Front. Med. 2024, 18(6): 1013−1025
https://doi.org/10.1007/s11684-024-1097-z

RESEARCH ARTICLE

Enhancing patient activation: a controlled implementation study of an interprofessional evidence-based counseling program for complementary and integrative healthcare in cancer patients ('CCC-Integrativ')

Jan Valentini (✉)[1], Daniela Froehlich[1], Inka Roesel[1,2], Regina Stolz[1], Cornelia Mahler[3], Peter Martus[2], Nadja Klafke[4], Markus Horneber[5], Claudia Witte[6], Klaus Kramer[7], Christine Greil[8], Barbara Gruen[9], Katrin Tomaschko-Ubelaender[10], Stefanie Joos[1], on behalf of the CCC-Integrativ Study Group

[1]Institute for General Practice and Interprofessional Care, University Hospital and Faculty of Medicine Tuebingen, Tuebingen, Germany; [2]Institute for Clinical Epidemiology and Applied Biostatistics, University Hospital and Faculty of Medicine Tuebingen, Tuebingen, Germany; [3]Department of Nursing Science, Institute for Health Sciences, University Hospital and Faculty of Medicine Tuebingen, Tuebingen, Germany; [4]Department of General Practice and Health Services Research, University Hospital Heidelberg, Germany; [5]Department of Internal Medicine, Division of Pneumology, Paracelsus Medical University, Klinikum Nuernberg, Germany; [6]aQua Institute for Applied Quality Improvement and Research in Health Care, Goettingen, Germany; [7]Department of Integrative Medicine, University Hospital and Faculty of Medicine Ulm, Germany; [8]Department of Medicine I, Medical Centre University of Freiburg, Faculty of Medicine, University of Freiburg, Germany; [9]Department of Medical Oncology, National Centre for Tumor Diseases, Heidelberg, Germany; [10]AOK Baden-Württemberg Hauptverwaltung, Fachbereich Integriertes Leistungsmanagement, Stuttgart, Germany

Abstract **Complementary and integrative healthcare (CIH) is increasingly recognized as a valuable approach to empowering and activating cancer patients. Studies have shown that higher patient activation is positively associated with improved health outcomes and reduced healthcare costs. The CCC-Integrativ study aimed to assess the implementation of an evidence-based counseling service on CIH at four Comprehensive Cancer Centers (CCC) in Germany. In this controlled implementation study, the patient-level intervention included three CIH consultations within a 3-month period delivered by interprofessional teams of physicians and nurses. The primary endpoint was patient activation using the PAM-13 at baseline (T1) and post-intervention (T2), and compared between control (CO, receiving routine care) and the intervention group (IG) using an analysis of covariance. Missing data were handled with multiple imputations. Maintenance effects at 6-month follow-up (T3) were investigated using a linear mixed model. A total of n = 1128 oncology patients (CO = 443, IG = 685) with diverse tumor entities and cancer stages were included in the study. The overall mean baseline PAM-13 score was 69.74 (SD = 14.24) (n = 959 (85.0%)). A statistically significant between-group difference in post-intervention PAM-13 scores was observed ($F_{group}(1, 1866.82) = 8.634$, $P = 0.003$), with an adjusted mean difference of 2.22 PAM-points. Age, gender, tumor entity, disease stage, or CCC study site did not significantly predict post-treatment PAM-13 scores. The maintenance effect of the intervention was not statistically significant ($F_{timeXgroup}(1, 3316.04) = 2.337$, $P = 0.096$). Individually tailored counseling on CIH, offered by specifically trained, interprofessional teams, significantly improved patient activation. Given the established positive effects of higher patient activation, the implementation of such a program at cancer centers may yield beneficial outcomes for both patients and the healthcare system.**

Keywords adult oncology; complementary medicine; complementary and integrative healthcare; herbal medicine; nutritional support; oncology; preventive medicine; patient activation; interprofessional counseling

Received April 5, 2024; accepted June 18, 2024

Correspondence: Jan Valentini, jan.valentini@med.uni-tuebingen.de

Introduction

Complementary and integrative healthcare (CIH) is widely used by cancer patients. According to international literature, as many as 40% of all oncology patients [1] and up to 80% of breast cancer survivors [2] report using CIH approaches. CIH encompasses a diverse range of interventions including nutritional approaches (e.g., special diets, dietary supplements, herbs), psychological techniques (e.g., mindfulness), and physical methods (e.g., massage) either individually or a combination of these (e.g., psychological and physical, such as yoga, tai ji, acupuncture or art therapies) [3]. As described by the National Center for Complementary and Integrative Health (NCCIH), "Integrative health aims for well-coordinated care among different providers and institutions by bringing conventional and complementary approaches together to care for the whole person" [4]. A growing body of evidence suggests that certain CIH approaches, such as acupuncture, mindfulness-based stress reduction, yoga and tai ji, and certain phytotherapeutics, may aid in managing cancer symptoms and mitigating treatment side effects [5–9]. As a holistic approach addressing physical, emotional as well as spiritual aspects, CIH is increasingly recognized as a valuable approach for enhancing patient-centered care [10]. Nevertheless, there are also risks associated with the use of CIH, for instance, phytotherapeutics and micronutrients that may interact with chemotherapy [11,12]. Hence, an evidence-based approach is crucial for patient safety and an increasing number of oncological guidelines offer recommendations on the use of various CIH approaches during cancer care [13–15].

In addition to their therapeutic effects, many CIH approaches have the potential to activate and empower cancer patients by providing self-care strategies [10,16]. By offering education and tools for managing their own health, CIH approaches promote patient activation and enhance their sense of control over their well-being [17].

Patient activation, originally introduced as a theoretical concept by Hibbard and colleagues, refers to the knowledge, skills and confidence patients possess in managing their own health and healthcare [18,19]. Thus, the promotion of patient activation serves as a comprehensive concept for self-management in chronic diseases [20]. Multiple studies have demonstrated a positive association between higher patient activation and improved health outcomes in cancer patients [21–24]. More actively engaged patients are better equipped to participate in decision-making, adopt healthier lifestyles [24–28], exhibit higher confidence in self-managing side effects from conventional oncological therapy [29], report more positive care experiences [20], and demonstrate better adherence to treatment plans [29–31]. Consequently, this leads to fewer hospitalizations [32,33] and ultimately lowers health care costs [34–36]. Thus, fostering patient activation emerges a crucial element of patient-centered cancer care with positive implications at both the patient and system levels. However, scientifically proven and scalable approaches for achieving this are still lacking in Germany.

To address this gap, we developed an evidence-based interprofessional counseling program on CIH for oncology patients and implemented it at four University Hospital Comprehensive Cancer Centers (CCC) (Freiburg, Heidelberg, Tuebingen-Stuttgart, Ulm) in Baden-Wuerttemberg, Germany. The primary objective of the CCC-Integrativ study was to assess the program's effects concerning patient activation.

Material and methods

Study design

The CCC-Integrativ study is a prospective controlled non-randomized implementation study with interventional elements and outcome measures on micro- (patient), meso- (provider) and macro-level (system) accompanied by a mixed-methods process evaluation and a health economic analysis [37]. The leading confirmatory evaluation refers to the patient-level based on primary data collection with respect to 3-month interprofessional CIH counseling program for oncology patients with a 6-month follow-up (FU) period.

A pre-post/treatment-control design was employed to compare the primary endpoint at post-intervention between control (CO) and intervention group (IG): the primary outcome parameter for assessing the intervention effect was patient activation, measured with the Patient Activation Measure questionnaire (PAM-13) at baseline (T1) and after the three-month intervention period (T2). Temporal trend and maintenance investigations at 6-month follow-up (T3) were conducted as a secondary endpoint.

The study was registered and approved by the ethics committees of the University of Tübingen, Germany (No. 658/2019BO1; Trial Registration Number, DRKS00021779). Further details on the study design of the main and the process evaluation are available in the study protocols [37,38]. Results for meso- and macro-levels and process evaluation will be published separately.

Intervention

Intervention group (IG)

The intervention is described according to the Template for Intervention Description and Replication (TIDieR) checklist [39] (see Supplement 1). The CCC-Integrativ

intervention is an evidence-based counseling service on CIH specifically designed for oncology patients. Counseling had a patient-oriented approach and incorporated evidence-based treatment options as well as nursing and physician experience. Based on results and knowledge from the CONGO study [40,41], the KOKON project [42,43] and a counseling service on CIH [44], an interprofessional blended learning training program was developed and manualized in order to provide standardized and evidence-based counseling. This training includes a knowledge database on the clinical efficacy and safety of complementary medicine in oncology, providing evidence-based information that has been used to develop various toolboxes for counseling teams, such as specific symptom-driven guidelines for the most relevant symptoms.

The interprofessional counseling teams (nurses, physicians) of the four CCCs completed the training program as a group in order to ensure that the processes across all counseling teams are standardized. The 10-month training program included 13 online sessions, each lasting 3–6 h, and utilized a web-based platform for concurrent learning. Participants included 11 nurses and 11 physicians from the four CCC sites in Baden-Wuerttemberg. The training covered various CIH approaches, such as acupressure, aromatherapy, external applications, and phytotherapy, as well as lifestyle topics like nutrition, exercise, and stress management. These sessions were led by experts in the field of CIH. In addition, interprofessional teambuilding sessions utilizing the Toolkit for Enhancing and Maintaining Team Collaboration (TEAMc) concept [45] were conducted for each CCC team. Counseling sessions, tailored to individual patients needs and to their baseline PAM-13 levels, focused on various aspects of CIH, including phytotherapy, acupuncture, nutrition, stress management, and exercise, but also on external applications such as wraps and compresses. To further support patient activation, information leaflets for CIH methods were developed and provided to patients.

Within three months, patients in the intervention group received three individual counselings on CIH. The first counseling session, lasting 60 min, was conducted face-to-face by an interprofessional team consisting of a physician and a nursing expert. The two follow-up counselings, lasting 30 min each, were flexible in terms of format (in-person, telephone, video), and took place inter- or monoprofessionally, depending on the patient's needs. For example, patients with a high need for counseling on potential interactions between phytotherapeutics and/or dietary supplements and ongoing chemotherapy were followed up by a physician, whereas patients with a high need for counseling on a more complex additional external application of yarrow liver compress were followed up by nurses. All counseling sessions were provided at the corresponding CCC site. Patients were reminded of the counseling appointments by e-mail and telephone. Further details of the intervention are described in the study protocol [37].

Control group (CO)

The control group received conventional standard healthcare provided by the CCCs (treatment as usual). As compensation for their time and due to ethical reasons, the patients were offered the CIH counseling service after the end of the observation period of 6 months (outside the study setting).

Participant eligibility and recruitment

Eligible participants of the IG were recruited from outpatient oncology clinics at the four CCCs using targeted convenience sampling (flyers, newspaper reports, word-of-mouth, invitation from treating physicians). The CO was recruited 6 months before the start of the intervention phase. A classical parallel-group design with randomization at the patient level was not considered feasible, as the study information would increase awareness of the topic CIH, potentially introducing a bias. Cluster randomization also had to be rejected due to possible contamination problems. Further details on the recruitment process and eligibility criteria have been described previously in the study protocol [37].

Outcome measures

Outcome measures were self-reported in questionnaires, collected and managed using REDCap electronical data capture tools hosted at the University Hospital Tuebingen [46,47]. Relevant clinical information was extracted from routine medical documentation.

Primary outcome: Patient Activation Measure 13 (PAM-13)

The Patient Activation Measure 13 (PAM-13) is a widely used, valid, and reliable self-reported measure that assesses patient knowledge, skill, and confidence for self-management and was originally developed by Hibbard *et al*. [19]. The questionnaire consists of 13 items on a 4-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = agree, 4 = agree strongly). Patient activation is quantified by calculating a raw sum score ranging from 13 to 52, which is then transformed to a standardized metric ranging from 0 to 100 (0 = low activation; 100 = highest activation). We used the standardised spreadsheet provided by the developers (Insignia Health), which transforms the German response options into standardised metrics. The continuous PAM scores can be categorized

into four hierarchical levels of activation: level 1 (≤ 47.0) – not believing activation is important; level 2 (47.1–55.1) – lacking knowledge or confidence in self-management of health; level 3 (55.2–67) – beginning to take action; and level 4 (≥ 67.1) – taking action but requiring support in maintaining positive behavior change. For this study the translated and validated German PAM-13 version [48] was used.

Further details on clinical and sociodemographic data can be found in Supplement 2.

Sample size

A sample size calculation was performed based on consistent data on the distribution of the primary endpoint PAM-13 and interventional effects found in the literature [49,50]. For details refer to the study protocol and Appendix 3.

Statistical analysis

For our primary endpoint, an analysis of covariance (ANCOVA) on the post-intervention scores (T2) with the independent variable *group* (IG, CO) was applied with adjustment for PAM-13 baseline scores (T1) and *study center* as categorical variable. Missing data were handled with multiple imputation. For further details refer to Appendix 4.

Results

Participants

Study flow

The study flow of participants is shown in Fig. 1. At baseline (T1) 1128 participants (CO = 443, IG = 685) recruited at the four CCC study sites (Tuebingen, 287; Freiburg, 322; Heidelberg, 280; Ulm, 239) fulfilled all eligibility criteria and provided questionnaire data. Overall, 986 (87.4%) patients (CO = 383, IG = 603) completed T2 (3-month follow-up); 892 (79.08%) individuals (CO = 338, IG = 554) completed the 6-month FU at T3.

Dropouts

The overall rate of patients who prematurely dropped out of the study at T2 (primary endpoint) amounted to 12.5% (n = 142) of the total sample, 13.5% (n = 60) in the control group and 11.8% (n = 82) in the intervention group. Reasons for dropout are displayed in Fig. 1. Factors related to dropout were assessed by comparing study completers and dropouts with respect to their socio-demographic characteristics and anamnesis (Supplement 3). The dropout rate at T3 (secondary endpoint) was 20.9% (23.7% CO, 19.1% IG), lower than the assumed 30% for sample size calculations.

Patient characteristics: socio-demographics and clinical characteristics

Table 1 presents the socio-demographic and clinical characteristics of the 1128 patients at baseline. The majority of participants were female, 68.8% in the control group and 75.6% in the intervention group, with a significantly higher proportion of women in the IG (P = 0.015). The age of participants ranged from 18 to 88 years, with a mean of 57.1 years (SD 12.2). Significant baseline differences between CO and IG were found in terms of age, body mass index (BMI), educational level, and occupational status. With respect to clinical data, 60.5% of participants entered the study with an initial cancer diagnosis, and 47.9% were being treated curatively. The most common primary diagnosis was breast cancer (for more detailed information on the main oncological diagnoses, please refer to Supplement 4). CO and IG differed significantly with respect to main diagnosis, treatment intention, and comorbidities.

Between the CCC centers some heterogeneity was found with regard to sex, age, education, and several clinical anamnesis variables (see Supplement 5).

Descriptives of PAM-13

PAM-13 scores at baseline (T1)

For 959 (85.0%) patients all PAM-13 items were completed and the composite PAM-13 score could be calculated at baseline (T1), resulting in an overall mean patient activation of 69.74 (SD = 14.24), ranging from 17.95 to 100. No statistically significant difference in mean baseline PAM-scores (P = 0.360) were found between IG and CO (Table 2). There were no statistically significant differences or associations of the mean PAM-13 scores with respect to patient characteristics and patient anamnesis at baseline except for education (P = 0.015; post-hoc Tukey-test: none/basic school vs. secondary school P = 0.007, all other pairwise comparisons n.s.) and cancer stage (P = 0.040; post-hoc Tukey HSD: progress vs. first diagnosis P = 0.032, relapse vs. first diagnosis n.s., relapse vs. progression n.s.). Accounting for the multiple tests conducted on the different variables (Bonferroni-adjustment), however, all P-values were insignificant.

Change in PAM-13 scores and levels over 3 months (T1 –T2)

The overall Pearson-correlation between baseline (T1)

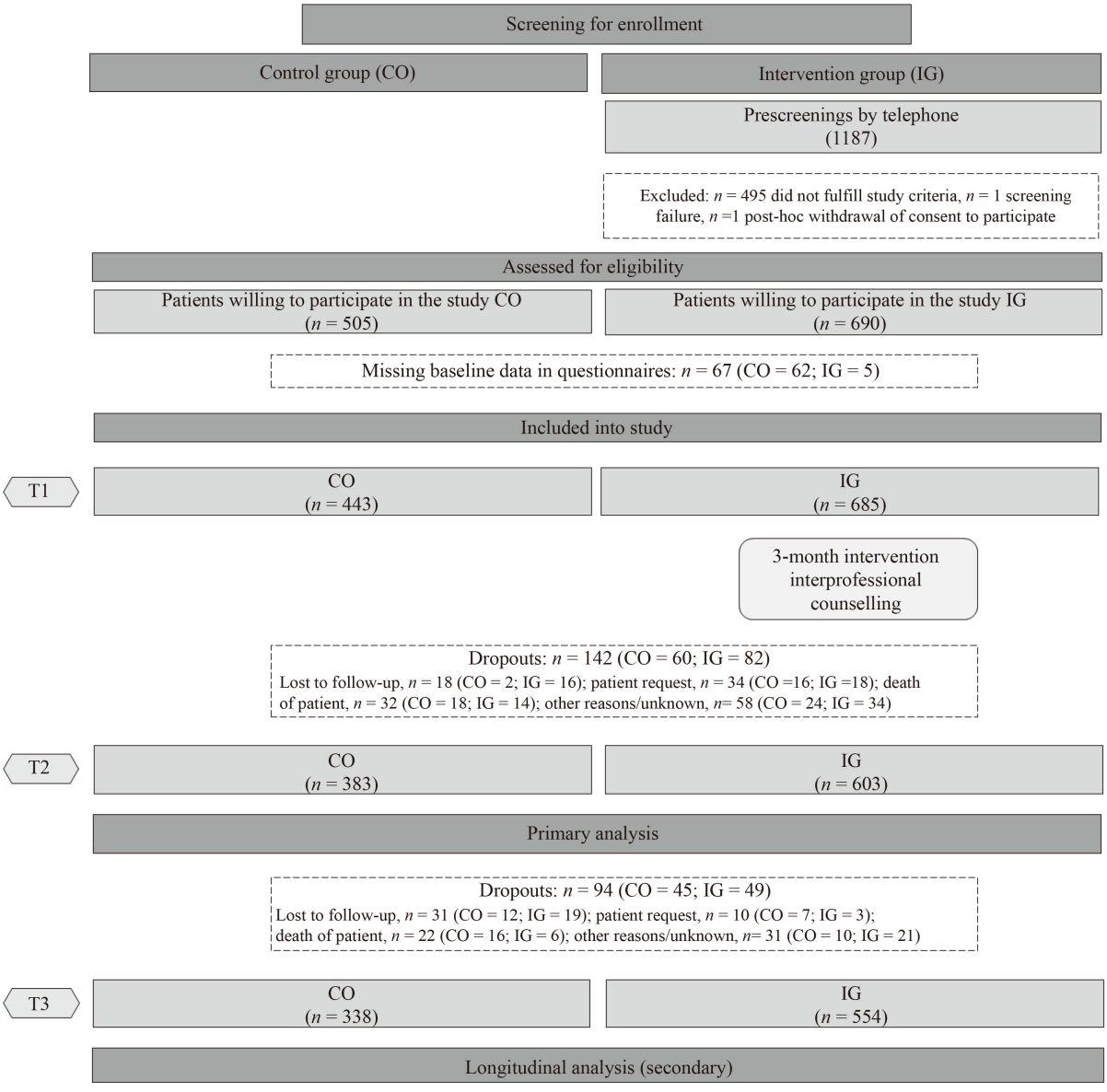

Fig. 1 Patient flowchart modified according to the CONSORT diagram.

and post-intervention (T2) PAM-13 score was r = 0.6. In the intervention group patients improved by 2.12 PAM-points on average from baseline to post-intervention, while the CO remained relatively stable at roughly 69 points. The difference-in-difference of change from baseline between intervention and control groups at T2 amounted to 1.85 PAM-points (Table 2).

Proportion of patients in PAM-13 levels

The majority's baseline (T1) activation score fell into the highest PAM-13 level 4 (*n* = 539, 56.2%; CO = 187, 54.0%; IG = 352, 57.3%), 287 (30.0%) patients started in level 3 (CO = 103, 29.8%; IG = 184, 30.0%), 73 (7.6%) individuals (CO = 28, 8.1%; IG = 45, 7.3%) in level 2.

Fig. 2 illustrates the changes in patient activation levels over 3 months for all participants who completed the PAM-questionnaires at both T1 and T2 (see also Sankey diagrams in Supplement 6). When not differentiating between the baseline PAM-levels, overall improvement by at least one level was nearly equally distributed among both groups with 20.2% (*n* = 54) in the CO and 20.5% (*n* = 105) in the IG, whereas the percentage of patients experiencing a deterioration of at least one level was higher in the CO at 23.6% (*n* = 63) compared to 16.0% (*n* = 82) in the IG. A two-sided Cochrane-Armitage test for trend (level change deteriorated, constant, improved) yielded a statistically non-significant result (*P* = 0.095) for these proportions. Considering positive or negative events combined, 8.0% of the level changes were in favor

Table 1 Baseline patient characteristics (socio-demographics and clinical data) and PAM-scores within strata

	Total (n = 1128)	CO (n = 443)	IG (n = 685)	P value	n	PAM-score (mean (SD))	P value	n
Socio-demographics								
Sex				0.015#	1128		0.635*	959
Male	305 (27.0%)	138 (31.2%)	167 (24.3%)			69.36 (15.30)		
Female	823 (73.0%)	305 (68.8%)	518 (75.7%)			69.87 (13.84)		
Age (year)	57.1 (12.2)	59.9 (12.3)	55.3 (11.8)	< 0.001*	1128	r = 0.038	0.234§	959
Education				< 0.001#	1115		0.015$	949
University/college degree	405 (36.3%)	123 (28.3%)	282 (41.5%)			69.73 (13.28)		
High school	179 (16.0%)	55 (12.6%)	124 (18.2%)			70.27 (13.31)		
Secondary school or similar	343 (30.8%)	150 (34.5%)	193 (28.4%)			71.10 (14.52)		
None/basic secondary school (8 years)	188 (16.8%)	107 (24.6%)	81 (11.9%)			66.49 (16.54)		
Working status				< 0.001#	1112		0.279$	946
Full-time	353 (31.7%)	125 (28.8%)	228 (33.6%)			70.28 (13.68)		
Part-time	272 (24.5%)	79 (18.2%)	193 (28.5%)			70.29 (13.43)		
Not working	96 (8.63%)	43 (9.91%)	53 (7.8%)			66.96 (15.55)		
Retired	391 (35.1%)	187 (43.1%)	204 (30.1%)			69.65 (14.95)		
Marital Status				0.169#	1102		0.160*	939
Single	240 (21.8%)	104 (24.0%)	136 (20.3%)			68.33 (15.68)		
In a relationship/married	862 (78.2%)	329 (76.0%)	533 (79.7%)			70.04 (13.88)		
BMI (kg/m^2)	24.9 (5.13)	25.4 (5.44)	24.5 (4.89)	0.010*	1109	r = −0.024	0.462§	1110
Clinical data								
Diagnosis stage				0.395#	1128		0.040$	960
Initial diagnosis	682 (60.5%)	273 (61.6%)	409 (59.7%)			70.54 (14.48)		
Progression	332 (29.4%)	132 (29.8%)	200 (29.2%)			67.97 (14.06)		
Relapse	114 (10.1%)	38 (8.58%)	76 (11.1%)			70.29 (13.02)		
Intention of treatment				0.002#	1128		0.554$	960
Curative	540 (47.9%)	194 (43.8%)	346 (50.1%)			70.22 (13.80)		
Palliative	407 (36.1%)	157 (35.4%)	250 (36.5%)			69.1 (14.17)		
Unclear	181 (16.0%)	92 (20.8%)	89 (13.0%)			69.1 (15.46)		
Chronic condition				0.005#	1127		0.447*	958
Yes	720 (63.9%)	305 (69.0%)	415 (60.6%)			69.52 (14.27)		
No	407 (36.1%)	137 (31.0%)	270 (39.4%)			70.25 (14.15)		
Main cancer diagnosis				0.038#	1128		0.885$	960
Breast cancer	467 (41.4%)	167 (37.7%)	300 (43.7%)			69.55 (14.15)		
Gastrointestinal	234 (20.7%)	103 (23.3%)	131 (19.1%)			69.53 (14.31)		
Gynecological	118 (10.5%)	56 (12.6%)	62 (9.04%)			70.81 (13.9)		
Other	310 (27.5%)	117 (26.4%)	193 (28.1%)			69.77 (14.52)		
Metastases				0.215#	1051		0.219*	886
Yes	472 (44.9%)	198 (47.4%)	274 (43.3%)			69.2 (14.10)		
No	579 (55.1%)	220 (52.6%)	359 (56.7%)			70.37 (14.21)		

*t-test, §Pearson correlation, $ANOVA, #Chi-square test.

of the intervention group. The number needed to treat (NNT), i.e., the number of patients you need to treat to prevent an additional bad outcome (deterioration) within the period of 3 months of the intervention, amounted to NNT = 13 (95% CI 7–63, Wald-type confidence interval). Looking at the level changes based on the baseline PAM-levels (Fig. 2), it was observed that the lower number of level deteriorations in the IG was most pronounced in the

Table 2 Patient activation scores at baseline (T1), post-intervention (T2) (primary outcome), and 6-month follow-up (T3) (secondary outcome)

	Total (n = 1128)	IG (n = 685)	CO (n = 443)
	PAM-13 score (0–100), mean (SD)		
T1 (n = 959, CO 346, IG 613)	69.74 (14.24)	70.08 (13.71)	69.16 (15.14)
T2 (n = 883, CO 323, IG 560)	71.16 (14.10)	72.20 (13.80)	69.43 (14.47)
T3 (n = 786, CO 280, IG 506)	71.19 (14.01)	72.00 (13.77)	69.84 (14.35)

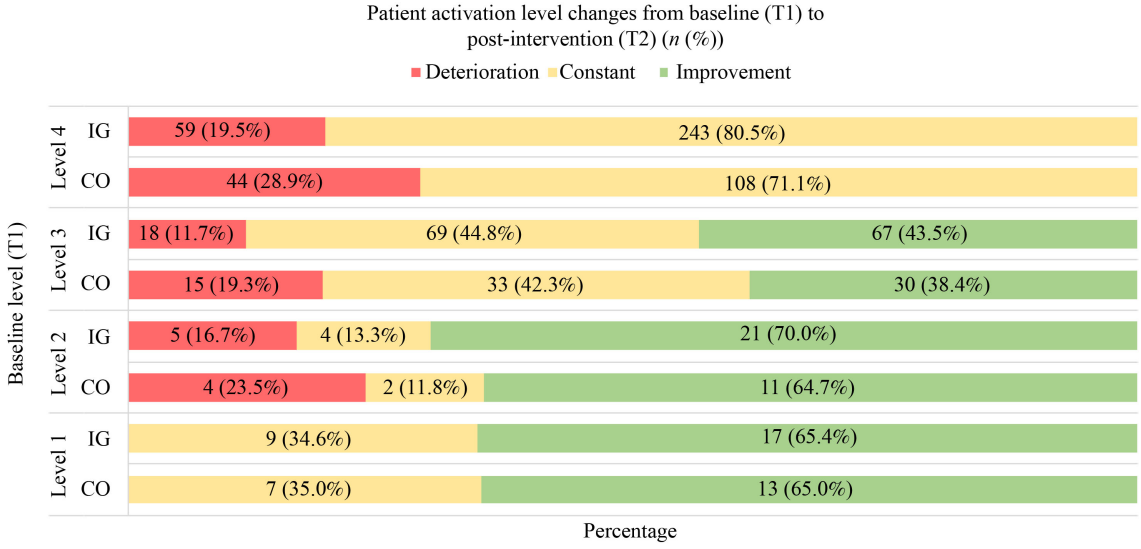

Fig. 2 Change in patient activation levels in CO and IG from baseline (T1) to post-intervention (T2).

highest baseline PAM-level 4 (IG 19.5% vs. CO 28.9%).

Primary analysis: effect of the 3-month intervention on the PAM-13 score (pre-post)

In the primary analysis (MODEL 1) a statistically significant difference in the post-intervention PAM-13 score between IG and CO was observed after adjustment for baseline PAM-13 scores and CCC study site ($F_{Group}(1,1866.82) = 8.634$, $P = 0.003$, $\eta_{partial}^2 = 0.005$) (Supplement 7). A higher baseline PAM-13 score was found to be significantly associated with higher follow-up PAM-13 scores (unstandardized Beta (B) = 0.61, 95% CI 0.55–0.66, $P < 0.001$), whereas CCC study site was not a statistically significant predictor of post-treatment PAM scores. Adjusted mean differences at T2 between IG and CO amounted to 2.22 (95% CI 0.74–3.71) in favor of the intervention group.

Sensitivity analysis

In line with the findings of the primary analysis, a sensitivity analysis including multiple baseline covariates (MODEL 2) also exhibited a statistically significant group effect ($F_{Group}(1, 2308.40) = 8.564$, $P = 0.003$, $\eta_{partial}^2 = 0.006$). In analogy to MODEL 1 only the PAM-13 baseline score (B = 0.60, 95% CI 0.55–0.66, $P < 0.001$) was found to be significantly associated with the follow-up PAM-13 scores. Adjusted mean differences in PAM-13 scores at T2 between IG and CO amounted to 1.97 (95% CI 0.41–3.54) in favor of the intervention group.

Running a linear mixed model as an additional sensitivity analysis for the primary endpoint T2 versus baseline showed that findings are robust and consistent with the results of our primary analysis: a statistically significant *time x group* interaction ($P = 0.036$) was found (Supplement 8). The estimated difference in change from baseline calculated from the estimated marginal means was slightly lower than in our ANCOVA models amounting to 1.71 (95% CI 0.11–3.32) PAM-points. This corresponds to an effect size of 0.12 (Cohen's d).

Follow-up: maintenance effects (T1–T3)

The mean PAM-13 scores at 6 months after baseline (T3) were 72.00 (SD = 13.77) in the intervention group and 69.84 (SD = 14.35) in the control group, which relates to a between-group difference of change from baseline of 1.24 PAM-points. In the longitudinal model including T1–T3 to test for maintenance effects of the intervention the *time x group* interaction was found to be statistically

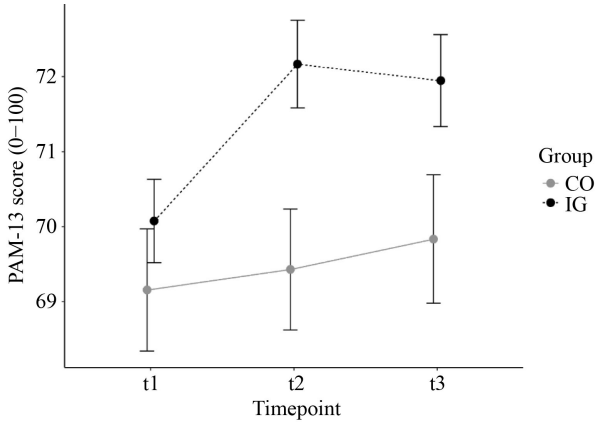

Fig. 3 Mean PAM-13 scores (+/−1 SE) estimated from the linear mixed model including T1–T3.

insignificant ($P = 0.096$) (Supplement 9 and Fig. 3).

Discussion

The CCC-Integrativ study aimed to evaluate the impact of up to three interprofessional counseling sessions by specifically trained nurses and physicians on patient activation, as measured by the PAM-13 among cancer patients from various CCC centers in Southern Germany. The primary analysis revealed a statistically significant difference in post-intervention PAM-13 scores between the intervention group (IG) and the control group (CO), with an adjusted mean difference of 2.22 points. Sensitivity analysis confirmed the robustness and consistency of the results. Considering covariates such as main diagnosis, disease stage, or CCC study site, did not show any statistically significant predictors of post-treatment PAM scores. Our study's findings align with prior research by Wolever *et al*. which demonstrated that participation in an Integrative Medicine Immersion Model significantly improved patient activation in patients with chronic conditions [51]. The presented data also confirm the results of Antol *et al*. indicating that patient-, provider-, and system-level interventions, including educational and professional development curricula enhance patient activation and self-management [52]. Remarkably, the mean baseline PAM-13 scores in the IG were already high, with an overall mean patient activation score of 69.74 (SD = 14.24), corresponding to PAM-13 level 4. These findings are consistent with several studies that have reported high baseline scores for patients with different chronic conditions such as cancer, musculoskeletal disorders or circulatory system diseases [52–57]. Overall, our findings show that patients initiating at lowest levels of activation experienced the greatest change in activation, indicating that they benefit the most from the intervention. This finding is consistent with the international literature, where Harvey *et al*. demonstrated that patients in level 1 achieved the most substantial gain in PAM score, while those starting in level 4 showed a slight, non-significant, decrease after an intervention within a traditional health promotion program [52,58]. Therefore, patients starting in level 4 are not at an endpoint but can continue to make significant improvements in health behavior by utilizing supportive complementary interventions in their cancer treatment [58].

Furthermore, our results demonstrate that level deterioration occurs significantly less often in patients in the IG compared to CO. This may suggest a preventive effect of the intervention, potentially strengthening resilience. This assumption is supported by the findings of Mosen *et al*., showing that individuals with higher PAM scores are more likely to engage in self-management behaviors, use self-management services, and report higher medication adherence compared to individuals with lower PAM scores [30]. In this context, Hibbard *et al*. reported that level 4 patients are in a better position to deal with new or unfamiliar situations, even during times of stress, as they exercise their acquired coping and problem-solving skills [59]. Furthermore a recent systematic review by Brändli *et al*. showed that nurse-led counseling interventions on the self- and symptom management of patients in oncology rehabilitation can affect patients' self-management [60].

Additionally, our results align with findings from international literature, indicating that a higher baseline PAM score was significantly associated with a higher follow-up PAM score [53]. Studies reporting on validation of PAM scores suggest that the minimal clinically important difference (MCID) is at least a 4-point difference in PAM score, combined with transitioning from lower to higher PAM levels [18,61]. In our study, the observed changes were less than 4 when considering the mean change across all PAM-13 baseline levels. However, it should be noted that the determination of MCID can vary widely depending on the condition and methodology used, and there is no standardized international approach for calculating MCIDs, leading to methodological and interpretation challenges [62–65].

Regarding health economic costs, the international literature describes a negative correlation between patient activation levels and healthcare costs [22,36,66,67]. These findings are linked to improved clinical outcomes, healthier behaviors and increased uptake of screening [36]. According to Hibbard *et al*., each point increase in PAM score is associated with a 2% decrease in hospitalization, a 2% increase in medication adherence and reduced emergency department visits [21]. Greene *et al*. found that health-related costs were significantly higher for those who experienced a level drop over one

year and significantly lower for those who increased a level, compared to those who remained at the same PAM level [36,68].

In the analysis of T3 overall PAM scores, the IG showed slightly lower scores compared to the end of the intervention at T2, suggesting a maintenance of the effect after the end of the intervention. However, this effect was no longer significant between the groups. Similar deterioration in the follow-up phase was observed by Krouse [69]. It is possible that some patients may have benefited from more frequent counselings over an extended period. Lunardi *et al*. reported the highest effects on patient activation for intervention durations between 3 and 6 months [70]. Several studies also report consistent results regarding patient activation in follow-up analyses [71,72].

Apart from the discussion on patient activation, counseling on CIH may offer several additional benefits. It can serve as a catalyst for fostering communication within the provider–patient relationship. A proactive approach addressing CIH topics encourages open dialog, mutual understanding, and shared decision-making, ultimately enhancing patient-centered care and facilitating communication [73]. Studies indicate that a considerable percentage of cancer patients, ranging from 20% to 77%, depending on the study setting, do not disclose their usage of CIH to their treating physicians [74–76]. This lack of communication can potentially undermine the doctor–patient relationship and, in the long run, exacerbate the risk of delayed diagnosis or discontinuation of conventional therapy [77,78]. Additionally, interactions between herbal remedies or dietary supplements and chemotherapeutic agents are potential risks that can be identified and addressed by the specially trained personnel during these counselings. Moreover, there may be an economic risk for patients, as many CIH procedures are not covered by public health insurance [79]. Therefore, the provision of counseling on CIH methods, which should be seamlessly integrated into comprehensive cancer therapy management, yields several beneficial effects, not only in terms of cost considerations but also with a primary focus on enhancing patient safety.

Strengths and limitations of the study

The CCC-Integrativ study exhibits numerous strengths. First, it represents the first multicenter study in Germany to implement and evaluate a transsectoral, interprofessional, evidence-based counseling program for CIH at CCCs. Secondly, the study represents the largest cohort of cancer patients examined using the PAM-13 scale in a pre-post comparison to date, offering valuable insights into the natural progression of PAM-13 at different time points in cancer patients, as assessed in the CO. Lastly, the interprofessional approach and individually tailored counseling based on patients' specific levels of PAM, resources and specific needs, represent a significant strength of our study. This approach aligns with recommendations from international literature [13,58].

One major limitation of the study is the absence of randomization. The decision to use a non-randomized naturalistic study design was based on ethical considerations, as a traditional randomized parallel-group design was not feasible due to strong patient preferences for counseling on CIH. Consequently, some significant baseline differences in the data, including main diagnosis, comorbidities, and age, may be attributed to this non-randomization. The study employed a timely offset recruitment strategy, with the control group recruited through study staff requests for participation, while the intervention group (IG) approached the counseling center based on eligibility criteria and perceived need for CIH counseling. This difference in recruitment may introduce a selection bias when comparing the control group to the intervention group. Technical limitations at the beginning of the study resulted in a paper-based completion of baseline questionnaires for the control group, leading to a higher proportion of missing data ($n = 62$), as mandatory completion of specific questions, such as the PAM-13, could not be verified. In contrast, the intervention group utilized electronic questionnaires with mandatory answer options for the PAM-13, resulting in fewer missing data ($n = 5$).

The study also leaves several questions unanswered, necessitating further investigation. One such question pertains to the specific dose–response relationship of the intervention, given the standardized three sessions over three months. Additionally, the study cannot conclusively determine the individual benefit of specific components of the intervention, as it was delivered and evaluated as a complex intervention. Moreover, our study does not provide a conclusive answer regarding the possible superiority of an interprofessional approach over a monoprofessional one in terms of patient activation outcomes. Comparing the effects of both approaches would be beneficial in determining the most effective model for delivering CIH counseling to cancer patients. However, we have undertaken an extensive exploration of these questions within our accompanying process evaluation [38].

Conclusions

Our results show that patient activation can be significantly enhanced through individually tailored counseling on CIH delivered by interprofessional teams specifically trained in CIH. Implementing such a program at cancer centers can effectively advance patient-centered

care with an emphasis on self-management, while also addressing the substantial patient demand for CIH methods. From a systemic perspective, the implementation of this program offers additional advantages, as the established positive effects of patient activation on health outcomes further support its utility.

Acknowledgements

This work was supported by the Innovationsfonds of the Federal Joint Committee 2019–2022 (No. 01NVF18004). The authors are gratefully for all patients who took part to the CCC-Integrativ study. We would also thank Holger Mauch for reviewing this manuscript. ChatGPT also assisted in linguistic revisions of the manuscript.

Compliance with ethics guidelines

Conflicts of Interest Jan Valentini, Daniela Froehlich, Inka Roesel, Regina Stolz, Cornelia Mahler, Peter Martus, Nadja Klafke, Markus Horneber, Claudia Witte, Klaus Kramer, Christine Greil, Barbara Gruen, Katrin Tomaschko-Ubelaender, and Stefanie Joos declare that they do not have any conflict of interests.

The study has been approved by the appropriate Institutional Ethical Committee of the University of Tuebingen (No. 658/2019BO1).

Trial Registration Number DRKS00021779

Collaborators: CCC-Integrativ study group A Schmitt, B Kröger, B Noack, B Wattenberg, E Kaschdailewitsch, H Mauch, K Gauß, K Harder, L Lohmüller, Institute for General Practice and Interprofessional Care, University Hospital and Faculty of Medicine Tuebingen, Germany; A Seckinger, D Zips, K Müller, Comprehensive Cancer Center Tübingen-Stuttgart, Germany; E Winkler, M Busacker-Scharpff, M Hoffmann, M Krug, M Reuter, S Eismann, Department of Medical Oncology, National Centre for Tumor Diseases, Heidelberg, Germany; A Kestler, B Leicht, C Nagat, C Raff, F Rapp, K Kraus, W Kmietschak, Department of Integrative Medicine, University Hospital and Faculty of Medicine Ulm, Germany; A Battran, A Frohn, B Held, C Perinchery, C Pfister-Jimenéz, Department of Medicine I, Medical Centre University of Freiburg, Faculty of Medicine, University of Freiburg, Germany; H Dürsch, J Bossert, J Szecsenyi, M Wensing, Department of General Practice and Health Services Research, University Hospital Heidelberg, Germany; A Kaltenbach, U Boltenhagen, Department of Nursing Science, Institute for Health Sciences, University Hospital and Faculty of Medicine Tuebingen, Germany; A Behzad, A Leppert. B Stein, Department of Internal Medicine, Division of Pneumology, Paracelsus Medical University, Klinikum Nuernberg, Germany; B Broge, C Witte, aQua Institute for Applied Quality Improvement and Research in Health Care, Goettingen, Germany; S Treffert, AOK Baden-Württemberg

Electronic Supplementary Material Supplementary material is available in the online version of this article at https://doi.org/10.1007/s11684-024-1097-z and is accessible for authorized users.

Funding note Open Access funding enabled and organized by Projekt DEAL.

References

1. Horneber M, Bueschel G, Dennert G, Less D, Ritter E, Zwahlen M. How many cancer patients use complementary and alternative medicine: a systematic review and metaanalysis. Integr Cancer Ther 2012; 11(3): 187–203
2. Boon HS, Olatunde F, Zick SM. Trends in complementary/alternative medicine use by breast cancer survivors: comparing survey data from 1998 and 2005. BMC Womens Health 2007; 7(1): 4
3. Academic Consortium for Integrative Medicine & Health. Definition of Integrative Medicine and Health. 2018. Available at the website of imconsortium.org
4. (NCCIH) NCfCaIH. Complementary, Alternative, or Integrative Health: What's In a Name? 2018. Available at the website of nccih. nih. gov
5. Greenlee H, DuPont-Reyes MJ, Balneaves LG, Carlson LE, Cohen MR, Deng G, Johnson JA, Mumber M, Seely D, Zick SM, Boyce LM, Tripathy D. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J Clin 2017; 67(3): 194–232
6. Hershman DL, Unger JM, Greenlee H, Capodice JL, Lew DL, Darke AK, Kengla AT, Melnik MK, Jorgensen CW, Kreisle WH, Minasian LM, Fisch MJ, Henry NL, Crew KD. Effect of acupuncture vs sham acupuncture or waitlist control on joint pain related to aromatase inhibitors among women with early-stage breast cancer: a randomized clinical trial. JAMA 2018; 320(2): 167–176
7. Hilfiker R, Meichtry A, Eicher M, Nilsson Balfe L, Knols RH, Verra ML, Taeymans J. Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: a systematic review incorporating an indirect-comparisons meta-analysis. Br J Sports Med 2018; 52(10):

651–658
8. Wayne PM, Lee MS, Novakowski J, Osypiuk K, Ligibel J, Carlson LE, Song R. Tai Chi and Qigong for cancer-related symptoms and quality of life: a systematic review and meta-analysis. J Cancer Surviv 2018; 12(2): 256–267
9. Haller H, Winkler MM, Klose P, Dobos G, Kümmel S, Cramer H. Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. Acta Oncol 2017; 56(12): 1665–1676
10. Liu R, Chang A, Reddy S, Hecht FM, Chao MT. Improving patient-centered care: a cross-sectional survey of prior use and interest in complementary and integrative health approaches among hospitalized oncology patients. J Altern Complement Med 2016; 22(2): 160–165
11. Ben-Arye E, Samuels N, Goldstein LH, Mutafoglu K, Omran S, Schiff E, Charalambous H, Dweikat T, Ghrayeb I, Bar-Sela G, Turker I, Hassan A, Hassan E, Saad B, Nimri O, Kebudi R, Silbermann M. Potential risks associated with traditional herbal medicine use in cancer care: a study of Middle Eastern oncology health care professionals. Cancer 2016; 122(4): 598–610
12. Posadzki P, Watson LK, Ernst E. Adverse effects of herbal medicines: an overview of systematic reviews. Clin Med (Lond) 2013; 13(1): 7–12
13. Leitlinienprogramm Onkologie. (Deutsche Krebsgesellschaft DK, AWMF.) S3-Leitlinie Komplementärmedizin in der Behandlung von onkologischen PatientInnen. 2021. AWMF Registernummer: 32/055OL (Langversion 1.1). Available at the website of leitlinienprogramm-onkologie.de
14. Lyman GH, Greenlee H, Bohlke K, Bao T, DeMichele AM, Deng GE, Fouladbakhsh JM, Gil B, Hershman DL, Mansfield S, Mussallem DM, Mustian KM, Price E, Rafte S, Cohen L. Integrative therapies during and after breast cancer treatment: ASCO endorsement of the SIO clinical practice guideline. J Clin Oncol 2018; 36(25): 2647–2655
15. Deng GE, Frenkel M, Cohen L, Cassileth BR, Abrams DI, Capodice JL, Courneya KS, Dryden T, Hanser S, Kumar N, Labriola D, Wardell DW, Sagar S; Society for Integrative Oncology. Evidence-based clinical practice guidelines for integrative oncology: complementary therapies and botanicals. J Soc Integr Oncol 2009; 7(3): 85–120
16. Yeh GY, Chan CW, Wayne PM, Conboy L. The impact of tai chi exercise on self-efficacy, social support, and empowerment in heart failure: insights from a qualitative sub-study from a randomized controlled trial. PLoS One 2016; 11(5): e0154678
17. Hübner J, Welter S, Ciarlo G, Käsmann L, Ahmadi E, Keinki C. Patient activation, self-efficacy and usage of complementary and alternative medicine in cancer patients. Med Oncol 2022; 39(12): 192
18. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. Health Serv Res 2004; 39(4p1): 1005–1026
19. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. Health Serv Res 2005; 40(6p1): 1918–1930
20. Alexander JA, Hearld LR, Mittler JN, Harvey J. Patient–physician role relationships and patient activation among individuals with chronic illness. Health Serv Res 2012; 47(3pt1): 1201–1223
21. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. Health Aff (Millwood) 2013; 32(2): 207–214
22. Blakemore A, Hann M, Howells K, Panagioti M, Sidaway M, Reeves D, Bower P. Patient activation in older people with long-term conditions and multimorbidity: correlates and change in a cohort study in the United Kingdom. BMC Health Serv Res 2016; 16(1): 582
23. Regeer H, van Empelen P, Bilo HJG, de Koning EJP, Huisman SD. Change is possible: how increased patient activation is associated with favorable changes in well-being, self-management and health outcomes among people with type 2 diabetes mellitus: a prospective longitudinal study. Patient Educ Couns 2022; 105(4): 821–827
24. Hibbard JH, Mahoney ER, Stock R, Tusler M. Do increases in patient activation result in improved self-management behaviors? Health Serv Res 2007; 42(4): 1443–1463
25. Salyers MP, Matthias MS, Spann CL, Lydick JM, Rollins AL, Frankel RM. The role of patient activation in psychiatric visits. Psychiatr Serv 2009; 60(11): 1535–1539
26. Cuevas H, Heitkemper E, Huang YC, Jang DE, García AA, Zuñiga JA. A systematic review and meta-analysis of patient activation in people living with chronic conditions. Patient Educ Couns 2021; 104(9): 2200–2212
27. Paukkonen L, Oikarinen A, Kähkönen O, Kaakinen P. Patient activation for self-management among adult patients with multimorbidity in primary healthcare settings. Health Sci Rep 2022; 5(4): e735
28. Westman B, Bergkvist K, Karlsson Rosenblad A, Sharp L, Bergenmar M. Patients with low activation level report limited possibilities to participate in cancer care. Health Expect 2022; 25(3): 914–924
29. Salgado TM, Mackler E, Severson JA, Lindsay J, Batra P, Petersen L, Farris KB. The relationship between patient activation, confidence to self-manage side effects, and adherence to oral oncolytics: a pilot study with Michigan oncology practices. Support Care Cancer 2017; 25(6): 1797–1807
30. Mosen DM, Schmittdiel J, Hibbard J, Sobel D, Remmers C, Bellows J. Is patient activation associated with outcomes of care for adults with chronic conditions? J Ambul Care Manage 2007; 30(1): 21–29
31. Acquati C, Hibbard J, Miller-Sonet E, Zhang A, Ionescu E. The moderating role of informal caregiver's involvement on the relationship between patient activation and adherence to treatment: Implications for self-management intervention in cancer care. J Clin Oncol 2021; 39(15 suppl): 12083
32. Janamian T, Greco M, Cosgriff D, Baker L, Dawda P. Activating people to partner in health and self-care: use of the Patient Activation Measure. Med J Aust 2022; 216(Suppl 10): S5–S8
33. Cronin RM, Dorner TL, Utrankar A, Allen W, Rodeghier M, Kassim AA, Jackson GP, DeBaun MR. Increased patient activation is associated with fewer emergency room visits and hospitalizations for pain in adults with sickle cell disease. Pain Med 2019; 20(8): 1464–1471
34. Lindsay A, Hibbard JH, Boothroyd DB, Glaseroff A, Asch SM. Patient activation changes as a potential signal for changes in health care costs: cohort study of us high-cost patients. J Gen Intern Med 2018; 33(12): 2106–2112

35. Hibbard JH, Greene J, Overton V. Patients with lower activation associated with higher costs; delivery systems should know their patients' 'scores'. Health Aff (Millwood) 2013; 32(2): 216–222
36. Greene J, Hibbard JH, Sacks R, Overton V, Parrotta CD. When patient activation levels change, health outcomes and costs change, too. Health Aff (Millwood) 2015; 34(3): 431–437
37. Valentini J, Fröhlich D, Stolz R, Mahler C, Martus P, Klafke N, Horneber M, Frasch J, Kramer K, Bertz H, Grün B, Tomaschko-Ubeländer K, Joos S. Interprofessional evidence-based counselling programme for complementary and integrative healthcare in patients with cancer: study protocol for the controlled implementation study CCC–Integrativ. BMJ Open 2022; 12(2): e055076
38. Bossert J, Mahler C, Boltenhagen U, Kaltenbach A, Froehlich D, Szecsenyi J, Wensing M, Joos S, Klafke N. Protocol for the process evaluation of a counselling intervention designed to educate cancer patients on complementary and integrative health care and promote interprofessional collaboration in this area (the CCC–Integrativ study). PLoS One 2022; 17(5): e0268091
39. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M, Lamb SE, Dixon-Woods M, McCulloch P, Wyatt JC, Chan AW, Michie S. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. BMJ 2014; 348: g1687
40. Klafke N, Mahler C, von Hagens C, Uhlmann L, Bentner M, Schneeweiss A, Mueller A, Szecsenyi J, Joos S. The effects of an integrated supportive care intervention on quality of life outcomes in outpatients with breast and gynecologic cancer undergoing chemotherapy: results from a randomized controlled trial. Cancer Med 2019; 8(8): 3666–3676
41. Klafke N, Mahler C, von Hagens C, Rochon J, Schneeweiss A, Müller A, Salize HJ, Joos S. A complex nursing intervention of complementary and alternative medicine (CAM) to increase quality of life in patients with breast and gynecologic cancer undergoing chemotherapy: study protocol for a partially randomized patient preference trial. Trials 2015; 16(1): 51
42. Klein GE, Guethlin C. Information and training needs regarding complementary and alternative medicine: a cross-sectional study of cancer care providers in Germany. Integr Cancer Ther 2018; 17(2): 380–387
43. Blödt S, Mittring N, Schützler L, Fischer F, Holmberg C, Horneber M, Stapf A, Witt CM. A consultation training program for physicians for communication about complementary medicine with breast cancer patients: a prospective, multi-center, cluster-randomized, mixed-method pilot study. BMC Cancer 2016; 16(1): 843
44. Horneber M, van Ackeren G, Fischer F, Kappauf H, Birkmann J. Addressing unmet information needs: results of a clinician-led consultation service about complementary and alternative medicine for cancer patients and their relatives. Integr Cancer Ther 2018; 17(4): 1172–1182
45. Orchard C, Bursey S, Peterson L, Verrilli S. Can workshops provide a way to enhance patient/client centered collaborative teams?: evidence of outcomes from TEAMc online facilitator training and team workshops. Int J Practice-based Learning Health Social Care 2016; 4(2): 73–87
46. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009; 42(2): 377–381
47. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, McLeod L, Delacqua G, Delacqua F, Kirby J, Duda SN, on behalf of the REDCap Consortium. Building an international community of software platform partners. J Biomed Inform 2019; 95: 103208
48. Brenk-Franz K, Hibbard JH, Herrmann WJ, Freund T, Szecsenyi J, Djalali S, Steurer-Stey C, Sönnichsen A, Tiesler F, Storch M, Schneider N, Gensichen J. Validation of the German version of the patient activation measure 13 (PAM13-D) in an international multicentre study of primary care patients. PLoS One 2013; 8(9): e74786
49. Rademakers J, Maindal HT, Steinsbekk A, Gensichen J, Brenk-Franz K, Hendriks M. Patient activation in Europe: an international comparison of psychometric properties and patients' scores on the short form Patient Activation Measure (PAM-13). BMC Health Services Research 2016; 16(1): 570
50. Bates JS, Auten J, Sketch MR, Patel T, Clark SM, Morgan KP, Muluneh B, McLaughlin JE, Pinelli NR, Foster MC, Amerine L. Patient engagement in first cycle comprehensive chemotherapy consultation pharmacist services and impact on patient activation. J Oncol Pharm Pract 2019; 25(4): 896–902
51. Wolever RQ, Webber DM, Meunier JP, Greeson JM, Lausier ER, Gaudet TW. Modifiable disease risk, readiness to change, and psychosocial functioning improve with integrative medicine immersion model. Altern Ther Health Med 2011; 17(4): 38–47
52. Antol SM. Predictors of patient activation among underserved patients in a nurse-managed health center: a pilot study. University of Maryland, College Park. 2016
53. John JR, Tannous WK, Jones A. Outcomes of a 12-month patient-centred medical home model in improving patient activation and self-management behaviours among primary care patients presenting with chronic diseases in Sydney, Australia: a before-and-after study. BMC Fam Pract 2020; 21(1): 158
54. Howell D, Pond GR, Bryant-Lukosius D, Powis M, McGowan PT, Makuwaza T, Kukreti V, Rask S, Hack S, Krzyzanowska MK. Feasibility and effectiveness of self-management education and coaching on patient activation for managing cancer treatment toxicities. J Natl Compr Canc Netw 2023; 21(3): 247–256.e8
55. Vohra Y, Brown CM, Moczygemba LR, Wilfong L. Evaluating the relationship between patient activation and health-related quality of life (HRQOL) in patients with pancreatic cancer (PwPC). Support Care Cancer 2023; 31(3): 191
56. Solomon M, Wagner SL, Goes J. Effects of a web-based intervention for adults with chronic conditions on patient activation: online randomized controlled trial. J Med Internet Res 2012; 14(1): e32
57. Welter S, Keinki C, Ahmadi E, Huebner J. Lay etiology, self-efficacy and patient activation among cancer patients. Cancer Invest 2021; 39(3): 219–228
58. Harvey L, Fowles JB, Xi M, Terry P. When activation changes, what else changes? the relationship between change in patient activation measure (PAM) and employees' health status and health behaviors. Patient Educ Couns 2012; 88(2): 338–343
59. Hibbard JH. Using systematic measurement to target consumer activation strategies. Med Care Res Rev 2009; 66(1 suppl):

9S–27S
60. Witzig Brändli V, Lange C, Kobleder A, Kohler M. Effectiveness and content components of nursing counselling interventions on self- and symptom management of patients in oncology rehabilitation—a systematic review. Nurs Open 2023; 10(5): 2757–2769
61. Hibbard JH, Greene J, Tusler M. Improving the outcomes of disease management by tailoring care to the patient's level of activation. Am J Manag Care 2009; 15(6): 353–360
62. Bloom DA, Kaplan DJ, Mojica E, Strauss EJ, Gonzalez-Lomas G, Campbell KA, Alaia MJ, Jazrawi LM. The minimal clinically important difference: a review of clinical significance. Am J Sports Med 2023; 51(2): 520–524
63. Copay AG, Subach BR, Glassman SD, Polly DW Jr, Schuler TC. Understanding the minimum clinically important difference: a review of concepts and methods. Spine J 2007; 7(5): 541–546
64. Wright A, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). J Manual Manip Ther 2012; 20(3): 160–166
65. Cook CE. Clinimetrics corner: the minimal clinically important change score (MCID): a necessary pretense. J Manual Manip Ther 2008; 16(4): E82–E83
66. Kanu C, Brown CM, Rascati K, Moczygemba LR, Mackert M, Wilfong L. Are health literacy and patient activation related to health outcomes in breast cancer patients? Health Lit Res Pract 2021; 5(3): e171–e178.
67. Palumbo R. Examining the impacts of health literacy on healthcare costs. An evidence synthesis. Health Serv Manage Res 2017; 30(4): 197–212
68. Greene J, Hibbard JH. Why does patient activation matter? An examination of the relationships between patient activation and health-related outcomes. J Gen Intern Med 2012; 27(5): 520–526
69. Krouse RS, Grant M, McCorkle R, Wendel CS, Cobb MD, Tallman NJ, Ercolano E, Sun V, Hibbard JH, Hornbrook MC. A chronic care ostomy self-management program for cancer survivors. Psychooncology 2016; 25(5): 574–581
70. Lunardi LE, Hill K, Xu Q, Le Leu R, Bennett PN. The effectiveness of patient activation interventions in adults with chronic kidney disease: a systematic review and meta-analysis. 2023; 20(3): 238–258
71. Frydenberg M, Maindal HT, Fletcher A, Juul L. Is patient activation a mediator of the effect of a health promoting intervention in adults at high risk of type 2 diabetes? A longitudinal path model analysis within a randomised trial. BMC Public Health 2022; 22(1): 439
72. Lemanska A, Poole K, Manders R, Marshall J, Nazar Z, Noble K, Saxton JM, Turner L, Warner G, Griffin BA, Faithfull S. Patient activation and patient-reported outcomes of men from a community pharmacy lifestyle intervention after prostate cancer treatment. Support Care Cancer 2022; 30(1): 347–358
73. Stub T, Quandt SA, Arcury TA, Sandberg JC, Kristoffersen AE. Complementary and conventional providers in cancer care: experience of communication with patients and steps to improve communication with other providers. BMC Complement Altern Med 2017; 17(1): 301
74. Davis EL, Oh B, Butow PN, Mullan BA, Clarke S. Cancer patient disclosure and patient–doctor communication of complementary and alternative medicine use: a systematic review. Oncologist 2012; 17(11): 1475–1481
75. Sanford NN, Sher DJ, Ahn C, Aizer AA, Mahal BA. Prevalence and nondisclosure of complementary and alternative medicine use in patients with cancer and cancer survivors in the United States. JAMA Oncol 2019; 5(5): 735–737
76. Arslan C, Guler M. Alternative medicine usage among solid tumour patients receiving chemotherapy. Eur J Cancer Care (Engl) 2017; 26(5): e12530
77. Johnson SB, Park HS, Gross CP, Yu JB. Complementary medicine, refusal of conventional cancer therapy, and survival among patients with curable cancers. JAMA Oncol 2018; 4(10): 1375
78. Hayward RA, Asch SM, Hogan MM, Hofer TP, Kerr EA. Sins of omission: getting too little medical care may be the greatest threat to patient safety. J Gen Intern Med 2005; 20(8): 686–691
79. Wardle JJL, Adams J. Indirect and non-health risks associated with complementary and alternative medicine use: an integrative review. Eur J Integr Med 2014; 6(4): 409–422