Bijlage 7 Evidence tabellen

Evidence tabellen behorende bij de oorspronkelijke uitgangsvragen die in deze richtlijn via de GRADE methodiek zijn uitgewerkt.

Uitgangsvraag kanker – warmtetherapie

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van warmtetherapie in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Warmtetherapie
Comparison: Geen warmtetherapie
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Yamamoto et al. (2011)**	• RCT • No conflicts of interest reported. • Setting: 1 hospitals in Japan. • Sample size: 31 • Median follow-up not reported. • No protocol existence reported.	• **Eligibility criteria:** Subjects were hospitalized patients with incurable cancer without inflammatory findings or leg sensory disturbances. Patients were defined as having incurable cancer according to the following criteria: Metastasis had occurred from the primary focus organ to other organs, and a complete cure was not possible. All patients had a diagnosis of incurable cancer by the doctor in charge. • **Patient characteristics:** • Age categories. 50-59, intervention: 2/9, control: 3/9. 60-69, intervention: 5/9, control 3/9. >70, intervention: 2/9, control: 3/9. • Sex categories: male, intervention: 6/9, control: 6/9. Female, intervention: 3/9, control: 3/9.	• Wrapped warm footbath versus • recumbent position for 80 minutes	**Pain (reported as VAS score)** • Intervention: 1.78 (SD: 1.82) • Control: 2.54 (SD: 2.54) • MD: -0.76 (95%-CI: -2.80 to 1.28)* **Quality of Life** • Not reported.	High risk of bias due to high amount of patients post-randomisation.	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Referenties

[1] Yamamoto K, Nagata S. Physiological and psychological evaluation of the wrapped warm footbath as a complementary nursing therapy to induce relaxation in hospitalized patients with incurable cancer: A pilot study. *Cancer nursing* 2011:185-92.10.1097/NCC.0b013e3181fe4d2d.

Uitgangsvraag kanker – massage

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van massage in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Massage
Comparison: Geen massage
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Jane** et al (2011)	• RCT • Conflicts of interest reported and none known. • Setting: 5 inpatient oncology units in a 3500-bed-capacity teaching medical center in northern Taiwan: Chang Gung Memorial Hospital (CGMH) • Sample size: 72 • Follow-up: 5 days • No protocol	• **Eligibility criteria:** • patients had to be age 18 years or older; orientated to person, place, and time; able to speak and read Chinese; radiologically diagnosed with evident bone metastases via bone scan; and reportedly experiencing at least moderate metastatic bone pain, with an intensity P4 on a 0–10 scale. • **Patient characteristics:** • Age: 49.9 years (SD:10.6) • Sex: 42% male, 58% female.	• massage therapy (n=36) versus • Social attention (n=36)	**Pain** (reported as score on present pain intensity-VAS at the fourth day. • Intervention:2.6 (SD: 2.5) • Control: 4.2 (SD:2.1) • MD: -1.60 (95%-CI: -2.67 to -0.53)* **Quality of life** • Not reported	• High risk of bias due to no blinding of patients and physical therapists	• Moderate quality of evidence due to risk of bias.
• **Kutner** et al (2008)	• RCT • No conflicts of interest reported • Setting: fifteen U.S. hospices that are members of the Population-based Palliative Care Research Network (PoPCRN) and the University of Colorado Cancer Center. • Sample size: 380 • Follow-up: 3 weeks. • Protocol: available upon request.	• **Eligibility criteria:** • English-speaking adults with advanced cancer (stage III or IV, all cancer types, any care setting) who had at least moderate pain (≥ 4 on a 0 – 10 scale) in the week prior to enrollment, anticipated life expectancy of at least three weeks and were able to consent. • **Patient characteristics:** • Age: intervention: 65.2 (SD: 14.4), control: 64.2 (SD: 14.4) • Sex (% female): intervention: 64%, control: 58%.	• Six 30-minute massage (n=188) versus • simple touch sessions (n=192)	**Pain** (reported as mean change from baseline with the MPCA questionnaire). • Intervention: -1.87 (95%-CI: -2.07 to -1.67) • Control: -0.97 (95%-CI: -1.18 to -0.76) • MD: -0.90 (95%-CI: -1.19 to -0.61) **Quality of life** (reported as mean change from baseline with the overall quality of life MQOL instrument). • Intervention: 0.36 (95%-CI: 0.04 to 0.68) • Control: 0.29 (95%-CI: -0.03.18 to 0.61) • MD: 0.08 (95%-CI: -0.37 to 0.53)	• High risk of bias due to no blinding of patients and physical therapists	• Pain: Moderate quality of evidence due to risk of bias. • Quality of life: Moderate quality of evidence due to risk of bias.
• **Soden** et al (2004)	• RCT • No conflicts of interest reported • Setting: three specialist palliative care units within the South Thames region • Sample size: 42 • Follow-up: 4 weeks.	• **Eligibility criteria:** • have a diagnosis of cancer and to be able to complete the assessment scales. Patients were excluded from the study if they had received aromatherapy, massage, chemotherapy or radiotherapy within the	• Massage therapy (n=13) versus • Control: no massage (n=13)	**Pain** (reported as mean change from baseline with a VAS score) • Intervention: 0.50 (no variability reported) • Control: 1.68 (no variability reported) • P-value: not reported. **Quality of life** Not reported	• High risk of bias due to no blinding of patients and physical therapists .	• Pain: Very low quality of evidence due to risk of bias and imprecision (once for low number of patients once for

	• No protocol	previous month. Patients entered the study with varying levels of physical and psychological symptoms. • **Patient characteristics:** • Median age: 73 (range: 44-85) • Sex: 76% female, 24% male.				no variability reported).
• **Stephenson** et al (2007)	• RCT • No conflicts of interest reported • Setting: oncology unit in a 314-bed regional hospital and on an oncology unit in a 734-bed tertiary hospital in the southeastern United States. • Sample size: 86 • Follow-up: 6 weeks. • No protocol	• **Eligibility criteria:** • Patient selection criteria included the presence of any type of metastatic cancer and a pain score of 2 or higher on the 0–10 pain scale during the current hospitalization. Additional criteria for the patient-partner dyad were being 21 years of age or older; living together as spouses or domestic partners, family members, or friends; English speaking; living within a 75- to 100-mile radius of the hospital; partner availability for 30 minutes from 2–10 pm; and willingness to participate as evidenced by verbalizing understanding and signing an informed consent form. • **Patient characteristics:** • Mean age: intervention: 60.5 (SD: 12.1), control: 56.1 (SD: 24.4) • Sex (% female): intervention: 57%, control: 46%.	• partner-delivered foot reflexology (n=42) versus • Usual care (n=44)	**Pain** (reported as mean change from baseline with a VAS score) • Intervention: 4.7 (no variability reported) • Control: 7.1 (no variability reported) • P-value: not reported. **Quality of life** Not reported	• High risk of bias due to no blinding of patients and physical therapists .	• Pain: Very low quality of evidence due to risk of bias and imprecision (once for low number of patients once for no variability reported).
• **Toth** et al (2013)	• RCT • Conflict of interest reported and none known. • Setting: Beth Israel Deaconess Medical	• **Eligibility criteria:** • Subjects were patients with metastatic cancer. • **Patient characteristics:** • Mean age: 55.1 (SD:11)	• Massage (n=20) versus	**Pain** (reported as median change from baseline with a VAS score) • Intervention: 0 (Q1: -1 to Q3: 0) • Control: -2 (Q1: -2 to Q3: -1) • P-value: 0.14	• High risk of bias due to no blinding of patients and physical therapists .	• Very low quality of evidence due to risk of bias and imprecision (once for low number of

	Center (BIDMC) in Boston • Sample size: 42 • Follow-up: 1 month. • No protocol	• Sex (% female): 82%	• Usual care (n=9)	**Quality of life** (reported as median change from baseline with a McGill total score) • Intervention: 0 (Q1: -0.42 to Q3: 0.3) • Control: 0 (Q1: 0 to Q3: 0.58) • P-value: 0.33		patients once for no variability reported).
• **Wyatt** et al (2012)	• RCT • No conflicts of interest reported. • Setting: Thirteen medical oncology settings in the midwestern United States • Sample size: 385 • Follow-up: 11 weeks. • No protocol	• **Eligibility criteria:** • Inclusion criteria were being aged 21 years or older; having a diagnosis of stage III or IV breast cancer, metastasis, or recurrence; being able to perform basic activities of daily living; being cognitively intact and without a documented diagnosis of mental illness; being able to speak and understand English; having access to a telephone; being able to hear normal conversation; receiving chemotherapy at intake into the study; and having a score of 11 or lower on the Palliative Prognostic Score which indicates a 30% probability of having a life expectancy of at least three months • **Patient characteristics:** • Mean age: intervention: 55.3 (SD:9.4), control: 57.3 (SD:11.8) • Sex: all female.	• Reflexology (n=95) versus • Usual care (n=95)	**Pain** (reported as mean score on VAS scale) • Intervention: 3.2 (SD: 3.1) • Control : 3.9 (SD: 3.1) • MD: -0.70 (95%-CI: -1.58 to 0.18)* **Quality of life** (reported as mean FACT-B total score) • Intervention: 101.1 (SD: 18.3) • Control : 100.4 (SD: 18.7) • MD: 0.70 (SD: -4.55 to 5.95)*	• High risk of bias due to no blinding of patients and physical therapists .	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Boyd** et al. (2016)	• Design: systematic review with meta-analysis.	• Eligibility criteria: Articles were included if they met all of the following criteria: (a)	• Massage therapy versus	**Pain** (reported as pain intensity / severity) • SMD: -0.203 (95%-CI: -0.992 to 0.585) (3 studies)	• Low risk of bias	• Low quality of evidence due to

	• Conflicts of interest reported and none known. • Search date: February 2014 • Searched databases: PubMed, CINAHL, Embase, and Psycinfo • Included study designs: RCTs • Number of included studies: 12 studies. • PROSPERO: CRD42014008867.	cancer patients experiencing pain, as defined above; (b) massage therapy, as defined above, administered (i) alone as a therapy; (ii) as part of a multi-modal intervention where massage effects can be separately evaluated; or (iii) with the addition of techniques commonly used with massage, as pre-defined by the EMT Working Group (i.e., external application of water, heat, cold, lubricants, background music, aromas, essential oils, and tools that may mimic the actions that can be performed by the hands); (c) sham, no treatment, or active comparator (i.e., those in which participants are actively receiving any type of intervention); (d) assessment of at least one relevant function outcome, as defined above; and (e) randomized controlled trial (RCT) study design published in the English language .	• No massage treatment or usual care	**Quality of life** • Not reported.		imprecision and inconsistency.
• **Chen** et al. (2016)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: July 2015 • Searched databases: PubMed and Cochrane library • Included study designs: RCTs • Number of included studies: 7 studies. • No protocol reported.	• Eligibility criteria: Studies were included if they met the following inclusion criteria: (1) the study design was randomized controlled trial, (2) the subjects were human, (3) the experimental group received massage with essential oil and the control group received usual care only, and (4) mean difference and standard deviation were reported in the article	• Massage therapy versus • No massage treatment or usual care	**Pain** (reported as pain reduction) • SMD: 0.01 (95%-CI: -0.23 to 0.24) (3 studies) **Quality of life** • Not reported.	• Unclear risk of bias due to no description of an 'a priori' design, complete search strategy, searching grey literature, independent data screening/extraction, and	• Low quality of evidence due to imprecision and risk of bias.

					data synthesis.	
• **Lee** et al. (2015)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: August 2013 • Searched databases: MEDLINE, EMBASE, CENTRAL, AMED, CINAHL. • Included study designs: RCTs and CCTs. • Number of included studies: 12 studies. • No protocol reported.	• Eligibility criteria: All RCT and nonrandomized controlled clinical trial (CCT) studies were included to investigate the effect of massage in patients with cancer pain. Each study was required to have intervention and control, which meant intervention with any type of massage therapy. All types of cancer were included for study population. No massage treatment or conventional care was considered the control group.	• Massage therapy versus • No massage treatment or usual care	**Pain** (reported as VAS score) (8 studies included) • SMD: -1.46 (95%-CI: -1.93 to -0.98) **Quality of life** • Not reported.	• Unclear risk of bias due to no description of an 'a priori' design, complete search strategy, searching grey literature, and data synthesis.	• Low quality of evidence due to risk of bias and inconsistency.

Referenties

[1-9]

[1] Jane SW, Chen SL, Wilkie DJ, et al. Effects of massage on pain, mood status, relaxation, and sleep in Taiwanese patients with metastatic bone pain: a randomized clinical trial. Pain. 2011; 152: 2432-42. 10.1016/j.pain.2011.06.021.

[2] Kutner JS, Smith MC, Corbin L, et al. Massage therapy versus simple touch to improve pain and mood in patients with advanced cancer: a randomized trial. Annals of internal medicine. 2008; 149: 369-79.

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[8] Chen TH, Tung TH, Chen PS, et al. The Clinical Effects of Aromatherapy Massage on Reducing Pain for the Cancer Patients: Meta-Analysis of Randomized Controlled Trials. Evidence-based complementary and alternative medicine : eCAM. 2016; 2016: 9147974. 10.1155/2016/9147974.

[9] Lee SH, Kim JY, Yeo S, et al. Meta-Analysis of Massage Therapy on Cancer Pain. Integrative cancer therapies. 2015; 14: 297-304. 10.1177/1534735415572885.

Uitgangsvraag kanker – oefentherapie

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van oefentherapie in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Oefentherapie
Comparison: Geen oefentherapie
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Cheville** et al (2013)	• RCT • Conflicts of interest reported and none known. • Setting: Mayo Clinic Outpatient Oncology Clinic • Sample size: 66 • Follow-up: 12 months • Protocol: NCT01334983	• **Eligibility criteria:** • Patients with pathology-confirmed Stage IV lung and colorectal cancers. • **Patient characteristics:** • Age: Intervention: 63.8 (SD:12.5), control: 65.5 (SD:8.9) • Sex (%male): Intervention: 48.5, control: 57.6	• one-on-one, 90-minute instructional session in REST as well as a pedometer-based walking program (n=33) versus • neither directed to exercise, nor was their activity monitored (n=33)	**Pain** (reported as mean difference between week 8 and baseline). • Intervention: -0.62 (SD:2.59) • Control: -0.50 (SD:2.01) • P-value (between groups): 0.87 **Quality of life** (reported as mean difference between week 8 and baseline on the FACT-G scale) • Intervention: 1.07 (SD:11.60) • Control: 0.12 (SD:10.22) • P-value (between groups): 0.54	• High risk of bias due to no blinding of patients, physical therapists, and the research coordinator.	• Low quality of evidence due to risk of bias and imprecision.
• **Cormie** et al (2013)	• RCT • Conflicts of interest reported and none known. • Setting: referred by oncologists and urologists in Perth, Western Australia from July 2011 through July 2012 • Sample size: 20 • Follow-up: 12 weeks • No protocol reported.	• **Eligibility criteria:** • Participants had a histological diagnosis of prostate cancer, established bone metastatic disease as determined by a whole-body bone scan and obtained written medical clearance from their physicians (general practitioner) • **Patient characteristics:** • Age: Intervention: 73.1 (SD:7.5), control: 71.2 (SD:6.9) • Sex: all male.	• twice-weekly resistance exercise sessions for 12 weeks (n=10) versus • Usual care (n=10)	**Pain** (reported as FACT-Bone Pain after 12 weeks). • Intervention: 50.7 (SD:4.5) • Control: 52.3 (SD:5.5) • P-value (between groups): 0.26 **Pain** (reported as bone pain – VAS after 12 weeks). • Intervention: 0.9 (SD:1.2) • Control: 0.8 (SD:1.6) • P-value (between groups): 0.60 **Quality of life** (reported as Physical Health composite of the SF-36 instrument after 12 weeks) • Intervention: 45.9 (SD:9.1) • Control: 45.8 (SD:8.5) • P-value (between groups): 0.96 **Quality of life** (reported as Mental Health composite of the SF-36 instrument after 12 weeks) • Intervention: 42.6 (SD:12.9) • Control: 43.9 (SD:11.4) • P-value (between groups): 0.48	• High risk of bias due to no blinding of patients and healthcare professionals.	• Low quality of evidence due to risk of bias and imprecision.
• **Henke** et al (2014)	• RCT • Conflicts of interest reported and none known.	• **Eligibility criteria:** • Patients, who were older than 18 years, diagnosed with non-small cell lung cancer (NSCLC) or small	• additional strength and endurance training (n=18)	**Pain** (reported as pain scale of the EORTC QLQ C-30 list) • Intervention: 25.0 (SD:29.2) • Control: 46.2 (SD:34.8) • MD: -21.2 (95%-CI: -45.8 to 3.4)*	• Unclear risk of bias due to no description of allocation concealment,	• Low quality of evidence due to risk of bias and imprecision.

	• Setting: Vivantes Hospital in Neukoelln/Berlin/ Germany. • Sample size:44 • No follow-up reported. • No protocol reported.	cell lung cancer (SCLC) in stage IIIA/IIIB/IV, who received an inpatient palliative platinum-based chemotherapy treatment at the Vivantes Klinikum Neukoelln/Berlin • **Patient characteristics:** • Mean age not reported. • Gender not reported.	versus • Conventional physiotherapy (n=11)	**Quality of life** (reported as QoL of the EORTC QLQ C-30 score) • Intervention: 57.8 (SD:17.3) • Control: 44.2 (SD: 29.5) • MD: 13.6 (95%-CI: -5.6 to 32.8)*	blinding, incomplete outcome data, and selective outcome reporting.	
• **Jensen** et al (2014)	• RCT • Conflicts of interest reported and none known. • Setting: oncologic outpatients clinic of the University Medical Center Hamburg-Eppendorf • Sample size:26 • No follow-up reported. • No protocol reported.	• **Eligibility criteria:** • patients with advanced gastrointestinal cancer, including gastric, colorectal, pancreatic, and biliary tract cancer, were included. Patients aged ≥18 years with a life expectancy ≥6 months • **Patient characteristics:** • Mean age: 55.0 (SD: 13.1) • Gender: Female: 11, Male: 10.	• a resistance (RET) training group (n=13) versus • aerobic exercise training group (AET) (n=13)	**Pain** (reported as pain scale of the EORTC QLQ C-30 list) • Intervention: 30.3 (SD:27.7) • Control : 36.6 (SD:34.1) • MD: -6.3 (95%-CI: -17.6 to 30.2)* **Quality of life** (reported as QoL of the EORTC QLQ C-30 score) • Intervention: 56.9 (SD: 45.6) • Control: 70.8 (SD:5.3) • MD: -13.9 (95%-CI: -11.1 to 38.9)*	• Unclear risk of bias due to no description of randomisation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting.	• Low quality of evidence due to risk of bias and imprecision.
• **Litterini** et al (2013)	• RCT • Conflicts of interest reported and none known. • Setting: oncology-specific exercise program at a hospital-based fitness facility • Sample size:66 • Follow-up: 10 weeks. • No protocol reported.	• **Eligibility criteria:** • Participants were patients aged >=18 years with advanced cancer who were recruited to attend an oncology-specific exercise program at a hospital-based fitness facility between February 2010 and March 2012 • **Patient characteristics:** • Mean age: 62.4 (SD: 13.5) • Gender: Female: 36, Male: 30.	• Resistance exercise (n=34) versus • Cardiovascular exercise (n=32)	**Pain** (reported as VAS 100-mm pain after 10 w) • Intervention: 15.8 (SD:20.7) • Control: 12.5 (SD:15.9) • MD: 3.3 (95%-CI: -7.8 to 14.4)* **Quality of life** • Not reported.	• High risk due to no blinding of personnel and patients.	• Very low quality of evidence due to risk of bias, indirectness, and imprecision.
• **Rief** et al (2014)	• RCT • Conflicts of interest reported and none known. • Setting: Radiooncology Department of the	• **Eligibility criteria:** • Inclusion criteria were an age of 18 to 80 years, a Karnofsky performance score, ≥ 70,written consent to participate, and already	• resistance training (n=30) versus	**Pain** (reported as VAS 100-mm pain after 6 months) • Intervention: 20.8 (SD:46.9) • Control: 76.7 (SD:103.6) • MD: -55.9 (95%-CI: -108.4 to -3.4)* **Quality of life** • Not reported.	• Unclear risk of bias due to no description of, allocation concealment, blinding, andincomplete outcome data.	• Very low quality of evidence due to risk of bias, indirectness, and imprecision.

	Heidelberg University Clinic • Sample size:60 • Follow-up: 6 months. • Protocol: NCT 01409720.	initiated bisphosphonate therapy. • **Patient characteristics:** • Mean age: intervention: 61.3 (SD:10.1), control: 64.1 (SD: 10.9) • Gender: intervention: male: 46.7, female: 53.3. control: male: 63.3%, female: 36.7	• passive physical therapy (n=30)			

* self-calculated

Referenties

[1-6][1] Cheville AL, Kollasch J, Vandenberg J, et al. A home-based exercise program to improve function, fatigue, and sleep quality in patients with Stage IV lung and colorectal cancer: a randomized controlled trial. Journal of pain and symptom management. 2013; 45: 811-21. 10.1016/j.jpainsymman.2012.05.006.

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Uitgangsvraag kanker - ontspanningstechnieken

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van ontspanningstechnieken in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Ontspanningstechnieken
Comparison: Geen ontspanningstechnieken
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Kwekkeboom** et al (2012)	• RCT • No conflicts of interest reported. • Setting: outpatient chemotherapy or radiation therapy clinics at a National Cancer Institute designated Comprehensive Cancer Center in the midwest U.S • Sample size: 86 • Follow-up: two weeks • Protocol: NCT00946803	• **Eligibility criteria:** Participants were receiving treatment for advanced (metastatic or recurrent) colorectal, lung, prostate or gynecologic cancers, and had experienced pain, fatigue, and sleep disturbance in the past week • **Patient characteristics:** • Age: 60.29 (SD:11.09) • Sex: 41% male and 59% female	• Patient-Controlled Cognitive-Behavioral Intervention (n=43) versus • Waitlist Control Condition (n=43)	**Pain** (reported as pain severity at 2 weeks follow-up): • Intervention: 1.65 (SD:1.61) • Control: 2.23 (SD:1.96) • MD: -0.58 (95%-CI: -1.37 to 0.21)* **Quality of life:** • Not reported	• High risk of bias due to no blinding of patients and research nurse.	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Referenties
[1] Kwekkeboom KL, Abbott-Anderson K, Cherwin C, et al. Pilot randomized controlled trial of a patient-controlled cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. Journal of pain and symptom management. 2012; 44: 810-22. PMC3484234.

Uitgangsvraag kanker - cognitieve gedragstherapie

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van cognitieve gedragstherapie in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Cognitieve gedragstherapie
Comparison: Geen cognitieve gedragstherapie
Outcome: Pijn en kwaliteit van leven.

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Kwekkeboom** et al. (2012)	• RCT • Conflicts of interest reported and none known. • Setting: outpatient chemotherapy or radiation therapy clinics at a National Cancer Institute designated Comprehensive Cancer Center in the midwest U.S • Sample size: 86 • Follow-up: two weeks. • Protocol: NCT00946803	• **Eligibility criteria:** Participants were receiving treatment for advanced (metastatic or recurrent) colorectal, lung, prostate or gynecologic cancers, and had experienced pain, fatigue, and sleep disturbance in the past week. • **Patient characteristics:** • Age: 60.29 (SD: 11.09) years • Sex: 41% male and 59% female.	• Patient-Controlled Cognitive-Behavioral Intervention (n=43) versus • Waitlist Control Condition (n=43)	**Pain** (reported as pain severity) • Intervention: 1.65 (SD: 1.61) • Control: 2.23 (SD: 1.96) • MD: -0.58 (95%-CI: -1.37 to 0.21)* **Quality of Life** • Not reported.	• High risk of bias due to no blinding of patients and outcome assessor.	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment

• **Kwekkeboom** et al. (2010)	• Design: systematic review. • No conflicts of interest reported • Search date: March 2009 • Searched databases: CINAHL, Medline, and PsycINFO • Included study designs: RCTs, cross-over studies, and pre- and post-test studies. • Number of included studies: 43 studies for all comparisons (21 studies for cognitive interventions). • No protocol reported.	• Eligibility criteria: Articles were selected for inclusion if they tested one of the mind-body interventions in a sample of patients with cancer and if pain, fatigue, or sleep disturbance was among the dependent variables.	• CBT / Coping Skills Training Interventions versus • Usual care.	**Solely a narrative synthesis of the results are provided in this systematic review. No meta-analysis has been performed.** **Pain** • Studies with a significant pain reduction: Dalton 2004,Robb 2006,Syrjala 1992, Syrjala 1995. • Studies with no significant effect on pain: Arathuzik 1994, Arving 2007, Clark 2006, Dalton 1987, Davidson 2001, Gaston-Johansson 2000, Vilela 2006. **Quality of Life** • Not reported.	• Unclear risk of bias due to no description of a protocol, independent data-extraction, searching grey literature, synthesis of evidence, and assessment of publication bias.	• Low quality of evidence due to risk of bias and imprecision.
• **Mustafa** et al. (2013)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: June 2011 • Searched databases: Cochrane library, MEDLINE, EMBASE, PsycINFO, CINAHL. • Included study designs: RCTs • Number of included studies: 10 studies • Cochrane protocol.	• Eligibility criteria: Studies involving women with metastatic breast cancer (that is stages three or four). This included women with metastatic disease present at first diagnosis (’contemporaneous’ metastatic disease) and those in whom metastatic disease was diagnosed after the initial diagnosis and treatment phases of disease (’delayed’ metastatic disease).	• Psychological intervention versus • Usual care.	**Pain** (reported as pain at one year) • Intervention: no mean score reported • Control: no mean score reported • MD: -0.58 (95%-CI: -0.98 to -0.18) **Quality of life** (reported as mean score of EORTC QLQ-C30 score) • Intervention: 59.7 (SD:20.2) • Control: 58.8 (SD:23.5) • MD: 0.90 (95%-CI: -5.51 to 7.31)	• Low risk of bias	• Pain: high quality of evidence. • Quality of life: moderate quality of evidence due to imprecision.

Referenties

[1-3]

[1] Kwekkeboom KL, Abbott-Anderson K, Cherwin C, et al. Pilot randomized controlled trial of a patient-controlled cognitive-behavioral intervention for the pain, fatigue, and sleep disturbance symptom cluster in cancer. Journal of pain and symptom management. 2012; 44: 810-22. 10.1016/j.jpainsymman.2011.12.281.

[2] Kwekkeboom KL, Cherwin CH, Lee JW, Wanta B. Mind-body treatments for the pain-fatigue-sleep disturbance symptom cluster in persons with cancer. Journal of pain and symptom management. 2010; 39: 126-38. 10.1016/j.jpainsymman.2009.05.022.

[3] Mustafa M, Carson-Stevens A, Gillespie D, Edwards Adrian GK. Psychological interventions for women with metastatic breast cancer. John Wiley & Sons, Ltd 2013.10.1002/14651858.CD004253.pub4.

Uitgangsvraag kanker - paracetamol

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van paracetamol in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Paracetamol
Comparison: Geen paracetamol
Outcome: Pijn en kwaliteit van leven.

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Cubero** et al. (2010)	• RCT • No conflicts of interest reported. • Setting: no information about the setting is reported • Sample size: 50 • Follow-up: 7 days. • No protocol reported.	• **Eligibility criteria:** Patients over 18 years old, on stable dose of morphine for at least 1 week, were considered eligible. Those who used acetaminophen in the last 48 h, receiving radiotherapy for pain control and presenting severe hepatic and/or renal dysfunction or cognitive alterations, were excluded. • **Patient characteristics:** • Median age: intervention: 58.1 (range: 19-81). Control: 59 (range: 25-76). • Gender (% male): intervention: 54, control: 52.	• Methadone and acetaminophen (n=25) versus • Methadone and placebo (n=25)	**Pain (**reported as VAS scale from 0-10 after 7 days) • Intervention: 4.26 (SD: 2.33) • Control: 3.31 (SD: 2.79) • MD: 0.95 (95%-CI: -0.49 to 2.39)* **Quality of Life** (reported as global health score on the QLQ-C30 questionnaire after 7 days). • Intervention: 55 (SD: 29) • Control: 49 (SD:25) • MD: 6.00 (95%-CI: -9.19 to 21.19)*	• Unclear risk of bias due to no description of blinding and selective outcome reporting.	• Low quality of evidence due to risk of bias and imprecision.
• **Israel** et al. (2010)	• RCT • No conflicts of interest reported. • Setting: Brisbane South Palliative Care Service and Mt. Olivet Palliative Care Service in Brisbane, Australia.	• **Eligibility criteria:** • Patients on stable (30% of total daily requirement) doses of opioid and nonopioid analgesics for at least one week before recruitment • Baseline pain score greater than or equal to two	• 4 g of paracetamol daily (n=11) versus • Placebo (n=20)	**Pain** (reported as pain on a VAS scale from 0-10 after 4 days). • Intervention: 3.59 (SD: 1.58) • Control: 3.43 (SD: 1.44) • MD: 0.16 (95%-CI: -0.47 to 0.79) **Quality of Life** • Not reported	• Unclear risk of bias due to no description of allocation concealment, blinding and selective outcome reporting.	• Low quality of evidence due to risk of bias and imprecision.

	• Sample size: 31 • Follow-up: 7 days. • No protocol reported.	• Prepared to take 4 g of oral paracetamol daily • If currently using paracetamol, prepared to stop their usual dose • Prepared to cease any breakthrough medications with a paracetamol additive • Ability to give informed consent in English • Mini-Mental State Examination (MMSE) score of at least 22 out of 30 (repeated at five-day intervals) • **Patient characteristics:** • Median age: 56.3 (range: 28-79) • Gender (male/female): 12/10				
• **Tasmacioglu** et al. (2009)	• RCT • No conflicts of interest reported. • Setting: Pain Clinic of Istanbul University, Cerralpasa Medical Faculty, Turkey. • Sample size: 43 • Follow-up: 1 day. • No protocol reported.	• **Eligibility criteria:** • Chronic cancer pain patients aged between 18 and 76 years without sufficient pain control despite step 2 treatment not including strong analgesics according to the World Health Organization analgesic ladder protocol. • **Patient characteristics:** • Median age: intervention: 52.8 (SD: 15.29) **&** control: 55.40 (SD: 16.16). • Gender (male/female): 9/31	• 1g of intravenous administration of paracetamol every 6 hours (n=20) versus • 100 ml of intravenous administration of saline (n=20)	**Pain.** • No quantitative levels of pain score are reported for both groups. Only the statement of statistically significance between the two groups is reported: “VAS levels were similar among the two groups throughout the study (p=0.269, two-way ANOVA for repeated measures). **Quality of Life** • Not reported	• Unclear risk of bias due to no description of randomisation, incomplete outcome data, selective outcome reporting.	• Very low quality of evidence due to risk of bias and imprecision.

* self-calculated

Referenties

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[1] Cubero DI, del Giglio A. Early switching from morphine to methadone is not improved by acetaminophen in the analgesia of oncologic patients: a prospective, randomized, double-blind, placebo-controlled study. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2010; 18: 235-42. 10.1007/s00520-009-0649-8.

[2] Israel FJ, Parker G, Charles M, Reymond L. Lack of benefit from paracetamol (acetaminophen) for palliative cancer patients requiring high-dose strong opioids: a randomized, double-blind, placebo-controlled, crossover trial. Journal of pain and symptom management. 2010; 39: 548-54. 10.1016/j.jpainsymman.2009.07.008.

[3] Tasmacioglu B, Aydinli I, Keskinbora K, et al. Effect of intravenous administration of paracetamol on morphine consumption in cancer pain control. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer. 2009; 17: 1475-81. 10.1007/s00520-009-0612-8.

Uitgangsvraag kanker – NSAID

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van NSAID (ibuprofen, diclofenac, naxproxen) in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: NSAID (ibuprofen, diclofenac, naxproxen)
Comparison: Geen NSAID (ibuprofen, diclofenac, naxproxen)
Outcome: Pijn en kwaliteit van leven

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Nabal** et al. (2012)	• Design: systematic review. • Conflicts of interest reported and none known. • Search date: 2010 • Searched databases: Medline, EMBASE, and CENTRAL. • Included study designs: only RCTs. • Number of included studies: 12 studies. • No protocol reported.	• Eligibility criteria: conducted in human, adult patients with chronic cancer pain; a randomized controlled trial (RCT) or a meta-analysis of reported data from RCTs; studies containing data on patient-reported efficacy and/or side effects of NSAIDs or paracetamol in addition to opioids compared to placebo or opioids alone; and written in English	• NSAID + opioids versus • Opioids	The results of this systematic review are only described narratively and no meta-analysis is performed. **Pain** Dipyrone + morphine versus morphine • 1 study: additive analgesic effect of dypirone. Ibuprofen + opioids versus opioids • 2 studies: addition of ibuprofen improved pain relief. Ketorolac + morphine versus morphine • 1 study: No difference in analgesic efficacy. Diclofenac+ morphine versus morphine • 1 study: No difference in analgesic efficacy. Choline magnesium trisalicylate + morphine versus morphine • 1 study: No difference in analgesic efficacy. Flurbiprofen + opioids versus opioids • 1 study: No difference in analgesic efficacy.	• Unclear risk of bias due to no description of a protocol, searching grey literature, no rating of scientific quality, synthesis of the results, and assessment of publication bias.	• Low quality of evidence due to risk of bias and imprecision.

				Quality of life: • Not reported		

Referenties

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[1] Nabal M, Librada S, Redondo MJ, et al. The role of paracetamol and nonsteroidal anti-inflammatory drugs in addition to WHO Step III opioids in the control of pain in advanced cancer. A systematic review of the literature. Palliative Medicine. 2012; 26: 305-12.

Uitgangsvraag kanker - TENS

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van TENS (transcutane elektrische zenuwstimulatie) in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: TENS (transcutane elektrische zenuwstimulatie)
Comparison: Geen TENS
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Bennett** et al. (2010)	• RCT • No conflicts of interest reported. • Setting: specialist palliative care services in 2 UK cities (initially in Leeds and then in Lancaster) • Sample size: 24 • Follow-up: not reported. • Protocol: ISRCTN = 92118149	• **Eligibility criteria:** Patients were required to have radiological evidence of bone metastases, pain rated at least 3 out of 10 on a numerical pain-intensity scale at rest or on movement at the first visit, and an estimated survival of longer than 4 weeks. • **Patient characteristics:** • Age: 72.0 (SD: 11.1) • Sex: 18 men and 6 women.	• Transcutaneous Electrical Nerve Stimulation (TENS) versus • placebo TENS	**Pain** (defined as pain intensity at rest 1 hour after intervention) • Intervention: 2.11 (SD: 2.42) • Control: 1.79 (SD: 2.18) • MD: 0.32 (95%-CI: -1.52 to 2.16)* **Pain** (defined as pain intensity on movement 1 hour after intervention) • Intervention: 2.84 (SD: 2.17) • Control: 3.05 (SD: 2.46) • MD: -0.21 (95%-CI: -2.07 to 1.65)* **Quality of life:** • Not reported	• Unclear risk of bias due to no description of allocation concealment, blinding, and incomplete outcome data.	• Very low quality of evidence due to risk of bias and imprecision (twice).

* self-calculated

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Hurlow** et al. (2012)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known.	• Eligibility criteria: Participants were 18 years of age or older. They had experienced cancer-related	• Transcutaneous Electrical Nerve Stimulation (TENS) versus	Systematic review conducted no meta-analyses and only described the results separately per study.	• Unclear risk of bias due to no description	• Very low quality of evidence due to risk of bias and imprecision (twice).

	• Search date: June 2011 • Searched databases: CENTRAL, MEDLINE, EMBASE, CINAHL and AMED • Included study designs: only RCTs. • Number of included studies: 3 studies. • Cochrane protocol.	pain, unspecified or persistent cancer treatment-related pain, or both, for aminimum of threemonths after any anticancer treatment had been completed. Pain was classified based on commonly used verbal rating scales or pain interference scales.	• placebo TENS	**Pain** (defined as pain intensity at rest 1 hour after intervention) • Intervention: 2.11 (SD: 2.42) • Control: 1.79 (SD: 2.18) • MD: 0.32 (95%-CI: -1.52 to 2.16) **Pain** (defined as pain intensity on movement 1 hour after intervention) • Intervention: 2.84 (SD: 2.17) • Control: 3.05 (SD: 2.46) • MD: -0.21 (95%-CI: -2.07 to 1.65) **Pain relief scores** • No significant differences in pain relief scores between TENS or sham TENS. Quality of Life • Not reported	of synthesis of results and no meta-analysis performed.	

Referenties

[[1] Bennett MI, Johnson MI, Brown SR, et al. Feasibility study of Transcutaneous Electrical Nerve Stimulation (TENS) for cancer bone pain. The journal of pain : official journal of the American Pain Society. 2010; 11: 351-9. 10.1016/j.jpain.2009.08.002.

[2] Hurlow A, Bennett MI, Robb KA, et al. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. The Cochrane database of systematic reviews. 2012; CD006276. 10.1002/14651858.CD006276.pub3.

Uitgangsvraag kanker - plexus coeliacusblokkade

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van plexus coeliacusblokkade in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Plexus coeliacusblokkade
Comparison: Geen plexus coeliacusblokkade
Outcome: Pijn en kwaliteit van leven

Primary studies

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Gao** et al (2014)	• RCT • Conflicts of interest reported and none known. • No information about the setting reported. • Sample size: 100 • Follow-up: 3 months • No protocol reported.	• **Eligibility criteria:** • patients of 18 and older; male or female; with unresectable (T4 or M1 or non-regional lymph nodes) or inoperable carcinoma of the pancreas as determined by CTor endoscopic ultrasound (EUS); staging as determined per 2010 AJCC staging manual; presence of midabdominal pain (3 on VAS scale) at least 2 days per week, lasting at least 1 h per day; no known coagulopathy as measured by prothrombin time (INR) 1.5; platelets are ≥50,000; and with life expectancy at >3 months • **Patient characteristics:** • Age: Intervention: 65.5 (SD:10.2), control: 66.6 (SD:9.9) • No information about gender reported.	• celiac neurolysis group (n=68) versus • sham group (same medication injected into gastric lumen) (n=32)	**Pain** (reported as pain symptom scale of QLQ-EORTC instrument after three months) • Intervention: 41.2 (SD:1.5) • Control: 75.1 (SD:1.9) • P-value (between groups): <0.01 **Quality of life** (reported as global quality on the QLQ-EORTC instrument after three months) • Intervention: 65.6 (SD:0.4) • Control: 51.3 (SD:0.5) • P-value (between groups): <0.05	• Unclear risk of bias due to no description of randomisation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting.	• Low quality of evidence due to risk of bias and imprecision.
• **Johnson** et al (2009)	• RCT • No conflicts of interest reported. • Setting: multicentre trial in the United Kingdom. Four teaching hospitals recruited patients. • Sample size: 65 • Follow-up: 8 weeks • No protocol reported.	• **Eligibility criteria:** • clinical, radiological or histological evidence of irresectable primary or secondary malignancy in the upper abdominal viscera (pancreas, stomach, oesophagus, duodenum, bile duct or gallbladder, or hepatic metastases of any origin), including recurrence after resection of a primary tumour, and if they had pain requiring any opioid medication at least once per day. • **Patient characteristics:**	• Medical management + celiac plexus block (n=20) versus • medical management (n=24)	**Pain** (reported as mean score of Brief Pain Inventory after two months) • Intervention: 2.46 (SD:1.75) • Control: 4.00 (SD:1.2) • MD: -1.54 (95%-CI: -3.02, -0.06) **Quality of life** • Not reported.	• High risk of bias due to selective outcome reporting (quality of life measured but data not shown).	• Low quality of evidence due to risk of bias and imprecision.

		• Age: Intervention: 60.5 (SD:9.2), control: 65.5 (SD:9.1) • Gender (% male): Intervention: 50%, control: 67% •				
• **Wyse** et al (2009)	• RCT • Conflict of interest reported and none known. • Setting: the Centre Hospitalier de l'Universite´ de Montreal in Montreal, Quebec, Canada • Sample size: 98 • Follow-up: 3 months • Protocol: clinicaltrials.gov	• **Eligibility criteria:** • patients were required to have suspected pancreatic cancer and any new-onset pain considered to be cancer-related (centrally located, constant, with no other obvious cause). • **Patient characteristics:** • Age: Intervention: 66.6 (SD:9.3), control: 66.5 (SD:10.0) • Gender (% male): Intervention: 53.1%, control: 42.9% •	• Early Endoscopic Ultrasound–Guided Celiac Plexus Neurolysis (n=49) versus • No Celiac Plexus Neurolysis (n=49)	**Pain** (reported as pain relief after three months) • Intervention change with baseline: -2.6 (95%-CI: -3.2 to -2.0) • Control change with baseline: -0.3 (95%-CI: -0.9 to +0.2) • MD between the two groups at three months: -60.7 (95%-CI: -86.6 to -25.5) **Quality of life** (reported as DDQ-15 score after three months) • Intervention change with baseline: 19 (95%-CI: 10-27) • Control change with baseline: 18 (95%-CI: 12 to 26) • MD at three months: not significant	• Low risk of bias.	• Low quality of evidence due to imprecision (twice).
• **Zhang** et al (2008)	• RCT • No conflicts of interest reported. • No information about the setting reported. • Sample size: 56 • Follow-up: 90 months • No protocol reported.	• **Eligibility criteria:** • patients with chronic upper-abdominal pain secondary to unresectable pancreatic cancer proved by histopathology • **Patient characteristics:** • No details about age + gender reported	• neurolytic coeliac plexus block (NCPB) guided by computerized tomography (CT) (n=29) versus • pharmacological therapy (n=27)	**Pain (**reported as VAS-score at day 90) • Intervention: 3.9 (SD: 1.2) • Control: 3.7 (SD: 1.3) • MD: 0.20 (95%-CI: -0.46 to 0.86)* **Quality of life** (reported as QOL was evaluated based on interference with appetite, sleep, communication) • No quantitative data reported, only the statement that it is not significant between the two groups.	• Unclear risk of bias due to no description of randomisation, allocation concealment, blinding, incomplete outcome data, and selective outcome reporting.	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment

• **Arcidiacono Paolo (**2011)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: December 2010 • Searched databases: CENTRAL, MEDLINE, GATEWAY, and EMBASE • Included study designs: only RCTs. • Number of included studies: 6 studies. • Cochrane protocol.	• Eligibility criteria: Adults of either sex, aged 18 years or over, suffering from abdominal or back pain due to pancreatic cancer at any stage, confirmed by CT or ultrasound, EUS and clinical criteria.	• percutaneous CPB, the surgical approach, and EUS-guided neurolysis versus • control group included patients treated with NSAIDs and morphine.	**Pain (**reported as VAS-score at day 8 weeks) (5 studies) • MD between the two groups: -0.44 (95%-CI: -0.89 to 0.01) **Quality of life** • Not reported	• Low risk of bias	• Moderate quality of evidence due to imprecision.
• **Nagels (**2013)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: May 2011 • Searched databases: MEDLINE, EMBASE, AMED, Web of Science, CINAHL. • Included study designs: only RCTs. • Number of included studies: 9studies. • No protocol	• Eligibility criteria: All study designs and case reports regarding percutaneous and EUS CPN in adults with abdominal pain due to intra-abdominal cancer were included in this review.	• percutaneous CPN versus • systemic analgesic therapy	**Pain (**reported as VAS-score at day 8 weeks) (4 studies) • MD between the two groups: -0.31 (95%-CI: -0.74 to 0.12) **Quality of life** • Not reported	• Unclear risk of bias due to no description of an 'a priori' design, duplicate study selection/data extraction, complete search strategy, searching grey literature, scientific quality, data synthesis, and publication bias.	• Low quality of evidence due to risk of bias and imprecision.
• **Puli (**2009)	• Design: systematic review with meta-analysis. • No conflict of interest. • Search date: June 2008 • Searched databases: EMBASE, CINAHL, ACP, DARE, MEDLINE, and CENTRAL. • Included study designs: only RCTs. • Number of included studies: 9studies. • No protocol	• Eligibility criteria: Studies using EUS-guided CPN for pain control due to chronic pancreatitis or unresectable pancreatic cancer were selected.	• EUS-Guided Celiac Plexus Neurolysis versus • systemic analgesic therapy	**Pain (**reported as proportion of patients that experienced pain relief) (6 studies) • Combined proportion of patients in the intervention group: 0.83 (95%-CI: 0.71-0.92) • Control group data: not reported. **Quality of life** • Not reported	• Unclear risk of bias due to no description of an 'a priori' design, duplicate study selection/data extraction, complete search strategy,	• Very low quality of evidence due to risk of bias, imprecision, and inconsistency.

					searching grey literature, scientific quality, data synthesis, and conflict of interest.	
• **Yan (**2007)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: August 2005 • Searched databases: MEDLINE, EMBASE, HealthStar, and the Cochrane library. • Included study designs: only RCTs. • Number of included studies: 5 studies. • No protocol	• Eligibility criteria: Only RCTs comparing NCPB to standard treatment in patients with pancreatic cancer were selected for inclusion in the review.	• Neurolytic Celiac Plexus Block versus • standard treatment	**Pain (**reported as VAS at 8 weeks) (4 studies) • WMD between the two groups: -0.60 (95%-CI: -0.82 to -0.37) **Quality of life** • Not reported	• Unclear risk of bias due to no description of an 'a priori' design, duplicate study selection/data extraction, complete search strategy, searching grey literature, scientific quality, and data synthesis.	• Low quality of evidence due to risk of bias and imprecision.
• **Zhong (**2014)	• Design: systematic review with meta-analysis. • Conflicts of interest reported and none known. • Search date: November 2012 • Searched databases: MEDLINE, Google Scholar, and Cochrane library. • Included study designs: only RCTs. • Number of included studies: 7studies. • No protocol	• Eligibility criteria: Studies were eligible for inclusion in the meta-analysis if they were randomized controlled trials comparing pain severity between patients receiving celiac plexus block and those receiving medical management for pain	• celiac plexus bloc versus • medical management for pain.	**Pain (**reported as VAS at 8 weeks) (6 studies) • MD between the two groups: -0.265 (SE: 0.217) • P-value: 0.223 **Quality of life** Not reported	• Unclear risk of bias due to no description of an 'a priori' design, duplicate study selection/data extraction, complete search strategy, searching grey literature, scientific quality, and	• Low quality of evidence due to risk of bias and imprecision.

					data synthesis.	

Referenties

[1-9]

[1] Gao L, Yang YJ, Xu HY, et al. A randomized clinical trial of nerve block to manage end-stage pancreatic cancerous pain. Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine. 2014; 35: 2297-301. 10.1007/s13277-013-1304-z.

[2] Johnson CD, Berry DP, Harris S, et al. An open randomized comparison of clinical effectiveness of protocol-driven opioid analgesia, celiac plexus block or thoracoscopic splanchnicectomy for pain management in patients with pancreatic and other abdominal malignancies. Pancreatology : official journal of the International Association of Pancreatology (IAP) [et al]. 2009; 9: 755-63. 10.1159/000199441.

[3] Wyse JM, Carone M, Paquin SC, et al. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2011; 29: 3541-6. 10.1200/jco.2010.32.2750.

[4] Zhang CL, Zhang TJ, Guo YN, et al. Effect of neurolytic celiac plexus block guided by computerized tomography on pancreatic cancer pain. Digestive diseases and sciences. 2008; 53: 856-60. 10.1007/s10620-007-9905-2.

[5] Arcidiacono Paolo G, Calori G, Carrara S, et al. Celiac plexus block for pancreatic cancer pain in adults. John Wiley & Sons, Ltd 2011.10.1002/14651858.CD007519.pub2.

[6] Nagels W, Pease N, Bekkering G, et al. Celiac plexus neurolysis for abdominal cancer pain: a systematic review. Pain medicine (Malden, Mass). 2013; 14: 1140-63. 10.1111/pme.12176.

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[8] Yan BM, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. The American journal of gastroenterology. 2007; 102: 430-8. 10.1111/j.1572-0241.2006.00967.x.

[9] Zhong W, Yu Z, Zeng JX, et al. Celiac plexus block for treatment of pain associated with pancreatic cancer: a meta-analysis. Pain practice : the official journal of World Institute of Pain. 2014; 14: 43-51. 10.1111/papr.12083.

Uitgangsvraag kanker - spinale toediening van opioïden

Uitgangsvraag:
Wat zijn de ongewenste en gewenste effecten van spinale toediening van opioïden in vergelijking met control voor patiënten met pijn en kanker?

Patiëntengroep: Patiënten met pijn en kanker
Intervention: Spinale toediening van opioïden
Comparison: Geen spinale toediening van opioïden
Outcome: Pijn en kwaliteit van leven

Systematic reviews

I Study ID	II Method	III Patient characteristics	IV Intervention(s)	V Results	VII Critical appraisal of study quality	GRADE assessment
• **Hayek** et al. (2011)	• Design: systematic review. • Conflicts of interest reported and none known. • Search date: October 2010 • Searched databases: Medline, EMBASE, and Cochrane library. • Included study designs: RCTs and observational studies (stratification between RCTs and observational studies done). • Number of included studies: 20 studies (1 RCT and 19 observational studies) • No protocol reported.	• Eligibility criteria: Studies should clearly show the use of intrathecal infusion device/system (programmable or fixed infusion rate) implanted for chronic pain for long-term use. Studies must have a specific indication for intrathecal infusion and the drug injected. A minimum of 3 months of follow-up was available for studies on cancer pain patients. A minimum of 12 months of follow-up was available for studies on non-cancer pain or studies involving both cancer and non-cancer pain patients. Clear documentation of patient outcomes and complications should have been provided. Number of patients evaluated must have been at least 24.	• Implemented intrathecal drug delivery system versus • Conservative Medical Management	**Pain** (reported as improvement in pain or reduction in toxicity) • Intervention: 60/71 • Control: 51/72 • OR: 2.25 (95%-CI: 0.99-5.10)* **Quality of life:** • Not reported	• Unclear risk of bias due to no description of a protocol, searching grey literature, synthesis of the results, and assessment of publication bias.	• Low quality of evidence due to risk of bias and imprecision.

• **Kurita** et al. (2015)	• Design: systematic review. • Conflicts of interest reported and none known. • Search date: February 2014 • Searched databases: Medline, EMBASE, and CENTRAL. • Included study designs: RCTs. • Number of included studies: 1 RCT • No protocol reported.	• Eligibility criteria: 1. Randomised controlled trials (RCTs), which have been conducted to investigate the effects of long-term epidural and/or subarachnoid analgesic treatment. 2. Adult patients with chronic pain due to cancer. 3. Patients previously treated with systemic opioids, which failed to control cancer pain and/or induced intolerable side effects. 4. Data on the relevant outcomes (efficacy on pain intensity and/or side effects). 5. Written in the English language.	• single neuraxial drug (ziconotide) (n=68) versus • neuraxial placebo (n=40)	**Pain** (reported as pain relief) • Intervention: 54% • Control: 18% • P-value: 0.02 **Quality of life:** Not reported	• Unclear risk of bias due to no description of a protocol, searching grey literature, quality assessment, synthesis of the results, and assessment of publication bias.	• Low quality of evidence due to risk of bias and imprecision.
• **Kurita** et al. (2011)	• Design: systematic review. • Conflicts of interest reported and none known. • Search date: November 2009 • Searched databases: Medline, EMBASE, and CENTRAL. • Included study designs: RCTs. • Number of included studies: 9 studies. • No protocol reported.	• Eligibility criteria: adults with cancer pain, long-term systemic opioids (at least days of treatment) that failed to control cancer pain and/or induced intolerable side effects, outcomes of spinal opioid treatment, and English language. Outcomes of spinal treatment were included as a result of pain intensity/relief and/or side effects control related to comparison before/after treatment, intervention/control groups, or after treatment.	• Implemented intrathecal drug delivery system versus • Conservative Medical Management	**Pain** (reported as improvement in pain or reduction in toxicity) • Intervention: 60/71 • Control: 51/72 • OR: 2.25 (95%-CI: 0.99-5.10)* **Quality of life:** Not reported	• Unclear risk of bias due to no description of a protocol, searching grey literature, quality assessment, synthesis of the results, and assessment of publication bias.	• Low quality of evidence due to risk of bias and imprecision.

* self-calculated

Referenties

[1-3]

[1] Hayek SM, Deer TR, Pope JE, et al. Intrathecal therapy for cancer and non-cancer pain. Pain physician. 2011; 14: 219-48.

[2] Kurita GP, Benthien KS, Nordly M, et al. The evidence of neuraxial administration of analgesics for cancer-related pain: a systematic review. Acta anaesthesiologica Scandinavica. 2015; 59: 1103-15. 10.1111/aas.12485.
[3] Kurita GP, Kaasa S, Sjogren P. Spinal opioids in adult patients with cancer pain: a systematic review: a European Palliative Care Research Collaborative (EPCRC) opioid guidelines project. Palliative medicine. 2011; 25: 560-77. 10.1177/0269216310386279.

Evidence table for intervention studies (randomized controlled trials and non-randomized observational studies [cohort studies, case-control studies, case series])[1]

This table is also suitable for diagnostic studies (screening studies) that compare the effectiveness of two or more tests. This only applies if the test is included as part of a test-and-treat strategy – otherwise the evidence table for studies of diagnostic test accuracy should be used.

Research question: Wat is het effect van zwakwerkende opioïden (codeïne of tramadol) op pijn bij patiënten met kanker?

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Comparison / control (C) [3]	Follow-up	Outcome measures and effect size [4]	Comments
Nunes, 2014	Type of study: RCT Setting: Hospital Country: Brazil Source of funding: not reported	Inclusion criteria: Patients with locally advanced and/or metastatic cancer. Exclusion criteria: Patients with difficultly in maintaining clinical follow-up, cognitive impairment and previous treatment with opioids. N total at baseline: Intervention: 30 Control:30 Important prognostic factors[2]: *age ± SD:* *I: 58.7 ± 12.4* *C: 57.5 ± 12.7* *Sex:* *I: M:F 25:5*	Treated according to the guidelines of the WHO analgesic ladder and started on the first step with paracetamol 1 g every six hours (maximum dose 4g/day); in the second step, codeine (30 mg) every four hours (maximum dose of 360 mg /day) and morphine 10 mg four hours in the third step	Morphine 10 mg every four hours	Length of follow-up: 3 months Loss-to-follow-up: Intervention:1 Control: 6	Pain intensity by visual analogue scale: 12th week I: 2.3±2.1 C: 2.9 ±2.5 p=0.3400 Satisfaction with treatment I: 20 C: 24 p=0.5275 Quality of life I: 92.2±11.7 C:93.0 ± 10.5 p=0.7816 Nausea I: 5 C: 20 p=0.0088 Constipation I: 14 C: 25 p=0.0071 Dizziness I: 6 C: 14 p=0.0376 Drowsiness I: 13 C: 27 p=0.0005	

		C: M:F 27:3 Groups comparable at baseline? yes					

Notes:

1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Evidence table for systematic review of RCTs and observational studies (intervention studies)

Research question: Wat is het effect van zwakwerkende opioïden (codeïne of tramadol) op pijn bij patiënten met kanker?

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Wiffen 2017 10 RCTs	SR and no meta-analysis Literature search up to Nov 2016 Study design: RCT Setting and country: UK Source of funding: Not reported	Inclusion criteria SR: 1) RCT's of any duration 2) adults and children of any age who expierenced cancer-related pain 3) tramadol with or without paracematol for cancer pain Exclusion criteria SR: 1) quasi-randomized studies 2) studies with <10 participants 3) non cancer related pain 4) no assessment of pain as outcome *10 studies included*	Intervention: Oral tramadol with or without paracematol for cancer pain	Comparison: Placebo or any active comparator	End-point of follow-up: One day to six months	Tramadol versus morphine: Participants with pain reduction of 30% or greater from baseline(1 study): not calculated Participants with pain reduction of 50% or greater from baseline (1 study): not calculated Participants with pain no worse than mild (1 study): no data Participants with Patient Global impression of Change (PGIC) of much improved or very much imporved (1 study): no data Serious adverse events (death) (2 studies): not calculated Other adverse events: no analysis possible For all comparisons: no firm conclusions could be drawn for any outcome in any comparison.	Pooling of results was not possible due to heterogeneity of studies

Straube, 2014 15 studies	SR Literature search up to March 2014 <u>Study design:</u> RCT <u>Setting and country:</u> UK <u>Source of funding:</u> Not reported	Inclusion criteria SR: 1) RCT's of any duration 2) adults and children of any age who expierenced cancer-related pain 3) codeine, alone or in combination with paracetamol, using any formulation, dosage regimen, and route of administration for cancer pain Exclusion criteria SR: 1) quasi-randomized studies 2) studies with <10 participants 3) non cancer related pain 4) no assessment of pain as outcome Exclusion criteria SR: *15 studies included*	Intervention: codeine, alone or in combination with paracetamol, using any formulation, dosage regimen, and route of administration for cancer pain	Comparison: Placebo or an alternative active treatment	<u>End-point of follow-up</u>: -	Codeine +/- paracetamol compared with placebo for cancer pain At least 50% reduction in pain or equivalent: not calculated "moderate"benefit; at least 30% reducation in pain: no data. Proportion below 30/100 mm on VAS: no data Patient Global Impression of Change much or very much improved : no data Adverse event withdrawals: no usable data Serious adverse events: non reported Death: not calculated	Although a number of different drugs or combinations of drugs were compared with codeine, no two studies made the same comparison, and the numbers involved were too small to draw any firm conclusion.

Author(s): Jos Kleijnen
Date: 2016-11-14
Question: Should neurolytic plexus hypogastricus block be used for pain due to cancer?
Settings: Treatment by anesthetists
Bibliography: Mishra S, Bhatnagar S, Rana SP, Khurana D, Thulkar S. Efficacy of the anterior ultrasound-guided superior hypogastric plexus neurolysis in pelvic cancer pain in advanced gynecological cancer patients. Pain Med. 2013;14(6):837-42. doi: 10.1111/pme.12106.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Neurolytic plexus hypogastricus block	Control	Relative (95% CI)	Absolute		
Global pain intensity[1] (follow-up 1-13 weeks; assessed with: 10cm VAS)												
1	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	-	-	-	-	EBEBOO LOW	CRITICAL
								0%		-		

1 The VAS-scores in the hypogastric-block-group had decreased significantly after 1 week, 1 and 2 months (about 20 at all times vs. 55, 45 and 35 respectively in the control group). At 3 months, there was no difference in pain scores. No numeric results were given, the data have to be estimated from a figure.

2 Doubts about adequate blinding

3 Small trail with 25 patients per group

Evidence table for systematic review of RCTs and observational studies (intervention studies)

Research question: Bijwerkingen van opioïden

Study reference	Study characteristics	Patient characteristics	Intervention (I)	Comparison / control (C)	Follow-up	Outcome measures and effect size	Comments
Dale 2010	Only narrative description of 11 studies, no RCTs	Studies including adult cancer pain patients switching from one strong opioid ladder to another. 11 studies	Opiods switching	Opioids switching	Not mentioned	Side effects narratively decribed in table 1	The evidence profiles for the outcome side effects started low. The data was considered imprecise with a high probability of reportingbias and therefore the evidence level was low
Langsand 2011	All kind of studies, 55 studies in total.	Adult cancer patients receiving opioids for chronic cancer pain, addressing management of nausea and vominting either as a primary or a secondary endpoint 55 studies	Several kind of treatment of nausea/vomiting	Several kinds of treatment of nausea/vomiting	Not mentioned	Only narrative summary of findings: Several antiemetics reported to be effective (metoclopramide, levosulpiride, olanzapine, risperidone, scopolamine, tropisetron)	
Sande 2019	15 RCTs	Patients with cancer ; >=18 years of age, on opioids (weak or strong opioid) as defined by WHO's Analgestic	Opioid switch	Other opioid switch	Not mentioned	Narrative summary of main findings	

		Laddeer for cancer pain relief; nausea and/or vomiting assessed as primary or secondary outcome					
Ahmedzai 2010	23 systematic reviews, RCTs or observational studies	Studies answering the questions: What are the effects of: orla laxatives, rectally applied medications, and opioi antagonists for constipation in people prescribed opioids?	Opioids	Opioids	Not mentioned	Narrative summary of findings	
Stone 2010	26 studies	Adult patients with chronic cancer pain, containing data on the efficacy of a treatment for the opioid central nervous system (CNS) adverse effect (sedation, cognitive impairment, myoclonus, hyperalgaesia, insomnia) 26 studies	Management of opioid-induced central side effects	Management of opioid-induced central side effects	Not mentioned	Only narrative summary of findings	The overall quality of the data wa low, and the few recommendations that can be made are weak and require confirmatory studies.
Mehta 2016	6 RCTs	Studies (RCTs) published after 2007,, studying the use of methylnaltrexone fot the treatment of Opioid-induced	Management of opioid-induced constipation	Management of opioid-induced constipation	Not mentioned	Risk difference for opioid induced constipation favors methylnaltrexone RD=0.33 (95%CI 0.27-0.39) p< 0.0001)	

		constipation, with the occurrence oif an rescue-free bowel movement (RFBM) within 4 hours as primary end point.					
Ruston 2013	Systematic review, however no studies included						
Sivanesan 2016	Systematic review, however only case reports included, no comparison						