Asia-Pacific Journal of Oncology Nursing 9 (2022) 39–47

Contents lists available at ScienceDirect

Asia-Pacific Journal of Oncology Nursing

journal homepage: www.ajon.org

Original Article

Randomized clinical trial to evaluate a cancer pain self-management intervention for outpatients

Sabine Valenta [a,b,*], Christine Miaskowski [c], Rebecca Spirig [a,d], Kathrin Zaugg [e,f], Kris Denhaerynck [a], Horst Rettke [g], Elisabeth Spichiger [a,h]

[a] Nursing Science, Department Public Health, University of Basel, Basel, Switzerland
[b] Department Theragnostik, Hematology, University Hospital Basel, Basel, Switzerland
[c] School of Nursing, University of California San Francisco, San Francisco, CA, United States
[d] Department of Nursing Science, University of Witten/Herdecke, Witten, Germany
[e] Department of Radiation Oncology, Stadtspital Triemli, Zurich, Switzerland
[f] Department of Radiation Oncology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[g] Center for Clinical Nursing Science, University Hospital Zurich, Zurich, Switzerland
[h] Department of Nursing, Inselspital, Bern University Hospital, Bern, Switzerland

ARTICLE INFO

Keywords:
Cancer pain
Opioid analgesics
Patient education
Qualitative research
Randomized controlled trial
Self-management

ABSTRACT

Objective: Unrelieved pain is common in patients with advanced cancer. Although psychoeducational interventions were found to decrease pain, effects were moderate. The purpose of this study was to evaluate the efficacy of a pain self-management intervention compared with usual care and to explore participants' experiences with pain management and study participation.

Methods: A multicenter randomized controlled trial design with post-trial interviews was used. Outpatients with cancer pain and their family caregivers were recruited from three Swiss university hospitals. The intervention group (IG) received the six-week intervention consisting of education, skills building, and nurse coaching. The control group (CG) received usual care. Outcome variables were analyzed using multilevel models. Interpretive description guided the qualitative study part.

Results: Twenty-one patients with advanced cancer and seven family caregivers completed the study. The group x time effect showed a statistically significant decrease in average pain ($P = 0.04$), but no significant group x time effect for worst pain ($P = 0.06$). Pain scores, pain-related knowledge, Pain Management Index, self-efficacy, and performance status improved in the IG ($P < 0.05$). Almost all of the interviewed participants perceived the pain management diary, tailored intervention sessions, and weekly support as useful. None experienced study participation as burdensome.

Conclusions: This study was the first to test the efficacy of a psychoeducational cancer pain self-management intervention in a German-speaking context, with most patients receiving palliative care. Clinicians can recommend the use of pain management diaries. Tailoring interventions to an individual's situation and dynamic pain trajectory may improve patients' pain self-management.

Registration number: This study has been registered via ClinicalTrials.gov: NCT02713919.https://clinicaltrials.gov/ct2/show/NCT02713919?term=NCT02713919&draw=2&rank=1.

Introduction

Unrelieved cancer pain is a frequent and distressing symptom,[1] with complex and dynamic trajectories.[2] However, despite increased attention to cancer pain management and effective treatments, between 55% and 66% of patients undergoing treatment for or living with advanced cancer report pain[3] that is treated with analgesics.[4]

In addition to health care– and system-related barriers, patient-related barriers can interfere with pain management. While these barriers include cognitive (e.g., patients' knowledge about pain and pain medication), affective (e.g., stress, anxiety, depression), and sensory (e.g., analgesic side effects) components, the major challenge for many patients is poor adherence with their analgesic regimen.[5,6] In addition, the implementation of pain self-management strategies into daily life is a

* Corresponding author.
E-mail address: sabine.valenta@unibas.ch (S. Valenta).

https://doi.org/10.1016/j.apjon.2021.12.003
Received 6 October 2021; Accepted 6 October 2021

complex process.[7] Patients and their family caregivers need to learn how to monitor their pain, obtain and administer their medications, react if pain is not alleviated, and manage side effects. Considering that they assume these tasks with little or no preparation, knowledge, resources, or skills, improving their competencies to effectively self-manage their pain is an important goal.[8]

Systematic reviews have examined the efficacy of interventions focused on cancer pain self-management.[9,10] While these reviews found statistically significant decreases in pain intensity, the clinical relevance of these decreases was moderate at best. Of note, of the 26 randomized controlled trials (RCTs) that were reviewed,[9] only eight reported statistically significant decreases in pain intensity. In addition, the lack of a standardized methodology decreases the ability to compare intervention effects. For example, educational interventions are prone to high levels of heterogeneity in terms of content, intensity, and duration, as well as length of follow-up and reported outcomes.[9,11] Additional research is needed to evaluate the efficacy of self-management interventions aimed at cancer pain and associated side effects.

One promising psychoeducational intervention identified in earlier meta-analyses was the PRO-SELF© Pain Control Program (PCP). This intervention demonstrated significant decreases in patients' pain intensity,[12] as well as increases in patients'[13] and family caregivers'[14] cancer pain management knowledge. Based on these findings, the PCP intervention was extended from six to ten weeks, resulting in the PRO--SELF© Plus PCP. The latter program was translated and culturally adapted to a German-speaking setting.[15] This adapted German PRO--SELF© Plus PCP was evaluated in a pilot RCT,[15] which became the basis for the Swiss multicenter RCT. For this RCT, while focusing primarily on testing the efficacy of the adapted German PRO-SELF© Plus PCP, we aimed to explore the intervention's effect on associated symptoms and other selected patient outcomes, as well as explore patients' and family caregivers' experiences with pain management and study participation.

Methods

A multicenter RCT design with post-trial interviews was used to evaluate the efficacy of the adapted German PRO-SELF© Plus PCP in outpatients with cancer and their family caregivers. Our qualitative component of the study was guided by interpretive description, a research approach for applied disciplines.[16]

Setting and sample

Patients and their family caregivers were recruited from oncology outpatient clinics at three university hospitals in Switzerland. Outpatients were eligible for inclusion if they (1) had experienced any type of cancer pain with an average pain of $\geq$3 on a 0–10 numeric rating scale (NRS) during the last two weeks; (2) had an estimated life expectancy of $>$6 months; (3) were aged 18 years or older; (4) were able to understand, read, and write German; and (5) had access to a telephone. Patients were excluded if they (1) had cognitive dysfunction or hearing impairment; (2) were hospitalized for $>$2 weeks during the study; or (3) experienced only neuropathic pain. Family caregivers who were aged 18 years or older; able to understand, read, and write German; had access to a telephone; and were willing to participate in all of the intervention sessions were included.

Study procedures

Research assistants (RAs), who worked as nurses in the outpatient clinics, were specially trained to screen patients and family caregivers for eligibility, to inform them about the study, to recruit and randomize them, and to collect data in the control group (CG). Patients who met the study's inclusion criteria were invited to participate during their routine outpatient visits. If family caregivers were involved in the patient's pain management, they were invited to participate.

Patients were stratified by site and randomized 1:1 by the RAs into either the intervention group (IG) or the CG. Using 2-, 4-, and 6-patient blocks, computerized randomization was done to create the two lists. While blinding was not possible for data collectors, treating clinicians were not informed about group allocation.

Participants in both groups received home visits at enrollment (week 0), week 1, and week 6. In addition, all of the patients completed a daily pain and symptom management diary. They were asked to complete the diary before bedtime to review their pain intensity, analgesic intake, side effects, and related strategies over a 24-h period of time.

Participants in both groups completed questionnaires at enrollment (week 0) and at week 6. Participants received a home visit at enrollment to explain the study questionnaires and the diary. Additional visits were done at week 1 and 6 to collect the questionnaires and diaries. For the CG, the RAs did the home visits. In addition, they called each patient/family caregiver every second week to ensure that the pain management diary was completed on a daily basis. In the IG, the intervention nurses (INs) performed the study visits and data collection.

Ethical considerations

The study was conducted according to the Helsinki Declaration[17] and was approved by all responsible ethics committees (Approval No. EKNZ BASEC 2015-00012). Written informed consent was obtained from all participants before enrollment.

Intervention

The PRO-SELF© Plus PCP was developed for patients who have pain from cancer and their family caregivers. It includes structured and tailored components and is based on three key strategies: nurse coaching, self-care skills building to manage pain and associated symptoms, and provision of information through academic detailing.[18] Academic detailing[19] focuses on enhancing knowledge by providing key information and positive reinforcement, while stimulating the learner to be an active partner.

The intervention was provided by four specially educated INs, all of whom were oncology nurses with a Master's degree in nursing. The INs' training occurred over two days and included a review of current pain theory and pain management guidelines as well as education on each intervention component.

In terms of the structured components of the PCP, patients/family caregivers were instructed to monitor pain and analgesic side effects (e.g., nausea, fatigue), to document analgesics taken, and to use a one-week pillbox. They were educated to use a script to communicate with clinicians if pain control was inadequate. In terms of the tailored components, the IN reviewed each pain management diary and assessed each patient's adherence with analgesic medications. In addition, she discussed the appropriateness of the analgesic prescription and side effect management with patients and family caregivers and taught them how to adjust their medications within the prescribed dose range in response to changing pain conditions and side effects. At each visit, the IN assessed the implementation and success of previous recommendations and discussed needed adaptations. Furthermore, she educated patients and their family caregivers to improve their self-management by evaluating their pain management diary entries. Then, based on these evaluations, patients/family caregivers were taught to set individual, achievable goals and establish a symptom management plan to achieve these goals. To identify patients' and family caregivers' pain management knowledge deficits, the INs evaluated their knowledge at enrollment using the Patient Pain Questionnaire (PPQ) and the Family Pain Questionnaire (FPQ).[20] To reinforce their education and enhance their knowledge, patients and family caregivers received a teaching booklet as well as individualized academic detailing sessions.[19]

The timing and dosing of the intervention followed a detailed protocol.[18] Each IG participant received home visits or telephone calls to provide structured and tailored components of the PCP on a weekly basis

for a total of seven intervention sessions. All participants received home visits after enrollment and at weeks 1 and 6. During study weeks 2 through 5, participants received weekly visits either in their homes or by telephone. The IN decided the format for the next visit using the following algorithm: pain score >3 on an NRS; the patient is dissatisfied with pain management; and/or patient adherence with pain medication or recommendations is <50%. If one or more of these criteria occurred, the IN scheduled a home visit; otherwise, the participant received a phone call. Home visits lasted no more than 1 h. Telephone calls lasted approximately 10 min. For quality assurance purposes, all intervention sessions and telephone calls were audio-recorded. The primary investigator reviewed these recordings to promptly discuss any deviations from the intervention protocol with the IN. Although no relevant protocol deviations occurred, the primary investigator and the INs discussed minor issues on a regular basis.

Usual care

The CG participants received usual care at participating centers (i.e., their physicians assessed pain and prescribed analgesic medications). No specific counselling was provided to this group. If participants raised concerns about pain or side effects during home visits or telephone calls for data collection, the RAs encouraged them to contact their physician.

Variables and measurement

As shown in Table 1, this study's primary outcomes were average and worst pain intensity scores. Using the pain management diary on a daily basis, patients reported average and worst pain intensity scores for the previous 24 h using a 0 (no pain) to 10 (worst imaginable pain) NRS. These items are part of the German version of the Brief Pain Inventory (BPI).[21]

Secondary outcomes included pain relief (as a percentage), pain duration (in hours), and types and doses of analgesic medications (e.g., opioid, nonopioid, co-analgesics) assessed on a daily basis by the BPI.[21] Pain interference with function was evaluated weekly using the BPI's Interference Scale.[21] Quality of pain treatment was assessed weekly using the Pain Management Index (PMI).[22] Daily doses of analgesics were converted to morphine equivalents (ME).[23] In addition, patients rated the severity of 12 analgesic side effects on a weekly basis using 0 (none) to 10 (excruciating) NRSs.

To report the presence and severity of constipation, patients completed the Constipation Assessment Scale (CAS). Each CAS item was rated on a 0 (no problem) to 2 (severe problem) scale, with any score of ≥2 indicating constipation.[24] Knowledge of cancer pain management was assessed using the PPQ and FPQ.[20] For these instruments, each item was rated on a 0 to 10 NRS, with higher scores indicating greater knowledge.[25,26] Self-efficacy was evaluated using the 15-item Self-Efficacy Questionnaire (SEQ).[27] This self-report measure evaluates perceived ability to manage specific aspects of pain using a 10 (very uncertain) to 100 (very certain) scale. Functional status was evaluated using the Eastern Cooperative Oncology Group Performance Status scale.[28] In addition, anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS).[29]

Quantitative data analysis

Data were retrieved from the SecuTrial® database and analyzed using SPSS, version 24.0.[30] Demographic and clinical data were systematically examined for out-of-range values and inconsistencies. For all of the study variables, descriptive statistics were calculated. Differences in enrollment characteristics between the patients in the IG and the CG were evaluated using Student's *t*-tests or Mann–Whitney tests. Due to the small sample size of family caregivers, only descriptive statistics are reported for them. All analyses followed an intention-to-treat strategy. The level of significance was set at 0.05.

We quantified the intervention's effect by calculating the mean differences between IG and CG average and worst pain intensity scores after four weeks and at the end of the intervention (week 6). To determine differences between the IG and CG regarding changes in average and worst pain intensity scores, daily duration of pain, pain relief, and

Table 1
Study variables and measurement timetable.

Study variable		Instrument	Assessed in patients	Assessed in FCs	Week 0	Week 1–5	Week 6
Primary outcomes	Average pain and worst pain	Pain management diary[a]:	X		X	X	X
	Pain alleviation through pain medication	BPI	X		X	X	X
	ATC and PRN analgesic prescribed and taken per day converted to ME		X		X	X	X
	Pain interference with function		X		X	X	X
	Duration of pain	Pain management diary[a]	X		X	X	X
	Bowel movements and use of laxatives						
	Side-effects of pain and cancer treatment						
Secondary outcomes	Quality of analgesic prescription	PMI	X		X	X	X
	Constipation	CAS	X		X	X	X
	Knowledge of cancer pain	PPQ	X		X		X
		FPQ		X	X		X
	Self-efficacy	SEQ in patients with cancer	X		X		X
		Caregiver version of the SEQ		X	X		X
	Anxiety and depression	HADS	X		X		X
	Functional status	ECOG performance status	X		X		X
Demographics and clinical data	Demographics, patient	Patient Information Questionnaire	X		X		
	Demographics, FC	FC Information Questionnaire		X	X		
	Clinical data	Medical Record Review Form	X		X		

ATC, around the clock; BPI, Brief Pain Inventory; CAS, Constipation Assessment Scale; ECOG, Eastern Cooperative of Oncology Group; FC, family caregiver; FPQ, Family Pain Questionnaire; HADS, Hospital Anxiety and Depression Scale; ME, morphine equivalents; PMI, Pain Management Index; PPQ, Patient Pain Questionnaire; PRN, pro re nata (as needed); SEQ, Self-Efficacy Questionnaire.

[a] Pain management diary: daily assessment of average and worst pain, pain alleviation, and pain interference with function via the Brief Pain Inventory (BPI), as well as duration of pain, bowel movements/use of laxatives, side effects of pain and of cancer treatment via pain management diary.

changes in medication scores from the initiation to the end of the intervention, we used multilevel modeling. This statistical procedure is well suited for this analysis because 1) it accounts for the hierarchical structure of the data resulting in more accurately estimated standard errors; 2) it offers the option to actively model the changes in study outcomes, using the information from all of the assessments; and 3) it allows for testing the effects of the intervention at level 1 (time) and level 2 (study group) as well as to test for cross-level interactions. The relevant variables (i.e., time, study group, and group × time interaction) were entered successively into the models. For each patient, a random intercept and random slope were estimated.[31]

In addition, independent t-tests or Wilcoxon tests were calculated to determine whether secondary outcome scores changed significantly within the groups over the six weeks of the study. If so, effect sizes (Cohen's d) were calculated.[32]

Qualitative data collection and analysis

After completing the RCT, patients and family caregivers from both groups were invited to participate in interviews to retrospectively explore participants' experiences with pain management and study participation. Initially, the plan was to use purposive sampling to ensure approximately equal numbers per site and variation regarding pain intensity, adherence with the intervention, age, gender, education, living situation, and type of cancer. After the first two months of the study, because of recruitment challenges, all patients and family caregivers

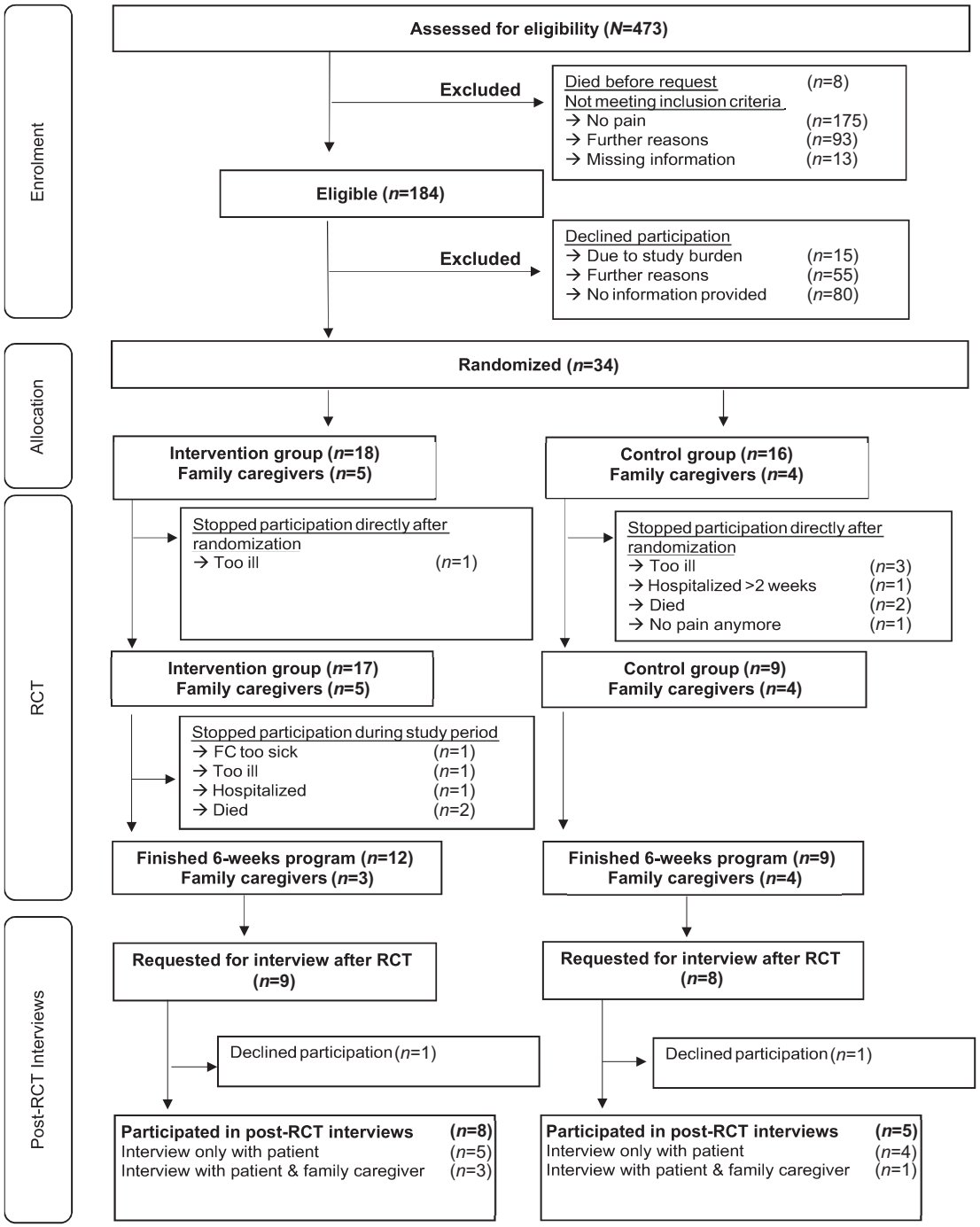

Figure 1. Flowchart of included participants. *Note.* Flowchart of study participation. FC, family caregiver; RCT, randomized controlled trial.

were invited to participate in an interview.

The interviews were conducted by specially educated nurses, the study coordinator, or the principal investigator in participants' homes. Following an interview guide, open-ended questions were asked to explore patients' and family caregivers' experiences with pain and side effect self-management, the pain management diary, and the intervention. Interviews lasted between 21 and 51 min (mean = 37 min). They were audio-recorded and transcribed verbatim. For the qualitative analysis, we applied the thematic analysis approach of Braun et al.[33] by following the six steps in an iterative process. To allow for integration of relevant new topics into the interview guide, the analysis started during the data collection period. For data analysis, the ATLAS.ti Scientific Software (version 8.0) was used.[34]

Results

Patient and family caregiver characteristics

From March 2016 until December 2018, 34 patients and nine family caregivers were included in this study. Figure 1 illustrates the flow of IG and CG participants over this period. Characteristics of the patients and family caregivers are shown in Table 2. Cancer diagnoses included breast, prostate, lung, colon, pancreas, adrenal cortex, urothelium, ovary, and multiple myeloma.

Primary outcomes: changes in pain intensity

For average pain, effect size calculations demonstrated that on the 0 to 10 NRS, the mean difference of change between the IG and the CG was −0.37 (95% confidence interval [CI]: −0.80 to 0.06; Cohen's d = 0.14) at week 4 and −1.12 (95% CI: −1.56 to −0.68; Cohen's d = 0.41) at week 6. The weekly mean pain scores are listed in Table 3. Figure 2A–D illustrate the changes in IG and CG pain scores over the course of the study. For average pain, a significant group × time interaction ($P = 0.04$) as well as a significant main effect of time ($P < 0.001$) were found. However, no significant main effect of group ($P = 0.67$) was found.

For worst pain, effect size calculations demonstrated that on the NRS, the mean difference of change between the IG and the CG was −1.05 (95% CI: −1.67 to −0.42; Cohen's d = 0.26) at week 4 and −1.53 (95% CI: −2.14 to −0.93; Cohen's d = 0.41) at week 6. No significant main effects of group ($P = 0.56$) or group × time interaction ($P = 0.06$) were found, whereas a significant main effect of time ($P < 0.001$) was found.

Secondary outcomes

For pain relief, pain duration, and ME intake, no significant group × time interactions were found (Table 3). Results for PMI, constipation, pain management knowledge, self-efficacy, and performance status for the IG and CG at enrollment, week 4, and week 6 are shown in Table 4. As illustrated in Figure 3, the analgesic side effects with the highest severity scores were fatigue, daytime sleepiness, difficulty concentrating, and nausea.

Qualitative results

As shown in Figure 1, of the 13 interviews conducted after RCTs, eight were with IG participants and five were with CG participants. Four family caregivers were included in joint interviews. Four patients declined to

Table 2
Characteristics of patients and families at enrollment.

Characteristics	Patients with cancer			Family caregivers	
	IG ($n = 17$)	CG ($n = 9$)	P	IG ($n = 5$)	CG ($n = 4$)
Demographic characteristics					
Age in years, mean (SD)	66.6 (14.5)	64.1 (11.0)	0.66	55.2 (2.0)	62.3 (9.8)
Female, *n* (%)	6 (35.3)	4 (44.4)	0.66	4 (80.0)	3 (75.0)
Married/partnered, *n* (%)	12 (70.6)	7 (77.8)	0.76	4 (80.0)	4 (100.0)
Employed, *n* (%)	1 (5.9)	1 (11.1)	1.0	3 (60.0)	2 (50.0)
Highest education, *n* (%)			0.52		
University degree	7 (41.1)	4 (44.4)		2 (40.0)	2 (50.0)
Elementary school	7 (41.1)	1 (11.1)		0 (0.0)	1 (25.0)
Vocational training	1 (5.9)	2 (22.2)		2 (40.0)	1 (25.0)
Commercial school	1 (5.9)	2 (22.2)		1 (20.0)	0 (0.0)
Other	1 (5.9)	0 (0.0)		0 (0.0)	0 (0.0)
Clinical characteristics[a]					
Therapeutic goal palliative, *n* (%)	14 (82.4)	7 (77.8)	1.0		
Current anticancer therapy[b], *n* (%)					
Chemotherapy	2 (11.8)	5 (55.6)	1.0		
Radiotherapy	4 (23.5)	3 (33.3)	1.0		
Steroids	12 (70.6)	8 (88.9)	10		
Bisphosphonates	16 (94.1)	8 (88.9)	1.0		
Pain and medication characteristics[a]					
Average pain, mean (SD)	4.3 (1.8)	3.7 (1.3)	0.27		
Worst pain, mean (SD)	5.3 (1.9)	5.1 (2.0)	0.46		
Total ME per day, mean (25/75 percentiles)	43.5 (23.8/48.3)	46.7 (26.9/56.1)	0.56		
PMI scores, mean (SD)	0.2 (0.8)	0.2 (1.0)	0.84		
Pain interference with function, mean (SD)	3.8 (1.6)	3.6 (1.7)	0.83		
Symptom severity scores					
CAS scores, mean (SD)[a]	0.6 (0.4)	0.5 (0.6)	0.79		
PPQ/FPQ total score, mean (SD)	5.7 (1.1)	6.0 (1.7)	0.67	6.1 (1.3)	6.5 (0.5)
SEQ total score, mean (SD)	69.2 (18.5)	69.9 (10.1)	0.68	43.5 (24.3)	50.2 (20.2)
HADS Anxiety score, mean (SD)[a]	1.4 (0.6)	1.6 (0.8)	0.42		
HADS Depression score, mean (SD)[a]	2.1 (0.3)	2.1 (0.2)	0.42		
ECOG performance status, mean (SD)[a]	2.9 (1.0)	2.9 (0.8)	0.97		

Note. Differences in demographic and clinical characteristics between the patients with cancer in the intervention and control groups at enrollment as well as family caregivers' demographic characteristics.

CAS, Constipation Assessment Scale; CG, control group; ECOG, Eastern Cooperative of Oncology Group; FPQ, Family Pain Questionnaire; HADS, Hospital Anxiety and Depression Scale; IG, intervention group; ME, morphine equivalence in mg/day; PMI, Pain Management Index; PPQ, Patient Pain Questionnaire; SD, standard deviation; SEQ, Self-Efficacy Questionnaire.

[a] Not applicable for family caregivers.

[b] Patients could be receiving more than one type of treatment simultaneously.

Table 3
Mean scores for the primary and secondary outcomes and *P*-values for the group × time interactions.

	Week	0	4	6	Group × time interactions
	n (IG/CG)	17/9	12/9	12/9	
Primary outcomes		Mean (SD)	Mean (SD)	Mean (SD)	*P*
Average pain	IG	4.3 (1.8)	2.6 (1.4)	2.0 (1.2)	0.04
	CG	3.7 (1.3)	3.0 (1.1)	3.1 (1.3)	
Worst pain	IG	5.3 (1.9)	3.1 (1.6)	2.3 (1.5)	0.06
	CG	5.1 (2.0)	4.1 (2.2)	3.8 (2.0)	
Secondary outcomes		Mean (SD)	Mean (SD)	Mean (SD)	
Pain relief (%)	IG	57.1 (20.4)	68.6 (25.8)	72.8 (28.6)	0.19
	CG	50.7 (23.2)	50.0 (30.8)	47.5 (31.5)	
Hours per day in pain	IG	10.6 (7.0)	9.0 (7.0)	8.9 (9.0)	0.29
	CG	7.0 (6.2)	9.3 (9.2)	10.3 (9.2)	
Total ME per day	IG	43.5 (20.7)	40.0 (19.1)	37.8 (16.8)	0.77
	CG	46.7 (22.2)	47.5 (23.5)	42.9 (21.9)	

CG, control group; IG, intervention group; ME, morphine equivalence in mg/day; SD, standard deviation.

participate in an interview. The findings were assigned to three main themes, namely, experiences with the pain management diary, experiences with the intervention, and experiences with study participation.

Experiencing the pain management diary as supportive

According to most participants, including all CG participants and all family caregivers, the pain management diary reinforced their pain self-management efforts. It assisted them in reviewing the course of their pain over the week, in becoming more attentive to their pain, in overviewing the timing and dosing of pain medications, and in reconstructing how they had managed previous pain situations or analgesic side effects (e.g., constipation). "I just filled it [the diary] out late in the evening, before going to bed. And accordingly, I could really look back at my day and deal with it," said a patient. Two IG participants used the diary to report pain to their physician. After the study, several participants in the IG continued using another diary that was recommended by the IN because it provided a sense of control and security and supported pain reporting to their physician. Three CG participants were willing to continue to use the diary. "For me, it [the diary] was such a companion. My husband and I, we have already discussed how I could actually keep a personal diary like this," mentioned one of them. However, eight participants experienced some difficulties with diary completion. For some, it was just forgotten or became boring after a while, assessing pain duration or pain relief was difficult, or rating pain using the NRS was problematic. For some patients, expressing pain in words would have been easier.

Experiencing the intervention as mostly beneficial

All IG participants and family caregivers noted that the structured individualized intervention sessions supported their daily pain self-management. They felt more secure and some were more confident in

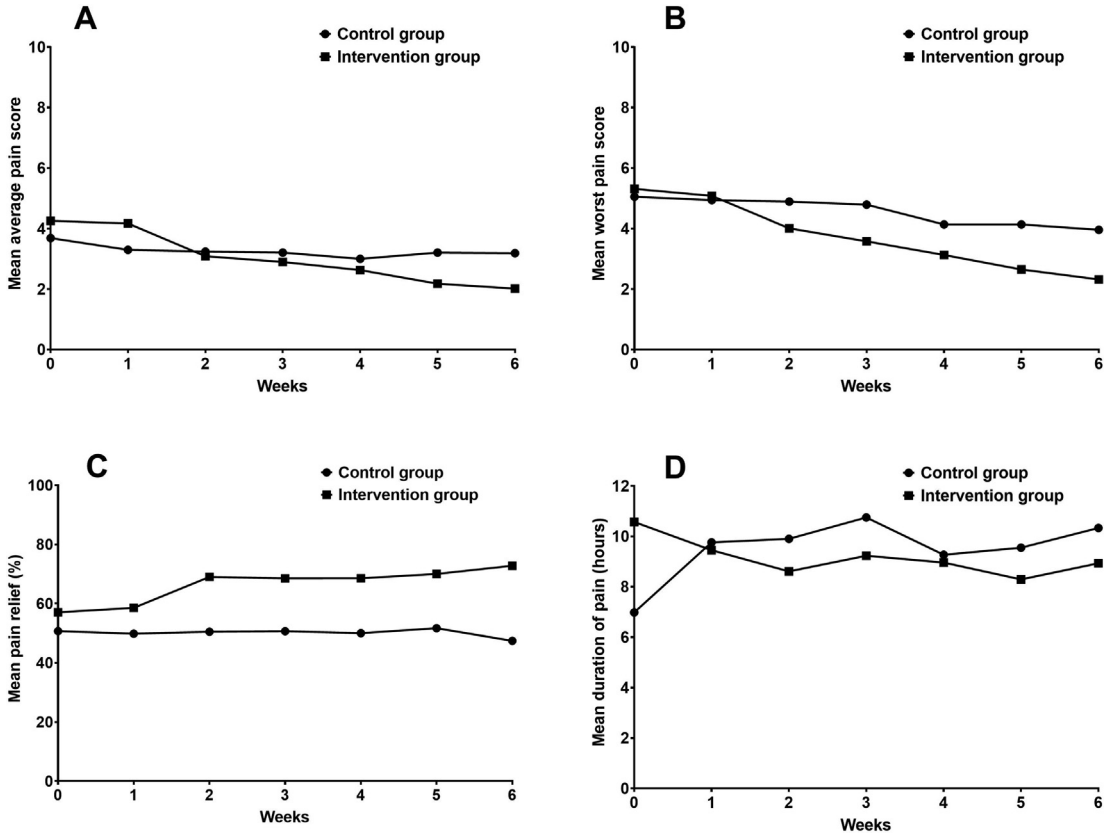

Figure 2. Changes over time in pain scores. *Note.* Changes over time in (**A**) average pain scores, (**B**) worst pain scores, (**C**) pain relief scores, and (**D**) duration of pain over time for patients with cancer in the intervention and control groups plotted as means.

Table 4
Mean scores for the secondary outcomes and effect sizes for intragroup changes.

	Week	0	4	6	Effect sizes
	n	17/9	12/9	12/9	
Secondary outcomes	IG/ CG	Mean (SD)	Mean (SD)	Mean (SD)	Cohen's d
PMI scores	IG	0.2 (0.8)	1.3 (0.7)	1.6 (0.5)*	0.51
	CG	0.2 (1.0)	0.8 (1.0)	0.7 (1.1)	–
CAS scores	IG	0.6 (0.4)	0.5 (0.4)	0.4 (0.5)	–
	CG	0.5 (0.6)	0.2 (0.2)	0.2 (0.2)*	0.78
ECOG performance status	IG	2.9 (1.0)	N/A	2.7 (1.1)	–
	CG	2.9 (0.8)	N/A	2.8 (0.7)	–
Pain interference with function scores	IG	3.8 (1.6)	2.3 (1.6)	2.6 (2.3)*	0.88
	CG	3.6 (1.7)	2.6 (1.8)	2.6 (2.1)	–
PPQ scores	IG	5.7 (1.1)	N/A	7.3 (1.2)*	0.77
	CG	6.0 (1.7)	N/A	6.4 (1.8)	–
SEQ scores	IG	69.2 (18.5)	N/A	79.9 (17.8)*	0.75
	CG	69.9 (10.1)	N/A	67.3 (12.8)	–
HADS Anxiety scores	IG	1.4 (0.6)	N/A	1.0 (0.7)	–
	CG	1.6 (0.8)	N/A	1.4 (0.9)	–
HADS Depression scores	IG	2.1 (0.3)	N/A	1.9 (0.1)	–
	CG	2.1 (0.2)	N/A	2.2 (0.2)	–

N/A, only assessed at enrollment (week 0) and after 6 weeks.
*$P < .05$.
CAS, Constipation Assessment Scale; CG, control group; ECOG, Eastern Cooperative Oncology Group; HADS, Hospital Anxiety and Depression Scale; IG, intervention group; PMI, Pain Management Index; PPQ, Patient Pain Questionnaire; SD, standard deviation; SEQ, Self-Efficacy Questionnaire.

adapting their analgesic regimen. One family caregiver stated: "It [the intervention] just provides security. You just know that you have one more contact point." These positive experiences were directly related to the IN: She listened attentively, had sufficient time to discuss individual problems, responded to previous experiences, supported individual goal setting, and provided useful explanations. One patient explained: "Mrs. S [IN] has written down goals with me that one wants to achieve. In any case, I have achieved all these goals. […] Well, actually through the study, this motivated me." In addition, the IN was perceived as knowledgeable, competent, and – most importantly for participants – trustworthy. In addition, several IG and CG participants found the repeated completion of the PPQ interesting and instructive.

Only three participants suggested improvements. One experienced the telephone call of a substituting IN as insufficient and would have preferred a face-to-face contact. Another individual was generally annoyed with the home visits and would have preferred telephone calls. One family caregiver felt slightly stressed because the intervention sessions had to be arranged after work and she thought that the IN would be bothered. She was very pleased with the IN's flexibility that made evening sessions possible.

Experiencing no burden from study participation

Participants reported no burden from study participation, and most would recommend it to others. Five IG participants and three family caregivers mentioned that they would still like to have a trustworthy contact person, and two participants experienced study participation as a privilege. "Yes, it [the study] could have gone on for us. Not in terms of a study, but simply in terms of support," stated a family caregiver.

Discussion

Our findings suggest that the intervention, the adapted German PRO-SELF© Plus PCP, decreased average pain intensity. In addition, most of the interviewed participants listed numerous benefits from the study and none found it to be burdensome. Effect sizes for average and worst pain intensity were higher in this RCT (−1.12 for average pain and −1.53 for worst pain) than for the pilot study (−0.55 for average pain and −0.73 for worst pain) of the adapted intervention.[15] The decreases in pain intensity in the IG may be attributable to two main factors. First, the intervention was tailored more closely to patients' individual pain trajectories by using an algorithm to determine the number and type of intervention sessions. In previous studies, both the number and types of intervention sessions were fixed.[15,35] However, in other studies, tailored interventions with individual support adapted to patients' needs, concerns, and knowledge gaps proved useful to decrease their pain intensity.[36,37]

Second, contrary to previous studies,[12,15] our CG participants did not receive an "attention control intervention." This change was based on the hypothesis that owing to the trustful nurse-patient/family caregiver relationship, an "attention control intervention" could have influenced pain self-management.[15] In their systematic review, Prip et al.[38] emphasized the importance of a trustful relationship and open communication with clinicians about the patients' ability to cope with cancer, its treatments, and daily life. Our participants highlighted their trustful relationship with the IN as an important and conducive factor in improving their pain self-management. These types of patient-family caregiver-provider relationships and good communication are considered as a central component of care for patients with cancer.[39]

Consistent with previous reports on the efficacy of the PRO-SELF© PCP,[15,40] both our IG and CG participants found the pain management diaries useful because they provided an overview of their daily medication plan, previous handling of pain situations, and changes in their pain scores throughout the day. This finding is consistent with the results of previous research[35,41] that highlighted the use of a pain management diary combined with tailored intervention sessions as an effective approach in decreasing present and average pain intensity.

Regarding pain medication doses, the decreases in pain in both groups were achieved even though patients in this study took lower doses of opioids than in previous studies.[12,15] In addition, CG participants took higher doses of opioids than the IG. A possible explanation for this finding could be that compared with our CG participants, our IG participants were better able to implement pain relief strategies to their current situation because crucial components of the intervention sessions were knowledge transfer, skills training, and empowerment to implement pain management strategies to meet their individual needs. The improved PMI in the IG suggests that their pain management regimen was adequate.[22] This finding is consistent with previous evidence[4,42] that emphasized that adequate pain relief is achieved not only by increasing the opioid dose but also by taking the prescribed doses, adjusting the individual opioid doses to current needs, and making appropriate modifications if pain is not relieved.

Regarding side effects, patients in this study were most affected by fatigue. Given the high prevalence of fatigue in patients with cancer,[43] this finding is not surprising. Other side effect scores were rather low in both the IG and the CG.

Limitations

This study's major limitation was its small sample size. Therefore, findings must be interpreted with caution. While multilevel modeling estimations using the restricted maximum likelihood method are relatively robust for small sample sizes, this limitation was primarily due to challenges with recruitment. Of the 473 patients who were screened, the majority reported no pain, leaving only 184 (39%) eligible patients. Of

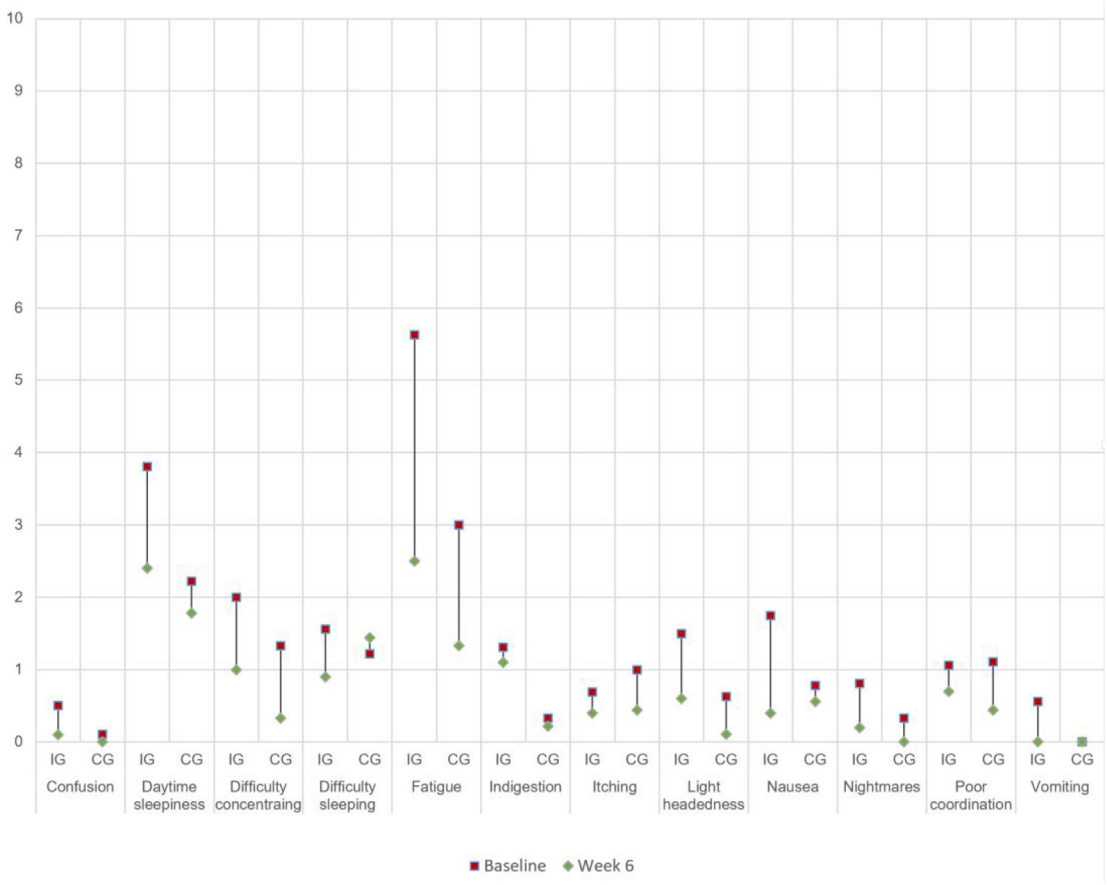

Figure 3. Means and changes in mean analgesic side effect scores. *Note.* Scores for both the intervention and control groups, using a 0 (none) to 10 (excruciating) numeric rating scale from enrollment (week 0) to week 6. CG, control group; IG, intervention group.

that number, only 34 (18%) agreed to participate. Several patients cited fear of additional burden as their reason for declining participation. Another explanation for the small sample size was an overestimation of the number of eligible patients by clinicians. In addition, a certain level of "gatekeeping" by the RAs cannot be excluded. Budgetary restrictions prevented the use of RAs not involved in the patient's care to recruit patients.

The attrition rate of 38% was very close to what was expected (35%). Thirteen participants dropped out owing to hospitalization or declining health status. Previous evidence suggests that the challenges with recruitment of patients with cancer are numerous and can be particularly difficult for symptom management studies because patients/family caregivers often feel too ill or too overwhelmed to participate in time-consuming studies or experience participation as burdensome.[44]

Conclusions

This study is the first to test the efficacy of a psychoeducational cancer pain self-management intervention in German-speaking outpatients with cancer. The implementation of post-RCT interviews was an excellent investment because these interviews increased our understanding of the efficacy of the adapted German PRO-SELF© Plus PCP. While none of the patients and family caregivers experienced study participation as burdensome, most participants appreciated the diary and the competent, trustworthy IN.

Based on our findings, we suggest that clinicians recommend the use of a pain management diary to patients with cancer pain. In addition, tailoring interventions to patients' individual situations and to their dynamic pain trajectories as well as coaching by a competent nurse may improve patients' and family caregivers' skills and knowledge to adequately implement pain self-management strategies in their daily lives.

Acknowledgments

We thank all of the patients and family caregivers for their participation; our intervention nurses, Monique Sailer Schramm, Hans-Rudolf Stoll and Anna Götz, as well as the research assistants for their engagement and support; all the nurse managers and clinicians of the participating hospitals for their contributions; and Chris Shultis for his linguistic assistance.

Funding

The PEINCA study was supported by unrestricted grants from the Domarena Foundation, Nursing Science Foundation Switzerland, the Foundation to Combat Cancer (Stiftung zur Krebsbekämpfung), the cantonal cancer leagues of Basel and Zurich, and the Giuliana and Giorgio Stefanini Foundation.

Declaration of competing interest

There are no conflicts of interest.

References

1. Reilly CM, Bruner DW, Mitchell SA, et al. A literature synthesis of symptom prevalence and severity in persons receiving active cancer treatment. *Support Care Cancer*. 2013;21:1525–1550. https://doi.org/10.1007/s00520-012-1688-0.
2. Schumacher KL, Plano Clark VL, Rabow MW, Paul SM, Miaskowski C. The experience of complex pain dynamics in oncology outpatients: a longitudinal qualitative

analysis. *Cancer Nurs*. 2021;44:136–144. https://doi.org/10.1097/ncc.0000000000000747.
3. van den Beuken-van Everdingen M, Hochstenbach LM, Joosten EA, Tjan-Heijnen VC, Janssen DJ. Update on prevalence of pain in patients with cancer: systematic review and meta-analysis. *J Pain Symptom Manag*. 2016;51:1070–1090. https://doi.org/10.1016/j.jpainsymman.2015.12.340.
4. Swarm RA, Paice JA, Anghelescu DL, et al. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Adult cancer pain, Version 3.2019. *J Natl Compr Cancer Netw*. 2019;17:977–1007. https://doi.org/10.6004/jnccn.2019.0038.
5. Kasasbeh MAM, McCabe C, Payne S. Cancer-related pain management: a review of knowledge and attitudes of healthcare professionals. *Eur J Cancer Care (Engl)*. 2017;26, e12625. https://doi.org/10.1111/ecc.12625.
6. Al-Ghabeesh SH, Bashayreh IH, Saifan AR, Rayan A, Alshraifeen AA. Barriers to effective pain management in cancer patients from the perspective of patients and family caregivers: a qualitative study. *Pain Manag Nurs*. 2020;21:238–244. https://doi.org/10.1016/j.pmn.2019.07.011.
7. Scarborough BM, Smith CB. Optimal pain management for patients with cancer in the modern era. *CA Cancer J Clin*. 2018;68:182–196. https://doi.org/10.3322/caac.21453.
8. Ullgren H, Tsitsi T, Papastavrou E, Charalambous A. How family caregivers of cancer patients manage symptoms at home: a systematic review. *Int J Nurs Stud*. 2018;85:68–79. https://doi.org/10.1016/j.ijnurstu.2018.05.004.
9. Oldenmenger WH, Geerling JI, Mostovaya I, et al. A systematic review of the effectiveness of patient-based educational interventions to improve cancer-related pain. *Cancer Treat Rev*. 2018;63:96–103. https://doi.org/10.1016/j.ctrv.2017.12.005.
10. Chi NC, Barani E, Fu YK, et al. Interventions to support family caregivers in pain management: a systematic review. *J Pain Symptom Manag*. 2020;60:630–656.e631. https://doi.org/10.1016/j.jpainsymman.2020.04.014.
11. Lee YJ, Hyun MK, Jung YJ, Kang MJ, Keam B, Go SJ. Effectiveness of education interventions for the management of cancer pain: a systematic review. *Asian Pac J Cancer Prev*. 2014;15:4787–4793. https://doi.org/10.7314/apjcp.2014.15.12.4787.
12. Miaskowski C, Dodd M, West C, et al. Randomized clinical trial of the effectiveness of a self-care intervention to improve cancer pain management. *J Clin Oncol*. 2004;22:1713–1720. https://doi.org/10.1200/JCO.2004.06.140.
13. Rustøen T, Valeberg BT, Kolstad E, Wist E, Paul SM, Miaskowski C. The PRO-SELF© Pain Control Program improves patients' knowledge of cancer pain management. *J Pain Symptom Manag*. 2012;44:321–330. https://doi.org/10.1016/j.jpainsymman.2011.09.015.
14. Valeberg BT, Kolstad E, Smastuen MC, Miaskowski C, Rustoen T. The PRO-SELF pain control program improves family caregivers' knowledge of cancer pain management. *Cancer Nurs*. 2013;36:429–435. https://doi.org/10.1097/NCC.0b013e3182747bcf.
15. Koller A, Miaskowski C, De Geest S, Opitz O, Spichiger E. Supporting self-management of pain in cancer patients: Methods and lessons learned from a randomized controlled pilot study. *Eur J Oncol Nurs*. 2013;17:1–8. https://doi.org/10.1016/j.ejon.2012.02.006.
16. Thorne S. *Interpretive Description: Qualitative Research for Applied Practice*. 2nd ed. New York: Taylor & Francis; 2016.
17. The World Medical Association. *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*; 2018. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/.
18. West CM, Dodd MJ, Paul SM, Schumacher KL, Tripathy D, Koo P, et al. The PRO-SELF©: Pain Control Program - an effective approach for cancer pain management. *Oncol Nurs Forum*. 2003;30:65–73. https://doi.org/10.1188/03.ONF.65-73.
19. Avorn J. Academic detailing: "marketing" the best evidence to clinicians. *JAMA*. 2017;317:361–362. https://doi.org/10.1001/jama.2016.16036.
20. Ferrell BR, Rhiner M, Ferrell BA. Development and implementation of a pain education program. *Cancer*. 1993;72:3426. https://doi.org/10.1002/1097-0142(19931201)72:11+<3426::aid-cncr2820721608>3.0.co;2-d, 3426.
21. Radbruch L, Loick G, Kiencke P, et al. Validation of the German version of the Brief Pain Inventory. *J Pain Symptom Manag*. 1999;18:180–187. https://doi.org/10.1016/s0885-3924(03)00073-3.
22. Cleeland CS, Gonin R, Hatfield AK, et al. Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med*. 1994;330:592–596. https://doi.org/10.1056/nejm199403033300902.
23. Gallizzi M, Gagnon C, Harden RN, Stanos S, Khan A. Medication Quantification Scale Version III: internal validation of detriment weights using a chronic pain population. *Pain Pract*. 2008;8:1–4. https://doi.org/10.1111/j.1533-2500.2007.00163.x.
24. McMillan SC, Williams FA. Validity and reliability of the Constipation Assessment Scale. *Cancer Nurs*. 1989;12:183–188.
25. Ferrell BR, Ferrell BA, Rhiner M, Grant M. Family factors influencing cancer pain management. *Postgrad Med J*. 1990;67:64–69.
26. Ferrell BR, Rhiner M, Rivera LM. Development and evaluation of the Family Pain Questionnaire. *J Psychosoc Oncol*. 1993;10:21–35. https://doi.org/10.1300/J077V10N04_02.
27. Keefe FJ, Ahles TA, Porter LS, et al. The self-efficacy of family caregivers for helping cancer patients manage pain at end-of-life. *PAIN®*. 2003;103:157–162. https://doi.org/10.1016/s0304-3959(02)00448-7.
28. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5:649–656.
29. Petermann F. Hospital anxiety and depression scale, (HADS-D), deutsche Version [German version]. *Z Klin Psychol Psychiatr Psychother*. 2015;59:251–253. https://doi.org/10.1024/1661-4747/a000077.
30. IBM Corp. Released. *IBM SPSS Statistics for Windows*. Version 24.0; 2016. https://www.ibm.com/analytics/spss-statistics-software.
31. Fokkema M, Edbrooke-Childs J, Wolpert M. Generalized linear mixed-model (GLMM) trees: a flexible decision-tree method for multilevel and longitudinal data. *Psychother Res*. 2021;31:313–325. https://doi.org/10.1080/10503307.2020.1785037.
32. Cohen J. *Statistical Power Analysis for the Social Sciences*. Vol Second. New York: Lawrence Erlbaum; 1988.
33. Braun V, Clarke V, Hayfield N, Terry G. Thematic analysis. In: Liamputtong P, ed. *Handbook of Research Methods in Health Social Sciences*. 1st ed. Singapore: Springer; 2019:843–860.
34. ATLAS.ti Scientific Software Development GmbH. *ATLAS.ti - Discover Insights for Your Research Projects*; 2019. https://atlasti.com/product/.
35. Coolbrandt A, Steffens E, Wildiers H, Bruyninckx E, Verslype C, Milisen K. Use of a symptom diary during chemotherapy: a mixed-methods evaluation of the patient perspective. *Eur J Oncol Nurs*. 2017;31:37–45. https://doi.org/10.1016/j.ejon.2017.09.003.
36. Devan H, Hale L, Hempel D, Saipe B, Perry MA. What works and does not work in a self-management intervention for people with chronic pain? Qualitative systematic review and meta-synthesis. *Phys Ther*. 2018;98:381–397. https://doi.org/10.1093/ptj/pzy029.
37. ElMokhallalati Y, Mulvey MR, Bennett MI. Interventions to support self-management in cancer pain. *Pain Rep*. 2018;3, e690. https://doi.org/10.1097/PR9.0000000000000690.
38. Prip A, Moller KA, Nielsen DL, Jarden M, Olsen MH, Danielsen AK. The patient-healthcare professional relationship and communication in the oncology outpatient setting: a systematic review. *Cancer Nurs*. 2018;41:E11–e22. https://doi.org/10.1097/ncc.0000000000000533.
39. Schulman-Green D, Brody A, Gilbertson-White S, Whittemore R, McCorkle R. Supporting self-management in palliative care throughout the cancer care trajectory. *Curr Opin Support Palliat Care*. 2018;12:299–307. https://doi.org/10.1097/spc.0000000000000373.
40. Schumacher KL, Koresawa S, West C, et al. The usefulness of a daily pain management diary for outpatients with cancer-related pain. *Oncol Nurs Forum*. 2002;29:1304–1313. https://doi.org/10.1188/02.onf.1304-1313.
41. Fan Z-Y, Lin J-X, Li X, Chen X-W, Huang X-Y. The effect of pain self-management based on pain control diary on breakthrough pain. *J Clin Oncol*. 2017;35. https://doi.org/10.1200/JCO.2017.35.15_suppl.10107, 10107-10107.
42. Luckett T, Davidson PM, Green A, Boyle F, Stubbs J, Lovell M. Assessment and management of adult cancer pain: a systematic review and synthesis of recent qualitative studies aimed at developing insights for managing barriers and optimizing facilitators within a comprehensive framework of patient care. *J Pain Symptom Manag*. 2013;46:229–253. https://doi.org/10.1016/j.jpainsymman.2012.07.021.
43. Henson LA, Maddocks M, Evans C, Davidson M, Hicks S, Higginson IJ. Palliative care and the management of common distressing symptoms in advanced cancer: pain, breathlessness, nausea and vomiting, and fatigue. *J Clin Oncol*. 2020;38:905–914. https://doi.org/10.1200/jco.19.00470.
44. Manohar N, MacMillan F, Steiner GZ, Arora A. Recruitment of research participants. In: Liamputtong P, ed. *Handbook of Research Methods in Health Social Sciences*. Singapore: Springer Nature; 2019:71–98.