

## EVIDENCE TABELLEN

**UITGANGSVRAAG: Leidt advance care planning bij patiënten met hartfalen (NYHA-klasse III-IV) tot een betere kwaliteit van leven en/of hogere tevredenheid van de patiënt en de familieleden?**

Systematic reviews

| Study ID     | Method   | Patient characteristics  | Intervention(s)                                       | Results   | Critical appraisal of review quality  |
|--------------|--|--|---|---|---|
| Kirolos 2014 | <ul style="list-style-type: none"> <li>• SR</li> <li>• Funding/Control: no CoI</li> <li>• Search date: Apr 2013</li> <li>• Databases: Medline; bibliographies</li> <li>• Study designs: controlled studies, before-after studies</li> <li>• N included studies: N=6</li> </ul> | <ul style="list-style-type: none"> <li>• Eligibility criteria: studies with a well-defined intervention, that identified as outcome either hospice referral or hospice enrollment, and quantitatively compared the outcome variable between the intervention group and a control group, or between time periods before and after the intervention was implemented; patients at the end of their lives</li> </ul> | Interventions to increase hospice referral/enrollment | <p>One study evaluated ACP in heart failure patients: Schellinger 2011:</p> <ul style="list-style-type: none"> <li>• The intervention included the process of referral and enrollment into disease specific advanced care planning (DS ACP), and encompassed 5 steps: (1) referral to DS ACP (through discharge orders, direct referral from medical provider, or referral request sent by facilitators to primary care physicians; (2) referral coordinators explained to patients the ACP process and scheduled a visit with program facilitators (registered nurses, and social workers); (3) Facilitators and patients discuss end-of-life wishes; (4) facilitators include needs and wishes in the EMR; and (5) the facilitators follow-up with the patients' providers</li> <li>• DS-ACP participants were more likely to have used hospice compared to nonparticipants (56% versus 37%, <math>p=0.002</math>)</li> <li>• 94.3% of those completing the DS-ACP process, had a health directive</li> </ul> | <ul style="list-style-type: none"> <li>• Low-quality review</li> <li>• English literature only</li> </ul> |

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|--------------------|--|--|--------------------------------------|--|---|
|                    |  |  |                                      | <p>compared to 24.8% of noncompleters (p&lt;0.001)</p> |   |
| <p>Singer 2016</p> | <ul style="list-style-type: none"> <li>• SR</li> <li>• Funding/Control: supported by grant R01 NR013372 from the National Institute of Nursing Research, a Cambia Health Foundation Sojourns Award, and the California HealthCare Foundation ; no Col</li> </ul> | <ul style="list-style-type: none"> <li>• Eligibility criteria: <ul style="list-style-type: none"> <li>○ Adults at least 18 years old with advanced illness, and/or their caregivers</li> <li>○ Health service interventions addressing patient and/or caregiver quality-of-life-related elements in intervention design and/or as outcomes</li> <li>○ Cancer, heart failure and other cardiac conditions, chronic</li> </ul> </li> </ul> | <p>Palliative care interventions</p> | <p>No RCT on ACP in heart failure patients</p>         | <ul style="list-style-type: none"> <li>• High-quality review</li> </ul> |

| Study ID | Method  | Patient characteristics   | Intervention(s) | Results | Critical appraisal of review quality |
|----------|---|---|-----------------|---------|--------------------------------------|
|          | <ul style="list-style-type: none"> <li>• Search date: Jan 2015</li> <li>• Databases: Medline, Embase, PsycInfo, CDSR, Web of Science, CareSearch Palliative Care Knowledge Network Review Collection</li> <li>• Study designs: RCTs</li> <li>• N included studies: N=124</li> </ul> | <p>pulmonary disease, dementia and other neurological conditions, end-stage liver disease, or end-stage renal disease, or any advanced illness populations receiving palliative care, hospice, or end-of-life care</p> <ul style="list-style-type: none"> <li>○ Randomized controlled trials</li> <li>○ Published between January 1, 2001, and January 8, 2015</li> </ul> |                 |         |                                      |

Primaire studies

| Study ID    | Method  | Patient characteristics  | Interventions                      | Results   | Critical appraisal of study quality |
|-------------|---|--|------------------------------------|---|-------------------------------------|
| Denvir 2016 | <ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Funding/Col:</li> </ul> | <ul style="list-style-type: none"> <li>• Eligibility criteria: patients during an</li> </ul> | <p><u>Future care planning</u></p> | <p><u>Quality of life: CRITICAL OUTCOME</u></p> | <p>Level of evidence: high</p>      |

| Study ID | Method  | Patient characteristics   | Interventions  | Results   | Critical appraisal of study quality  |
|----------|---|---|--|---|--|
|          | <p>funded by Marie Curie Research (Project Grant A15867); no Col</p> <ul style="list-style-type: none"> <li>• Setting:</li> <li>• Sample size: N=50</li> <li>• Duration: enrolment Oct 2013 – Sept 2014; 24w follow-up</li> </ul> | <p>unscheduled hospital admission with heart failure and/or acute coronary syndrome based on European Society of Cardiology guidelines; predicted 12-month mortality risk of 20% or greater estimated using the Global Registry of Acute Coronary Syndrome (GRACE) score for ACS and the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) score for heart failure and patients with aortic stenosis who presented with heart failure; no dementia, prognosis &lt; 30d</p> | <p>(N=25): 3 main components, i.e. (1) initial one hour semi-structured meeting with the trial cardiologist (MD) and the trial nurse specialists involving the patient and their carer; followed by two 1 hour meetings with the trial nurse in the patient's home at 6 and 12 weeks; (2) Discussion and documentation of an agreed personal Future Care</p> | <ul style="list-style-type: none"> <li>• EQ-5D: no significant adjusted mean difference at the 12 (-0.01; 95%CI -0.16 to 0.13) or 24 week time points (-0.07; 95%CI -0.25 to 0.11)</li> </ul> <p><u>Quality of death:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Deaths: 4 vs. 3</li> <li>• Place of death: home 1 vs. 0</li> </ul> <p><u>Satisfaction of patient:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Patients appreciated the ongoing contact and communication</li> </ul> <p><u>Satisfaction of family:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• No difference in mean QoL score, anxiety/distress score and caregiver burden between the intervention groups</li> </ul> <p><u>Readmission:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• No difference in the number of unscheduled readmissions to hospital: 12</li> </ul> | <p>risk of bias</p> <ul style="list-style-type: none"> <li>• Risk of selection bias: out of 137 eligible patients, 87 were not randomised, of which 54 for unclear reasons</li> <li>• Very probably unblinded</li> <li>• No intention-to-treat analysis for some outcomes</li> </ul> |

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|----------|--|---|---|---|---|
|          |  | <p>or on palliative care register</p> <ul style="list-style-type: none"> <li>• <i>A priori</i> patient characteristics: intervention vs. control <ul style="list-style-type: none"> <li>○ Mean age: 81.9 vs. 80.2y</li> <li>○ Male : 68% vs. 52%</li> <li>○ Heart failure: 56% vs. 80%</li> </ul> </li> </ul> | <p>Plan which was sent to each patient and uploaded by the general practitioner using the electronic KIS; (3)</p> <p>Ongoing telephone support (available Monday to Friday, 9am–5pm) from the trial nurse for the 12 weeks offering advice, support and information about their healthcare and social needs</p> <p><u>Usual care</u> (N=25)</p> | <p>weeks RR 1.25 (95%CI 0.54-2.89), 6 months RR 1.23 (95%CI 0.64-2.34)</p> <ul style="list-style-type: none"> <li>• No difference in the number of unscheduled cardiovascular readmissions: 12 weeks RR 1.22 (95%CI 0.41-3.62), 6 months RR 0.83 (0.33-2.11)</li> </ul> <p><u>% CPR in end stage:</u><br/>CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Not reported</li> </ul> |   |
| Dev 2012 | <ul style="list-style-type: none"> <li>• Design: comparative observationa</li> </ul> | <ul style="list-style-type: none"> <li>• Eligibility criteria: patients hospitalised with</li> </ul>  | <p><u>DNR order</u> (N=26): do not</p>  | <p><u>Quality of life:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Time-trade-off utility:</li> </ul>   | <p>Level of evidence: high risk of bias</p> |

| Study ID | Method  | Patient characteristics   | Interventions  | Results   | Critical appraisal of study quality  |
|----------|---|---|--|---|--|
|          | <p>I study</p> <ul style="list-style-type: none"> <li>• Funding/Col: National Heart, Lung, and Blood Institute (N01-HV-98177); Duke Clinical Research Institute, Durham, NC, USA; no Col</li> <li>• Setting: multicentre, US</li> <li>• Sample size: N=375</li> <li>• Duration: inclusion Jan 2000 – Nov 2003; 1 month follow-up</li> </ul> | <p>advanced heart failure</p> <ul style="list-style-type: none"> <li>• <i>A priori</i> patient characteristics: intervention vs. control <ul style="list-style-type: none"> <li>○ Median age: 64 vs. 56y</li> <li>○ Male : 65% vs. 74%</li> </ul> </li> </ul> | <p>resuscitate</p> <p><u>Full code order</u> (N=349): 'attempt CPR' or 'attempt CPR but do not intubate'</p> | <p>median willingness to trade 12 versus 1of 24 months of theoretical survival time</p> <ul style="list-style-type: none"> <li>• Seven of 13 (54%) DNR patients expressed a desire for 'half time-trade-off' (willingness to trade <math>\geq</math>12 months of 24 month survival) compared with 60 of 279 (22%) Full Code patients (<math>p=0.007</math>, <math>X^2</math>)</li> </ul> <p><u>Quality of death:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Not reported</li> </ul> <p><u>Satisfaction of patient:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Not reported</li> </ul> <p><u>Satisfaction of family:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• Not reported</li> </ul> <p><u>Readmission:</u> CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>• DNR patients did not differ in 6-month rehospitalization rate (<math>p=0.79</math>, log-rank test)</li> </ul> <p><u>% CPR in end stage:</u> CRITICAL OUTCOME</p> | <ul style="list-style-type: none"> <li>• Patients were included in the ESCAPE randomised trial</li> <li>• Lost-to-follow-up for time-trade-off: 13 vs. 70</li> </ul> |

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|--------------|--|---|--|---|---|
|              |  |   |  | <ul style="list-style-type: none"> <li>Not reported</li> </ul>  |   |
| Dunlavy 2012 | <ul style="list-style-type: none"> <li>Design: comparative observational study</li> <li>Funding/Col: supported by grants from the National Institutes of Health (HL72435) and the Rochester Epidemiology Project from the National Institute of Aging (R01 AG034676); some authors have links with Boston Scientific</li> <li>Setting: population-based study, US</li> <li>Sample size: N=608</li> </ul> | <ul style="list-style-type: none"> <li>Eligibility criteria: patients presenting with heart failure</li> <li>A priori patient characteristics: intervention vs. control <ul style="list-style-type: none"> <li>Mean age: 79.8 vs 70y</li> <li>Male : 49% vs. 59%</li> <li>NYHA 3 or 4: 63% vs. 67%</li> </ul> </li> </ul> | <p><u>Advance directive</u> (N=249)</p> <p><u>No advance directive</u> (N=359)</p> | <p><u>Quality of life</u>: CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>Not reported</li> </ul> <p><u>Quality of death</u>: CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>Patients with AD specifying limits were less likely to receive mechanical ventilation compared with others who died without an AD or with an AD without limits (adjusted OR 0.26; 95%CI 0.06–0.88; p=0.03)</li> <li>No difference in risk of ICU care (adjusted OR 0.45; 95%CI 0.16 –1.29; p=0.14)</li> </ul> <p><u>Satisfaction of patient</u>: CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>Not reported</li> </ul> <p><u>Satisfaction of family</u>: CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>Not reported</li> </ul> <p><u>Readmission</u>: CRITICAL OUTCOME</p> <ul style="list-style-type: none"> <li>No difference in the risk of hospitalization in the last month of life in those with an</li> </ul> | <p>Level of evidence: high risk of bias</p> <ul style="list-style-type: none"> <li>No blinding</li> </ul> |

| Study ID | Method   | Patient characteristics | Interventions | Results   | Critical appraisal of study quality |
|----------|--|-------------------------|---------------|---|-------------------------------------|
|          | <ul style="list-style-type: none"> <li>Duration: inclusion Oct 2007 – Oct 2011; mean follow-up 1.8y</li> </ul> |                         |               | AD with limits compared with those without (adjusted OR 1.26; 95%CI 0.64 –2.48; p=0.51)<br><br><u>% CPR in end stage:</u><br><b>CRITICAL OUTCOME</b> <ul style="list-style-type: none"> <li>Not reported</li> </ul> |                                     |

Abbreviations: 95%CI: 95% confidence interval; ACP: advanced care plan; Col: conflicts of interest; CPR: cardiopulmonary resuscitation; MA: meta-analysis; MD: mean difference; NS: not significant; OR: odds ratio; QOL: quality of life; RCT: randomized controlled trial; RR: relative risk; SR: systematic review.

### Referenties

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Dev S, Clare RM, Felker GM, et al. Link between decisions regarding resuscitation and preferences for quality over length of life with heart failure. *Eur J Heart Fail.* 2012;14(1):45-53.

Dunlay SM, Swetz KM, Mueller PS, et al. Advance directives in community patients with heart failure. *Circ Cardiovasc Qual Outcomes.* 2012;Cardiovascular Quality & Outcomes. 5(3):283-9.

Kirolos I, Tamariz L, Schultz EA, et al. Interventions to improve hospice and palliative care referral: a systematic review. *J Palliat Med.* 2014;17(8):957-64.

Singer AE, Goebel JR, Kim YS, et al. Populations and Interventions for Palliative and End-of-Life Care: A Systematic Review. *J. Palliative Med.* 2016;19(9):995-1008