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The effect of the Carer Support Needs Assessment Tool intervention (CSNAT-I) in the Danish specialised palliative care setting: a stepped wedge cluster randomised controlled trial

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ABSTRACT

Background: The Carer Support Needs Assessment Tool intervention (CSNAT-I) has been shown to improve end-of-life care support for informal caregivers. This study investigated the impact of the CSNAT-I on caregivers of patients recently enrolled in specialised palliative care (SPC) at home in Denmark.

Methods: A stepped-wedge cluster randomised controlled trial with nine clusters (i.e., SPC teams). Outcome measures were collected using caregiver questionnaires at baseline (T0) and two (T1) and four (T2) weeks follow-up. ClinicalTrials.gov ID: NCT03466580.

Results: A total of 437 caregivers were enrolled (control group, n=255; intervention group, n=182). No intervention effect was found on the primary outcome, caregiver strain at T1 ($p = 0.1865$). However, positive effects were found at T1 and T2 on attention to caregivers' wellbeing ($p < 0.0001$), quality of information and communication ($p < 0.0001$), amount of information (T1: $p = 0.0002$; T2: $p < 0.0001$), involvement (T1: $p = 0.0045$; T2: $p < 0.0001$), talking about greatest burdens ($p < 0.0001$) and assistance in managing greatest burdens ($p < 0.0001$). The effect sizes of these differences were medium or large and seemed to increase from T1 to T2. At T1, positive effects were found on distress ($p = 0.0178$) and home care responsibility ($p = 0.0024$). No effect was found on the remaining outcomes.

Conclusion: Although no effect was found on caregiver strain, the CSNAT-I showed positive effects on caregiver distress, home care responsibility and key outcomes regarding caregivers' experience of the interaction with health care professionals.

INTRODUCTION

Informal caregivers are central to the support and care of patients,[1;2], particularly when the patient is cared for at home,[3;4]. However, caregivers themselves can be considered 'hidden patients',[5] as they may experience physical, psychological and social morbidity,[6] because the role as caregiver can be overwhelming, go on for years, and may increase towards the end of life,[7;8].

Yet, even in modern specialised palliative care (SPC) where caregiver support is a core function,[9], caregivers do not always feel well supported: they may lack information,[10] and feel overlooked and that their care expertise is not taken into consideration,[11]. In a study amongst Danish patients who were in contact with an SPC team/hospice, a large proportion reported room for improvement in caregiver support, and in the qualitative comments, the patients asked for more support for the family,[12]. Also, in a survey amongst 590 Danish cancer caregivers, a large proportion of caregivers reported lack of support, attention, and information, and insufficient involvement in the patients' disease, treatment and/or care,[13]. Evidence-based interventions and strategies to assess and respond to caregivers' needs have been lacking,[14;15].

The Carer Support Needs Assessment Tool intervention (CSNAT-I) was developed to respond to these problems,[16;17]. The intervention specifically targets caregivers of patients receiving end-of-life care at home and was developed on the basis of qualitative research (focus group and telephone interviews with 75 bereaved caregivers),[16] and validated in 225 caregivers in Hospice Home Care services,[17]. The CSNAT-I is underpinned by a person-centred framework in which the caregiver is taking the lead, and the health care professional (HCP) is working 'with' rather than doing 'to' the caregiver,[18] The CSNAT-I has shown positive effects in studies from Australia and the UK,[19-21] and has been valued by both caregivers and HCPs,[22-24].

Whilst the CSNAT-I seems to be a promising, available method to improve support to caregivers of patients in SPC at home in Denmark, evaluation of the intervention in this setting has not been done.

Thus, the aim of the present study was to investigate the impact of the CSNAT-I on caregivers of patients who recently started in SPC at home in Denmark: what is the effect of the intervention on caregiver strain, distress, positive caregiving appraisals, experiences of the interaction with HCPs, workload, emotional functioning, fatigue and quality of life?

METHODS

Setting

In Denmark, SPC is delivered as in-patient care at hospices or hospital SPC departments, or as out-patient care from these units in the home or in out-patient clinics. SPC teams are interdisciplinary and comprise specialised medical doctors and nurses and e.g., physiotherapists, social workers, psychologists and priests. Of the 24 SPC teams delivering out-patient care in Denmark (in 2017), nine consented to participate in the present study (Figure 1).

Study design

The study was a stepped-wedge cluster randomised controlled trial (SW-CRT),[25;26]. In an SW-CRT, every cluster first acts as a control and later as an intervention site. The time of transition varies and is determined by randomisation. The SW-CRT design was chosen to account for variation between SPC units, to prevent contamination, and to make participation in the study attractive for SPC units as all units ultimately will deliver the intervention,[25;26].

All participating SPC teams (i.e., clusters) had an enrolment period of 12 months. The shift from pre-intervention period (control period) to intervention period was at either 3, 6 or 9 months (Figure 1). The randomisation was computer based (carried out by the research group) and allocated three SPC teams to shift to intervention period at each of the three time points.

Study population

The study population was primary caregivers of patients recently started in SPC delivered by an SPC team. In Denmark, patients receiving SPC are almost exclusively cancer patients. Cancer patients starting in SPC have a very high symptom load (especially fatigue, anorexia and pain), poor level of physical functioning and low quality of life. In 2018 and 2019, the median survival time from start of SPC was 42 and 40 days, respectively,[27;28]

'Primary caregiver' was defined as the lay person whom the patient considered most involved in his/her disease course. Caregivers had to be adults (18 years and over) who were able to read and understand Danish and who were caring for adult patients who were able to read and understand Danish and who had not received any kind of SPC before. Caregivers were not eligible for the study if they had a known cognitive impairment precluding participation or, based on the HCP's clinical judgement, were too distressed to cope with research.

Enrolment procedure

HCPs briefly introduced caregivers and patients to the study and if they both consented, the research group contacted the caregiver, provided comprehensive information about the study and enrolled him/her in the study. Details of the enrolment procedure are shown in Figure 2.

Intervention

Content and delivery

The CSNAT-I has two parts: 1) an evidence-based tool (the CSNAT) consisting of 14 support domains covering the support that caregivers need to a) care for the patient (caregiver as co-worker) and b) look after their own health and well-being (caregiver as client),[16] (Box 1). The tool itself is integrated into 2) a five-stage person-centred framework which is HCP facilitated, but caregiver led (The CSNAT Approach),[18].

Delivery of the CSNAT-I followed the stages of the CSNAT Approach,[18]. First, the CSNAT was introduced to the caregiver by the HCP and/or research group during enrolment and once again when the HCP called the caregiver to plan a CSNAT conversation. Then, the caregiver was given time to consider in which areas he/she needed more support and complete the tool. Subsequently, a CSNAT conversation between the caregiver and the HCP was held, in which the caregiver had the opportunity to identify his/her individual support needs within the highlighted domains and was asked which support needs were the most urgent, what the caregiver felt would help him/her, and whether he/she needed assistance to access the support. The conversation formed the basis for developing a shared action plan which could contain e.g. the caregiver's planned actions to access support or the HCP's planned actions to facilitate support (by e.g. delivering support such as information or comfort, or to refer the caregiver to other services or sources of support such as a social worker or caregiver groups). Finally, a shared review of the caregiver's support needs and action plans was included in a second CSNAT-I.

The CSNAT-I was delivered to each caregiver individually. The CSNAT was either self-completed (preferably) by the caregiver or completed jointly with the HCP. When possible, the subsequent conversation was carried out face-to-face, but phone and video were also allowed. The intervention was delivered by nurses in all SPC teams and additional professionals in some teams. The intervention was delivered twice to each caregiver: first within 13 days of study enrolment and the second 15-27 days after enrolment (Figure 2).

Training

All HCPs delivering the CSNAT-I received training from the research group (LL and LR). Training consisted of one group training session lasting 2-3 hours provided shortly before the shift to intervention period. The CSNAT training materials can be accessed via http://csnat.org. If needed, refresher training sessions were conducted during the intervention period.

Documentation

After each intervention, the HCP filled in a standardised documentation form describing the intervention framework (place, duration, etc.).

Data collection and outcome measures

Caregiver completed standard measures

Outcome measures were collected at study enrolment (baseline, T0) and at follow-up two (T1) and four (T2) weeks later (Figure 2). These follow-up times were selected to minimize drop-out and to ensure that the intervention was also feasible for caregivers of patients with only a short survival time. The caregiver could choose paper questionnaires, electronic questionnaires, or telephone interviews. If the patient died during the study, subsequent data collection was cancelled.

The primary outcome was caregiver strain at T1 assessed by the eight item strain subscale of the Family Appraisal of Caregiving Questionnaire for Palliative Care (FACQ-PC),[29].

Secondary outcomes were caregiver strain at T2 and the following at T1 and T2:

Experiences of the interaction with HCPs

Lack of attention from HCPs to caregivers' wellbeing (four item subscale); problems with quality of information from and communication with HCPs (seven item subscale); caregiver involvement (single item); and selected items from the subscale Lack of information from HCPs (six items, reported as one subscale as Cronbach's Alpha: 0.88), all from the Cancer Caregiving Tasks, Consequences and Needs Questionnaire (CaTCoN),[13;30;31]. Minor adjustments were made to some CaTCoN items to adapt them to the current study (Appendix 1).

Talking to HCPs about greatest burdens and assistance from HCPs in managing greatest burdens, assessed by two newly developed items.

Experiences of caregiving

Caregiving workload, assessed by four items (selected from a five item subscale) from the CaTCoN,[13;30;31]

Positive caregiving appraisals and caregiver distress, assessed by the respective two subscales (four and seven items, respectively) from the FACQ-PC,[29].

Caregiver wellbeing

Emotional functioning and fatigue, assessed by subscales consisting of their respective four and three items from the EORTC Quality of Life Questionnaire Core 30 (EORTC QLQ-C30),[32;32] each supplemented with three selected items from the EORTC Computerized Adaptive Test (EORTC CAT Core) emotional functioning and fatigue item banks, respectively,[33;34], in order to optimize measurement.

Positive emotional functioning (positive affect), assessed by a subscale (validation not published) of five positively formulated emotional functioning items (originally developed for the EORTC CAT Core emotional functioning item bank, but not included in the final version as they formed a distinct scale).

Caregiver quality of life, assessed by the two-items subscale assessing overall health and quality of life in EORTC QLQ-C30,[32].

For each of the instruments, items and subscales were scored according to usual practice,[13;29;31-37]. The FACQ-PC subscale scores were calculated when at least half of the items were completed. The two newly developed items were scored using the CaTCoN scoring procedure,[13].

The questionnaire package (except the positively formulated emotional functioning items which were included later in the process) was evaluated in cognitive interviews with caregivers, ensuring that all items were understood in the context of the present study (Appendix 2).

An overview of the complete caregiver questionnaire is given in Appendix 3.

Caregiver and patient data

Caregiver socio-demographic data concerning age, gender, relationship to the patient, level of education, employment, and place of residence were collected at baseline (included in the caregiver questionnaire).

Data concerning enrolled patients' diagnosis and SPC course as well as the total number of patients starting SPC at home in the study period in the participating SPC units were extracted from the

Danish Palliative Database (DPD). Patient age and gender were provided by the patient when consenting to data extraction.

CSNAT-I data

Data about delivery of the CSNAT-I were obtained from the HCPs' documentation of the intervention (time, place, duration, whether the patient was present, and the HCP's profession), and all SPC teams were asked to keep a record with the number of caregivers not participating in the study and reasons for non-participation.

Translation

The CSNAT and FACQ-PC were not available in Danish and were therefore translated following the EORTC Quality of Life Group translation procedure,[38].

Sample size

This study used the same primary outcome and principles for sample size estimation as the CSNAT study by Aoun,[19]: a moderate effect size of 0.41 for the primary outcome, a power of 0.80, and an adjustment for cluster effect of 1.62. The required sample size was 308 caregivers (154 in each group). We anticipated that at least 90% of those who consented would complete baseline measures, and that the drop-out at two weeks follow-up would be 30% (based on the study by Aoun et al. (2015) which had a mean follow-up time of 43 days and drop-out rate of 45%). Based on these assumptions, a total of 490 caregivers had to be enrolled.

Statistical analyses

All analyses were carried out in SAS Enterprise Guide v.7.11, using a level of significance of 5%. No imputations for missing data were made.

Distribution of background variables in the intervention and control groups were compared using Chi^2 and Wilcoxon rank sum tests.

The effects of the intervention were assessed by comparing differences in change scores from baseline (T0) to follow-up at two (T1) and four weeks (T2) in the intervention and control group, respectively, using a multiple linear regression analysis, adjusting for background variables (shown in Table 1) as well as for baseline score. Effect sizes were calculated using Cohen's d (i.e., 0.2 small; 0.5 medium; 0.8 large,[39]). Analyses were based on intention to treat. Two sensitivity analyses were carried out: a per protocol analysis (S1) where intervention caregivers who did not

receive the CSNAT-I were considered part of the control group, and an analysis excluding intervention caregivers who did not receive the CSNAT-I (S2). Furthermore, a sensitivity analysis investigating the possible confounding effect of (calendar) time was carried out using Wilcoxon rank sum test.

Table 1. Characteristics (self-reported and obtained from the Danish Palliative Database) of the participating 437 caregivers

	TOTAL (n=437)	**INTERVENTION GROUP (n=182)**	**CONTROL GROUP (n=255)**	**P-value[a]**
Gender				0.7971
Male	135 (31%)	55 (30%)	80 (31%)	
Female	302 (69%)	127 (70%)	175 (69%)	
Age				**0.0009**
Mean	59.8	57.3	61.7	
Median	61.0	58.0	63.0	
Range	23.0-90.0	23.0-84.0	24.0-90.0	
Missing	23	5	18	
Relationship to the patient				**0. 0010**
Spouse/partner	27 (64%)	99 (57%)	171 (70%)	
(Adult) child	125 (30%)	69 (39%)	56 (23%)	
Other (e.g., parent, sibling, friend)	24 (6%)	7 (4%)	17 (7%)	
Missing	18	7	11	
Level of education				0.1149
University education	60 (14%)	33 (19%)	27 (11%)	
Longer theoretical education (3-4 years)	152 (36%)	62 (35%)	90 (37%)	
Short theoretical education (1-3 years)	101 (24%)	36 (20%)	65 (26%)	
Other (short education (< 1 year), non-theoretical education, ongoing education, no education)	110 (26%)	46 (26%)	64 (26%)	
Missing	14	5	9	
Employment				0.2909
Currently working (full or part time)	148 (34%)	63 (35%)	85 (34%)	
Currently on sick leave or has care leave	92 (21%)	43 (24%)	49 (20%)	
Retired	169 (39%)	62 (35%)	107 (43%)	
Other (student, un-employed, housewife)	21 (5%)	11 (6%)	10 (4%)	
Missing	7	3	4	
Place of residence				0.1355
City or suburbs	147 (34%)	64 (36%)	83 (33%)	
Provincial town	93 (22%)	33 (18%)	60 (24%)	
Village	98 (23%)	37 (21%)	61 (25%)	
Countryside	90 (21%)	46 (26%)	44 (18%)	
Missing	9	2	7	
Related to patients with				
Gender				0.0880
Male	218 (50%)	82 (45%)	136 (53%)	
Female	219 (50%)	100 (55%)	119 (47%)	

Table 1, continued

Age				0.5388
Mean	69.2	69.5	69.0	
Median	71.0	71.8	70.5	
Range	27.1-96.9	29.9-90.6	27.1-96.9	
Diagnosis				0.6550
Respiratory system cancer	93 (21%)	41 (23%)	52 (20%)	
Breast cancer	42 (10%)	16 (9%)	26 (10%)	
Pancreas cancer	37 (9%)	18 (10%)	19 (7%)	
Colorectal cancer	38 (9%)	16 (9%)	22 (9%)	
Prostate	36 (8%)	13 (7%)	23 (9%)	
Gynecological cancer	26 (6%)	14 (8%)	12 (5%)	
Upper gastrointestinal cancer	28 (6%)	11 (6%)	17 (7%)	
Urinary cancer	22 (5%)	7 (4%)	15 (6%)	
Cancer in brain and central nerve system	17 (4%)	9 (5%)	8 (3%)	
Liver/biliary cancer	16 (4%)	9 (5%)	7 (3%)	
Hematological cancer	14 (3%)	6 (3%)	8 (3%)	
Head and neck cancer	12 (3%)	4 (2%)	8 (3%)	
Other cancer (e.g., melanoma, sarcoma)	23 (5%)	10 (5%)	13 (5%)	
Unknown cancer	9 (2%)	3 (2%)	6 (2%)	
Not cancer (heart, lung, kidney or neurological disease)	24 (5%)	5 (3%)	19 (7%)	
SPC team from				**< 0.0001**[b]
Bispebjerg Hospital	56 (13%)	36 (20%)	20 (8%)	
Hospice Soendergaard	20 (5%)	9 (5%)	11 (4%)	
South Jutland Hospital	58 (13%)	46 (25%)	12 (5%)	
Arresoedal Hospice	24 (5%)	10 (5%)	14 (5%)	
Diakonissestiftelsens Hospice	23 (5%)	12 (7%)	11 (4%)	
North Zealand Hospital	61 (14%)	22 (12%)	39 (15%)	
Odense University Hospital & Hospital Svendborg	95 (22%)	29 (16%)	66 (26%)	
Rigshospitalet	30 (7%)	5 (3%)	25 (10%)	
Zealand University Hospital	70 (16%)	13 (7%)	57 (22%)	
Time from start SPI to study enrolment (days)				0.0788
Mean	7.8	8.4	7.4	
Median	6.0	6.0	5.5	
Range	0.0-52.0	0.0-52.0	0.0-49.0	
Missing	5	0	5	

[a] Chi Square for categorical variables and Wilcoxon for continuous variables

[b] That different proportions of caregivers were recruited to either control or intervention group in the different SPC teams was due to and a natural consequence of the study design

RESULTS

Study population

For six SPC teams, the enrolment period was from 15th March, 2018 to 15th April, 2019 (extended by one month to increase sample size in the intervention group) (Figure 1). Start of enrolment in the remaining three teams was delayed due to practical matters and took place from 15th June, 2018 to 15th June, 2019. To increase the sample size in the intervention group (due to slowing of caregiver enrolment in the intervention period), the largest SPC team shifted to the intervention period after six months instead of nine as decided by the randomisation (Figure 1).

A study flow chart (CONSORT diagram) is shown in Figure 3. Consent rates (proportion consenting to participate out of those invited) were 50% and 34% in the control and intervention group, respectively. A total of 437 caregivers were enrolled: 255 in the control group; 182 in the intervention group. Ninety-one caregivers were lost to follow-up at T1 (exclusion/attrition rate: 21%), and 139 at T2 (exclusion/attrition rate: 32%), resulting in 346 (T1) and 298 (T2) returned caregiver questionnaires.

Caregivers predominantly chose to complete the baseline questionnaires on paper (87%) compared to electronically (12%) or over the phone (<1%) whereas they preferred to complete the follow-up questionnaires electronically (63%) followed by on paper (36%) and rarely over the phone (<1%).

Characteristics of the 437 caregivers are shown in Table 1. Compared to the control group, the intervention group contained significantly more adult children of the patients (p=0.0010) and thus caregivers of younger age (p=0.0009). No other significant differences between caregivers in the two groups were found.

The intervention

Of the 142 caregivers in the intervention group completing the follow-up questionnaire at T1, 130 (92%) had, as intended, received their first CSNAT-I. Of these, four caregivers (3%) had also received their second CSNAT-I. Twelve caregivers (9%) had not received a CSNAT-I.

Of the 123 caregivers in the intervention group completing the follow-up questionnaire at T2, 93 (76%) had, as intended, received two CSNAT-I. Twenty-five caregivers (20%) had received only one CSNAT-I, and five caregivers (4%) had still not received a CSNAT-I.

CSNAT conversations were carried out predominantly by a nurse (93% and 91% of the first and second conversations, respectively) and in the remaining cases by a social worker, priest, psychologist, physiotherapist, medical doctor, or a nurse and a medical doctor together.

Most CSNAT conversations took place in out-patient clinics (37% and 35% of the first and second conversations, respectively) followed by the joint home of the patient and caregiver (24% and 22% of the first and second conversations, respectively) and over the phone (19% and 28% of the first and second conversations, respectively). 'Other places' and information not completed by the HCP totalled 20% and 15% of the first and second conversations, respectively.

Ninety-seven percent and 98% of the first and second conversations, respectively, were conducted with the caregiver alone (i.e., without the patient being present).

The mean duration of the first and second CSNAT conversations was 43 minutes (range 10-90) and 32 (10-70) minutes, respectively.

Effect of the intervention

No significant effect of the intervention on the primary outcome, caregiver strain at T1, was found ($p = 0.1865$) (Table 2).

However, at T1, positive intervention effects were found on caregiver distress ($p = 0.0178$, $d = 0.12$), attention to the caregivers' wellbeing ($p < 0.0001$, $d = 0.84$), quality of information and communication ($p < 0.0001$, $d = 0.57$), amount of information ($p = 0.0002$, $d = 0.51$), responsibility in relation to home care ($p = 0.0024$, $d = 0.17$), caregiver involvement ($p = 0.0045$, $d = 0.49$), talking about greatest burdens ($p < 0.0001$; $d = 0.98$) and assistance in managing greatest burdens ($p < 0.0001$, $d = 0.75$).

At T2, positive intervention effects were found on attention to the caregivers' wellbeing ($p < 0.0001$, $d = 0.95$), quality of information and communication ($p < 0.0001$, $d = 0.88$), amount of information ($p < 0.0001$, $d = 0.73$), caregiver involvement ($p < 0.0001$, $d = 0.70$), talking about greatest burdens ($p < 0.0001$, $d = 1.10$) and assistance in managing greatest burdens ($p < 0.0001$, $d = 0.84$).

The two sensitivity analyses (S1 and S2) supported the findings from the main analysis, except that additional, positive intervention effects were seen at T1 on caregiver strain (primary outcome) (S1: $p = 0.0048$, $d = 0.28$; S2: $p = 0.0288$, $d = 0.23$) as well as on emotional functioning (S1: p =

0.0319, d = 0.19), fatigue (S1: p = 0.0181, d = 0.28; S2: p = 0.0433, d = 0.25) and the caregivers' provision of practical help to the patient (S1: p=0.0108, d = 0.21).

No confounding effect of (calendar) time was found.

Table 2. The intervention effect on the primary and secondary outcomes from the Family Appraisal of Caregiving Questionnaire for Palliative Care (FACQ-PC)[a], the Cancer Caregiving Tasks, Consequences and Needs questionnaire (CaTCoN)[b], the EORTC Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)[c] and EORTC Computerized Adaptive Test (EORTC CAT Core) item banks[c], and two newly developed items[b] at T1 (two weeks follow-up) and T2 (four weeks follow-up).

	Time	**Intervention**			**Control**			**Difference between change scores[d]**	**Effect size (Cohen's d)**	**P[e]**
		N	**Baseline mean (SD)**	**Change from baseline to 2 weeks follow-up (SD)**	**N**	**Baseline mean (SD)**	**Change from baseline to 2 weeks follow-up (SD)**			
PRIMARY OUTCOME										
Caregiver strain (FACQ-PC eight item subscale)	T1	140	2.89 (0.78)	-0.02 (0.48)	199	2.89 (0.79)	0.05 (0.47)	-0.07	0.15	0.1865
	T2	122	2.90 (0.74)	-0.04 (0.52)	170	2.90 (0.76)	0.06 (0.54)	-0.10	0.19	0.1533
SECONDARY OUTCOMES										
FACQ-PC										
Caregiver distress (four item subscale)	T1	140	2.81 (0.95)	-0.10 (0.69)	200	2.99 (0.92)	-0.02 (0.70)	-0.08	0.12	**0.0178**
	T2	122	2.80 (0.98)	-0.03 (0.73)	171	2.95 (9.96)	0.00 (0.73)	-0.03	0.04	0.4424
Positive caregiving appraisals (seven item subscale)	T1	141	4.06 (0.57)	-0.08 (0.39)	200	3.96 (0.58)	-0.05 (0.41)	-0.03	0.08	0.6792
	T2	123	4.08 (0.57)	-0.10 (0.44)	169	3.95 (0.58)	-0.05 (0.41)	-0.05	0.12	0.4409
CaTCoN										
Lack of attention from health care professionals to the caregivers' wellbeing (four item subscale)	T1	125	29.27 (24.25)	-11.82 (22.81)	173	34.20 (26.55)	8.03 (24.62)	-19.85	0.84	**<0.0001**
	T2	110	30.13 (25.72)	-12.42 (27.52)	144	34.57 (27.63)	14.47 (29.21)	-26.89	0.95	**<0.0001**
Problems with the quality of information from and communication with health care professionals (seven item subscale)	T1	121	21.55 (15.73)	-2.07 (15.34)	172	23.73 (18.63)	7.38 (17.50)	-9.45	0.57	**<0.0001**
	T2	102	20.90 (15.90)	-3.17 (13.06)	139	23.66 (19.11)	11.12 (18.80)	-14.29	0.88	**<0.0001**
Lack of information from health care professionals (six item (modified) subscale)	T1	130	42.03 (28.79)	-10.11 (23.65)	186	41.71 (28.09)	2.65 (25.86)	-12.76	0.51	**0.0002**
	T2	113	41.05 (29.00)	-15.05 (25.84)	154	42.36 (28.07)	4.39 (27.07)	-19.44	0.73	**<0.0001**
Provision of practical help (single item)	T1	141	64.30 (32.52)	-6.38 (27.86)	193	66.67 (31.37)	-2.76 (25.76)	-3.62	0.13	0.0981
	T2	121	63.36 (31.74)	-7.16 (35.54)	166	66.87 (30.81)	-5.02 (27.86)	-2.14	0.07	0.4277
Provision of personal care (single item)	T1	138	25.85 (30.41)	-1.69 (21.43)	187	26.56 (31.14)	1.78 (25.57)	-3.47	0.15	0.5960

	T2	120	25.56 (27.92)	-1.39 (27.80)	157	23.57 (29.30)	4.25 (27.66)	-5.64	0.20	0.5419
Provision of psychological support (single item)	T1	141	61.23 (32.76)	-5.91 (30.42)	190	61.23 (31.42)	0.18 (25.77)	-6.09	0.22	0.1255
	T2	122	58.47 (32.72)	-5.19 (30.91)	163	61.15 (31.48)	-2.04 (32.44)	-3.15	0.10	0.2817
Too much responsibility in relation to home care (single item)	T1	134	30.85 (33.86)	-4.48 (31.07)	188	37.94 (34.16)	0.89 (31.49)	-5.37	0.17	**0.0024**
	T2	115	27.54 (31.92)	0.00 (32.74)	160	37.71 (33.25)	2.50 (30.27)	-2.50	0.08	0.0902
Caregiver involvement (single item)	T1	113	20.65 (26.47)	-3.83 (27.37)	151	21.85 (25.25)	11.70 (35.11)	-15.53	0.49	**0.0045**
	T2	97	20.62 (27.82)	-6.19 (26.06)	123	22.22 (24.39)	15.45 (34.75)	-21.64	0.70	**<0.0001**
EORTC QLQ-C30										
Quality of life (two item subscale)	T1	141	47.08 (8.83)	-0.64 (6.44)	203	47.47 (8.53)	-0.46 (7.48)	-0.18	0.03	0.9274
	T2	122	47.12 (8.61)	-0.57 (7.63)	174	47.96 (8.25)	-1.50 (8.97)	0.93	0.11	0.7534
EORTC QLQ-C30 + EORTC CAT Core										
Emotional functioning, short-form (seven item subscale)	T1	137	42.79 (7.78)	1.07 (6.01)	193	42.47 (8.41)	0.40 (6.32)	0.67	0.11	0.2446
	T2	118	43.71 (8.06)	1.24 (7.53)	166	42.15 (8.75)	0.82 (6.58)	0.42	0.06	0.6286
Fatigue, short-form (six item subscale)	T1	137	56.55 (9.48)	-0.05 (6.36)	194	55.41 (9.62)	0.84 (6.55)	-0.89	0.14	0.1796
	T2	116	55.79 (9.44)	0.19 (7.36)	164	55.36 (9.47)	0.79 (6.80)	-0.60	0.08	0.7799
EORTC CAT Core (excluded items)										
Positive emotional functioning (five item subscale)	T1	141	45.55 (6.96)	-0.32 (5.37)	201	45.29 (6.86)	-0.41 (4.88)	0.09	0.02	0.6964
	T2	121	45.71 (6.83)	-0.50 (5.38)	172	45.60 (6.88)	-0.20 (4.80)	-0.30	0.06	0.6329
Newly developed items										
Talking about greatest burdens (single item)	T1	95	60.35 (32.72)	-34.04 (38.59)	122	63.39 (34.66)	0.82 (32.49)	-34.86	0.98	**<0.0001**
	T2	83	60.24 (34.32)	-38.96 (40.26)	109	67.28 (31.09)	1.83 (33.59)	-40.79	1.10	**<0.0001**
Assistance in managing greatest burdens (single item)	T1	80	56.25 (32.52)	-24.17 (32.68)	104	59.62 (36.18)	0.64 (33.16)	-24.81	0.75	**<0.0001**
	T2	70	56.19 (35.23)	-29.52 (40.74)	90	60.37 (33.48)	3.70 (38.53)	-33.22	0.84	**<0.0001**

In the analyses, diagnosis was collapsed into eight groups (as opposed to 15 as shown in Table 1)
SD: Standard deviation
[a]Expressed on a scale of 1 (no strain/distress/positive caregiving appraisals) to 5 (maximum strain/distress/positive caregiving appraisals). Subscales are shown in Appendix 3.
[b]Expressed on a scale of 0 (no problems/unmet needs/tasks) to 100 (maximum problems/unmet needs/tasks). Items and subscales are shown in Appendix 3.
[c] Scores are transformed to T-scores, i.e., scored so the European general population has mean=50 and SD=10. The lower the score, the lower the level of quality of life, fatigue, emotional functioning, and positive emotional functioning. Subscales are shown in Appendix 3.
[d]For the outcomes 'Positive caregiving appraisals', 'Quality of life', 'Emotional functioning', and 'Positive emotional functioning', a positive value for the 'Difference between change scores in intervention and control groups' indicates that the intervention group had a more favourable development from baseline to follow-up than the control group. For all other outcomes, a negative value for the 'Difference between change scores in intervention and control groups' indicates that the intervention group had a more favourable development from baseline to follow-up than the control group.

[e]All background variables shown in Table 1 and baseline score for the particular outcome were included in the multiple linear regression (non-reduced model)

DISCUSSION

We found no effect of the CSNAT-I on the primary outcome, caregiver strain at T1, in the primary analysis. However, positive intervention effects were found at both T1 and T2 on the caregivers' evaluation of attention to their wellbeing, quality of information and communication, amount of information, caregiver involvement, talking about greatest burdens and assistance in managing greatest burdens. For all of these outcomes, the effect sizes were found to be medium or large and seemed to increase from T1 to T2 (Table 2). Furthermore, at T1, positive effects were found on distress and home care responsibility.

Lack of an intervention effect on the primary outcome may be due to increased caregiver strain being an inevitable consequence of providing end-of-life care for a loved one. However, it should be noted that a reduction in caregiver strain was found at T1 in both sensitivity analyses, and this may indicate some intervention effect. Furthermore, the positive intervention effect (d =0.35) after two CSNAT-Is reported by Aoun et al. (2015) was based on a per protocol analysis (i.e., as our sensitivity analysis S1), not on intention to treat analysis.

Caregiver strain was chosen as the primary outcome as we wished to replicate the study by Aoun et al (2015), but in addition we included several secondary outcomes which we consider highly relevant and important for the caregivers. The fact that the CSNAT-I had positive effects on caregiver distress, home care responsibility and a wide range of aspects of caregiver-HCP interaction is very encouraging.

It is noteworthy that positive effects were obtained at T1, i.e. after one CSNAT conversation only, that is, an effect obtained quickly and with minimal intervention. This suggests that caregivers of patients with a very limited life expectancy have the potential to benefit from the intervention. Furthermore, as the effect sizes seemed to increase at T2, i.e. after two CSNAT conversations, a dose-response relationship is suggested, and further research could investigate the impact of additional interventions.

Baseline levels of caregiver strain in the current study (2.89; 2.90) and in Aoun et al.'s (2015) study (2.92 in both groups) were very similar. However, it appears that a substantial proportion of caregivers were not informed about our project as HCPs judged the patient or caregiver too burdened for the caregiver to participate (Figure 3). This 'gate keeping' may have excluded some caregivers with a high level of caregiver strain (and/or other problems) and thereby a pronounced need for support from participation.

Our consent rates of 50% and 34% in the control and intervention group, respectively, indicate that compared to agreeing to complete standard measures only (i.e., in the control period), some caregivers may have perceived the CSNAT-I as time consuming and as an additional obligation they preferred to avoid. Therefore, when using the CSNAT-I in routine practice it should be introduced in a way that does not make caregivers feel that 'this is an extra thing to deal with' but rather as an opportunity to have a conversation about their support needs.

A limitation of the study is that the SW-CRT design was not optimal due to differences in the sizes of SPC teams and the slower enrolment rate during the intervention period, and thus minor modifications to the study design were required to ensure sufficient statistical power in analyses. Another limitation is that randomisation was skewed regarding caregiver age and relationship to the patient. However, the study has significant strengths: it is the first multi-centre RCT investigating the effect of the CSNAT-I, and for a palliative care study where enrolment is a known difficulty it has a large sample size (i.e., 36% more caregivers than in the study by Aoun (2015)) and a low exclusion/attrition rate (32% at T2 vs. 45% in the study by Aoun et al (2015)).

There are several areas of further research indicated by the present study. It would be highly relevant to investigate the Danish HCPs' experiences of delivering the CSNAT-I and whether the intervention also has positive effects on the patients (e.g. on their acute hospitalizations, survival time and place of death). Positive HCP experiences and patient effects would further strengthen the case for implementation of the CSNAT-I as standard care in daily clinical practice.

CONCLUSIONS

This study of the CSNAT-I in the Danish SPC setting found no effect of the intervention on the primary outcome, caregiver strain at two weeks follow-up, in the primary analysis. Yet, positive intervention effects were found on caregiver distress and home care responsibility at two weeks follow-up and on several key outcomes regarding caregivers' experience of the interaction with the HCPs at both two and four weeks follow-up, suggesting that the CSNAT-I is of great value to caregivers.

Compliance with Ethical standards

The study was carried out in accordance with the 1964 Helsinki Declaration and its later amendments.

The study was registered at ClinicalTrials.gov (ID: NCT03466580) and was approved by the Danish Data Protection Board (VD-2018-46). The protocol was presented to the Scientific Ethical Committee system (no. H-16042063) and was found not to require formal approval from the committee.

Informed consent: Patient and caregiver gave informed consent to the caregiver's participation in the study. Furthermore, the patients gave informed consent to extraction of data concerning their diagnosis and SPC course from Danish registers.

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FIGURE LEGENDS

Figure 1: The stepped wedge trial design of the study. The planned enrolment period for all participating SPC teams (i.e., clusters) was 12 months. The shift from control period to intervention period was after either 3 (period 1), 6 (period 2) or 9 (period 3) months. For six SPC teams, the enrolment period was extended by one month.

Figure 2: Study course

Figure 3: Study flow chart (CONSORT diagram)

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