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Providing a nurse-led complex nursing INtervention FOcused on quality of life assessment on advanced cancer patients: The INFO-QoL pilot trial

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ABSTRACT

Purpose: Unmet needs for advanced-disease cancer patients are fatigue, pain, and emotional support. Little information is available about the feasibility of interventions focused on patient-reported outcome measurement developed according to the Medical Research Council (MRC) Framework in advanced-disease cancer patients. We aimed to pilot a nurse-led complex intervention focused on QoL assessment in advanced-disease cancer patients.

Methods: The INFO-QoL study was based on an exploratory, nonequivalent comparison group, pre-test-post-test design. Study sites received either the INFO-QoL intervention or usual care.

Adult advanced-disease cancer patients admitted to hospice inpatient units that gave their informed consent were included in the study. Subjects were 187 patients and their families and 19 healthcare professionals.

We evaluated feasibility, acceptability, and patients' outcomes using the Integrated Palliative Care Outcome Scale.

Results: Nineteen healthcare professionals were included. The mean competence score increased significantly over time ($p < 0.001$) and the mean usefulness score was high 8.63 (± 1.36).

In the post-test phase, 54 patients were allocated to the experimental unit and 36 in the comparison unit. Compared to the comparison unit, in the experimental unit anxiety ($R2 = 0.07$; 95% CI = −0.06; 0.19), family anxiety ($R2 = 0.22$; 95% CI = −0.03; 0.41), depression ($R2 = 0.31$; 95% CI = −0.05; 0.56) and sharing feelings ($R2 = 0.09$; 95% CI = −0.05; 0.23), were improved between pre-test and post-test phase.

Conclusions: The INFO-QoL was feasible and potentially improved psychological outcomes. Despite the high attrition rate, the INFO-QoL improved the quality and safety culture for patients in palliative care settings.

1. Introduction

The worldwide global cancer burden is significant, and cancer is one of the leading causes of death. Most cancer patients, in addition to active treatments need physical, psychological, social and spiritual support that also impact on their families as informal caregivers ('WHO | WHO Definition of Palliative Care', 2019). Advanced-disease cancer patients in their final stage of life, experiencing complex symptoms, should receive palliative care in one of the designated settings, such as hospice inpatient care or homecare ('WHO | WHO Definition of Palliative Care', 2019).

Nevertheless, a recent systematic review, aimed at identifying unmet care needs of patients in their final cancer disease trajectory, found that the most commonly reported unmet needs for patients were fatigue,

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pain, and emotional support (Wang et al., 2018).

In the context of a life-limiting disease, these patients' needs and Quality of Life (QoL) have been conceptualized and grouped as patient-centered outcomes (Locklear et al., 2015). Concurrently, the Institute of Medicine refers to patient-centered care as care that respects patients' needs and preferences (IOM, 2001). Thus, it is essential to plan care processes according to patients' point of view collected through validated Patient-Reported Outcome Measures (PROMs) (Antunes et al., 2014). A systematic review found that most of the high-quality evidence on PROMs implementation in clinical practice was conducted in cancer outpatient settings (Etkind et al., 2015). However, knowledge about PROMs use in inpatient palliative care routine practice is still lacking. Furthermore, recent recommendations have pointed out that successful use of PROMs in clinical settings requires local tailoring, having a coordinator of PROM process, offering all staff an educational program, and recognizing the ongoing cognitive and emotional processes in each individual (Antunes et al., 2014). An empirical conceptualization preliminary to this study concluded that outcome measurements in clinical settings (e.g., quality of life) do not only entail using a measure in clinical practice but involve training healthcare professionals, educating patients, and having treatments/interventions available to address patients' needs. Each of these interrelated components leads to changes in patients' outcomes, thus making the implementation of a clinical intervention focused on measuring quality of life (QoL) a complex intervention (Catania et al., 2013). However, little information is available about the feasibility and potential effectiveness of interventions focused on PRO measurement developed according to the MRC Framework in advanced-disease cancer patients. Furthermore, research gaps identified by organizations such as the Oncology Nursing Society (Von Ah et al., 2019), and the National Institute of Nursing Research (National Institute of Nursing Research, 2016) concluded that it is a research priority to determine the effective interventions to improve patients' QoL. Therefore, we developed and modeled a nurse-led INtervention FOcused on Quality of Life (INFO-QoL) assessment.

The primary study aim of this pilot study was to assess the INFO-QoL intervention involving inpatient palliative care team members and their patients in terms of feasibility and acceptability. The secondary aim was to determine the potential effectiveness of the INFO-QoL intervention in improving patient's QoL and informing a larger phase III trial in the future.

Feasibility was assessed in terms of 1) timing to educate healthcare professionals, 2) fidelity through a checklist, and 3) team members' competence and confidence level in delivering the intervention across three time points. Furthermore, the feasibility of the study included patient recruitment and dropout rates.

The acceptability of the INFO-QoL intervention was evaluated in terms of overall rate of eligible patients who accepted to participate in the study. Also, relevance, appropriateness, and usefulness of the intervention in addressing patients' needs and QoL from team members perspective were measured.

2. Methods

2.1. Study design and participants

The INFO-QoL study was based on a nonequivalent comparison group, pre-test-post-test design. Pretest measurements on both groups allowed comparability of the two groups. In the context of quasi-experimental studies, this design is described as more robust from a methodological point of view (Polit and Beck 2017). The study was conducted in two 12-bed inpatient units in two hospice sites in Italy that admitted adult patients. The two study sites admitted cancer patients in their last phase of life who could not be cared for at home, in hospital, or a nursing home. The staff of the study sites included palliative care physicians, registered nurses, and nursing assistants. They were educated and trained in palliative care and communication in end-of-life stage, and adopted the Liverpool care pathway. The inclusion criteria were adult advanced-disease cancer patients admitted to hospice inpatient units who agreed to give their informed consent. Cognitively impaired patients were excluded (Catania et al., 2017).

The Ethics Committee of the Liguria Region approved the study (Registration n. 335REG2014), which was registered in the ISRCTN registry (ISRCTN41201864). The study was reported according to the CONSORT checklist for randomized pilot trials (Eldridge et al., 2016). This study was conducted from January 2016 to January 2019.

2.2. The intervention

The INFO-QoL intervention aimed at improving patients' outcomes and overall QoL in advanced-disease cancer patients with palliative care needs. Its development was conceptually based on the QoL Assessment Principles in Palliative Care framework (Catania et al., 2013); it postulates that QoL assessment is a complex intervention made of different components and underlying mechanisms that were carefully considered as a whole before implementing them in clinical practice, and may determine improved outcomes. Thus, the INFO-QoL intervention consisted of three main components: 1) a small group interdisciplinary team educational program focusing on QoL issues and interventions that promote better outcomes in advanced-disease cancer care; 2) nurse-patient and nurse-family face-to-face interaction to educate patients and their families on QoL issues; 3) patients' outcomes and QoL assessment and appointing a nurse in charge of the process. The INFO-QoL intervention may determine practice changes in the unit that impact on decision making and on the activities of all team members.

The three components were delivered as follows: 1) the team education program lasted for 4 h. To allow the participation of all the team members 3 sessions were scheduled. The educational and workshop session contents were developed according to the team's learning needs (i.e., knowledge and attitude) which were evaluated using the INFO-QoL questionnaire. Ten days before attending the session, each team member received the Italian version of the "Outcome Measurement in Palliative Care - The Essential" (Bausewein et al., 2011) guidance and the Palliative care Outcome Scale user guide (Aspinal et al., 2002). All the members of the team (i.e., 2 physicians, 10 nurses, 7 nursing assistants) attended the educational program. 2) Nurse-patient and family face-to-face interaction was based on a handout on QoL, and it aimed at presenting the purpose of QoL assessment to patients and their families and teaching them how to complete the Italian version of the Integrated Palliative care Outcome Scale (I-POS) (Costantini et al., 2016). Each session took 10–15 min 3) Patients' outcomes and QoL assessment was conducted under the supervision of a nurse responsible for the following process tasks: scheduling the measurement, preparing the documentation required to perform the assessment and discussing each patient's needs during the daily staff briefing, assigning the patients to the nurse, and overseeing the completion of assessments.

According to the I-POS scores, the care plan was developed during the daily multidisciplinary staff briefing and included changing treatments/route of administration, monitoring vital signs, providing emotional support, educating patients and their families about the illness and options for care based on their goals and preferences, and initiating decision-making conversations.

2.3. Standard care

In the hospice inpatient unit randomly assigned to receive usual care, the team members did not receive the educational program. Patients received clinical and nursing care based on routine assessment and did not receive QoL assessment, and the results were not discussed during daily staff briefing.

2.4. Procedures

The pre-test phase served as a baseline assessment for both groups. In the post-test phase, all the team members of the experimental group received the INFO-QoL questionnaire aimed at assessing their knowledge and attitude toward QoL in advanced-disease cancer patients with palliative care needs. About two weeks later, they participated in the INFO-QoL educational program.

Subsequently, all potentially eligible patients admitted to the hospice inpatient unit were screened by a nurse who discussed the purpose and procedures of the study in detail. Subjects who agreed to participate were asked to sign the informed consent form.

All the process activities were conducted under the supervision of two nurses of the team, who were responsible for the correct implementation of the INFO-QoL intervention. Within 3 days from admission (T0) subjects received a handout about addressing patient's needs and a nurse-led brief educational session to motivate patients on QoL as the ultimate goal of the healthcare professional team. During the morning shift, subjects were assessed at T0, 8–10 days later (T1), and 15–18 days from admission (T2). During daily briefing, team members discussed the data collected at each assessment, they developed or updated their care plan and shared results and details of the plan with the subjects and their family.

3. Outcome measures

Trained nurses performed the assessment in all the subjects. Demographic and clinical information were collected from the patients' charts when they were enrolled in the study. Patients' outcomes were measured using the self-report QoL measure. We used the validated Italian version of the Integrated Palliative care Outcome Scale (IPOS) (Veronese et al., 2019) both for the INFO-QoL intervention and the outcome study measure. The IPOS is a 17-item valid, reliable, and widely used measure including physical and psychological symptoms, and communication, spiritual and practical patients' needs. Each item is scored on a Likert scale ranging from 0 to 4, where 0 indicates the best and 4 the worst possible care. The overall score ranges from 0 to 68, where 68 indicates severe impairment (Murtagh et al., 2019).

3.1. Feasibility

The feasibility of the INFO-QoL intervention was measured through 1) timing to educate healthcare professionals, 2) fidelity through a checklist, and 3) team members' level of competence and confidence in delivering the intervention across the 3-time points. Data were collected through 2 questions (i.e., *To what extent do you feel competent/confident about carrying out the INFO-QoL intervention?*), which were both rated on an 11-point Likert scale from 0 (*not at all*) to 10 (*very much*) and at 3-time points: baseline (T0), 3 months (T1), and 6 months (T2).

Furthermore, the feasibility of the study included patient recruitment and dropout rates.

3.2. Acceptability

The acceptability of the INFO-QoL intervention was evaluated in terms of overall rate of eligible patients who accepted to participate in the study. Also, relevance, appropriateness, and usefulness of the intervention in addressing patients' needs and QoL from team members perspective were measured through three 11-point Likert scales ranging from 0 (*not at all*) to 10 (*very much*).

3.3. Potential effectiveness

Patients' QoL was measured at baseline and every week up to 15 ± 3 days from admission to both inpatient units, before and after the intervention implementation using the IPOS tool. In both units, blinding of the assessors took place to prevent that groups differed in the way outcomes information was gathered. Therefore, research assistants conducted data collection throughout the phases of the study except for the intervention unit, during the post-test phase, where the assessment was performed by healthcare professionals as part of the INFO-QoL intervention.

3.4. Patient management

Patient management data were collected using a composite patient management score (Detmar et al., 2002). Patient management actions included medications, interventions, nutrition and diet, vital signs, diagnostic tests, referrals and consultations, patient and family counseling, and education. The score was calculated by summarizing all the actions undertaken by multidisciplinary staff per patient.

3.5. Data analyses

A sample size of 23 patients per unit/phase was estimated assuming a small effect size of 0.3 and a statistical power of 80%; an attrition rate of 30% was set (Hui et al., 2013). We used descriptive statistics to summarize the study results; the Student T test was used to compare the mean age between groups, and the $\chi 2$ test was applied to analyze the distribution differences between groups. Outliers were detected via studentized residuals. For the overall quality of life score and each patients' outcome score, the Kolmogorov-Smirnov Z test and the Levene test were applied to assess the normality of the distribution and the homogeneity of variance of our data, respectively. The Mauchly test of sphericity was used to validate the correlation of the repeated measures, and tests of within-subject (i.e. study phase) and between-subject (i.e. group variable) effects were applied by two-way repeated measures of ANOVA in a general linear model. When the assumption of sphericity was not met, correction was made using the Greenhouse-Geisser Epsilon.

The primary purpose of two-way repeated measures of ANOVA was to understand if there was an interaction between the two independent variables (i.e., the group variable – experimental vs comparison group - and the study phase variable – pre-test vs post-test) on the mean of the dependent continuous and ordinal variables (i.e. overall quality of life score and each patient's outcomes score). Covariates that were imbalanced across the treatment groups were the Karnofsky Performance Status and the item about who completed the IPOS questionnaire (i.e., self-administered, relative/friend, staff).

Moreover, the Mann-Whitney *U* test was performed to compare the median of each patient's need, before and after the intervention at each of the timepoints within the two nonequivalent groups. We calculated Effect Sizes (ES) as r = z/square root of N where N = total number of cases; 95% Confidence Interval (CI) was estimated as the standard error of R^2. According to Cohen's guidelines, r of 0.5 was considered a large, 0.3 a medium, and 0.1 a small effect (Cohen et al., 2003; Fritz et al., 2012).

For all the statistical procedures, p values < 0.05 were considered statistically significant. Two-way repeated measures of the ANOVA analysis was performed on an intention-to-treat basis. All remaining analyses were performed on an intention-to-treat and per-protocol analysis basis. Intention-to-treat analysis considered subjects with at least two time point assessments, per-protocol analyses included adherent subjects with three time point assessments. Version 26 of the SPSS software was used to conduct the analyses (IBM SPSS Inc., Chicago, IL).

4. Results

4.1. Feasibility of intervention at team level ($n = 19$)

Educational training on QoL measurement for the healthcare professionals lasted 4 h as planned. All the staff members took part in one of

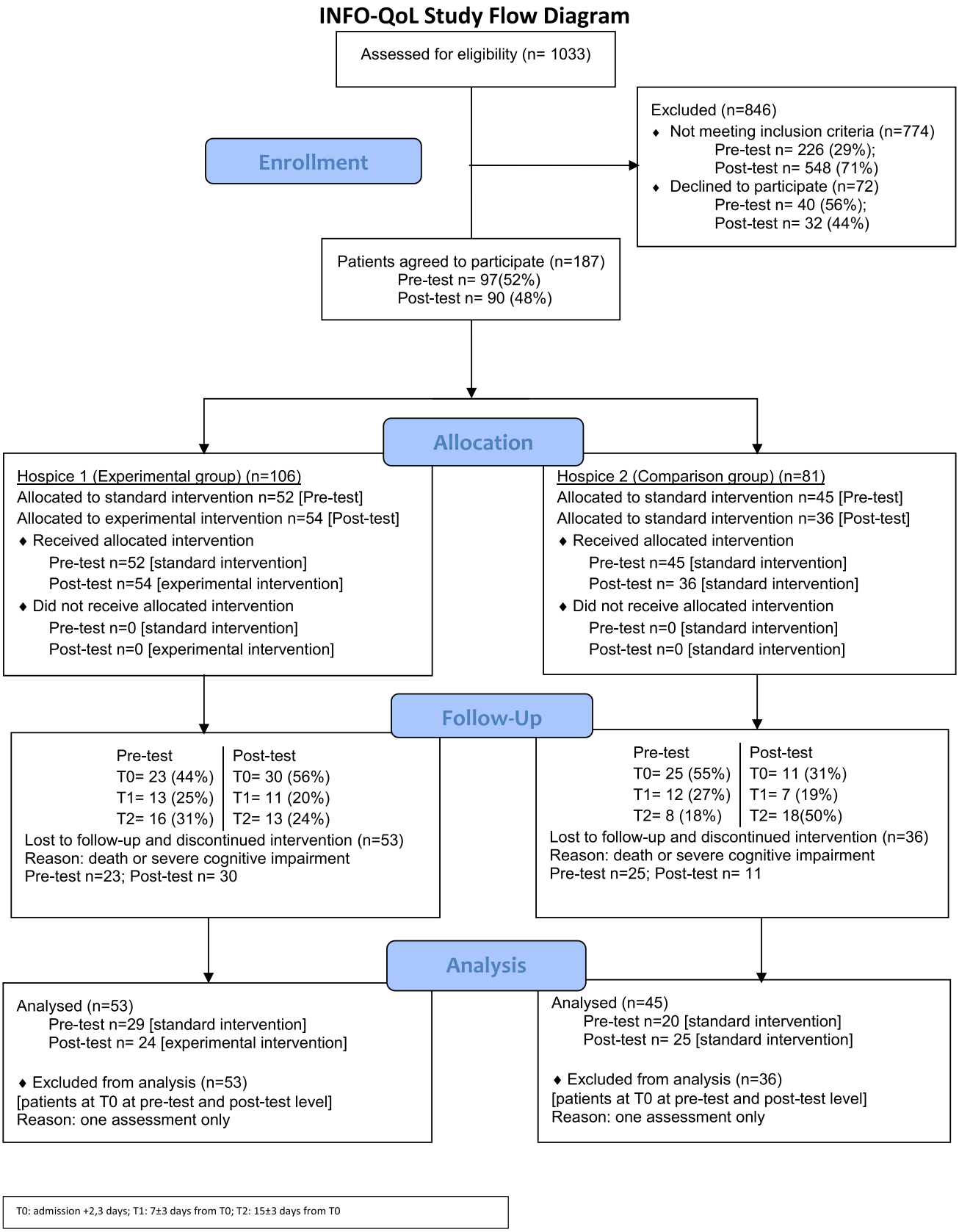


Fig. 1. INFO-QoL study flow diagram.

the three scheduled events to allow all staff to participate. All the sample (N = 19) attended the educational workshop, of whom 79% (N = 15) were female. The mean age was 44 years (±11). Mean years in their professional role and in palliative care was 15 (±9) and 8 (±7), respectively. Eight team members missed one or more intervention feasibility assessments because they were on vacation or sick leave during the scheduled assessments. Eleven (79%) healthcare professionals completed all the three assessments. Competence and confidence scores were normally distributed, as assessed by Shapiro-Wilk's test of normality (P = 0.097). The mean competence score increased significantly over time so that it increased from 4.55 (±2.11) (T0) to 6 (±1.78) (T1) to 7.09 (±1.04) (T2), F (2.22) = 10.120, P < 0.001. In contrast, although the mean confidence score increased over time from 5.45 (±2.11) (T0) to 5.91 (±1.7) (T1) to 6.82 (±1.53) (T2), the effect of the workshop on staff's perceived confidence to deliver the INFO-QoL intervention was not statistically significant, F (2.22) = 2.648, P = 0.095.

4.2. Acceptability of the study at team level (n = 16)

Overall, 16 out of the 19 team members (1 physician, 9 nurses, 6 nursing assistants) shared their points of view about the relevance, appropriateness, and usefulness of the INFO-QoL intervention.

One physician retired during the study period, one nurse and one nursing assistant did not score the acceptability of the study. The mean scores of the healthcare professionals for each of the three variables were all particularly close to the maximum score: relevance 8.31 (±1.6); appropriateness 7.75 (±2); and usefulness 8.63 (±1.37). Most of them agreed to continue to use the INFO-QoL intervention (n = 13; 81%) even after the study ended.

4.3. Feasibility of intervention at patient level (n = 106)

In the experimental group (n = 106), all the patients in the after phase (n = 54) at T0 (n = 30), T1 (n = 11), and T2 (n = 13) were assessed according to the study procedures. Data showed that all the activities were conducted as planned in the study protocol, except for the number of scheduled assessments where only 13 patients (24%) completed the three scheduled assessments. Lost to follow-up reasons were death or severe cognitive impairment.

4.4. Feasibility of the study at patient level

We assessed for eligibility 1033 patients, of which 846 were excluded because they did not meet the inclusion criteria (n = 774; 91%) or declined to participate (n = 72; 9%).

Overall, in the pre-test phase 363 patients were invited (included n = 97; 27%; excluded n = 266; 73%), and in the post-test phase 670 patients (included n = 90; 13%; excluded n = 580; 87%) (P < 0.001). In both phases, recruitment goals were extended from three to six months because of poor enrollment. In both units, dropout reasons were either death or severe cognitive impairment (Fig. 1).

Table 1
Patient's demographic and clinical characteristics.

	Experimental group			Comparison group		
	Pre-test (n = 29)	*Post-test* (n = 24)	*p value*	*Pre-test* (n = 20)	*Post-test* (n = 25)	p value
Age, years	74.6 (11.1)	73.9 (11.0)	0.827	69.9 (16.7)	70.5 (9.9)	0.880
Sex						
Female	19 (66%)	11 (46%)	0.150	12 (60%)	11 (44%)	0.286
Male	10 (34%)	13 (54%)		8 (40%)	14 (56%)	
Karnofsky Performance Status						
Requires occasional assistance	0 (0%)	2 (8%)	0.216	0 (0%)	0 (0%)	0.034
Requires considerable assistance	2 (7%)	3 (13%)		0 (0%)	4 (16%)	
Disabled	13 (45%)	13 (54%)		15 (75%)	10 (40%)	
Severely disabled	12 (41%)	6 (25%)		5 (25%)	11 (40%)	
Very sick	2 (7%)	0 (0%)		0 (0%)	0 (0%)	
Tumour Site						
Gastrointestinal	13 (45%)	6(26%)	0.269	3 (15%)	9 (36%)	0.274
Genitourinary	6 (21%)	3 (13%)		5 (25%)	5 (20%)	
Lung	3 (10%)	8 (35%)		4 (20%)	5 (20%)	
Breast	2 (7%)	1 (4%)		3 (15%)	2 (8%)	
Head and neck	2 (7%)	1 (4%)		0 (0%)	1 (4%)	
Hematologic	2(7%)	4 (17%)		1 (5%)	1 (4%)	
Melanoma	1(3%)	0 (0%)		2 (10%)	0 (0%)	
Central nervous system	0 (0%)	0 (0%)		2 (10%)	0 (0%)	
Sarcoma	0 (0%)	0 (0%)		0 (0%)	2 (8%)	
Who completed the IPOS						
T0. Self-administered	7 (24%)	6 (25%)	0.539	6 (30%)	1 (4%)	0.015
T0. Relative or friend	5 (17%)	7 (29%)		5 (25%)	3 (12%)	
T0. Staff	17 (59%)	11 (46%)		9 (45%)	21 (84%)	
T1. Self-administered	6 (21%)	7 (30%)	0.152	5 (25%)	1 (4%)	<0.001
T1. Relative or friend	3 (10%)	6 (26%)		8 (40%)	0 (0%)	
T1. Staff	20 (69%)	10 (44%)		7 (35%)	24 (96%)	
T2. Self-administered	2 (13%)	6 (46%)	0.131	2 (25%)	0 (0%)	0.006
T2. Relative or friend	2 (13%)	1 (8%)		2 (25%)	0 (0%)	
T2. Staff	12 (74%)	6 (46%)		4 (50%)	17 (100%)	
Data are mean (SD) or n (%)						

IPOS= Integrated Palliative Outcome Scale; T0 = admission +2,3 days; T1: 7 ± 3 days from T0; T2: 15 ± 3 days from T0.

Table 2
Interaction effect between study phases and study sites on patients' physical outcomes.

Variable	Experimental group		Comparison group		Source [a]	*F*	*p value*
	Pre-test (n = 29)	*Post-test (n = 24)*	*Pre-test (n = 20)*	*Post-test (n = 25)*			
Pain T0	0.94 (0.77)	1.23 (1.30)	2.13 (1.55)	1.35 (0.86)	A	1.230	0.302
Pain T1	0.81 (1.05)	0.92 (0.95)	1.88 (1.55)	1.00 (1.28)	A x P	0.788	0.461
Pain T2	1.00 (1.21)	1.08 (1.04)	1.13 (1.25)	1.00 (1.00)	A x H	3.370	**0.043**
					A x P x H	1.081	0.348
Dyspnea T0	0.63 (0.81)	0.69 (0.95)	1.00 (0.93)	1.35 (1.12)	A	0.266	0.767
Dyspnea T1	0.44 (0.63)	0.69 (0.86)	0.75 (1.17)	1.12 (1.05)	A x P	0.249	0.780
Dyspnea T2	0.63 (0.72)	1.00 (1.23)	0.63 (0.74)	1.18 (1.19)	A x H	1.229	0.302
					A x P x H	0.744	0.481
Fatigue T0	1.44 (0.89)	2.23 (1.09)	1.43 (1.13)	2.29 (0.99)	A	2.371	0.105
Fatigue T1	1.19 (0.91)	2.15 (0.99)	1.71 (1.50)	1.94 (0.97)	A x P	0.966	0.389
Fatigue T2	1.38 (0.96)	2.00 (1.16)	1.86 (0.90)	1.88 (1.67)	A x H	0.712	0.496
					A x P x H	1.784	0.180
Nausea T0	0.25 (0.45)	0.38 (0.65)	0.63 (0.92)	0.94 (1.20)	A	1.299	0.283
Nausea T1	0.31 (0.60)	0.46 (0.78)	0.13 (0.35)	0.71 (1.21)	A x P	2.534	0.091
Nausea T2	0.44 (0.73)	0.23 (0.60)	0.88 (1.36)	0.65 (1.17)	A x H	2.809	0.071
					A x P x H	0.230	0.796
Vomiting T0	0.00 (0.00)	0.08 (0.28)	0.00 (0.00)	0.94 (1.39)	A	0.474	0.625
Vomiting T1	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	0.53 (1.18)	A x P	1.200	0.311
Vomiting T2	0.13 (0.34)	0.00 (0.00)	0.00 (0.00)	0.47 (1.01)	A x H	0.665	0.519
					A x P x H	0.298	0.744
Poor appetite T0	1.25 (0.93)	1.00 (1.10)	1.29 (1.11)	1.82 (1.33)	A	0.087	0.917
Poor appetite T1	1.44 (0.73)	1.15 (1.28)	1.43 (1.27)	1.24 (1.44)	A x P	1.702	0.194
Poor appetite T2	1.44 (0.81)	1.00 (0.91)	1.57 (0.98)	0.88 (0.99)	A x H	1.371	0.264
					A x P x H	1.261	0.293
Constipation T0	1.63 (0.81)	1.17 (1.64)	1.43 (0.79)	1.60 (1.40)	A	0.393	0.678
Constipation T1	1.44 (0.89)	1.42 (1.56)	0.86 (0.90)	1.33 (1.18)	A x P	3.927	**0.028**
Constipation T2	1.50 (0.97)	0.50 (1.00)	1.43 (1.51)	0.80 (0.86)	A x H	1.537	0.227
					A x P x H	0.167	0.846
Sore/Dry mouth T0	0.75 (1.07)	1.23 (0.93)	1.38 (0.92)	1.18 (0.95)	A	0.015	0.985
Sore/Dry mouth T1	0.56 (1.03)	1.38 (0.87)	1.25 (0.89)	1.00 (1.00)	A x P	0.558	0.576
Sore/Dry mouth T2	0.75 (1.13)	1.23 (1.24)	1.25 (1.39)	0.82 (0.73)	A x H	0.401	0.672
					A x P x H	0.587	0.560
Drowsiness T0	1.13 (1.15)	1.31 (1.11)	1.57 (0.98)	1.82 (1.07)	A	1.597	0.214
Drowsiness T1	0.88 (0.96)	1.62 (1.12)	1.29 (1.38)	2.12 (1.22)	A x P	1.301	0.283
Drowsiness T2	0.94 (0.93)	1.31 (1.03)	1.57 (1.27)	1.76 (0.90)	A x H	0.213	0.809
					A x P x H	0.271	0.764
Poor mobility T0	1.44 (1.15)	1.92 (1.26)	2.13 (1.36)	2.59 (0.80)	A	0.948	0.395
Poor mobility T1	1.31 (1.14)	2.23 (1.24)	2.25 (1.28)	2.12 (0.93)	A x P	0.813	0.450
Poor mobility T2	1.50 (1.21)	1.85 (1.14)	2.63 (1.30)	2.29 (1.16)	A x H	0.982	0.382
					A x P x H	0.893	0.417
Overall symptoms T0	9.44 (4.32)	11.31 (6.41)	13.00 (5.18)	15.71 (6.07)	A	0.559	0.576
Overall symptoms T1	8.38 (4.79)	12.15 (5.89)	11.13 (7.74)	12.94 (7.52)	A x P	3.188	**0.051**
Overall symptoms T2	9.68 (5.77)	10.15 (6.28)	13.25 (7.13)	11.65 (5.30)	A x H	1.697	0.195
					A x P x H	0.978	0.384

Data are mean (SD); T0: admittance ±3 days; T1: 7 ± 3 days from admission; T2: 15 ± 3 days from admission.
[a] multivariate tests of two-way repeated measures analysis of variance; A = assessment; P = phase; H= Hospice.

4.5. Acceptability of the study at patient level (n = 122)

In the post-test phase, 122 patients were eligible, of which 32 declined to participate (experimental group, n = 20 (63%); comparison group, n = 12 (37%)). The main reasons for declining were tiredness, reduced energy, and mental exhaustion (Fig. 1).

4.6. Potential effectiveness (n = 98)

Preliminary, we evaluated the distribution of values, there were 10 outliers out of 52 variables, which had studentized residual values ranging from 6.00 to 3.03. As they were neither the results of a data entry error nor measurement errors, we did not reject them as invalid. The variables were not normally distributed ($P < 0.05$) as assessed by Shapiro-Wilk's test of normality on the studentized residuals. However, there was homogeneity of variance as assessed by Levene's Test for Equality of Variances except for nausea and vomiting items ($P < 0.05$).

In both phases, patients with at least one assessment were n = 187, two assessments were completed in n = 98 patients; n = 53 in the experimental group (pre-test n = 29; post-test n = 24) and n = 45 in the comparison group (pre-test n = 20; post-test n = 25). Dropout reasons were death or severe cognitive impairment.

In the post-test phase, more than half of the patients were males, both in the intervention and in the comparison group, 54% and 56%,

Table 3
Interaction effect between study phases and study sites on patients' psychosocial and spiritual outcomes.

Variable	Experimental group		Comparison group		Source [a]	*F*	*p value*
	Pre-test (n = 29)	*Post-test (n = 24)*	*Pre-test (n = 20)*	*Post-test (n = 25)*			
Anxiety T0	2.50 (1.27)	1.77 (1.36)	1.63 (1.41)	2.18 (1.07)	A	1.797	0.177
Anxiety T1	2.19 (1.05)	1.62 (1.19)	1.13 (1.46)	1.88 (1.05)	A x P	0.566	0.572
Anxiety T2	2.44 (1.15)	1.77 (1.24)	0.88 (0.84)	2.06 (1.14)	A x H	0.594	0.556
					A x P x H	0.573	0.568
Family Anxiety T0	3.00 (1.16)	2.77 (1.17)	2.50 (1.31)	3.24 (0.90)	A	0.713	0.496
Family Anxiety T1	2.88 (1.09)	2.38 (1.26)	2.13 (1.55)	2.59 (1.18)	A x P	0.650	0.527
Family Anxiety T2	2.94 (1.06)	2.38 (1.33)	2.13 (1.13)	2.65 (1.41)	A x H	0.297	0.745
					A x P x H	0.200	0.819
Depression T0	2.25 (0.93)	1.00 (1.35)	1.57 (1.13)	1.53 (1.28)	A	4.415	**0.018**
Depression T1	2.25 (1.07)	1.38 (1.45)	0.86 (0.90)	0.76 (0.90)	A x P	0.276	0.760
Depression T2	2.31 (1.20)	0.85 (1.35)	0.85 (1.35)	1.06 (1.14)	A x H	6.202	**0.004**
					A x P x H	1.279	0.289
Feeling at peace T0	1.13 (1.31)	1.31 (1.49)	1.00 (1.07)	1.29 (1.26)	A	0.541	0.586
Feeling at peace T1	1.06 (1.29)	0.69 (1.11)	0.75 (0.71)	1.06 (1.09)	A x P	0.464	0.632
Feeling at peace T2	1.13 (1.26)	0.85 (1.07)	0.75 (0.71)	0.94 (0.97)	A x H	0.218	0.805
					A x P x H	0.708	0.498
Share feelings T0	1.56 (1.09)	0.92 (1.50)	1.63 (1.19)	1.00 (1.06)	A	0.094	0.910
Share feelings T1	1.69 (1.01)	1.46 (1.56)	1.00 (1.20)	1.76 (1.20)	A x P	2.811	**0.071**
Share feelings T2	1.31 (0.87)	0.92 (1.32)	1.25 (1.04)	1.18 (1.63)	A x H	0.502	0.609
					A x P x H	0.329	0.721
Information T0	1.56 (1.26)	0.50 (0.80)	0.38 (0.74)	0.82 (1.19)	A	1.908	0.161
Information T1	1.13 (1.20)	1.17 (1.75)	0.13 (0.35)	1.12 (0.99)	A x P	3.977	**0.026**
Information T2	1.19 (1.22)	0.92 (1.56)	0.50 (0.54)	1.18 (1.13)	A x H	0.507	0.606
					A x P x H	0.494	0.614
Practical Problems T0	0.81 (1.05)	1.31 (1.50)	1.13 (0.84)	0.76 (1.15)	A	0.071	0.931
Practical Problems T1	0.63 (0.89)	1.23 (1.30)	0.88 (0.84)	0.47 (0.94)	A x P	1.214	0.307
Practical Problems T2	0.69 (1.08)	0.92 (1.18)	0.88 (0.64)	0.35 (0.61)	A x H	0.117	0.890
					A x P x H	0.599	0.554

Data are mean (SD); T0: admittance ±3 days; T1: 7 ± 3 days from admission; T2: 15 ± 3 days from admission.
[a] multivariate tests of two-way repeated measures analysis of variance; A = assessment; P = phase; H= Hospice.

Table 4
Interaction effect between study phases and study sites on patients' overall quality of life.

Variable	Experimental group		Comparison group		Source [a]	*F*	*p value*
IPOS overall score	*Pre-test (n = 29)*	*Post-test (n = 24)*	*Pre-test (n = 20)*	*Post-test (n = 25)*			
IPOS total score T0	22.25 (6.59)	20.85 (9.96)	22.63 (6.19)	26.53 (8.56)	A	1.058	0.355
IPOS total score T1	20.19 (6.59)	22.00 (9.41)	17.88 (7.75)	22.59 (9.19)	A x P	2.332	0.109
IPOS total score T2	21.69 (7.77)	18.85 (11.06)	20.75 (7.57)	21.06 (7.13)	A x H	2.455	**0.097**
					A x P x H	0.630	0.537

Data are mean (SD); T0: admission ±3 days; T1: 7 ± 3 days from admission; T2: 15 ± 3 days from admission.
[a] multivariate tests of two-way repeated measures analysis of variance; A = assessment; P = phase; H= Hospice.

respectively (P = 0.897). The mean age was 73.9(±11) in the experimental group and 70.5 (±9.9) in the comparison group (P = 0.269). Demographic and clinical characteristics of the patients are described in Table 1 (Table 1).

No differences between patients' characteristics admitted to the hospice inpatient units were present, except for the post-test phase where the subjects in the comparison group were more severely disabled and completion of the IPOS was performed more frequently by the staff (i.e., research assistant) compared to the pre-test phase across the three assessments.

Mauchly's test of sphericity indicated that the assumption of sphericity had been violated for the two-way interaction for the following patients' outcomes: nausea (P = 0.004), vomiting (P < 0.001), poor appetite (P = 0.019), depression (P = 0.002), and practical problems (P < 0.001).

Two-way repeated measures ANOVA revealed significant interactions between the two groups (assessment*hospice) and the following individual outcomes scores: pain (P = 0.043) (Table 2); depression (P = 0.004, ε = 0.799) (Table 3) indicating that the changes between the groups were significantly different.

Also, the p value from patients' outcomes scores and study phase interaction (assessment*phase) was statistically significant for both constipation (P = 0.028) (Table 2), and practical problems (P = 0.026) (Table 3) indicating that the changes between the pre-test and post-test study phases were significantly different within the two groups. Furthermore, the analysis detected a trend toward a difference statistically significant two-way interaction between quality of life (all dimensions) scores and experimental and comparison group (assessment*hospice), (P = 0.097) (Table 4), and between overall symptoms (physical dimension) scores and study phase, (P = 0.051) (Table 2).

A Mann-Whitney *U* test, the *r* ES and 95% CI were run to detect if there were differences in the patients' outcomes score between the pre-test and post-test phase in the two nonequivalent groups (Table 5a,

Table 5a
Significant median change in dependent variable score for the experimental and comparison group with effect sizes and 95% Confidence Interval (CI) – intention-to-treat analyses.

Variable	Median score (IQR)	Median score (IQR)	Mann-Whitney test U score	Z test	p value	Effect sizes	R^2	95% CI
	Experimental group							
	Pre-test (n = 29)	*Post-test* (n = 24)						
Anxiety								
T1	2 (1–3)	2 (1–2)	236	−1.865	0.062	−0.26	0.07	−0.06 and 0.19
Family anxiety								
T0	4 (3–4)	3 (2–3.75)	237	−2.103	0.035	−0.29	0.08	−0.05 and 0.22
T1	4 (3–4)	2 (1–3)	157	−3.385	0.001	−0.47	0.22	0.03 and 0.41
Depression								
T0	2 (1.50–3)	1.50 (0–2)	237.5	−2.050	0.040	−0.28	0.08	−0.05 and 0.21
T1	2 (1–3)	2 (0–2)	208	−2.379	0.017	−0.33	0.11	−0.04 and 0.26
T2	2.50 (1–3)	0 (0–1.50)	38	−2.975	0.003	−0.55	0.31	0.05 and 0.56
Share feelings								
T0	2 (1–2)	0 (0–2)	239	−2.043	0.041	−0.28	0.08	−0.05 and 0.21
T1	2 (1–2)	1 (0–2)	223	−2.115	0.034	−0.29	0.09	−0.05 and 0.23
	Comparison group							
	Pre-test (n = 20)	*Post-test* (n = 25)						
Pain								
T0	2.50 (1–3)	1 (1–2)	162.5	−2.072	0.038	−0.31	0.10	−0.06 and 0.25

Table 5b
Significant median change in dependent variable score for the experimental group with effect sizes and 95% Confidence Interval (CI) – Per-protocol analysis.

Variable	Median score (IQR)	Median score (IQR)	Mann-Whitney test U score	Z test	p value	Effect sizes	R^2	95% CI
	Experimental group							
	Pre-test (n = 16)	*Post-test* (n = 13)						
Constipation								
T2	2 (1–2)	0 (0–0.75)	44	−2.556	0.015	−0.47	0.23	−0.02 and 0.47
Depression								
T0	2 (2–3)	0 (0–2)	44.5	−2.695	0.008	−0.50	0.25	0.00 and 0.50
T2	2.50 (1–3)	0 (0–1.50)	38	−2.975	0.003	−0.55	0.31	0.05 and 0.56
Information								
T0	1 (1–2)	0 (0–1)	46	−2.437	0.020	−0.45	0.20	0.02 and 0.39

Table 5b,Supplemental file 1: Table S1).

4.7. Experimental group (n = 53)

4.7.1. Physical dimension

In the experimental group, the distributions of the following physical dimension outcomes median scores were statistically significantly worse between the pre-test and post-test phases: dyspnea at T1 (P = 0.024); fatigue both at T0 (P = 0.012) and at T1 (P = 0.042); sore/dry mouth both at T0 (P = 0.015) and at T1 (P = 0.001); poor mobility both at T0 (P = 0.012) and at T1 (P = 0.01) (Table 5; Supplemental file 1: Table S1a). On the contrary, a significant improvement was observed for constipation at T2 (P = 0.015; ES = −0.35).

4.7.2. Psychosocial dimension

In the experimental group, the distribution of practical problems at T0 was worse in the post-test phase compared to the pre-test phase (P = 0.016).

On the contrary, the distribution of the following psychosocial dimension scores was statistically significantly better between the pre-test and post-test phase at each timepoint: family anxiety at T0 (P = 0.035; ES = −0.29), T1 (P = 0.001; ES = −0.47), depression at T0 (P = 0.040; ES = −0.28) T1 (P = 0.017; ES = −0.33), T2 (P = 0.003; ES = −0.55); and share feelings T0 (P = 0.041; ES = −0.28) and T1 (P = 0.034; ES = −0.29) (Table 5, Fig. 2a and Fig. 3a, Supplemental file 1: Table S1a). Anxiety at T1showed a borderline significant reduction (P = 0.062; ES = −0.26).

4.8. Comparison group (n = 45)

4.8.1. Physical dimension

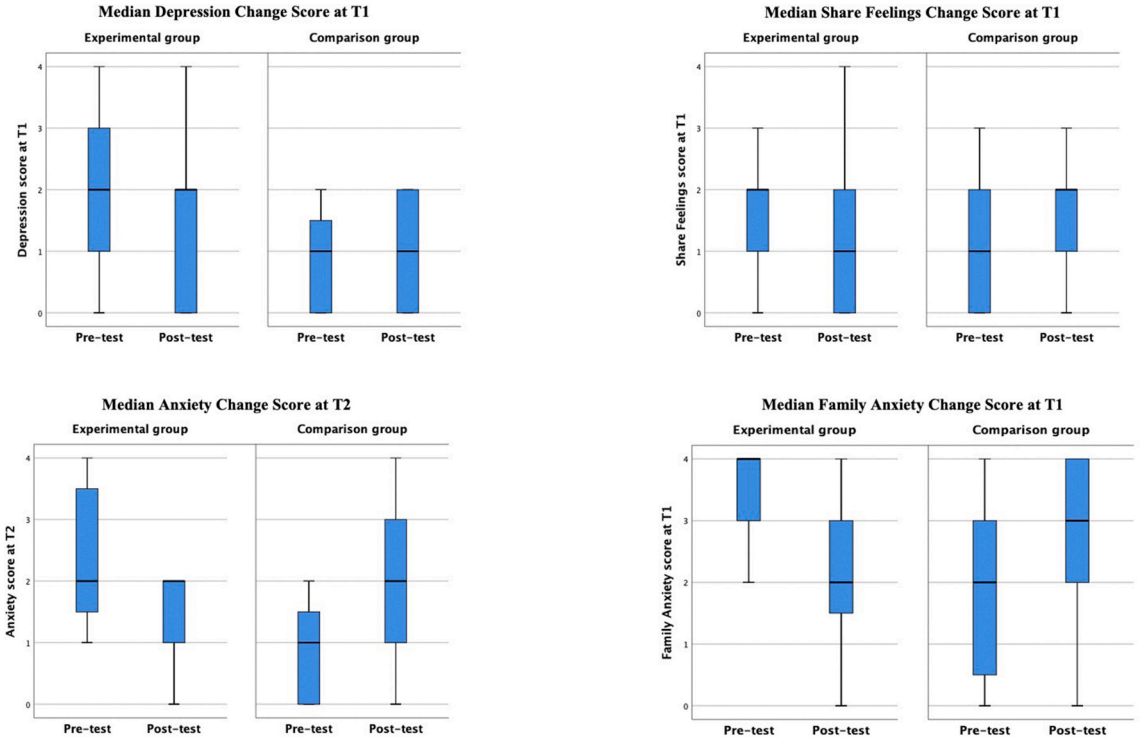
In the comparison group, statistically significant differences were found in the pain item. The distribution of pain score was significantly better between the pre-test and post-test phase at T0 (P = 0.038; ES = −0.31) (Table 5).

4.8.2. Psychosocial dimension

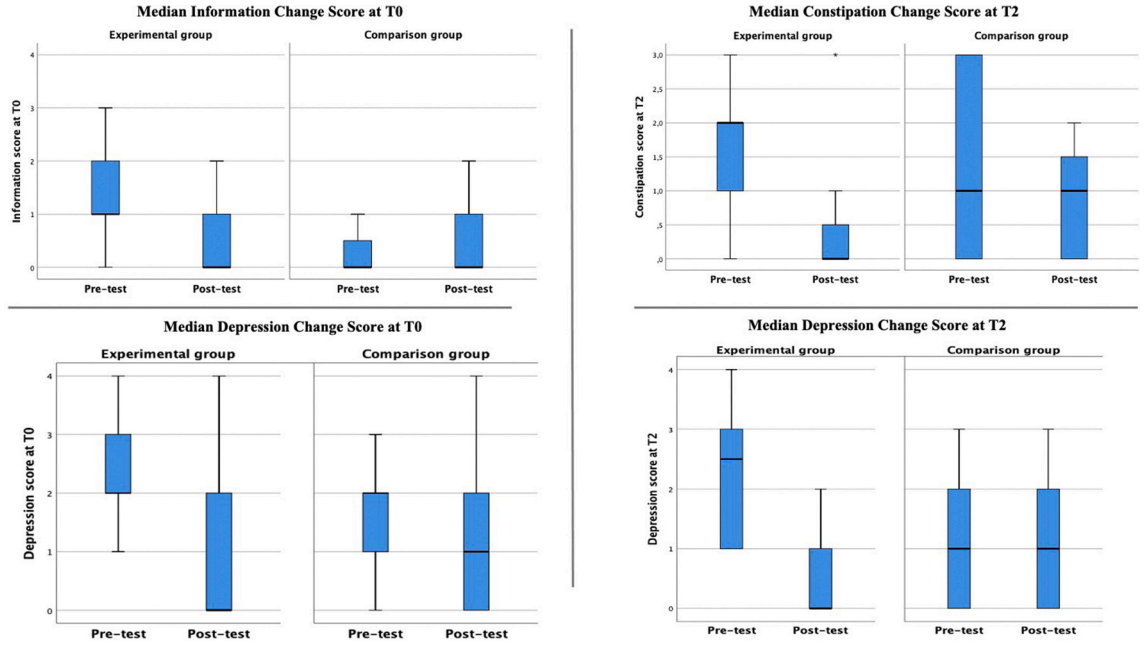
In the comparison group, the distribution of patient anxiety was statistically significantly worse between the pre-test and post-test phase at T2 (P = 0.019); family anxiety at T0 (P = 0.006) and T1 (P = 0.016); share feelings at T1 (P = 0.031); and information need outcomes at T1 (P = 0.024) (Table 5a, Figs. 2a, Fig. 3a, Supplemental file 1: Table S1a).

4.8.3. Patient management

The chi-square test for association was conducted between the composite patient management score (i.e., number of activities delivered to patients for each of the impaired QoL dimensions resulting from the IPOS score) and hospice units. In the post-test phase, there was a statistically significant association between the number of activities delivered to patients and sore/dry mouth (P = 0.031) and patient and family anxiety; (P = 0.019; P = 0.004 respectively) (Table 6) showing that in the experimental group the number of interventions delivered to address patients' needs were higher compared to the comparison group. For the experimental group, the participants received interventions such as painkillers and chlorhexidine mouthwash for treating sore/dry mouth, art therapy and emotional support from nurses, and psychologists to address patient and family anxiety.

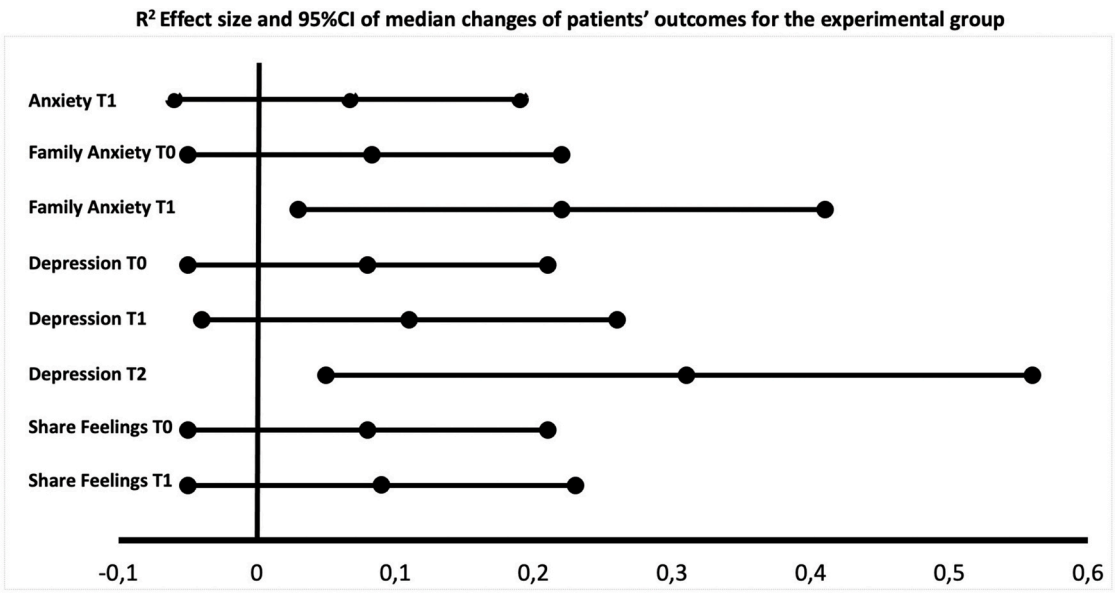


a. Median change score by group and phase – intention-to-treat analyses
Box and whisker plots indicate median and IQR (boxes) and range (whiskers).

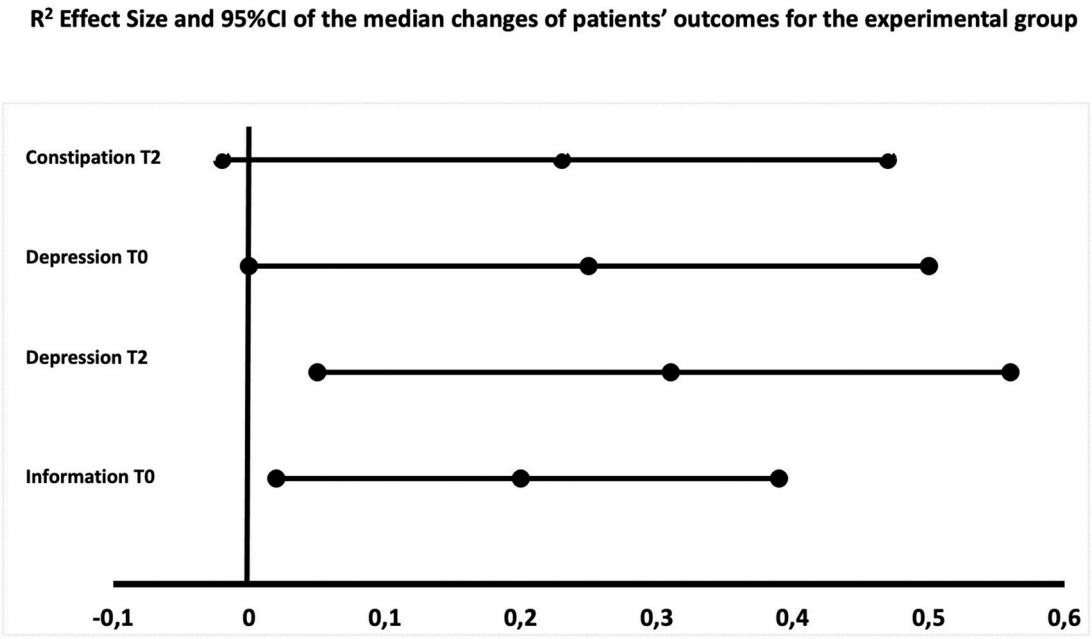


b. Median change score by group and phase – per-protocol analyses
Box and whisker plots indicate median and IQR (boxes) and range (whiskers). Dots represent outliers.

Fig. 2. a. **Median change score by group and phase – intention-to-treat analyses**. Box and whisker plots indicate median and IQR (boxes) and range (whiskers). b. **Median change score by group and phase – per-protocol analyses**. Box and whisker plots indicate median and IQR (boxes) and range (whiskers). Dots represent outliers.



a. R^2 effect sizes and 95% Confidence Interval – intention-to-treat analyses



b. R^2 effect sizes and 95% Confidence Interval – per-protocol analyses

Fig. 3. a. R^2 effect sizes and 95% Confidence Interval – intention-to-treat analyses.bR^2 effect sizes and 95% Confidence Interval – per-protocol analyses.

4.9. Per-protocol analyses (n = 55)

A total of 55 subjects were included in the per-protocol analyses; n = 29 in the experimental group (pre-test n = 16; post-test n = 13) and n = 26 in the comparison group (pre-test n = 8; post-test n = 18). Overall, in the post-test phase in the experimental group the per-protocol analyses showed a significant improvement for constipation at T2 (ES = −0.47), depression at T0 (ES = −0.50) and T2 (ES = −0.55), and information need (ES = −0.55). Fatigue score at T1 and sore/dry mouth score at T1 were significantly worse.

In the comparison group, in the post-test phase a significant worsening for anxiety at T2 and information at T1 was shown (Table 5b, Figs. 2b, Fig. 3b, Supplemental file 1: Table S1b).

5. Discussion

To our knowledge, this was the first study that developed an intervention to assess QoL in cancer patients with advanced disease in palliative care according to the MRC Framework. Our findings were interpreted for statistical significance and positive clinical impact on patient's outcomes. The INFO-QoL procedures were feasible and did not meet any barriers to their implementation. On the contrary, study feasibility showed critical issues regarding patients' enrollment. Despite recommendations on early palliative care (Haun et al., 2017), patients were referred too late to specialist palliative care determining an unequal distribution across study groups, which we tried to tackle by doubling enrollment time from three to six months. Consistent with recommendations on research in palliative care (Gysels et al., 2013), our

Table 6
Patient management score from T0 to T1. Number of QoL-related management actions delivered to patients for each of the impaired QoL dimensions.

	Pre-test					Post-test				
	Experimental group (n = 29)		Comparison group (n = 20)			Experimental group (n = 24)		Comparison group (n = 25)		
	Action	No action	Action	No action	p value*	Action	No action	Action	No action	p value*
Pain	22 (76)	7 (24)	17 (85)	3 (15)	0.435	3 (43)	4 (57)	8 (42)	11 (58)	0.973
Dyspnea	8 (28)	21 (72)	6 (30)	14 (70)	0.854	1 (17)	5 (83)	2 (12)	15 (88)	0.759
Fatigue	0 (0)	29 (100)	1 (5)	19 (95)	0.224	2 (33)	4 (67)	2 (13)	14 (87)	0.259
Nausea	4 (14)	25 (86)	6 (30)	14 (70)	0.167	2 (29)	5 (71)	2 (13)	14 (87)	0.349
Vomiting	1 (3)	28 (97)	2 (10)	18 (90)	0.347	0 (0)	6 (100)	1 (6)	15 (94)	0.531
Poor appetite	3 (10)	26 (90)	8 (40)	12 (60)	**0.014**	1 (14)	6 (86)	1 (6)	15 (94)	0.529
Constipation	17 (59)	12 (41)	10 (50)	10 (50)	0.551	3 (43)	4 (57)	4 (23)	13 (77)	0.344
Sore/Dry mouth	4 (14)	25 (86)	5 (25)	15 (75)	0.319	6 (67)	3 (33)	4 (23)	13 (77)	**0.031**
Drowsiness	2 (7)	27 (93)	1 (5)	19 (95)	0.785	2 (29)	5 (71)	5 (28)	13 (72)	0.968
Poor mobility	9 (31)	20 (69)	9 (45)	11 (55)	0.319	5 (56)	4 (44)	12 (55)	10 (45)	0.959
Anxiety	12 (43)	16 (57)	8 (40)	12 (60)	0.843	6 (75)	2 (25)	5 (26)	14 (73)	**0.019**
Family anxiety	6 (21)	23 (79)	3 (15)	17 (85)	0.613	6 (67)	3 (33)	2 (12)	15 (88)	**0.004**
Depression	10 (35)	19 (65)	2 (10)	18 (90)	**0.050**	4 (50)	4 (50)	3 (18)	14 (82)	0.093
Feeling at peace	2 (7)	27 (93)	1 (5)	19 (95)	0.785	2 (25)	6 (75)	3 (18)	14 (82)	0.668
Share feelings	3 (10)	26 (90)	0 (0)	20 (100)	0.138	3 (33)	6 (67)	2 (12)	15 (88)	0.184
Information	6 (21)	23 (79)	5 (25)	15 (75)	0.722	3 (33)	6 (67)	1 (6)	16 (94)	0.065
Practical problems	3 (10)	26 (90)	0 (0)	20 (100)	0.138	–	6 (100)	–	16 (100)	–

Data are n (%); T0: within day 3 from admission; T1 = 7 ± 3 days from T0; *Chi-square test.

pilot study suggested flexibility in the data collection schedule. Although most of the patients in the experimental group were lost to follow-up leading to missed scheduled assessments, our findings showed an improvement in patients' outcomes over time because of outcomes assessments by trained healthcare providers and the review of the care plans, accordingly. A future definitive INFO-QoL study trial should address this issue by including a new component as a part of the complex intervention. We hypothesize the need to add an evidence-based component characterized by a nurse-led early assessment outcomes system embedded into oncology settings with the use of shared criteria to identify patients at highest need of a referral to palliative care (Hui et al., 2018).

The data about acceptability of the study in terms of relevance, appropriateness, usefulness, and willingness to continue using the INFO-QoL suggested that healthcare professionals require and need to implement interventions to address patients' outcomes and guarantee the principle of equity in assessing patients with a systematic approach. Also, healthcare professionals felt significantly competent in delivering the intervention across the time frame of the study.

After implementing the INFO-QoL intervention, the experimental group was found to show a more significant improvement than the comparison group with regard to constipation, patient and family anxiety, depression and sharing feelings. Per-protocol analyses confirmed a stronger effect for constipation and depression and showed a moderate effect for need for information.

Furthermore, healthcare professionals' actions delivered to manage patients' outcomes were significantly higher for patient and family anxiety and xerostomia. In fact, compared to the pre-test phase, in the post-test phase, it was interesting to note that improved family anxiety in the experimental group, matched with a significantly higher number of actions delivered by the team.

Although this was a pilot exploratory trial study, it showed that when patients' outcomes are systematically assessed and addressed in clinical practice, the benefits for psychological and social outcomes are improved. Although the INFO-QoL intervention did not show an improvement in overall QoL, a more extensive study may impact positively on patients' QoL.

These results are reassuring as they confirm that interventions focusing on QoL assessment are complex (Catania et al., 2013) and should be addressed under this perspective to ensure better evidence-based practice. Our findings were consistent with other studies included in a systematic review (Catania et al., 2015) where the majority had a medium-low methodological quality and were observational. In addition, our study may represent a response to unmet needs of advanced cancer patients highlighted in a recent systematic review, which showed that emotional needs are mostly unmet (Wang et al., 2018).

This study demonstrates that the development and implementation of an intervention based both on specific conceptual frameworks (Catania et al., 2013; Craig et al., 2008) and recommendations (Antunes et al., 2014) on barriers and facilitators that influence outcome measurement in clinical practice, may impact positively on cancer patient outcomes.

The INFO-QoL intervention is innovative because it is based on delivering a response to patients' needs under the guidance of nurses. This was achieved as staff completed a practical training on the use of the outcome measure and how to analyze and interpret the IPOS scores. Also, patients' outcomes were collected, recorded, and shared among multidisciplinary staff members to promote coordinated patient and family centered care. Although the intervention was piloted in palliative care units, it may set the stage for implementing it also in cancer care units to improve feasibility. The enrolled subjects came from cancer units and they reported unmet needs, some of which (i.e., family anxiety, depression, and share feelings) were improved through the INFO-QoL intervention. This study has some limitations. The main limitation was the high rate of attrition. In addition, future research could involve designing a similar pilot study as a cluster randomized trial. However, as barriers to conduct research in palliative care were well described also in terms of the challenging characteristics of the population, including the recruitment and retainment of research subjects (Khalil et al., 2018), we were concerned that a pilot cluster trial with just two units included could be exposed to different subject recruitment rates between the two study sites. Furthermore, accurate records of treatments delivered to manage patients' outcomes would have been beneficial for the study.

6. Conclusions

The INFO-QoL intervention was feasible, acceptable, and potentially improved outcomes in terms of family anxiety, depression, and sharing feelings. The findings could support nurses in developing and implementing nurse-led interventions focused on PROMs. Furthermore, our results indicated that to address unmet patients' needs, nurses play a crucial role in developing and putting evidence into practice. They have to identify and model the components of the intervention and test them using innovative nursing strategies. This can lead to better knowledge

that may further refine nursing strategies that engage advanced-disease cancer patients and promote personalized interventions to better assess and manage patients' outcomes.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejon.2021.101961.

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