Symptoms in the cancer patient –

of importance for their caregivers' quality of life and mental health?

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Subtitle: Cancer patients' symptoms affecting caregivers' quality of life and mental health

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Purpose: To examine the level of symptom burden in a sample of cancer patients in a curative and palliative phase. In addition to determine a) whether the patients' symptom burden and patients' demographic variables, and b) the caregivers' demographic variables' impact on the caregivers' quality of life and mental health.

Method: This descriptive, cross-sectional study combines data from two samples. The first group consists of caregivers of hospitalized patients with cancer in the late palliative phase and the second group is caregivers of outpatients with cancer who have pain and/or use of analgesics.

Results: The main result showed that the symptom burden was close to equal when we compared the cancer patients in the palliative and the curative phase respectively. The whole sample of patients seemed extremely tired because they score high on items capturing fatigue or weakness. They also had problems with pain and constipation. For patients having trouble sleeping, the caregivers' reported higher level of depression, whilst caregivers' gender had impact on the caregivers' anxiety. The younger the patients the more impact on caregivers' QOL mental health.

Conclusion: In this study no significant differences were revealed when comparing symptom burden among cancer patients in different stages of the disease. Caregivers reported more depression when patients had trouble sleeping and more declined mental quality of life when patients were younger. Female caregivers reported more anxiety than male caregivers.

Key words: Patient symptoms, cancer, caregivers, quality of life, mental health

Introduction

Caregivers of cancer patients are suggested to be affected by different factors regarding their health and well-being during the patient's disease trajectory (Weitzner et al., 1999; Grunfeld et al., 2004; Grov et al., 2006a). The caregivers may be defined as partners, close relatives, next-of-kin, and significant others depending on their relationship to the patient (McClement et al., 1998). According to the Norwegian legal definition (Patient's right law, §3-3), the primary caregiver (caregiver) is the one defined by the patient regardless of their family connection. The caregivers are to be informed about the patient's health condition when the patient wants to share such information.

Cancer patients may experience multiple disease or treatment related symptoms (Donnelly, 1995). In a study of 796 consecutive patients with advanced cancer the most prevalent symptoms (≥50 %) were pain, easy fatigue, anorexia, weakness, lack of energy, dry mouth, dyspnoea, constipation, and early satiety. Most of these symptoms did not differ between primary cancer sites in either prevalence or severity. They were not able to correlate symptoms with disease stage or separate treatment related symptoms from cancer related symptoms (Kirkova et al., 2011a). However, a comprehensive clinical review of cancer symptom clusters showed that disease and treatment related symptoms are influenced by primary cancer site, disease stage and antitumor treatment (Kirkova et al., 2011b).

When staying at home with advanced cancer, the patient and his/her caregiver coordinates the support needs necessary in collaboration with the community oncology nurse. The impact of the involvement and responsibility during the cancer journey might leave concerns on caregivers. Studies have been performed during different stages of the cancer patients' disease trajectory, and for caregivers there are reported burden (Given et al., 2004; Goldstein et al., 2004; Doorenbos et al., 2007; Higginson et al., 2008), reaction in terms of particular burden and well-being (McCorkle et al., 1993; Nijboer et al., 1999; Hagedoorn et al., 2002; Grov et al., 2006c), quality of life (QOL) (Grov, 2005; Clark, 2006; Grov et al., 2006b), mental health (Edwards et al., 2004; Grov, 2005) , and a large number of specific aspects influencing the caregivers' situation, e.g. work and economy (Goldzweig et al., 2009), and the impact of educational level and educational programs facilitated for caregivers (Clark, 2006; Goldzweig et al., 2009). In a recent study 38% of caregivers reported depressive symptoms in the clinical range as measured by Center for Epidemiological Studies – Depression scale (CES-D) (Steel et al., 2011).

Weitzner et al. (1999) compared QOL measured by the Short form 36 (SF-36) in caregivers of cancer patients in the palliative versus the curative phase. The caregivers of patients in the palliative phase generally reported lower QOL than those caring for patients in the curative phase. The latter mentioned study suggested that caregivers' QOL was dependent on factors related to the patient's condition as well as individual characteristics of the caregiver. The main findings were that caregivers' physical QOL was dependent on the patient's performance status as well as the education level of the caregivers. They recommend research to focus on caregivers' situation in terms of QOL and emotional distress and factors influencing these variables. Others have also stated that the patients' illness characteristics may be factors that influence the families' level of depression and anxiety (Edwards Clarke, 2004), and a study of 82 adult caregivers showed that patients' pain were significantly correlated with caregivers' depression, but they found no correlation between patients' fatigue and caregivers depression (Bush et al., 2004).

Cancer stage of the patients is shown as a predictor of caregivers' physical QOL in addition to health behaviour and overload (Matthews et al., 2004). Besides the effect of the direct stress or burden of caring for the cancer patients, differences in caregivers' QOL may be linked to gender and partner role expectations. Stressors that have a strong effect on female family caregivers may have a weaker effect on male family caregivers and vice versa. Previous studies have indicated that female caregivers are more distressed by factors involving social and family relationships, and male caregivers are more worried about work related and financial issues (Goldzweig et al., 2009). Supportiveness, mood and partners' health condition seem to be more sternly related to female caregivers' than to male caregivers' psychological well-being (Hagedoorn et al., 2002).

Fridriksdottir et al. (2011) have studied QOL, anxiety, and depression in family members of cancer patients and found high prevalence of anxiety and depression. The latter mentioned study did not specifically report differences for caregivers when studying patients in curative versus palliative phase.

The curative phase is defined as a stage where the patients are admitted to a curative treatment intention, while the palliative phase is defined according to the definition of palliative care stated by World Health Organization (WHO) (1990) (WHO (World Health Organization) 2005) (http://www.who.int/cancer/palliative/definition/en/) and European Association for Palliative Care (EAPC) (2002)(EAPC (European Association for Palliative Care) 2005) (http://www.eapcnet.org/about/definition.html). Since Weitzner et al., (1999) have reported lower QOL among caregivers of cancer patients in the palliative phase compared to those caring for patients in the curative phase, and that explanation for the findings might be related to aspects of the patient's condition as well as individual characteristics of the caregivers, we wanted to shed light on the impact of the patients' symptoms and demographic variables in the cancer patients and their caregivers.

The aims of this study are therefore to examine;

1) The level of symptom burden in a sample of cancer patients in the curative phase compared to the palliative phase

2) The impact of patients' symptom burden, demographic variables of the patients and demographic variables of the caregivers on caregivers' QOL and mental health.

Since the symptom burden is expected to increase during the cancer trajectory, and the symptom load therefore is presumed higher in the palliative than in the curative phase, our hypothesis is that the QOL will be affected negatively by patients defined in the palliative phase, and those with high symptom load. The same argument is given for the caregivers' mental health, and we expect higher level of anxiety and depression for caregivers of patients in the palliative phase and those with high symptom load. In addition we hypothesize that female caregivers' experience higher level of anxiety and depression than men (Hagedoorn et al., 2002; Goldzweig et al., 2009).

Material and methods

Samples

This descriptive, cross-sectional study is a secondary analysis which combines data from two different studies in which patients were recruited together with their family members. The first group of patients were recruited between February 2002 and October 2003. At the recruitment time these patients were hospitalized with cancer in the palliative phase staying in a large, tertiary referral cancer hospital in Norway, but the intention was to leave the hospital for staying at home during this part of the cancer trajectory. All patients had metastatic cancer with estimated survival time of < 4 month at the recruitment time. Of the patients recruited to this study 31 % died within four month following up and 63 % patients were dead after one year (Grov, 2006b). Eligible patients and family caregivers were consecutively invited to participate and given an information letter and a consent form to complete. A total of 96 dyads consented and completed the questionnaires.

The second group of patients was recruited between January and June 2005 from outpatient oncology clinics (i.e., general, gynaecology, lung, pain, chemotherapy, radiotherapy) at the same hospital as the first patient-group. All patients coming to the outpatient clinics during selected periods of time were screened for pain as one of the main purposes of the primary study was to describe cancer patients' pain prevalence (Valeberg et al., 2008). Treatment intention (curative or palliative) was assessed from the medical charts by an experienced physician. Patients with pain and their family caregivers received written information about the study and were invited to participate. A total of 73dyads consented and completed the questionnaires and is part of this study.

Patients in both studies were included if they were: >18 years of age; had a diagnosis of cancer; were able to read, write, and understand Norwegian. Patients from the first sample had to understand that they had metastatic cancer, have an estimated survival time of more than four months, an ECOG performance status ≥ 1, and to be managed at home with support from caregivers and/or health care personnel. The exclusion criterion was known mental disorder. In the second sample, all patients had self-reported pain of any intensity and/or use of analgesics. The recruitment procedure is described more thoroughly elsewhere, for the first sample (Grov et al., 2005) and for the second sample (Valeberg et al., 2008).

All patients and their caregivers provided written informed consent. This study was approved by the Regional Ethics Committee, the Norwegian Radium Hospital's Protocol Review Board, and The Norwegian Data Inspectorate.

Instruments and scoring procedures

Demographic data from patients included gender, age, marital status (married/partnered or not), educational level (primary school (i.e., up to 10 years at school), secondary school (i.e., from 11 to 14 years at school), or college/university), and employment status (working full- or part-time or not working). From the caregivers, demographics included age, gender, education and work were assessed.

Medical Record Review

Patients' medical records were reviewed by two experienced physicians to obtain information on cancer diagnosis, presence of metastasis and whether the treatment intention was palliative or curative.

Functional status

In the first sample of patients performance status was measured using The Eastern Cooperative Oncology Group (ECOG) Performance status assessment tool. The WHO-index (ECOG performance status) assesses individual's status to perform daily activities. It is categorized as a score from 0 to 4, (0 = a function of full activity, 1 = with restriction related to physically strenuous activity, 2 = capable of self-care, but unable to carry out any work activities, up and about more than 50% of waking hours, 3 = capable of only limited self-care, confined to bed or chair more than 50% of waking hours, 4 = completely disabled, cannot carry out any self- care, totally confined to bed or chair) (Oken et al., 1982)**.**

Patients in the second sample reported their functional status using a modified Karnofsky Performance Status (KPS) scale that ranged from 40 (i.e., disabled, need special help and care) to 100 (i.e., adequate health status with no complaints and no evidence of disease). Reliability and construct validity of the KPS are well established and it is considered to be a global indicator of the functional status of patients with cancer (Schag et al., 1984). In order to compare patients from the different settings, patients scoring 80 or higher on the Karnofsky scale were labelled as having high function, and patients scoring 40-70 were labelled impaired. For ECOG status the cut off was defined to be 0 and 1 to represent high function while 2-4 represent impaired.

Hospital Anxiety and Depression Scale (HADS)

Anxiety and depression of caregivers was assessed by the HADS in both samples. The HADS has been found to perform well for studying mental health in the general population, in cancer patients, and in primary care patients (Mykletun, 2001). The instrument consists of 14 items, 7 on the depression sub-scale (HADS-D) and 7 on the anxiety sub-scale (HADS-A). Each item is scored on a four-point scale from 0 (not present) to 3 (considerable), and the item scores are added, giving HADS-D and HADS-A scores from zero (minimum symptom load) to 21 (maximum symptom load). A score ≥ 8 - 10 on anxiety or depression is defined as borderline abnormal and a score above 10 as abnormal (Zigmond et al., 1983).

Health Related Quality of Life (QOL): SF-36

Health related QOL of the caregivers was assessed by SF-36 in both samples. The SF-36 contains 36 items grouped into the eight multi-item health dimensions including physical functioning (PF, 10 items), role limitations due to physical problems (RF, 4 items), bodily pain (BP, 2 items), social functioning (SF, 2 items), mental health (MH, 5 items), role limitations due to emotional aspects (RE, 3 items), vitality (VT, 4 items), and general health perceptions (GH, 5 items) (Ware et al., 1992; Ware J.E. et al., 2000). The items are answered in “yes” or “no” alternatives, or in scales with three to six response alternatives. For each dimension questions are coded, summed, and transformed to a scale from zero (worst) to 100 (best). The SF-36 can also be divided into two component scores, physical and mental health sum-scores, named PCS and MCS.

In order to assess the patient’s condition, eleven items from the EORTC-QLQ-C30 was used (Aaronson et al., 1993). These conditions are fatigue, pain, nausea and vomiting, dyspnea, insomnia, need to rest, weakness, tired, appetite loss, constipation, and diarrhea. The conditions are scored from 1 to 4, with higher scores indicating more severe symptoms.

Statistical analysis

Data were analyzed using SPSS Version 17.0 (SPSS, Inc.). Descriptive statistics were calculated for the patients' and family members' demographics. To examine if patients' disease stage had an impact on the caregivers' mental health and QOL, the samples were divided into caregivers of patients in the palliative phase (n=124) and caregivers of patients in the curative phase (n=32).

The continuous variables were examined with t-tests, and categorical variables with χ^2-tests, or Fisher's exact test. Variables that showed a significant difference when comparing the groups of patients according to the disease stage (e.g. curative and palliative phase) were used further into the regression analysis. Four linear regression analyses were performed with the mental and physical health components of the SF 36 and anxiety and depression in the family caregivers respectively as the dependent variables. Significance level was set at $p < .05$, and two-sided tests were applied.

Results

Demographics patients and family caregiver

Demographics and clinical characteristics for the patient samples are given in Table 1. The patients' age ranged from 23 to 86 years and the majority was unemployed (or home working), married women. When we compared patients in the palliative and curative phase, significant differences were found in age, education, cancer sites, and presence of metastases.

Table 1 approximately here

The majority of the caregivers were men and their age ranged from 19 to 82 years. About 50 % of the caregivers worked full time. There are statistically differences between the caregivers of patients in the palliative and curative phase as the family caregivers' are more often older women in the palliative phase (Table 2).

Table 2 approximately here

Symptom burden of patients

Regarding symptoms from EORTC-C30, patients in the curative phase had statistically more trouble sleeping than patients in the palliative phase, and patients' in the palliative phase vomited more compared to patients in the curative phase . The highest scores on the individual symptoms of the EORTC is "need to rest", pain, tired, and "felt weak" (Table 3).

Table 3 approximately here

The independent variables used in the regression analysis are: caregivers' age and gender. The demographics and clinical variables of the patients are: age, trouble sleeping, vomiting, and curative and palliative phase. The palliative phase was identical to 'the presence of metastasis' and this variable was not brought into the regression analysis to avoid redundancy. Linear regression analysis was performed for the physical (PCS), mental (MCS) QOL sum-scores and anxiety and depression. For the PCS of the QOL none of the independent variables showed significant contribution to the model. For the MCS only the patients' age reached significance. For the anxiety dimension of the HADS, caregivers' gender revealed significant, and for the depression dimension of the HADS, only patients' report of trouble with sleep reached significance.

Table 4 approximately here

Discussion

The main result of this study was that the symptom burden was close to equal when we compared the cancer patients in the palliative and the curative phase respectively. The regression analysis showed that patients having trouble sleeping had impact on the caregivers' depression, whilst caregivers' gender had impact on the caregivers' anxiety. Women scored higher on anxiety than men. For the caregivers', the mental dimension of QOL showed that the patients' age contributed significantly to the model, the younger the patient the worse QOL for the caregivers.

We expected the symptom burden to be higher for patients in the palliative compared to the curative phase, but differences were only found in trouble sleeping and vomiting. An explanation for the lack of differences between the two groups may be that the symptom burden is the same regardless of where in the cancer trajectory the patients are assessed. Symptom burden may be more linked to the treatment and not whether they are considered as patients being in a palliative or curative phase. The sample size, especially in the curative phase is small, and may not capture the symptom burden present for these patients.

Patients in the curative phase scored higher on trouble sleeping compared to the patients in the palliative phase. The reason for this is not obvious, but one explanation may be that the patients in the palliative phase may have adapted to a larger extent to their situation, and are more often on medication regulating sleep (Sela et al., 2005) or have learnt to use techniques to relax. Patients in the palliative phase vomited more than patients in the curative phase. The reason for this is not apparent, but maybe patients in this group are getting treatments that have more side-effects than the patients in the curative phase? Unfortunate, we do not have available data on the patients' treatments.

The scores on the individual symptoms of the EORTC indicate that the whole sample of patients is extremely tired because they score high on the items capturing fatigue or weakness. This finding is supported by previous research (Kirkova et al., 2011a; Roscoe, 2007; Radbruch et al., 2008). In a study of 1,000 patients in an American Palliative care Program, 84% of the patients reported fatigue, 66% reported weakness and 61% reported lack of energy (Walsh et al., 2000).

The high value in the patients' pain score shows that the patients also had problems with this symptom. This scoring pattern is also in accordance with finding in previous research (Kirkova et al., 2011 ;Valeberg et al., 2008), but the result may also be attributed to the fact that the sample of outpatients were screened for pain when invited to participate in the study.

A previous study from Norway has argued that caregivers of patients in the palliative phase have lower scores on the mental dimension on QOL and higher scores on anxiety than the general population (Grov et al., 2005). We therefore expected the palliative phase to be more challenging for caregivers, suggesting differences between the scorings on the mental dimension on QOL and higher anxiety level for caregivers of patients in the palliative than for caregivers of patients in the curative phase. We did not find support for that hypothesis. The reason for this may be that the palliative and the curative phase are equally stressful or challenging. In addition we have to bring into consideration that the definition of curative and palliative phase does not capture or differentiate patients' overall condition in a meaningful manner.

In the regression analysis we brought in variables that showed statistically significant differences between patients in the palliative and curative phase. The only demographic variable included for the patients was age which revealed significant impact on the mental dimension of QOL for caregivers. A possible reason for this finding may be that the stress and burden are higher when a younger relative has advanced cancer. We suggested that the scenario of a younger person facing death is harder to take in compared to the fact that an older person to a kind of extent is expected to die. In this study the patients' mean age is 59 years, so the age might be characterized as 'middle age'. However, even with a middle age patient sample, it seems worse for the caregivers as younger the age of the patient.

Demographic variables of the caregivers entered into the regression analyses were age and gender, of which only caregivers' gender had significant impact on the caregivers' anxiety. Female caregivers report higher anxiety level than men, a finding that is supported by several studies (Hagedoorn et al., 2002; Grov et al., 2005; Goldzweig et al., 2009). For oncology nurses it seems important to have in mind female caregivers' expression of a higher level of anxiety when helping caregivers of cancer patients.

Clinical variables included in the regression analysis were palliative and curative phase, vomiting and trouble sleeping, where only the latter mentioned variable revealed significant impact on the caregivers' depression. An explanation may be related to the fact that for patients that have trouble sleeping the caregivers interpret such sign as patients' concerns. Our finding is in accordance with the study performed by Carter and Chang (2000), where they found that 64% of caregivers' depression was predicted by sleep problems in the patients. From a clinical point of view we recommend oncology nurses to highlight patients' problems with insomnia as this symptom may be important for caregivers' mental health. We have no data on the caregivers' eventually problems with sleep related symptoms, and therefore further research should focus on such aspects in caregivers as insomnia and mental health is shown to be highly correlated in a large Norwegian survey (Neckelmann et al., 2007; Sivertsen et al., 2009).

The limitations in this study reflect the abovementioned statement that we have not included instruments covering phenomenon that may be important for caregivers' mental health and QOL, e.g. sleeping problems. Patients in this study represent a large time span of the disease journey and maybe patients' symptoms affect their caregivers more in the terminal stage? Further research is recommended to explore this more closely. This study lacks information regarding the cancer patients' medical treatment. As treatment may have great impact on symptom burden in the patients, such data should be incorporated in future research. In addition to treatment having impact on symptoms, the symptoms may vary from one day to another. There is a need for more longitudinal data to capture this kind of variation.

Even though we used two different samples of family caregivers to increase the sample size, the sample size, especially in the curative phase is small and low statistical power and risk for type II statistical error may be present.

However, bringing into a study well-documented and psychometric tested instruments as the SF-36, the HADS, and variables from the EORTC give basis for valuable insight into these aspects for this particular sample-groups.

Conclusion

This study showed that trouble sleeping in cancer patients, regardless of the disease stage, has significant impact on the caregivers' mental health. Additionally, female caregivers seem more vulnerable than male caregivers for higher level of anxiety. The mental dimension of the QOL for caregivers is affected by the patients' age, where younger patients have greater impact on caregivers' mental QOL. Oncology nurses are to pay attention to the patient's trouble sleeping as an indicator for caregivers' experience of their mental health.

Conflict of interest

None declared.

Table 1 – Demographic and clinical characteristics of the total sample and among the two patient groups

Characteristics	**Total Sample N=159**	**Palliative phase n=127**	**Curative phase n=32**	**P-value**
Age, mean (SD)	58.6 (11.3)	60.0 (10.9)	52.3 (10.2)	**.001**
Gender, n (%)				
Men	50 (31)	43 (34)	7 (22)	.19
Women	109 (69)	84 (66)	25 (78)	
Education, n (%)				
Primary school	35 (23)	34 (27)	1 (3)	**.01**
Secondary school	59 (38)	43 (35)	16 (52)	
College/university	61 (39)	47 (38)	14 (45)	
Employment status, n (%)				
Not working	136 (87)	110 (88)	26 (81)	.32
Working full/part time	21 (13)	15 (12)	6 (19)	
Function, n (%)				
High function	103 (65)	80 (63)	23 (72)	.35
Impaired	56 (35)	47 (37)	9 (28)	
Cancer diagnosis, n (%)				
Breast	74 (46)	61 (49)	13 (41)	**.003**
Prostate	29 (18)	28 (22)	1 (3)	
Gynecologic	7 (5)	4 (3)	3 (9)	
Colorectal	20 (13)	17 (13)	3 (9)	
Other	29 (18)	17(13)	12 (38)	
Metastases, n (%)				
Yes	129 (81)	124 (98)	5 (16)	**.001**
No	30 (19)	3 (2)	27 (84)	

Table 2 – Demographic characteristics of the caregivers of the two patients groups

Characteristic	**Total sample Caregivers N=159**	**Palliative phase n=127**	**Curative phase n= 32**	**P- value**
Age, mean (SD)	57 (12.3)	57.7 (12.1)	52.2 (11.3)	**.002**
Gender, n (%)				
Men	102 (61)	70 (55)	32 (80)	**.005**
Women	65 (39)	57 (45)	8 (20)	
Relation to patient				
Married	140 (89)	109 (87)	31 (97)	.43
Daughter/ son	7 (4)	7 (6)	0 (0)	
Friend	9 (6)	8 (6)	1 (3)	
Sibling	1(1)	1 (1)	0 (0)	
Education, n (%)				
Primary school	37 (23)	29 (24)	8 (29)	.77
Secondary school	62 (38)	45 (36)	17 (43)	
College/university	65 (40)	50 (40)	15 (38)	
Employment status, n (%)				
Not working	77 (47)	62 (50)	15 (38)	.18
Working full/part time	88 (53)	63 (50)	25 (62)	

Table 3 – Comparisons of symptoms between cancer patients in the palliative and the curative phase

Characteristic Scoring range: 1-4	All patients (N=159)	Palliative phase (n= 127) mean (SD)	Curative phase (n= 32) mean (SD)	T-test P-value
Need to rest	2.85 (.83)	2.90 (.82)	2.66(.87)	.15
Pain	2.70 (.88)	2.66 (.91)	2.84 (.77)	.31
Tired	2.68 (.84)	2.66 (.84)	2.75 (.80)	.57
Felt weak	2.64 (.86)	2.68 (.86)	2.53 (.84)	.37
Lack of appetite	2.04 (1.03)	2.05 (1.0)	1.88 (.94)	.39
Trouble sleeping	2.02 (.97)	1.97 (.92)	2.34 (1.2)	**.05**
Constipated	1.98 (1.03)	2.02 (1.03)	1.84 (1.0)	.40
Short of breath	1.81 (1.01)	1.86 (1.0)	1.63 (.94)	.24
Nausea	1.80 (.93)	1.85(.96)	1.59 (.80)	.17
Diarrhea	1.51 (.73)	1.52 (.72)	1.50 (.84)	.91
Vomited	1.32 (.69)	1.38 (.74)	1.09 (.39)	**.03**

Table 4 - Linear regression analyses with physical and mental QOL, anxiety and depression as dependent variables

		Std. β	t	P-value
PCS				
Patient:	Age	-0.07	-0.52	0.61
	Vomiting	0.01	0.14	0.89
	Trouble sleeping	0.06	0.65	0.52
	Curative/palliative phase	0.03	0.29	0.77
Caregiver:	Gender	0.05	0.48	0.64
	Age	-0.23	-1.86	0.06
MCS				
Patient:	Age	0.30	2.12	**0.04**
	Vomiting	-0.10	-1.17	0.24
	Trouble sleeping	0.00	0.00	1.00
	Curative/palliative phase	-0.03	-0.32	0.75
Caregiver:	Gender	0.17	1.61	0.11
	Age	-0.09	-0.68	0.50
HADS-A				
Patient:	Age	-0.25	-1.77	0.08
	Vomiting	0.08	0.94	0.35
	Trouble sleeping	0.16	1.87	0.07
	Curative/palliative phase	0.05	0.59	0.56
Caregiver:	Gender	-0.21	-2.08	**0.04**
	Age	0.23	1.80	0.07
HADS-D				
Patient:	Age	-0.19	-1.33	0.19
	Vomiting	0.08	0.93	0.37
	Trouble sleeping	0.17	1.97	**0.05**
	Curative/palliative phase	0.03	0.34	0.74
Caregiver:	Gender	-0.08	-0.83	0.41
	Age	0.18	1.45	0.15

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