A systematic review of the effectiveness of patient-based educational interventions to improve cancer-related pain

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General and Supportive Care

A systematic review of the effectiveness of patient-based educational interventions to improve cancer-related pain

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ABSTRACT

Background: Despite existing guidelines to assess and manage pain, the management of cancer-related pain is often suboptimal with patients often being undertreated. Inadequate pain management may be due to patient-related barriers. Educating patients may decrease these barriers. However, the effect of pain education on patient-related outcomes is still unclear. This review aimed to study the effect of educational interventions on cancer-related pain.

Design: We performed a systematic review of randomized controlled trials (RCTs) identified from Medline and Cinahl, from 1995 to May 2017. Two reviewers independently selected trials comparing educational intervention to usual care or an active control intervention. The methodological quality was assessed and data extraction was done independently. Primary outcome measures were pain intensity and interference. Secondary outcome measures were knowledge/barriers, medication adherence and self-efficacy.

Results: Twenty-six RCTs totaling 4735 patients met our inclusion criteria. Compared to the control group, 31% of the studies (including 19% of all patients) reported a significant difference in pain intensity in favor of the intervention group. Twelve studies measured pain interference and four (30%) found a significant improvement. With regard to secondary endpoints, significant differences in favor of the experimental arms were found for pain knowledge or barriers (15/22 studies; 68%), medication adherence (3/6 studies; 50%) and self-efficacy (1/2 studies).

Conclusions: Patient-based pain educational programs may result in improvements of relevant patient-reported outcomes. However, the interventions are heterogeneous and improvement of pain was only seen in less than one third of the studies and in less than 20% of all included patients.

Introduction

Pain continues to be a frequently occurring symptom in patients with cancer, with a prevalence of 66% in patients with advanced, metastatic or terminal disease. In addition, 38% of all patients with cancer-related pain report moderate or severe pain (≥5 on a 0–10 numeric rating scale) [1]. Pain is associated with interference with daily activities, sleep, mood and social interactions [2–4]. Despite existing guidelines to assess and manage pain [5–7], the management of cancer-related pain is often suboptimal [8] and patients are regularly undertreated [9]. Inadequate pain management seems to be related to professional as well as patient-related barriers. The most commonly reported professional-related barriers include inadequate assessment and inadequate knowledge of pain management. The three most frequently described patient-related barriers are: poor knowledge and misconceptions about pain medication and their side-effects, non-adherence to treatment regimens and a deficit in communication about pain with health care providers [2,10]. Different

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educational interventions to reduce patient-related barriers and to improve their knowledge and communication with healthcare professionals have been developed and studied. Because these interventions vary greatly in type, content and duration the effects are still uncertain [3,10–12]. Moreover, it remains unclear which intervention components are most effective to improve cancer pain management [3,10–14].

In the Netherlands we recently updated our national evidence-based guideline "Diagnostics and treatment of pain in patients with cancer" [7]. As part of this guideline update, the literature on the effectiveness of educational interventions was systematically reviewed, since various new randomized controlled trials (RCTs) were published in the last 7 years and the existing reviews did not report all possible relevant outcomes. It was hypothesized that educating patients about pain improves their knowledge, reduces pain-related barriers and improves medication adherence and self-efficacy, which will all lead to better pain control and less interference with daily life [15]. The aim of this systematic review is to investigate the effectiveness of educational interventions in patients with cancer-related pain on all these relevant outcomes.

Materials and methods

Search methods

A systematic search of the literature published between January 1st 1995 and May 8th 2017 was performed using the following databases: Medline (OVID) and Cinahl. Together with a literature search specialist (IM), we developed a comprehensive search strategy combining key terms using a series of free text terms and MESH terms for: profession and/role (e.g. nurse; nurse practitioner; cancer nurse; oncology nurse) and Cancer (e.g. neoplasm; tumor, etc.). Boolean operators were used in order to maximize the penetration of terms searched, and appropriate "wild cards" were used to account for plurals, variations in databases and spelling. Previous reviews included randomized controlled trials, as well as studies with nonrandomized designs. Because there are many studies investigating the effect of educational interventions, in this review only randomized controlled trials were included. An example search strategy is provided in Supplementary file 1.

Only articles published in English, Dutch or German were considered. Bibliographies of selected studies and relevant Cochrane reviews were also hand-searched in order to identify any further relevant studies not detected by the electronic search.

Criteria for considering studies for this review

Studies were selected if the patient population consisted of adult patients with cancer-related pain. Nociceptive, neuropathic as well as mixed nociceptive and neuropathic pain were included. Only studies regarding patients with solid malignancies were included. All studies describing interventions in which patients received education about the management of their cancer-related pain were eligible. We defined educational interventions as information, behavioral instructions and advice given for the management of cancer-related pain (by verbal, written, audio- or videotaped or computer-aided modalities), which are given by a healthcare professional. Interventions aimed only at family caregivers and studies in which patients' pain intensity was not self-reported were excluded. For inclusion of studies, no restraints regarding the duration of follow-up were made.

The intervention could be compared to no intervention (care as usual) or an active control intervention (e.g. attention visits or education about nutrition).

Primary outcome measurements considered in this review were pain intensity and pain interference, measured before and after intervention. Secondary outcome measures were: knowledge about cancer-related pain, pain barriers, medication adherence and self-efficacy.

Study selection

One reviewer conducted the searching and initial screening. A second reviewer (JG, WO, or IM) independently assessed all titles with or without abstracts identified by the search. In case of potentially relevant articles, the full text was obtained to judge if they fulfilled the inclusion criteria. For the articles that met our inclusion criteria, data were extracted independently by two authors (WO, IM and/or JG), after which extracted data were compared. All studies were assessed in a standard manner. For each trial included, information was extracted on study design, number of patients, length of follow-up, kind of intervention, pain intensity, knowledge about pain, pain barriers, pain interference with daily life, medication adherence and self-efficacy.

Assessment of risk of bias in included studies

The quality of each RCT was assessed by two authors (WO, IM) by examining the risk of bias of each paper based on the adequacy of randomization, blinding, presence of selective outcome reporting, information provided on withdrawals and dropouts and potential violation of intention-to-treat analysis [16]. Disagreement on methodological quality was resolved, when necessary, by discussion between these two authors.

Results

Characteristics of included studies.

The literature search identified 680 titles. Fig. 1 shows the selection process. A total of 53 papers was selected for full text assessment. A high level of concordance was achieved as there was disagreement in only 4 out of 53 papers. These 4 papers were discussed with two additional authors until consensus was achieved. Twenty-nine articles fulfilled our inclusion criteria, describing 26 different studies as three studies [17–22] were described in several articles.

A total of 4735 patients were included. The study population varied from 30 to 1256 patients at baseline. Twelve studies were conducted in the USA [18,23–33], eight in Europe [20,21,34–39], three in Asia [40–42], two in Australia [43,44] and one in Canada [45].

Most studies (20) included outpatients [18,20,21,23–29,31–33, 35–37,41,43–45], five studies included inpatients [34,38–40,42] and one study included both inpatients and outpatients [30]. Three studies included both patients and family caregivers [29,30,41].

In 13 studies, the control group received care as usual [21,24, 27–29,34,36–39,41,43,45], in the other studies an active control intervention was given (Supplementary Table 1).

Although the interventions varied widely in content and intensity, 22 out of the 26 (85%) studies provided face-to-face sessions with the patients; 19 of these studies provided repeated contacts: four studies several face-to-face sessions and additional phone calls, five studies only repeated face-to-face sessions, and ten studies one face-to-face contact and additional phone calls. Seventeen studies combined these sessions with a booklet or video. The three studies without face-to-face contacts provided a booklet and/ or educational video supplemented with phone calls in two of them. Follow-up varied from 5 days to 6 months (median 8 weeks) (Supplementary Table 1).

All studies had some degree of risk of bias. As shown in Table 2, almost all studies had problems with blinding of the treatment allocation, (the participants and/or providers and/or outcome assessors). Overall, the majority of the studies reported most measured outcomes. However, three studies are very likely to have a bias here [24,41,43]. Due to the heterogeneity in study design, type of intervention, and the outcome measures, it was not possible to pool the results of the studies.

Primary outcomes

Pain intensity

All studies measured patients' pain intensity. Most studies reported on worst and average pain [18,20,21,25,26,30,34,35,40,43,45]. Composite scores were used by Kravitz (mean of worst and usual pain), Ward (2008, 2009-1 and 2009-2) (mean of worst, least and current pain) and Williams (mean of worst, least, current and usual pain). The remaining studies measured another type of pain intensity (e.g. current pain) or did not specify what type of pain intensity was measured (Table 1).

A 0–10 Numeric Rating Scale (NRS) was used in 22 of the 26 studies and a 0–100 Visual Analogue Scale (VAS) in two studies [31,33]. Two studies used a combination of a 0–10 NRS and a 4 or 5-point Likert scale [29,39]. One study reported only on pain relief on a 0–100 NRS [32].

Eight of the 26 studies (31%) reported a statistically significant difference in pain intensity in favor of the intervention group [18,21,25,39–41,43,45]. However, these studies measured pain intensity in different ways; average pain intensity (six studies), worst pain intensity (four studies), current pain intensity (three studies), and least pain intensity (two studies; Table 1). These eight studies included 19% of all included patients. In six out of these eight studies, the intervention existed of a face-to-face session (nurse-led in five studies), followed by repeated face-to-face sessions (n = 4) or follow-up phone calls (n = 2). All studies provided written and/or videotaped information. The control group received

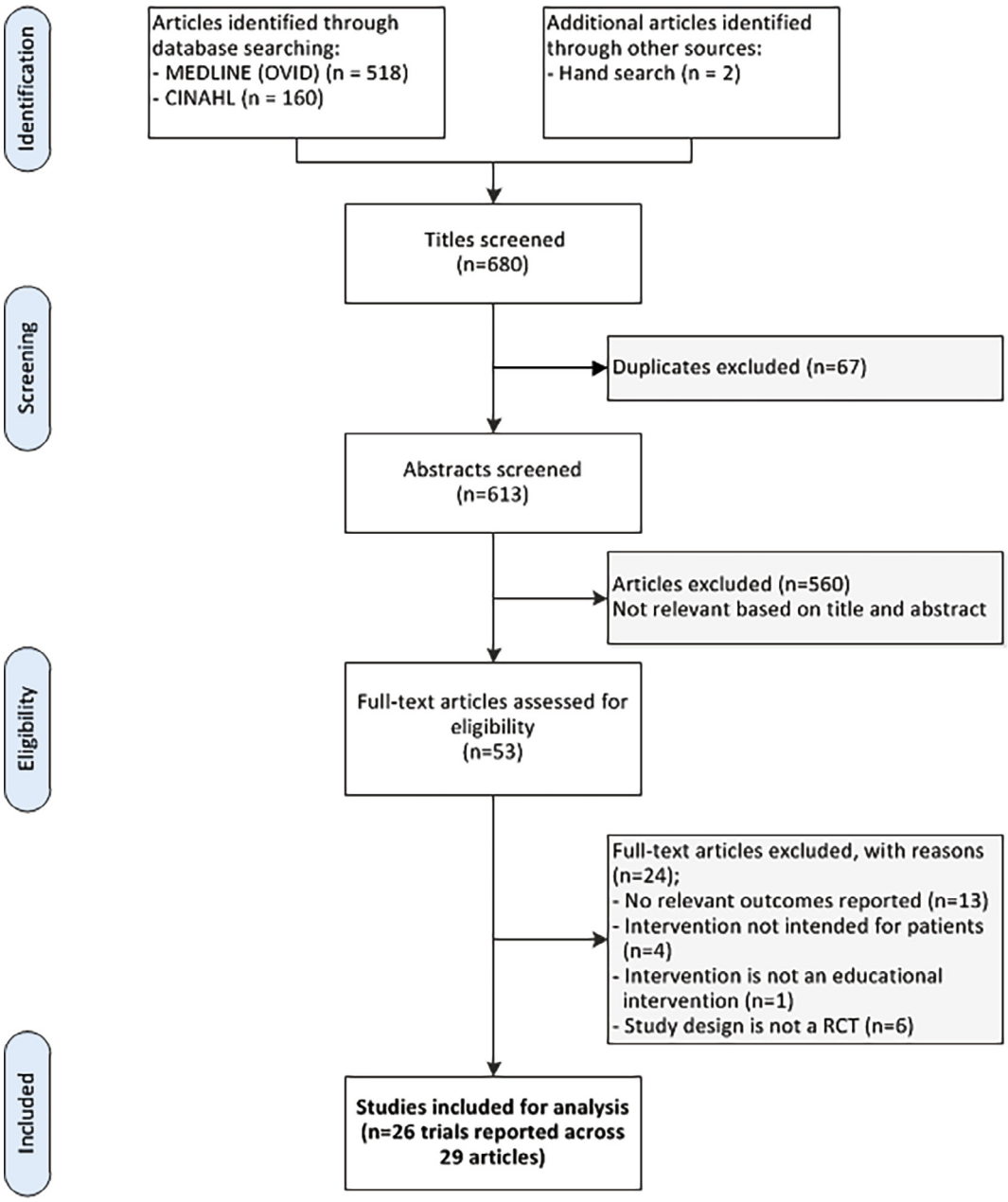

Fig. 1. Prisma flow diagram.

Table 1
Summary of the difference in main outcomes between the different groups of the included RCTs.

Study	Intervention	Number of patients: total (inter- vention)	Follow-up	PID average pain intensity	PID worst pain intensity	PID pain intensity others	Knowledge about pain	Pain barriers	Pain interference with daily life	Medication adherence	Self-efficacy
Anderson (2004)	Video + booklet	97 (50)	10 weeks	–	*BPI (0–10)* DNR; NS	–	*SPA* DNR; NS	–	*BPI (0–10)* DNR; NS	*Self-reported adherence* 14%; NS	–
Jahn (2014)	SCION-PAIN	263 (128)	1 week	*BPI (0–10)* DNR; NS	*BPI (0–10)* DNR; NS			*BQ II* 0.49 (CI −0.87 to −0.12) p = .02		*MAS* Better adherence in intervention group, p = .02 DNR	–
Koller (2013)	PRO-SELF	39 (19)	22 weeks	*BPI (0–10)*-0.51 (CI: −1.95 to 0.94); NS	*BPI (0–10)*-0.47 (CI: −2.81 to 1.87); NS		*PPQ (0–10)* 22%; P < .01	–	*BPI (0–10)* 1.5; (P = .02)	–	*SEQ (Null-100)* 7.3; NS
Kravitz (2012)	Tailored education and coaching	307 (150)	12 weeks			*0–10 scale* *Composite scale:* DNR; NS	–	*SBQ* 0.02; NS	–	–	*CPSE* (2 weeks) Communication 0.22, P < .001 Pain control: −0.03, NS
Lai (2004)	Patient Education Program	30 (15)	5 days	*BPI (0–10)* 1.6 P < .05	*BPI (0–10)* 0.13 NS	*BPI (0–10)* *Current pain:* 1.93; P < .05	*POABS-CA* 1.09 P < .005		*BPI (0–10)* .76 NS	–	–
Lin (2006)	Pain education program	61 (31)	4 weeks	*BPI (0–10)* DNR	*BPI (0–10)* 1.33; P = .04		–	*BQ-T* 0.78 (P < .0001)	*BPI (0–10)* −1.24 (P = .03)	*MAS (0–4)* 1.78 P < .0001 Use of pain medication: 0.16; P = 0.05	–
Lovell (2010)	Video + booklet	217 (163)	4 weeks	*BPI (0–10)* −1.17; P = .02	*BPI (0–10)* −1.12; P < .05	–	–	*BQ* −0.13; NS	*BPI (0–4)* DNR	–	–
Miaskowski (2004)/Kim (2004)	PRO-SELF	174 (93)	6 weeks	*NRS (0–10)* 34% P < .001	*NRS (0–10)* 26% P < .001	*NRS (0–10)* *Least pain:* 43% P < .001	FPPQ (0–100) 12.7; P < .001		–	Diary 25% increase vs. 9.0%; NS	–
Oldenmenger (2011)/ Oldenmenger (2017)	PC-PEP	73 (35)	8 weeks	*BPI (0–10)* −31% vs. −20% P = .03	*BPI (0–10)* 0.12 NS	*BPI (0–10)* *Current pain:* 30% vs. 16%, P = .016	*FPPQ (0–100)* 7; P = .002	–	*BPI (0–10)* 20% vs.2.5%; P = .01	*MEMS* 9%; P = .028	–
van der Peet (2009)	PEP	120 (58)	8 weeks		–	*BPI (0–10)* *Current pain*: −0.9; NS	*FPPQ (0–100)* DNR; P < .001	–	–	–	–
Rustøen (2012)/(2013)	PRO-SELF	179 (87)	6 weeks	*NRS (0–10)* DNR; NS	*NRS (0–10)* DNR; NS		*PES* 18.5; P < .001	–	–	–	–
Smith (2010)	PECS	89 (47)	12 weeks		–	*BPI pain relief (0–100%)* −5.1; NS	–	*BQ* −10.5; P = .04	–	–	–
Syrjala (2008)	Patient training	93 (48)	6 months	*BPI (0–10)* −0.81 ± 0.36 P = .03	*BPI (0–10)* 0.27 ± 0.38 NS			*BQ* −0.32 ± 0.09 P < .001	*BPI (0–10)* −0.62 ± 0.38 NS	–	–
Thomas (2012)	Education or coaching	317 (103); (105)	6 months	*BPI (0–10)* DNR; NS	*BPI (0–10)* DNR; NS			*BQ* DNR; NS	*0–10 scale* DNR P = .02	–	–
Tse (2012)	PMP	43 (22)	1 week	–	–	*NRS (0–10)* 0.72; NS	–	*BQ-T* Total score DNR; NS	–	–	–
Vallieres (2006)	Intervention session + pain diary	64 (33)	3 weeks	*NRS (0–10)* 2.2 P = .01	*NRS (0–10)* 1.7 NS		–	–	–	–	–
Ward (2008)	RID Cancer Pain	176 (92)	2 months		–	*BPI (0–10)* 0.17; NS	–	*BQ-r (0–5)* 0.07 P = .025	*BPI (0–10)* 0.26; NS	–	–
Ward (2009_1)	TBI	1256 (391)	4 weeks	–		*BPI (0–10)* *composite scale* 0.13; NS	–	*BQ-II* DNR P < .001	*BPI (0–10)* NS	–	–
Ward (2009_2)	1 dyads and 2 solo	161 (104)	9 weeks	–		*BPI (0–10)* 1.49; NS	–	*BQ-II* Dyads vs control 0.64 P = .001 Solo vs control 0.38 p = .018	*BPI (0–10)* 0.03; NS	–	–

(*continued on next page*)

Table 1 (*continued*)

Study	Intervention	Number of patients: total (inter- vention)	Follow-up	PID average pain intensity	PID worst pain intensity	PID pain intensity others	Knowledge about pain	Pain barriers	Pain interference with daily life	Medication adherence	Self-efficacy
Wells (2003)	PEP	64 (40)	6 months	*BPI (0–10)* DNR; NS	*BPI (0–10)* DNR; NS	–	–	*BQ-r* Total score DNR; NS	*BPI (0–10)* DNR; NS	–	–
Wilkie (2010)	Coaching on pain related variables	151 (76)	4 weeks			*VAS (0–100) Current pain*: 0; NS	–	–	–	–	–
Williams (2015)	Pain treatment and education by pain team	149 (75)	3 months	*BPI (0–10)* DNR; NS	*BPI (0–10)* DNR; NS	*BPI (0–10)* *Composite scale:* 0.36 (CI: −0.29–1.01); NS	–	–	–	–	–
De Wit (1997), EJP (2001)	PEP	313 (159)	8 weeks	*NRS (0–10)* 0.4; NS		*NRS (0–10)* *Current pain*: 0 (NS)	*FPPQ* 7; P < .01	–	–	–	–
Wright Oliver (2001)	Individualized intervention	67 (34)	2 weeks	*VAS (0–100)* 6.26; NS	–		*APSG-Q* DNR; NS	–	–	–	–
Yates (2004)	PMI	189 (97)	2 months	*BPI (0–10)* 0.0; NS		–	*0–10 scale* 0.4; NS	*BQ* DNR; NS	*BPI (0–10)* 3.3; NS	–	–
Yildirim (2009)	PEP	40 (20)	8 weeks		*Likert (1–5)* 0.7; NS	*NRS (0–10)* *Current pain* 1.55; P < .01	–	*BQ-r* 0.81; P < .05	–	–	–

APSG-Q: American Pain Society Guidelines for the Treatment of pain Patient Outcome questionnaire; BPI: Brief Pain Inventory; BPI-SF: Brief Pain Inventory Short Form; BQ: Barriers Questionnaire; BQ-II: Barriers Questionnaire II; BQ-r: Barriers Questionnaire Revised; BQ-T: Barriers Questionnaire Taiwanese version; CI: 95% confidence Interval; CPSE: Chronic Pain Self Efficacy Scale; DNR: data not reported; FPPQ: Ferrell's Patient Pain Questionnaire; MAS: Medication Adherence Scale; MEMS: Medication events monitoring system; NRS: Numeric Rating Scale; NS: No statistical Significant differences; PC: pain consultation; PCP: pain control program; PECS: Pain Education/Communication Skills; PEP: pain education program; PES: Pain Experience Scale; PID: Pain Intensity Difference; PMI: Pain Management Intervention; PMP: Pain management program; POABS-CA: Pain Opioid Analgesic Beliefs Scale – Cancer; PPQ: Patient Pain Questionnaire; SBQ: Short Barriers Questionnaire; SCION-PAIN: Self Care Improvement through Oncology Nursing; SEQ: Self Efficacy Questionnaire); SPA: Survey of Pain Attitudes; TBI: tailored Brief Intervention; TEC: tailored education and coaching (lay-administered); VAS: Visual Analogue Scale – : not reported.

care as usual in five studies. In all but one study, the follow-up was ≤ 8 weeks (Supplementary Table 1).

Pain interference

Twelve studies investigated pain interference with daily life [21,23,26–30,35,40,41,43,44]. Ten of these studies reported interference on a 0–10 NRS scale, measured with the Brief Pain Inventory (BPI). Two studies used an adapted version to measure interference (Table 1).

Four studies (33%) found a statistically significant difference between the intervention and the control group [21,32,35,41]. Two of these studies also found a significant difference in pain intensity (Table 1) [21,41].

Secondary outcomes

Knowledge about cancer-related pain/pain barriers

Twenty-two studies (85%) reported on pain knowledge and/or pain barriers. A version of the Barriers Questionnaire (BQ) was used in 14 studies (Table 1). Fifteen studies (68%) showed a significant difference in pain knowledge or barriers (increased knowledge or less barriers; Table 1). In all these studies, the intervention existed of a face-to-face session (nurse-led in 11 studies), followed by repeated face-to-face sessions and/or follow-up phone calls in 14 studies. Twelve studies provided written and/or videotaped information. The control group received care as usual in nine studies. In 11 studies, the follow-up was ≤ 8 weeks (Supplementary Table 1).

Seven out of the eight studies that reported a statistically significant difference in pain intensity, also measured pain knowledge or barriers, in which six studies found a statistically significant difference (Table 1).

Medication adherence

Six studies reported on medication adherence (Table 1). All studies measured medication adherence in a different way. Two studies used a questionnaire: the Medication Adherence Scale [34,41]. Four studies used patients' self-report: in one study patients were questioned whether they used the prescribed analgesics [23,31], in one study a diary was used [18], and one study measured actual use with the Medication Event Monitoring System [21].

Three studies (50%) found a statistically significant increase of medication adherence in the intervention group [21,34,41], of which two (33%) also found a statistically significant difference in pain intensity (Table 1) [21,41].

Self-efficacy

Two studies reported on self-efficacy measured with a questionnaire (Table 1). Kravitz et al. measured self-efficacy after only 2 weeks and found a statistically significant difference on self-efficacy regarding communication [24]. There were no significant differences between the groups regarding pain-control and self-efficacy (Table 1).

None of the included studies reported on all outcome measurements. Four studies reported four of the five selected outcome measurements [21,23,35,41]. One study found no statistically significant differences in any outcome measurement [23]. Another study found statistically significant differences in pain knowledge and pain interference, with no significant differences in pain intensity and self-efficacy [35]. Two studies found statistically significant differences in all reported outcomes: pain intensity, pain interference, pain knowledge or pain barriers and medication adherence [21,41].

Discussion

This systematic review of 26 randomized controlled trials shows that in eight studies (31%) including 19% of all included patients, education has a statistically significant effect on reported pain. None of the included studies reported all pre-defined outcome measurements. Significant improvements in daily pain interference were found in 33% of the studies. A statistically significant improvement in patients' knowledge was reported in 66% of the studies. Medication adherence and self-efficacy were reported in only six and three of the included RCTs, respectively. The included studies were too heterogeneous to prove their effects.

Heterogeneousness was seen in the educational interventions, control interventions, lengths of follow-up and reported outcome measures. The educational interventions varied in content, intensity and duration. Some interventions existed of only written and/or audio-visual information, while other interventions combined this information with single or multiple face-to-face sessions or follow-up phone calls. The interventions were not always clearly described (Supplementary Table 1), so it was hard to see

Table 2
Risk of bias for the included randomized controlled trials.

Study reference (first author, publication year)	Describe method of randomisation[1]	Bias due to inadequate concealment of allocation?[2] (unlikely/likely/unclear)	Bias due to inadequate blinding of participants to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of care providers to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to inadequate blinding of outcome assessors to treatment allocation?[3] (unlikely/likely/unclear)	Bias due to selective outcome reporting on basis of the results?[4] (unlikely/likely/unclear)	Bias due to loss to follow-up?[5] (unlikely/likely/unclear)	Bias due to violation of intention to treat analysis?[6] (unlikely/likely/unclear)
Anderson, 2004	Not described	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unlikely	Unlikely
Jahn, 2014	1) Pair-matched randomization of 2 patients on a ward 2) concurrently on all wards prior to study 3) by a reproducible SAS PROC PLAN 4) by an external department	Unlikely	Likely	Likely	Unclear	Unlikely	Unlikely	Unlikely
Koller, 2013	Computerized permuted blocks procedure, 1:1. Sequentially numbered opaque envelopes	Unlikely	Likely	Unlikely	Unclear	Unlikely	Unclear	Unlikely
Kravitz, 2012	Computer-generated blocked randomization	Unlikely	Likely	Likely	Unclear	Likely	Unlikely	Unlikely
Lai, 2004	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Unclear	Unclear
Lin, 2006	"randomly assigned"	Unclear	Unclear	Unclear	Unclear	Likely	Unclear	Unclear
Lovell, 2010	Central randomization by telephone: random numbers table	Unlikely	Likely	Likely	Likely	Likely	Unlikely	Unclear
Miaskowski, 2004/ Kim 2004	"randomly assigned"	Unclear	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Unclear
Oldenmenger, 2011	Computer-generated randomization procedure with variable block length (1-4 repetition blocks)	Unlikely	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear
Van der Peet, 2009	Computer-generated randomization procedure	Unlikely	Unclear	Unclear	Unclear	Unlikely	Likely	Unclear
Rustøen, 2012/2013	Randomized by lot	Likely	Unclear	Unclear	Unclear	Unclear	Unlikely	Unlikely
Smith, 2009	Randomization utility routine in SPSS	Unlikely	Unclear	Unclear	Unlikely	Unlikely	Unlikely	Unclear
Syrjala, 2007	Randomly assigned in blocks based on stratifications	Unlikely	Likely	Likely	Likely	Unlikely	Likely	Likely
Thomas, 2012	Permuted blocks with variable sizes	Unlikely	Unlikely	Unlikely	Unlikely	Unlikely	Likely	Unclear
Tse, 2012	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Unlikely	Likely
Vallieres, 2006	Randomly assigned (no further description)	Unclear	Unclear	Unclear	Unclear	Unlikely	Unclear	Unclear
Ward, 2008	Excel's RAND function	Unlikely	Likely	Likely	Likely	Unlikely	Unlikely	Unclear
Ward, 2009_1	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear
Ward, 2009_2	Excel's RAND function in repeating blocks of 30	Unclear	Likely	Likely	Likely	Unlikely	Unlikely	Unclear
Wells, 2003	Not reported	Unclear	Likely	Likely	Likely	Unlikely	Unclear	Unclear
Wilkie, 2010	Sequentially numbered opaque envelopes	Unlikely	Likely	Unlikely	Unclear	Unlikely	Unclear	Unclear
Williams, 2015	Randomization was performed in blocks based on stratifications	Unlikely	Likely	Unclear	Unclear	Unlikely	Unlikely	Unclear
De Wit, 1997	Not reported	Unclear	Unclear	Unclear	Unclear	Unlikely	Likely	Unclear
Wright Oliver, 2001	Randomization in blocks of 20	Unclear	Unclear	Unclear	Unlikely	Unlikely	Unclear	Unclear
Yates, 2003	Computer-generated table of random numbers	Likely	Likely	Likely	Likely	Unlikely	Unlikely	Unlikely
Yildirim, 2009	Not described	Unclear	Unclear	Unclear	Unclear	Unlikely	Unclear	Unclear

[1] Randomization: generation of allocation sequences have to be unpredictable, for example computer generated random-numbers or drawing lots or envelopes. Examples of inadequate procedures are generation of allocation sequences by alternation, according to case record number, date of birth or date of admission.
[2] Allocation concealment: refers to the protection (blinding) of the randomization process. Concealment of allocation sequences is adequate if patients and enrolling investigators cannot foresee assignment, for example central randomization (performed at a site remote from trial location) or sequentially numbered, sealed, opaque envelopes. Inadequate procedures are all procedures based on inadequate randomization procedures or open allocation schedules.
[3] Blinding: neither the patient nor the care provider (attending physician) knows which patient is getting the special treatment. Blinding is sometimes impossible, for example when comparing surgical with non-surgical treatments. The outcome assessor records the study results. Blinding of those assessing outcomes prevents that the knowledge of patient assignment influences the process of outcome assessment (detection or information bias). If a study has hard (objective) outcome measures, like death, blinding of outcome assessment is not necessary. If a study has "soft" (subjective) outcome measures, like the assessment of an X-ray, blinding of outcome assessment is necessary.
[4] Results of all predefined outcome measures should be reported; if the protocol is available, then outcomes in the protocol and published report can be compared; if not, then outcomes listed in the methods section of an article can be compared with those whose results are reported.
[5] If the percentage of patients lost to follow-up is large, or differs between treatment groups, or the reasons for loss to follow-up differ between treatment groups, bias is likely. If the number of patients lost to follow-up, or the reasons why, are not reported, the risk of bias is unclear
[6] Participants included in the analysis are exactly those who were randomized into the trial. If the numbers randomized into each intervention group are not clearly reported, the risk of bias is unclear; an ITT analysis implies that (a) participants are kept in the intervention groups to which they were randomized, regardless of the intervention they actually received, (b) outcome data are measured on all participants, and (c) all randomized participants are included in the analysis.

differences and similarities between the interventions. The control interventions differed from care as usual to friendly visits or educational interventions regarding nutrition. The length of follow-up also varied widely, from 5 days to 6 months.

Although patients' pain intensity was measured in all included studies, the way this was reported varied widely. Different types of pain intensity were reported (e.g. average, worst, current, least pain intensity or combinations of these types), and with different time frames (e.g. at this moment, last 24 h or last two weeks; Supplementary table 1). Besides this, different methods to measure pain intensity were used (Table 1). This variation was previously reported in several articles, and these articles were calling for more standardization in outcome measurements [11,46,47], but, as our present review shows, in the more recent studies there is still no improvement in standardization of outcome measurements.

We included interference of pain with daily activities also as a primary outcome. To our opinion it is not only important to evaluate patients' pain intensity, but also the impact of pain on daily life. Improved pain management can be achieved by a lower pain intensity, or by lower interference with the same pain intensity, making it possible for patients to increase their daily. This should be an important topic in patients' pain education, because it is not only important to decrease patients' pain intensity but also to improve their daily activities.

It is a common theory that improvements in patients' pain knowledge lead to improved self-efficacy and medication adherence, and ultimately lead to reductions in patients' pain intensity [15,42,44]. However, in the 88% of the included RCTs reporting data regarding pain knowledge and/ or barriers, we were not able to find a relation with pain intensity nor adherence. Medication adherence was measured in different ways, with a questionnaire, a single statement, and the measurement of the actual analgesic use (Table 1). As described by Oldenmenger et al. [22], these adherence rates should be interpreted in different ways. Therefore, it is hard to compare adherence rates when different methods were used [22]. Moreover, most studies only reported whether patients took their medication (taking adherence), without giving details on the analgesic use during the day (e.g. with the right intervals, timing adherence). In the paper by Oldenmenger et al. [22] on adherence to analgesics in oncology outpatients, the authors concluded that the true problem considering adherence is that patients do not take their pain medication at the right time intervals. This finding is an argument for education and coaching of patients to take their analgesics more regularly using correct dosing intervals [22].

Because most patients with cancer-related pain stay at home, they are expected to have an active and involved role in the monitoring of and communication about their symptoms. With patients' pain education, nurses may stimulate patients' self-efficacy. However, almost none of the included RCTs have measured the effect of pain education on patients' self-efficacy. Future studies should include self-efficacy as a process variable.

Over the years, different reviews on the effectiveness of patient educational interventions were published [3,10,11,13,14]. All these reviews included RCTs as well as studies with other designs, like (quasi-) experimental or pre-posttest designs. In one review, various articles describing different outcomes of the same study were included as separate studies [14]. In this review, the investigators found a significant decrease of pain intensity in 52% of all included studies [14], much more than the 31% of the included studies in our review. An explanation of this discrepancy could be the inclusion of non-randomized studies in their review, as five out of the six non-randomized studies showed a significant decrease in pain intensity.

In the review of Koller et al. [13], educational interventions were categorized into structure and content components and evaluated their efficacy. No single component, or combination of components were found to have a discernible influence on effect sizes. After their review, only one RCT was published reporting a significant decrease in pain intensity [21]. It remains unclear which components or aspects of educational interventions contribute to a decrease in pain intensity. It is remarkable that of the seven RCTs published after 2011 and included in our review, none reported a significant decrease in pain intensity. It is imaginable that over the years, the quality of standard care is improved. This is illustrated by a decrease in pain intensity in both the intervention and the control group in four of these RCTs [26,35,37,42] and the improvement of adequate prescription of analgesics. Three studies investigated the adequacy of analgesic prescription, measured with the Pain Management Index (PMI) [18,21,37]. Miaskowski et al. reported in 2004 an adequate prescription of opioids in 29% of the patients at baseline and 37% in the intervention group at the end of the study [18]. In 2011, Oldenmenger et al. reported that about 61% of the patients had an adequate opioid prescription at baseline [21]. In 2015, Williams et al. reported an adequate opioid prescription of 45–49% at baseline [37].

Strengths and limitations

To our knowledge this is the first systematic review that studies the effect of pain education in patients with cancer-related pain, and provides a clear overview of the risk of bias of these studies. Because of the earlier described heterogeneity, in both the intervention and outcome measurements, it was not possible to pool the results and perform a meta-analysis. The strength of this review is that only RCT's were included, with all relevant outcomes of patient pain education programs, to give a clear overview of the existing evidence. This systematic review described an improvement in pain intensity in 31% of the studies. An explanation for this is the possible contamination of the control group [21], whereby the actual effect of the pain education programs could be much larger. The interpretation of the results of this review is complicated by differences in the quality of the included RCTs. It is striking that in so many RCTs the methodology was unclearly described and therefore the risk of bias was hard to assess. For educational programs it is hard to adhere to all criteria, and therefore we decided not to score the quality of the RCTs nor to exclude studies based on their risk of bias, but to give an overview of the risk of bias. In the future, authors should report the used methodology better, regarding both the interventions and the outcome measurements.

In conclusion, patient pain education programs can improve patients' knowledge about cancer-related pain. However, because of the heterogeneity of both the description of the intervention as the outcome measurements', the effect of education programs on pain intensity and interference of pain with daily activities remains unclear, and no recommendation on types of interventions can be made. A more standardized reporting should be advised in order to enlarge the study populations and to strengthen the evidence.

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Conflict of interest

None.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ctrv.2017.12.005.

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