoff (2012) B. Perry (2005)	Type of study: RCTs and quasi-RCTs Search date: 27 June 2016 Number of included studies: N= 2 Country A. USA B. USA Source of funding: None Inclusion criteria: Studies with people with end-stage kidney disease (ESKD) Exclusion criteria: Studies with people with clinically-diagnosed mental illness, and people with ESKD not on haemodialysis	N total at baseline: A. 313 B. 203 Age, years (mean): A. Intervention group: 71.4; control group 70.6 B. 44 Disease category: A. Coronary heart failure (n=179), ESKD (n=134) B. Patients receiving haemodialysis	A. Patient Centred-Advance Care Planning: an interview with patient and a surrogate, delivered by a trained facilitator and lasting 1 to 1.5 hours. B. Peer mentoring (group 1), printed material (group 2)	A. Usual Care B. Usual Care	Length of follow-up: A. Not reported B. 2-4 months post intervention Loss-to-follow-up: Not reported.	Both studies did not report on any of the pre-specified primary or secondary outcomes. Quality of death: - Patient Centred-Advance Care led to higher rates of concordance between patients' preferences and end-of-life care among intervention group participants, including cardiopulmonary arrest. - The intervention resulted in a higher proportion of participants completing an advance directive or expressing a desire to complete one.	

Lin, 2019							
Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments

A. El-Jawahri (2010) B. Epstein (2013) C. Volandes (2013) D. Jones (2011) E. Stein (2013) F. Clayton (2007) G. Rodenbach (2017) H. Epstein (2017) I. Walczak (2017)	Type of study: RCTs Search date: 31 March 2017 Number of included studies: N=9 Country A. USA B. USA C. USA D. UK E. Australia F. Australia G. USA H. USA I. Australia Source of funding: None Inclusion criteria: All RCTs testing an ACP intervention for advanced cancer patients in the last 12 months of their life Exclusion criteria: Paediatric patients, studies focusing on interventions for promoting ACP completion rates or reporting non-primary data.	N total at baseline: A. 50 B. 56 C. 150 D. 77 E. 120 F. 174 G. 180 H. 265 I. 110 Age: Not reported. Disease category: A. Malignant giloma B. Progressive pancreas or hepatobiliary cancer C. Lung, colon, or breast cancer (advanced) D. Bowel, prostrate, or gynaecological cancer (recurrent, advanced) E. Colorectal, lung, other cancer (metastatic) F. Gastrointestinal, lung, other cancer (advanced) G. Non-hematologic cancer (advanced) H. Stage III or IV cancer I. Lung, prostate, or bowel/anus cancer (advanced)	A. 6-min video with verbal narrative of goals-of-care B. 30min video decision aids with image of cardiopulmonary resuscitation and mechanical ventilation C. 3-min video depicting a patient on a ventilator and cardiopulmonary resuscitation being performed on a simulated patient D. Meeting with a trained medical staff using a checklist of topic domains E. Semi-structured discussion with a psychologist using a pamphlet called 'Living with Advanced Cancer' F. Provision of a question prompt list to patients before consultation with physicians G. Communication coaching with a question prompt list for patients before the consultation with oncologist H. Values and options in cancer care (VOICE) I. Communication support programme	A. Verbal narrative of goals-of-care B. Verbal narrative about cardiopulmonary resuscitation and mechanical ventilation C. Verbal narrative describing cardiopulmonary resuscitation D. Usual care E. Usual care F. Standard consultation G. Usual care H. Usual care I. Usual care	Length of follow-up: Not reported. Loss-to-follow-up: Not reported.	Quality of life / Symptoms: Studies showed no difference in patients' depression and anxiety, or quality of life.	The systematic review was mainly focused on the conceptual models of ACP.

Brinkman-Stoppelenburg, 2014							
Included studies in the review	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
For all included studies, see reference list in the review.	Type of study: Empirical studies on ACP. Experimental (n=6) and	Number of patients in study: 0-100: n=13 101-500: n=35 501-1000: n=16 >1000: n=49	Type of ACP in study: Do Not Resuscitate order: n=52 Do Not Hospitalize order: n=16 Advance directive/living will/durable power of attorney: n=45	Not reported	Length of follow-up: Not reported Loss-to-follow-up: Not reported	Quality of life/quality of care/satisfaction: Decreased (n=1), increased (n=5), mixed results (n=1), no difference (n=12)	

	observational (n=107) Search date: December 2012 Number of included studies: N= 113 Country US (n=91) Canada (n=5) Other (n=17) Source of funding: No funding Inclusion criteria: - Studies concerning quantitative research - Reporting on: effects on medical treatment in the last phase of life, effects on quality of life and patients' and families' satisfaction with care, effects on patients' and families' prevalence and/or severity of symptoms - Both intervention and observational studies with control group - Studies published on paper in English between January 2000 and December 2012 Exclusion criteria: - Studies in which ACP is only part of a more complex intervention	Setting: Community (n=9) Nursing home (n=37) Hospital (n=37) Hospital ICU (n=18) Outpatient clinic (n=1) Mixed (n=12)	Complex ACP intervention: n=20			Patients' and families' symptoms: Decreased (n=5), mixed results (n=1), no difference (n=7) Life-sustaining treatment: Decreased (n=28), increased (n=3), mixed results (n=7), no difference (n=13) Hospice and/or palliative care: Increased (n=18), mixed results (n=3), no difference (n=2) Hospitalization/length of stay: Decreased (n=21), Increased (n=5), mixed result (n=1), no difference (n=8) ICU admission/length of stay: Decreased (n=2), increased (n=3), no difference (n=3) Cardiopulmonary resuscitation: Decreased (n=4), no difference (n=1) Compliance with patients' end of life wishes: Increased (n=3), no difference (n=3)	

	- Studies on children - Studies on psychiatric patients - Studies on hypothetical situations - Studies solely on effects on costs of care, on patients' preferences or on completion of ACP documents						

Tabellen karakteristieken geselecteerde studies – RCT's en observationeel onderzoek

Duenk, 2017

Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: pragmatic cluster controlled trial Setting: general hospitals Country: the Netherlands Source of funding: the Netherlands Organization for Health Research and Development-ZonMw	Inclusion criteria: - Acute exacerbation of COPD - Above 18 years of age - Poor prognosis as defined by meeting two or more of the 11 indicators for poor prognosis Exclusion criteria: - Unable to speak Dutch - Severe cognitive disorder - Already treated by a specialized palliative care team (SPCT) N total at baseline: Intervention: 90 Control: 138 Important prognostic factors: age ± SD: I: 68.67 (9.08) C: 68.45 (9.54) Sex: I: 51.1% M C: 46.4% M In the intervention group, compared to the control group, more patients had severe dyspnea scores, were living alone, and were suffering from congestive heart failure. No substantial differences were seen between groups on baseline outcome measures.	Additional proactive palliative care from a specialized palliative care team (SPCT). Patients had a first consultation with the SPCT during the initial hospitalization, or the latest within 1 week after hospital discharge. Thereafter, the SPCT had monthly meetings with the patient in the outpatient setting for 1 year or until death.	Usual care	Length of follow-up: 12 months Loss-to-follow: Not reported Incomplete outcome data: Intervention: 46 (51%) Reasons not reported Control: 82 (59%) Reasons not reported	Quality of Life / Symptoms: - Measured with the St George Respiratory Questionnaire (SGRQ) at 3, 6, 9 and 12 months. No significant differences between both groups at all timepoints for the SGRQ total score and the symptoms and activity subscales. There was a significant difference between groups in the change scores of the impact subscale at 6 months (-5.73 vs 0.86, p=0.04). - There were no differences in QoL as measured with the McGill Quality of Life questionnaire. - There were no differences in anxiety or depression during follow-up. Patient burdening: No differences in readmission rates.	

Lyon, 2014

Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: RCT Setting: Through oncology physicians	Inclusion criteria: - Adolescents 14-21 years - Patient aware of cancer diagnosis	Lyon Family-Centered Advance Care Planning (3 sessions): 1. the Lyon Family-Centered Advance Care Planning Survey,	An ACP education brochure.	Length of follow-up: 3 months Loss-to-follow-up: Intervention:	Quality of life / Symptoms: - No differences between groups as measured with the Pediatric Quality of	

Country: USA Source of funding: American Cancer Society and Chidren's National Medical Center	- Legal guardian available or family member who was at least 21 years of age Exclusion criteria: - Severe depression - Homicidality, suicidality - Psychosis - Being in foster care - Severe developmental delays - Impaired mental status N total at baseline: Intervention: 17 Control: 13 Important prognostic factors: age: I: 16.5 C: 16.0 Sex: I: 71% M C: 46% M There were no statistically significant differences in baseline characteristics.	which engage the participant in end of life questions 2. the Respecting Choices Disease Specific Advance Care Planning Interview 3. the Five Wishes, a legal document that helps people express how they want to be treated if they are seriously ill and unable to speak for themselves.		1 (6%) Control: 1 (8%) Reasons: One patient died and one was too ill to participate. Incomplete outcome data: None.	Life Inventory 4.0 (ß 3.1, p=0.61). - No difference in reported Beck Anxiety Inventory change (ß -3.1, p=0.35) between groups. Lower Beck Depression Inventory scores over time in the intervention group (ß -5.4, p=0.03). Patient burdening: The intervention group had higher scores on the Spiritual Well-Being Scale of the Functional Assessment of Chronic Illness Therapy (ß 8.1, p=0.03) Caregiver burdening: Anxiety scores dropped in the control group (ß -1.2, p=0.03) but increased in the intervention group (ß -1.2 + 2.0 =.8).	

Johnson, 2018						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: RCT Setting: Outpatient and inpatient departments of oncology centres Country: Australia Source of funding: The National Health and Medical Research Council	Inclusion criteria: - Age 18 years or older - Diagnosis of incurable cancer - Expected survival time of 3-12 months - Prior systemic anticancer therapy - Ability to complete questionnaires and have an ACP conversation in English Exclusion criteria: - Previously completed formal ACP - Patients without an adult family member/friend (FM) to participate in the trial with them	The ACP intervention is delivered in a structured meeting between the patient, their FM and the ACP facilitator, conducted within 2 weeks of study enrolment. The ACP facilitator reviewed the patient's medical notes and met with the patient's oncologist prior to intervention delivery to discuss medical goals of care, appropriate treatment options and the patient's prognosis.	Usual Care	Length of follow-up: Max. 3 years Loss-to-follow-up: Intervention: 37 (35.6%) Reasons: withdrew (n=16), died before first follow-up (n=17), missed session (n=4) Control: 27 (26.0%) Reasons: withdrew (n=5), died before first follow-up (n=19), missed session (n=3) Incomplete outcome data: Intervention: 51 (49.0%)	Patient satisfaction: No difference in patient satisfaction with care or FM satisfaction with care. Patient burdening: Concordance between documented preferences and end of life care received was higher in the ACP arm for CPR (75% vs 23%, p<0.01), ICU admissions (28% vs 11%, p<0.01), and ventilation (49% vs 12%, p<0.01). There was no difference in concordance between chemotherapy received in last 4 week,	

	N total at baseline: Intervention: 104 Control: 104 Important prognostic factors: age: I: 66 years C: 65 years Sex: I: 53.9% M C: 52.9% M Baseline demographic and clinical variables were similar between the arms.			Reasons not reported. Control: 41 (39.4%) Reasons not reported.	surgery, 'other' significant interventions in the last 2 weeks, or other goals of care. Caregiver burdening: There was no evidence of differences between groups in FM stress, distress, physical well being before or after death. There was greater improvement in mental well being from baseline to the bereavement interview in the usual care group (p<0.01). Quality of death: Concordance between documented preferences and place of death (49% vs 26%, p<0.01) was higher in the ACP arm.	

DeCourcey, 2019						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: Cross-sectional survey Setting: Bereaved parents of deceased children Country: USA Source of funding: Agency for Healthcare Research and Quality	Inclusion criteria: - Bereaved parents of children, adolescents or young adults with complex chronic conditions - English-speaking - resided in North America - At least 12 months elapsed after their child's death - child had received care at the Boston Children's Hospital and died between January 2006 and December 2015 Exclusion criteria: - None N total at baseline: Intervention: 70 Control: 37 Important prognostic factors: age: I: 47 years	ACP communication as measured through the survey.	No ACP communication.	Length of follow-up: Not applicable Loss-to-follow-up: Not applicable Incomplete outcome data: Not applicable	Quality of life: Increased perceived good to excellent quality of life during EOL care in the ACP group (aOR 3.59, 95%CI 1.23,10.37). Caregiver burdening: - Increased Parental preparedness for circumstances during the last 2 days of child's life in the ACP group (aOR 3.78, 95%CI 1.33,10.77). - Increased ability to plan child's location of death in ACP group (aOR 2.93, 95%CI 1.06,8.07). - No difference in decisional regret (aOR 0.52, 95%CI 0.19,1.41).	

	C: 48.5 years Sex: I: 15% M C: 24% M There were no differences in demographics of parents whose children had ACP versus those without. Children whose parents reported ACP were more likely to have resuscitation orders (78% vs 34%, p<0.01), palliative care involvement (94% vs 50%, p<0.01), and less likely to have intensive life-sustaining therapies at end of life (18% vs 42%, p<0.01).					

Peltier, 2017						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: Retrospective review of prospectively collected observational data Setting: Tertiary oncology setting Country: USA Source of funding: Not reported.	Inclusion criteria: - Patients referred to Surgical or Medical Oncology - Met a certified facilitator - Died following the implementation of the program Exclusion criteria: None reported. N total at baseline: Intervention: 24 Control: 45 Important prognostic factors: Sex: I: 41.7% M C: 57.8% M Patients enrolled in the intervention program were proportionally more likely to belong to a racial minority (20% vs 83%).	Honoring Choices Wisconsin: a state-wide initiative designed to increase advocacy and education around ACP, utilizing a trained facilitator framework modelled after “Respecting Choices”.	Usual care	Length of follow-up: 4 months Loss-to-follow-up: Not applicable Incomplete outcome data: Not applicable	Patient burdening: No difference in risk to be submitted to an ICU (17.8% vs 12.5%, p=0.57) or to be admitted to a hospice (74.4% vs 79.2%, p=0.66), Quality of death: No difference in risk to die in a hospice (53.3% vs 70.8%, p=0.37).	Pilot trial with limited comparable outcome data. High risk of bias.

GRADE Evidence Profile

ACP vergeleken met gewone zorg in patiënten die palliatieve zorg ontvangen

Patiënten of populatie: Patiënten die palliatieve zorg ontvangen of zorgverleners die palliatieve zorg verlenen
Setting: Palliatieve zorg
Interventie: ACP
Controle: Gewone zorg

Uitkomsten	Impact	Aantal deelnemers (studies)	Certainty of the evidence (GRADE)
Patiënttevredenheid	Combinatie van observationele studies met enkele RCT's. De meeste studies vonden geen verschil in patiënttevredenheid, wat op veel verschillende manieren werd gemeten.	(observationele studies)	⨁◯◯◯ ZEER LAAG a,b
Kwaliteit van leven	Combinatie van observationele studies en RCT's. Er was geen uniforme methode voor het meten van kwaliteit van leven. Sommige studies toonden een verbetering in kwaliteit van leven in de interventiegroep. Andere studies vonden geen verschil tussen beide groepen. Geen van de studies vond een negatief effect van de interventie op kwaliteit van leven.	(observationele studies)	⨁◯◯◯ ZEER LAAG a,c
Belasting van de patiënt	Combinatie van observationele studies en RCT's. Belasting werd voornamelijk uitgedrukt in zorggebruik. Enkele studies toonden een afname in ziekenhuisopnames en ligduur en een toename in hospice gebruik. Anderen toonden geen verschil.	(observationele studies)	⨁◯◯◯ ZEER LAAG a,d
Belasting van de mantelzorger	Combinatie van observationele studies en RCT's. Er was geen uniforme meetmethode. Richting van de resultaten was zowel positief als negatief.	(observationele studies)	⨁◯◯◯ ZEER LAAG a,e
Kwaliteit van sterven	Combinatie van observationele studies en RCT's. Een meerderheid van studies toonde een gunstig effect van de interventie op sterfte in de gewenste locatie.	(observationele studies)	⨁◯◯◯ ZEER LAAG a

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Toelichtingen
a. Risk of bias van toepasselijke studies als hoog gescoord.
b. Geen uniforme methode voor het meten van patiënttevredenheid en inconsistentie van resultaten.
c. Geen uniforme methode voor het meten van kwaliteit van leven en inconsistentie van resultaten.
d. Geen uniforme methode voor het meten van belasting van de patiënt en inconsistentie van resultaten.
e. Geen uniforme methode voor het meten van belasting van de mantelzorger en inconsistentie van resultaten.

Screening op cognitieve functiestoornissen en gedragsverandering

Op welk moment tijdens het behandeltraject is screening op cognitieve functiestoornissen en gedragsverandering bij mensen met ALS gewenst?

Patients	Mensen met ALS
Intervention	Screening op cognitieve functiestoornissen en gedragsverandering bij diagnose ALS middels ECAS (Edinburgh Cognitive and Behavioural ALS Screen)
Control	Screening op ander moment dan bij diagnose ALS
Outcomes	Accuratesse, belasting van de patiënt (afnemen van de vragenlijst), kwaliteit van zorg, begeleiding naasten, Advance Care Planning

Wat is de waarde van vervolg screening op cognitieve functiestoornissen en gedragsverandering ten opzichte van eenmalig screenen op cognitieve achteruitgang bij mensen met ALS?

Patients	Mensen met ALS
Intervention	Meer dan één keer screenen op cognitieve functiestoornissen en gedragsverandering middels ECAS (Edinburgh Cognitive and Behavioural ALS Screen)
Control	Eenmalig screenen op cognitieve functiestoornissen en gedragsverandering
Outcomes	Accuratesse, belasting van de patiënt (afnemen van de vragenlijst), kwaliteit van zorg, begeleiding naasten, Advance Care Planning

Burkhardt, 2017

Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: observational study Setting: ALS disease center Country: Switzerland Source of funding: Schweizerischer Nationalfonds	Inclusion criteria: - Patients who fulfilled the criteria for possible, probable, probable laboratory-supported or definite ALS according to the revised El Escorial criteria Exclusion criteria: - A clinical diagnosis of dementia according to ICD-10 criteria or other relevant central neurological diseases affecting cognition - Known co-morbid frontotemporal dementia N total at baseline: 40 ALS patients	Repeated assessment with the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS) at baseline, 6 months and 12-18 months.	Not applicable.	Length of follow-up: 18 months Loss-to-follow-up: At 6 months (n=24) 9 died 2 unable to come to outpatient clinic 5 wished to dropout At 12-18 months (n=10): 3 dead 4 unable to come to outpatient clinic 7 wished to dropout	No significant difference between baseline and 6 months follow-up was present on the total ECAS score, ALS specific and ALS non-specific subscores or in any of the subdomains. Re-test of the ECAS after more than 12 months compared to initial examination at baseline showed unchanged scores in the domains, subscores, ECAS total score and test duration.	Bias towards slow progressors in patients tested after 12 months, which may not fully reflect the general ALS population.

	Important prognostic factors: Age, mean: 61.6 years Years of education: 14.1 years Mean time since symptoms onset at baseline: 44.4 months					

Crockford, 2018						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: observational study Setting: 3 research sites Country: UK, Ireland Source of funding: ALS Association, University of Edinburgh	Inclusion criteria: - Patients who fulfilled the criteria for possible, probable, or definite ALS according to the revised El Escorial criteria Exclusion criteria: - History of dyslexia, marked premorbid reading, or writing difficulties or a learning disability - Non-fluent premorbid English reading and writing abilities - History of other neurologic conditions that could affect cognition - Alcohol and drug dependencies - Severe physical disability or weakness at the time of assessment N total at baseline: 161 Important prognostic factors: Age ± SD: 61.4 years (11.6) Gender: 108 (67%) male Years of education: 13.9 years Median time since diagnosis: 3 months	Assessment with the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS) and the King's Clinical Staging System.	Not applicable.	Length of follow-up: Cross-sectional. Loss-to-follow-up: Not applicable.	A significant effect, corrected for multiple comparisons, was observed for ALS specific score (TJT = 3,804.5, p = 0.022), ECAS total score (TJT = 3,845.5, p = 0.026), and number of behavioural features (TJT = 5,295.5, p < 0.001), demonstrating lower cognitive ability and a higher number of behavior features across advancing disease stages. No significant effect was observed for ALS-nonspecific functions. Analysis of the behavioral domains showed that apathy (z = 4.00, p < 0.001), disinhibition (z = 2.65, p = 0.012), loss of sympathy or empathy (z = 3.06, p = 0.005), perseveration (z = 1.68, p = 0.036), and eating behaviors (z = 2.76, p = 0.012) were significantly related to disease stages after correction for multiple comparisons.	Patients with lower cognitive functioning and more severe behavioural abnormalities may have been less likely to participate. Thus, it may be that the present results underestimate the prevalence of neuropsychological impairment across disease stages.

Diaz, 2019						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: observational study Setting: Respiratory care unit Country: Spain Source of funding: Institute of Health Research INCLIVA, Valencian Thoracic Society	Inclusion criteria: - Probably or definitive diagnosis of ALS - Managed at the respiratory care unit - Clinically stable Exclusion criteria: - Previous pulmonary disease - Dementia - Other serious mental or neurologic illness N total at baseline: 40 Important prognostic factors: Age ± SD: 64.5 years (11.6) Gender: 22 (55%) male Mean time since symptoms onset at baseline: 65.6 months Mean time since definitive diagnosis: 56.4 months	Assessment with the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS)	Not applicable.	Length of follow-up: Cross-sectional. Loss-to-follow-up: Not applicable.	There was no relationship between cognitive-behavioral impairment and time since onset of symptoms, nor between cognitive-behavioral impairment and time since diagnosis (P=0.844 and 0.583, respectively).	Limited study sample.

Poletti, 2018						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: observational study Setting: Department of Neurology Country: Italy Source of funding: Italian Ministry of Health	Inclusion criteria: - Patients who fulfilled the criteria for possible, probable, probable laboratory-supported or definite ALS according to the revised El Escorial criteria Exclusion criteria: - In terminal stage of disease - Major comorbid medical, neurological, psychiatric, or cardio-vascular diseases N total at baseline: 168 ALS patients Important prognostic factors: Age ± SD: 62.3 years (12.1) Gender: 114 (68%) male Years of education: 11.1 years Mean time since symptoms onset at baseline: 19.0 months	Repeated assessment with the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS) at baseline, 6, 12, and 24 months.	Not applicable.	Length of follow-up: 24 months Loss-to-follow-up: At 6 months (n=48): 12 died 8 unable to come to outpatient clinic 51 out-of-region 33 lost to follow-up 16 to do At 12 months (n=18): 2 died 2 unable to come to outpatient clinic 4 out-of-region 10 lost to follow-up 5 wished to drop out 1 not administrable 8 to do At 24 months (n=5): 1 died 4 lost to follow-up 1 not administrable 7 to do	No statistically significant difference was found between any ECAS score from baseline to 6 months of follow-up. When considering the subgroup who performed the assessments at baseline, and 6 and 12 months of follow-up (n=18), results from ANOVA demonstrated a significant increase in ECAS total and ALS non-specific scores among the follow-ups.	Results indicative of potential practice effect.

Psycho-educatie

Wat zijn de (on)gunstige effecten van psycho-educatie versus standaardzorg bij mensen met ALS en cognitieve functiestoornissen of gedragsverandering?

Patients	Mensen en naasten met ALS en cognitieve functiestoornissen of gedragsverandering
Intervention	Psycho-educatie
Control	Standaard zorg
Outcomes	Kwaliteit van leven, ervaring van mensen en naasten

Er kon geen literatuur geïncludeerd worden.

Seksualiteit

Hoe vaak ervaren mensen met ALS seksualiteit- en intimiteitproblemen ten opzichte van gezonde mensen?

Patients	Mensen met ALS en hun partners
Exposure	Seksuele problemen
Control	Normale/gezonde populatie
Outcomes	Rapportage door respondenten en/of partner over het voorkomen van seksuele- en intimiteitproblemen

Wat zijn de effecten van verschillende interventies bij mensen met ALS die problemen ervaren met seksualiteit of intimiteit?

Patients	Mensen met ALS en hun partners
Exposure	Gespreksvoering of medicatie
Control	Reguliere zorg/niet bespreken
Outcomes	Rapportage door patiënt en/of partner over seksuele- en intimiteitproblemen ten gevolge van ALS, welbevinden, kwaliteit van leven

Nasimbera 2018

Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: cross-sectional case-control Setting: not reported Country: Argentina Source of funding: not reported	Inclusion criteria: patient with ALS, Parkinson's disease, multiple sclerosis, or stroke. Exclusion criteria: not reported N total at baseline: ALS patients: 9 Age-matched controls: 29 Important prognostic factors: age ± SD: ALS: 52.8 (10.8) Control: 49.4 (19.3) Sex: ALS: 44.4% male Control: 41.4% male	Sexual function was rated with the International Index Erectile Function for men and the Female Sexual Function Index for women.	Not applicable.	Not applicable.	Prevalence of (overall) sexual dysfunction: ALS: 77.8% Control: 31.0% Prevalence of severe sexual dysfunction: ALS: 55.6% Control: 20.7%	No statistical tests performed.

Kaub-Wittemer 2003						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: cross-sectional Setting: nation-wide survey Country: Germany Source of funding: not reported	Inclusion criteria: ALS patients all over Germany who were recorded on file to be ventilated (non-invasive ventilation or invasive (tracheostomy) ventilation) Exclusion criteria: None N total at baseline: 53 Important prognostic factors: age (range): NIV: 60.0 (46-74) TV: 61.6 (47-82) Sex: NIV: 72% male TV: 91% male	Reported possibility of sexual activity.	Not applicable.	Not applicable.	31% of patients with non-invasive ventilation were still able to have sex. 14% of patients with invasive ventilation reported to still be able to have sex.	

Shahbazi 2017						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: cross-sectional Setting: outpatient ALS clinic at Hospital for Special Surgery in New York Country: United States Source of funding: None	Inclusion criteria: Patient with definite or probable ALS, over the age of 18, seen at the clinic Exclusion criteria: Incomplete response on questionnaire N total at baseline: 21 Important prognostic factors: Age: 71.4% above the age of 55	11-item questionnaire asking about decrease in sexual activity due to ALS	Not applicable.	Not applicable.	52.4% of respondents reported that ALS had affected their sexual activity. 47.6% of the ALS population experienced a decrease in intercourse.	

	Sex: 35% male					

Wasner 2004						
Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Type of study: cross-sectional Setting: outpatient clinic of the Munich University Hospital Country: Germany Source of funding: Not reported	Inclusion criteria: Patients with definite or probable ALS Exclusion criteria: None N total at baseline: 33 Important prognostic factors: age (range): 56 (32-73) Sex: 57.6% male	Sexuality self-reporting scale	Not applicable.	Not applicable.	Before disease onset 94% of patients reported having sexual intercourse at least once a month. This had decreased to 76% at time of survey. Satisfaction with their sexual life decreased from 73% to 44%. 62% of the patients reported sexual problems at time of survey, compared to 19% before disease onset. Disturbances in sexual function (erection, ejaculation) were rarely mentioned.	