Bijlage Evidence tabellen

Vraag 1: Wat is het effect van rehydratie op de kwaliteit van leven en/of levensduur bij patiënten in de palliatieve fase met dehydratie in de palliatieve fase (exclusief de stervensfase)?

Systematische reviews

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Broadhurst 2020	• Design: systematic review • Funding: partially supported via an unrestricted project grant provided by Becton Dickinson, Canada; CoI: see article • Search date: June 2020 • Databases: PubMed, Embase, Cinahl, CDSR, Joanna Briggs Institute of Systematic Reviews, DARE • Study designs: systematic reviews • N included studies: N=26	• Eligibility criteria: reviews that assessed interventions that used subcutaneous infusion (for a duration of around 2 hours or more) as an alternate route for fluid or medication therapy • Exclusion: reviews that included other routes as comparators (such as intravenous and intraosseous) were excluded if data on subcutaneous infusions could not be extracted separately	Subcutaneous hydration and medications infusions	• See individual reviews	• Review process in duplicate • Restriction to English language • Included relevant SR: Forbat 2016, Good 2014
Forbat 2016	• Design: systematic review • Funding: internship programme of the Australian Catholic University; CoI: none • Search date: Sep 2015 • Databases: CENTRAL, Medline, EMBASE, Web of Science, CINAHL • Study designs: not specified • N included studies: N=14	• Eligibility criteria: adult patients with advanced illness • Exclusion: extravasation, acute illness, IV therapy	Subcutaneous fluids	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: not reported • Complications: not reported • Hydration status: not reported • Thirst: not reported	• Review process in duplicate • Restriction to English language • Included relevant RCT: Bruera 2013
Good 2014	• Design: systematic review	• Eligibility criteria: adult palliative care patients	Medically assisted hydration	CRITICAL OUTCOMES • Quality of life: not reported	• Review process in duplicate

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	• Funding: NIHR Directly Commissioned Cochrane Incentive Scheme 2013 Award Reference Number 13/180/04; CoI: none • Search date: Mar 2014 • Databases: CENTRAL, MEDLINE, EMBASE, CINAHL, CANCERLIT, Caresearch, Dissertation abstracts, SCIENCE CITATION INDEX • Study designs: RCTs, prospective controlled studies • N included studies: N=6, of which 3 RCTs	• Exclusion: medically assisted hydration as part of a perioperative, chemotherapy or radiotherapy regimen, or because of chemotherapy or radiotherapy adverse effects		• Lifespan: Bruera 2013: no difference in survival between the hydration and control groups • Complications: ○ Bruera 2005: no differences between the groups ○ Cerchietti 2000: one participant with erythema and pain at the puncture site in the intervention group • Hydration status: not reported • Thirst: not reported	• Included RCTs: Bruera 2013, Bruera 2005, Cerchietti 2000
Kingdon 2021	• Design: systematic review • Funding: Health Education East of England (EoE) Academic Clinical Fellowship, National Institute for Health Research (NIHR) Applied Research Collaboration EoE programme; CoI: none • Search date: Dec 2019 • Databases: Medline, CINAHL, PsycINFO all via EBSCO, Embase via OVID, Web of Science Core Collection, the Cochrane Library, ASSIA via Proquest and AMED via NHS HDAS • Study designs: not specified • N included studies: N=15, of which 3 relevant RCTs	• Eligibility criteria: adult persons in the last days of life (mean/median survival <7 days; if average survival data not reported, evidence that the majority of participants were in the last 7 days of life) • Exclusion: case series, case reports	Clinically assisted hydration	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: ○ Davies 2018: timing of death was slightly delayed in the hydration arm (4.3 vs. 2.9 days, p=0.038) ○ Cerchietti 2000: no difference in survival • Complications: not reported • Hydration status: not reported • Thirst: ○ Cerchietti 2000: no impact on experience of thirst	• Review process in duplicate • Restriction to English language • Included RCTs: Bruera 2013, Cerchietti 2000, Davies 2018

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Viola 1997	• Design: systematic review • Funding: not reported; CoI: not reported • Search date: Mar 1996 • Databases: Medline, Cinahl, Current Contents ; journals • Study designs: controlled studies • N included studies: N=6, of which no RCTs	• Eligibility criteria: human patients described as dying or terminally ill or as receiving hospice care, palliative care, or terminal care • Exclusion: survey of attitudes or opinions of caregivers only; case report; case series	Fluid therapy	Not applicable	• Review process by one researcher • Restriction to English language

Abbreviations: 95%CI: 95% confidence interval; CoI: conflict of interest; RCT: randomised controlled trial.

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Vraag 2: Wat is het effect van hypodermoclyse en rectoclyse/proctoclyse (rectale toediening van vocht) op de kwaliteit van leven, levensduur en mate van rehydratie bij patiënten in de palliatieve fase met dehydratie, vergeleken met parenterale, enterale of rectale toediening?

Systematische reviews

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Barreto Annes 2020	• Design: systematic review + meta-analysis • Funding: not reported; CoI: not reported • Search date: -2019 • Databases: PubMed, Embase, Cinahl, Lilacs • Study designs: RCTs • N included studies: N=3	• Eligibility criteria: older adults over 60 years of age submitted to SC or IV fluid administration for the treatment of mild-to-moderate dehydration • Exclusion: quasi-RCTs, crossover trials	SC vs. IV rehydration	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: not reported • Complications: ○ Phlebitis: 2 studies, N=163, RR 0.10 (95%CI 0.01-0.76) ○ Cellulitis: 2 studies, N=163, RR 1.51 (95%CI 0.21-10.94) ○ Edema: 3 studies, N=197, RR 1.65 (95%CI 0.93-2.73) ○ Erythema: 2 studies, N=130, RR 1.09 (95%CI 0.53-2.23) ○ Hyponatremia: 2 studies, N=111, RR 0.49 (95%CI 0.13-1.79) ○ Pain: 1 study, N=96, RR 0.75 (95%CI 0.28-2.0) • Hydration status: ○ Serum osmolarity at 24h: 2 studies, N=101, MD 7.64 (95%CI 1.38-13.89) ○ Serum osmolarity at 48h: 2 studies, N=101, MD 5.80 (95%CI -2.42 to 14.02) • Thirst: not reported	• Review process in duplicate • No language or date restrictions • Included relevant RCTs: Challiner 1993, Noriega 2014 (Spanish), Slesak 2003
Broadhurst 2020	• Design: systematic review • Funding: partially supported via an unrestricted project grant provided by Becton Dickinson, Canada; CoI: see article • Search date: June 2020 • Databases: PubMed, Embase, Cinahl, CDSR, Joanna Briggs Institute of Systematic Reviews, DARE • Study designs: systematic reviews • N included studies: N=26	• Eligibility criteria: reviews that assessed interventions that used subcutaneous infusion (for a duration of around 2 hours or more) as an alternate route for fluid or medication therapy • Exclusion: reviews that included other routes as comparators (such as intravenous and intraosseous) were excluded if data on subcutaneous infusions could not be extracted separately	Subcutaneous hydration and medications infusions	See individual reviews	• Selection partly in duplicate; data extraction in duplicate • Limited to English language • Included relevant SR: Forbat 2016, Turner 2004

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Danielsen 2020	• Design: systematic review + meta-analysis • Funding: funded by the Department of Clinical Medicine, Aalborg University, and the Department of Geriatric Medicine, Aalborg University Hospital; CoI: none • Search date: Nov 2019 • Databases: Medline, Embase, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science • Study designs: any • N included studies: N=29, of which 7 RCTs	• Eligibility criteria: age >65y; studies on SC hydration as an intervention with hydration as an indication for infusion; studies with IV hydration as a comparator or observational studies with no comparator • Exclusion: studies on the SC infusion of drugs, parenteral nutrition, and the relevance of hyaluronidase, or studies without patient information; cross-sectional studies and case reports without any information on adverse effects	SC hydration	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: death rate RR 1.26, 95%CI 0.25-6.34 • Complications: SC vs. IV, RR 0.69, 95%CI 0.53-0.88 (4 RCTs, N=1093) • Hydration status: ○ Serum osmolality: MD 5.75, 95%CI 0.13-11.37 (2 studies, N=101) • Thirst: not reported	• Review process in duplicate • No language or date restrictions • Included relevant (comparative) studies: Delamaire 1992 (abstract), Challiner 1994, O'Keeffe 1996, Slesak 2003, Luk 2008 (Letter), Noriega 2014 (Spanish), Esmeray 2018
Forbat 2016	• Design: systematic review • Funding: internship programme of the Australian Catholic University; CoI: none • Search date: Sep 2015 • Databases: CENTRAL, Medline, EMBASE, Web of Science, CINAHL • Study designs: not specified • N included studies: N=14	• Eligibility criteria: adult patients with advanced illness • Exclusion: extravasation, acute illness, IV therapy	Subcutaneous fluids	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: not reported • Complications: not reported • Hydration status: not reported • Thirst: not reported	• Review process in duplicate • Restriction to English language • Included relevant (comparative) studies: Dasgupta 2000, O'Keeffe 1996
Wells 2020	• Design: systematic review • Funding: Canada's federal, provincial, and territorial governments; CoI: not reported • Search date: Jan 2015 – June 2020 • Databases: Medline, Embase, Cochrane Library, CRD	• Eligibility criteria: patients in any setting (e.g. acute, long term care, or palliative care) who are frail (as noted by the authors or according to a frailty scale or index) who are at risk of or who are dehydrated; or, geriatric patients (i.e., age 65 and older) receiving long term care who are at risk of or who are dehydrated	Hypodermoclysis vs. intravenous infusion, oral rehydration, no hypodermoclysis	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: not reported • Complications: ○ Dasgupta 2000: local reactions were lower in hypodermoclysis group (p=0.02) ○ Esmeray 2018: all complications 11.1% vs. 75.6%, p=0.001; redness 40.0% vs. 74.4%, p=0.001; edema 4.4% vs. 22.2%, p=0.002; bleeding 12.2% vs. 73.3%, p=0.001 • Hydration status: not reported • Thirst: not reported	• Review process by one reviewer • Restriction to English language • Included relevant studies: Forbat 2016, Duems-Noriega 2015 (Spanish), Esmeray 2018

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
	databases, HTA websites • Study designs: all • N included studies: N=3	• Exclusion: articles were excluded if they were not clear on the population being examined or were mixed populations with no indication of how many individuals fit the inclusion criteria of this report; articles were also excluded if the patients were not in long term care (e.g., acute care or palliative care) and were not specified as being frail			

Primaire studies

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
Chanthong 2022	• Design: RCT • Funding: Division of research, Golden Jubilee Medical Center; CoI: none • Setting: single university centre, Thailand • Sample size: N=26 • Duration: unclear	• Eligibility criteria: palliative care patients aged 18 years and older who required hydration and admission to a palliative care unit • Exclusion criteria: any skin infection at the needle insertion site, edema, heart failure, volume overload, chronic kidney disease, known allergy to the administered fluid, or refusal to consent • *A priori* patient characteristics: ○ Mean age: 73.1 vs. 74.5y ○ M/F: 4/8 vs. 6/8 ○ Cancer diagnosis: 11/12 vs. 14/14 ○ Dehydration: 7/12 vs. 5/14	Hypodermoclysis (N=12) vs. IV infusion (N=14)	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: not reported • Complications: ○ Pain (NRS): day 1 4.2 (SD 2.3) vs. 0.9 (1.4), p=0.006; day 2 1.2 vs. 1.3 (p=0.75) ○ One patient switched from IV to SC infusion because of venipuncture failure ○ Phlebitis: 0% vs. 21.4% ○ Leakage: 8.3% vs. 21.4% ○ Erythema: 16.7% vs. 0% ○ No systemic side effects • Hydration status: not reported • Thirst: not reported	Level of evidence: unclear risk of bias • Random allocation was generated by the four-sealed-envelopes method • Allocation concealment unclear • Blinding unclear
Danielsen 2022	• Design: RCT • Funding: none; CoI: none • Setting: single university centre, Denmark • Sample size: N=51 • Duration: recruitment Jan 2019 – Nov 2020	• Eligibility criteria: age 65 years or older, a prescription of 1–2 litres of parenteral fluid over the next 24 hours (mild dehydration or at risk of dehydration), and admission to either acute assessment unit, an orthopaedic ward with a hip fracture, or admission to a short-term care facility • Exclusion criteria: severe dehydration (expected to need	SC fluid (N=24) vs. IV fluid (N=27)	CRITICAL OUTCOMES • Quality of life: not reported • Lifespan: death during hospitalisation 0% in both groups • Complications: ○ At least one adverse event: 28% vs. 43%, p=0.012 ○ Mean pain score for insertion (0-100): 7.3 (SD 10.4) vs. 13.0 (13.4), p=0.13 • Hydration status: serum osmolality at 24h 290 (SD 8.8) vs. 290 (11)	Level of evidence: unclear risk of bias • Data manager generated the randomisation sequence as block randomisation with unknown block sizes • Blinded study • 1 dropout in SC group vs. 4 dropouts in IV group before start of treatment

Study ID	Methods	Patient characteristics	Intervention	Results	Critical appraisal of study quality
		more than 2 L of parenteral fluid over the next 24 hours), fluid restriction, unable to give informed consent, severe general oedema, or planned discharge from the hospital or care facility within the next 24 hours • *A priori* patient characteristics: ○ Mean age: 79 vs. 83y ○ M/F: 8/16 vs. 10/17		• Thirst: not reported	• After treatment 2 dropouts in SC group

Abbreviations: 95%CI: 95% confidence interval; CoI: conflict of interest; IV: intravenous; MD: mean difference; M/F: male/female; NRS: numeric rating scale; RCT: randomised controlled trial; RR: relative risk; SC: subcutaneous; SD: standard deviation.

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