

Symptoms of advanced cancer in palliative medicine: a longitudinal study

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Received 20 February 2021

Accepted 5 June 2021

Published Online First

23 June 2021

ABSTRACT

Objectives This study aimed to examine the symptomatology of patients with advanced cancer at admittance to palliative care services and to investigate how the symptomatology changed during the first month, and whether these changes were associated with various patient characteristics.

Methods In a longitudinal study in Chile, outpatients with advanced cancer completed the questionnaires European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care and the Hospital Anxiety and Depression Scale. Prevalence and severity of symptoms and problems (S/Ps) at baseline were calculated. Differences in S/P scores from baseline to follow-up were calculated overall and according to patient characteristics. Multiple linear regression was used to study the associations between patient characteristics and changes in S/P scores.

Results At baseline, 201 patients answered the questionnaires and 177 completed the follow-up. Fatigue, pain and sleeping difficulties were the most prevalent S/Ps reported, and also had the highest mean scores at baseline. S/P scores at baseline varied significantly according to sex, age, civil status, residence, children, prior and current antineoplastic treatment. Emotional functioning, pain, sleeping difficulties, constipation and anxiety improved significantly during the first month of palliative care. Residence, cohabitation status, diagnosis and current antineoplastic treatment were associated with changes in S/P scores.

Conclusions Patients reported moderate-to-severe levels of S/Ps at admittance to palliative care. Several S/Ps improved the first month. Certain patient characteristics were associated with changes in S/P scores. This information may guide clinicians to more effective interventions that can improve the quality of life of patients receiving palliative care.

Key messages

What was already known?

- ⇒ Cancer patients report high symptom burden at the start to palliative care, but which symptoms improve or worsen following initiation of palliative care differs across previous studies.
- ⇒ Little is known about the association between patient characteristics and changes in symptomatology of patients in palliative care.

What are the new findings?

- ⇒ Patients reported moderate-to-severe levels of symptoms at admittance to palliative care and overall emotional functioning, pain, sleeping difficulties, constipation and anxiety improved significantly during the first month.
- ⇒ Residence, cohabitation status, diagnosis and current antineoplastic treatment were associated with changes in symptomatology.

What is their significance?

- ⇒ The high level of symptoms reported at the admittance to palliative care and changes over time, emphasises the importance of using patient-reported outcomes questionnaires to ensure that patients systematically report all their symptoms and thus, are potentially treated.
- ⇒ Changes in symptomatology may be affected by certain patient characteristics that must be considered in clinical decisions toward more effective palliative care interventions and in further research.



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To cite: Rojas-Concha L, Hansen MB, Petersen MA, et al. *BMJ Supportive & Palliative Care* 2023;13:e415–e427.

INTRODUCTION

Preserving quality of life (QOL) and relieving symptoms in patients with advanced cancer are desired outcomes of palliative care.¹ Assessment of patients' QOL and symptomatology at the start and during palliative care may help clinicians to initiate relevant palliative care interventions and evaluate their effect.

Changes in symptomatology following initiation of palliative care have been investigated by using patient-reported outcomes (PRO) questionnaires, but the results were inconsistent across the studies on whether pain, fatigue, appetite loss, QOL, insomnia, constipation, nausea/vomiting and physical or emotional function improved or worsened after 2–4 weeks of palliative care.^{2–6} In addition, we only identified few studies assessing the association between changes in symptomatology and patient characteristics.^{7–9}

Chile has a population of 17.5 million inhabitants and has 52 hospital-based palliative care services/units in tertiary hospitals of the public healthcare system.¹⁰ Palliative care in the tertiary sector is provided by physicians (oncologists, internists or surgeons) and non-physicians such as nurses, paramedics and psychologists.^{10 11} In 2005, the national programme 'Pain relief for advanced cancer and palliative care' was enhanced by the Explicit Guarantees for Free Access Law (GES), aimed at providing palliative care treatment for all patients diagnosed with advanced cancer (defined as incurable progressive cancer) by a specialist.^{11 12} A national report showed that 67% of patients with cancer admitted to the programme in 2013 self-reported more than nine symptoms. The most prevalent symptoms and problems (S/Ps) listed were pain (90%), digestive symptoms, that is, anorexia, weight loss, nausea and vomiting (85%) and emotional symptoms, that is, anxiety, insomnia and depression (55%).¹³ However, to our knowledge no studies have investigated changes in S/Ps and overall QOL of patients receiving palliative care in Chile.

The aims of the current study were (1) to examine the symptomatology of patients with advanced cancer at admittance to palliative care services in Chile, (2) to investigate how the symptomatology changed during the first month of palliative care, and (3) to investigate whether these changes were associated with various patient characteristics.

METHODS

Design

This longitudinal study was carried out between October 2017 and January 2018 in four hospital-based palliative care services in Santiago, Chile. The symptomatology assessments were done at admittance, and 1 month later. The study was approved by two local ethics committees in Chile. All patients gave written consent.

Patients

This study included outpatients admitted to one of the four palliative care services. All patients had advanced cancer and were ≥ 18 years of age, had knowledge of their diagnosis, Karnofsky Performance Status (KPS) score of at least 50%,¹⁴ and provided informed, written consent. Patients who declined participation, were non-Spanish speakers, or were considered too

ill to participate by the staff were excluded. Socio-demographic data on sex, age, civil status, residence, cohabitation, children and education were collected at admittance. Clinical data on diagnosis, prior and current antineoplastic treatment, hospital and KPS score assessed by the physician at baseline were collected from the medical record.

Assessments

Patients were invited to participate in the study at their first contact with the palliative care service. Consenting patients received a booklet with the self-assessment questionnaires, that is, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care (EORTC QLQ-C15-PAL), the Write In three Symptoms/Problems (WISP) instrument and the Hospital Anxiety and Depression Scale (HADS). The first page of the booklet contained questions on sociodemographic information and a question on whether the patient had completed the questionnaires by herself/himself or with the help of a trained clinician. After 1 month of palliative care, patients who had any appointment or phone calls with the palliative care service were asked to complete the questionnaires again.

The EORTC QLQ-C15-PAL questionnaire consists of 15 items: two functional scales (physical and emotional functioning), seven symptom scales (pain, fatigue, nausea/vomiting, dyspnoea, sleeping difficulties, appetite loss and constipation) and one item referring to overall QOL. Fourteen items employ 4-points scales from 1 (not at all), 2 (a little), 3 (quite a bit) to 4 (very much), and QOL is rated from 1 (very poor) to 7 (excellent).¹⁵ The WISP is an open-ended instrument that permits patients to report up to three S/Ps not covered by the EORTC QLQ-C15-PAL and rate their severity from 1 (not at all) to 4 (very much).¹⁶

HADS is a self-reporting scale that contains 14 items divided into two subscales, one for anxiety and one for depression. Each subscale comprises seven items, which are scored on scales ranging from 0 to 3 points, giving a maximum of 21 points per subscale. According to Zigmond and Snaith's criteria, 0–7 points on a subscale represents a 'non-case', 8–10 points a 'doubtful' or possible case and 11–21 points a 'definite case' of anxiety or depression.¹⁷

Statistical analyses

The EORTC QLQ-C15-PAL scores were converted to 0–100 scales according to the Scoring Manual.¹⁸ High scores on the two functioning scales and overall QOL represent better function/QOL, while high scores on symptom scales reflect worse symptoms. Mean scores and SD of the scales in the EORTC QLQ-C15-PAL and HADS were calculated overall and according to patient characteristics at baseline. Differences in the distribution of these S/P scores across patient characteristics were tested with non-parametric analyses

using Mann-Whitney U test and Kruskal-Wallis test because S/P baseline scores were non-normally distributed. Patient characteristic categories with under 5% were grouped into an 'other' category.

At baseline we calculated the prevalence of having a 'symptom/problem' as the proportion of patients who reported EORTC QLQ-C15-PAL scores at least 'a little' (functioning scores ≤ 67 or symptom scores ≥ 33). Prevalence of 'severe symptom/problem' was calculated with patients scoring at least 'quite a bit' (functioning scores ≤ 34 or symptom scores ≥ 66), using the cut-points described in previous studies^{19 20} for all scales except overall QOL. The prevalence of patients with possible anxiety or depression (score ≥ 8), and definite anxiety or depression (≥ 11) were calculated for the HADS.¹⁷ Qualitative responses obtained from WISP were grouped into S/P categories using the list of 61 S/P-categories reported previously.¹⁶ The prevalence of patients reporting each additional S/P on WISP and the distribution of severity ratings were calculated.

For patients who completed the study, differences in S/P scores from baseline to follow-up were calculated overall and in relation to patient characteristics; change scores were tested using Wilcoxon signed-rank test. In addition, we performed multiple linear regressions with backwards stepwise selection to identify patient characteristics significantly associated with change in S/P scores from baseline to follow-up. The significance level used was 0.05. All analyses were performed using the statistical software Statistical Package for Social Sciences V.23.

RESULTS

Patient characteristics

Figure 1 shows the inclusion of patients. Of the 394 patients admitted to the four palliative care services, 201 (80% of the eligible patients) answered the

EORTC QLQ-C15-PAL, WISP and HADS at baseline (figure 1). Of these, 21 patients had died at 1-month follow-up, and 3 were too ill to participate, and the remaining 177 patients completed the follow-up questionnaires.

Around half of the participants were men (51.7%) and were married (55.7%). Their median age was 66 years and the median KPS score was 90. Most patients lived in their private residence with someone, had older children and had a low education level. The most frequent diagnoses were stomach cancer, colorectal cancer and breast cancer. At admittance to palliative care, 51.7% of patients had not received any prior antineoplastic treatment and 94% were not in a current antineoplastic treatment. Further details can be seen in table 1.

Symptomatology at the admittance to palliative care

The prevalences of having a S/P and a severe S/P, respectively, at baseline are presented in figure 2. The most prevalent S/Ps reported on the EORTC QLQ-C15-PAL were fatigue 71% (28% severely), pain 59% (29% severely) and sleeping difficulties 54% (31% severely). Nausea/vomiting (12%) and dyspnoea (21%) were the least prevalent S/Ps. Possible anxiety was reported by 21% of patients on HADS and possible depression by 19%. Definite anxiety and depression were reported by 11% and 10% of patients, respectively.

A total of 72 patients out of 201 (35.8%) reported S/Ps using the WISP instrument at baseline. These patients reported 91 S/Ps in total: 60 were additional S/Ps; 20 were elaborations of S/Ps already covered by the EORTC QLQ-C15-PAL, and 11 were diagnoses or symptoms that could not be coded. In total 80 S/Ps were grouped into 23 S/P categories. The most prevalent additional S/Ps reported on WISP were cough (5.5%), bloating (3.5%) and diarrhoea (2.5%).

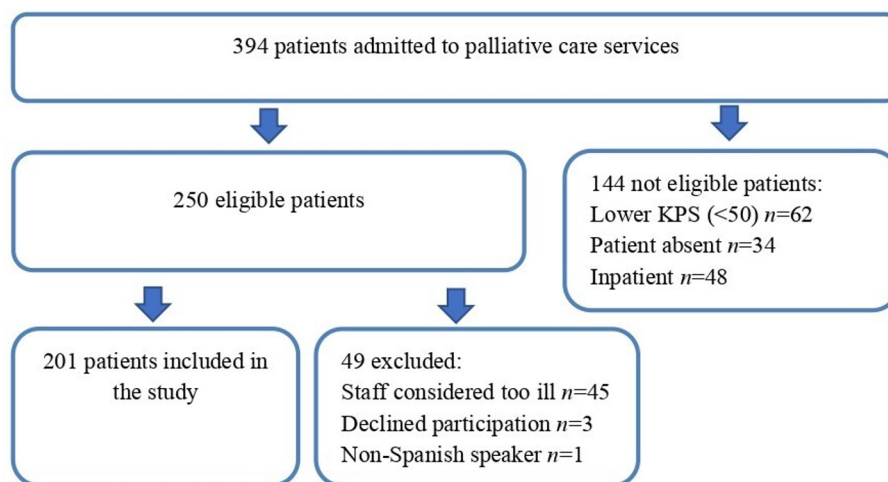


Figure 1 Inclusion of patients. KPS, Karnofsky Performance Status.

Table 1 Sociodemographic and clinical characteristics at baseline for the 201 patients included in the study

	N	%
Sex		
Men	104	51.7
Women	97	48.3
Age		
Median (range)	66	(24–90)
<65 years	86	42.8
≥65 years	115	57.2
Civil status		
Single*	89	44.3
Married/cohabiting	112	55.7
Residence		
Private residence (house, flat, etc)	143	71.1
Relatives' residence	49	24.4
Others' residence	9	4.5
Cohabitation		
Living alone	11	5.5
Living with spouse/partner	44	21.9
Living alone with children	39	19.4
Living with others	46	22.9
Living with spouse/partner and children	61	30.3
Children		
No children	22	10.9
Children, at least one younger than 18 years	24	11.9
Children, all at least 18 years old	155	77.1
Education		
Primary education or lower†	94	46.8
Secondary education‡	74	36.8
Higher education§	33	16.4
KPS score		
Median (range)	90	(50–100)
50–60	30	14.9
70–80	36	17.9
90–100	135	67.2
Diagnosis (cancer site, ICD-10)		
Stomach (C16)	26	12.9
Colorectal (C18–C20)	24	11.9
Breast (C50)	21	10.4
Lung (C33–C34)	18	9
Prostate (C61)	18	9
Gallbladder (C23)	11	5.5
Ovarian (C56,570–C574)	9	4.5
Leukaemia (C91–C95)	8	4
Liver (C22)	7	3
Oesophageal (C15)	6	3
Pancreatic (C25)	6	3
Melanoma skin cancer (C43)	6	3
Kidney (C64–C66)	6	3
Lymphoma (C81–C85)	5	2.5
Head and neck (C00–C14, C32)	4	2
Cervical (C53)	4	2
Bladder (C67)	4	2

Continued

Table 1 Continued

	N	%
Unknown primary cancer (C76–C80)	4	2
Multiple myeloma (C90)	3	1.5
Other cancer (all other C codes)	11	5.5
Any prior antineoplastic treatment		
Yes	97	48.3
No	104	51.7
Current antineoplastic treatment		
Yes	12	6
No	189	94
Hospital		
Sotero del Rio	99	49.3
San Juan de Dios	46	22.9
Salvador	36	17.9
Felix Bulnes Cerda	20	10

*Including: divorced, separated and widowed.

†Compulsory education of 8 years or less.

‡Compulsory education from 9 to 12 years.

§Education >12 years including university, technical or further studies.

ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; KPS, Karnofsky Performance Status.

Overall, 70% of the additional S/Ps were reported as 'quite a bit' to 'very much' (table 2).

Table 3 shows the EORTC QLQ-C15-PAL and HADS scores overall and according to patient characteristics at baseline. Overall, high symptom levels were found for fatigue, pain and sleeping difficulties. Women reported more severe fatigue than men ($p=0.022$), and younger patients had more severe nausea/vomiting ($p=0.033$), dyspnoea ($p=0.023$) and sleeping difficulties ($p=0.008$) compared with older patients. Single patients ($p=0.003$) and patients living in others' residence ($p=0.017$) reported more impaired physical functioning. Patients with younger children experienced higher levels of fatigue ($p=0.008$) and nausea/vomiting ($p=0.039$) than patients with older children. Patients who did not receive any prior antineoplastic treatment experienced more severe appetite loss ($p=0.037$) than patients who did. Patients in current antineoplastic treatment experienced more impaired physical and emotional functioning ($p=0.010$), as well as more severe nausea/vomiting ($p=0.039$), anxiety ($p=0.007$) and depression ($p<0.001$) compared with those not in treatment.

Changes in symptomatology

Table 4 shows change in the S/P scores of the EORTC QLQ-C15-PAL and HADS after 1 month of palliative care. Overall, no symptoms significantly worsened. There was significant improvement in the overall mean scores of emotional functioning ($p<0.001$), pain ($p<0.001$), sleeping difficulties ($p=0.005$), constipation ($p=0.005$) and anxiety ($p<0.001$).

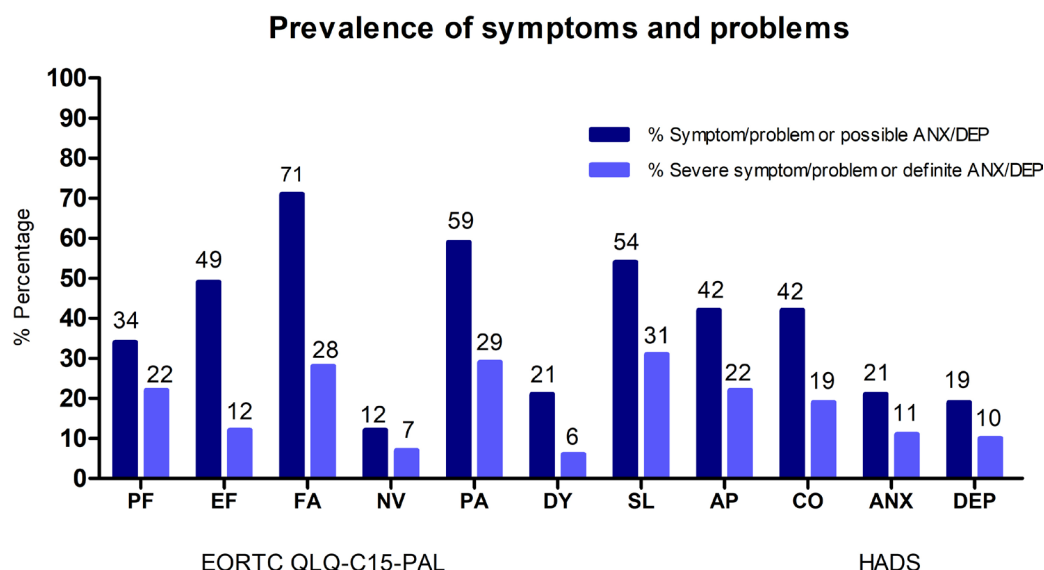


Figure 2 Prevalence of symptoms and problems in 201 patients who completed the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care (EORTC QLQ-C15-PAL) and the Hospital Anxiety and Depression Scale (HADS) at baseline. ANX, anxiety; AP, appetite loss; CO, constipation; DEP, depression; DY, dyspnoea; EF, emotional functioning; FA, fatigue; NV, nausea/vomiting; PA, pain; PF, physical functioning; SL, sleeping difficulties.

The multivariate analyses are shown in [table 5](#). For 7 of 12 scales a subgroup difference in change over time was found, that is, for physical functioning, emotional functioning, nausea/vomiting, appetite loss, quality of life, anxiety and depression. Of the seven scales, where subgroup differences in change over time were seen, two scales (emotional functioning and anxiety) also showed an overall significantly change over time ([table 4](#)). Despite the overall improvement in emotional functioning scores, emotional function deteriorated for patients living alone with children ([table 5](#)). A larger reduction in anxiety scores was observed for patients in current antineoplastic treatment compared with those who were not receiving antineoplastic treatment.

For the remaining five scales with significantly different changes over time between subgroups, that is, physical functioning, nausea/vomiting, appetite loss, quality of life and depression, no significant overall change over time was seen. Diagnosis was associated with change in appetite loss scores: patients with gallbladder and prostate cancer improved compared with other diagnoses ([table 5](#)). A reduction in nausea/vomiting scores was seen for patients living in a private residence compared with those living in others' residence, and for patients living with others compared with the remaining cohabitation categories. A negative change in QOL scores was seen for patients living in others' residence compared with those who lived in their private residence. A more positive change in physical functioning and depression scores was observed for patients in current antineoplastic treatment compared with those not in antineoplastic treatment.

DISCUSSION

In this longitudinal study we obtained a high consent rate of 80% (201/250 patients). Although the difficulties of conducting a longitudinal study with patients with advanced cancer experiencing mental and physical deterioration are well known, we had a good retention of patients, as 88% of 201 patients who answered the questionnaires at baseline completed the study after 1 month. This retention is higher compared with what was observed in some previous studies, where 59%–65% of patients completed a second symptom assessment after 1 month in palliative care.^{3 4}

Our main findings were that patients reported moderate-to-severe levels of symptoms at admittance to palliative care in Chile. Importantly, emotional functioning, pain, sleeping difficulties, constipation and anxiety improved significantly after the first month of palliative care. Moreover, residence, cohabitation status, diagnosis and current antineoplastic treatment were associated with changes in S/P scores.

At admittance to palliative care, we found that fatigue, pain and sleeping difficulties were the most prevalent S/Ps and had the highest mean scores. An earlier study in Chile also found that fatigue (83%) and pain (69%) were among the most prevalent symptoms reported in the FACT-G by 77 patients admitted to a single palliative care service.²¹ In previous studies from Europe and Northern America, fatigue and pain have also been reported among the most prevalent S/Ps by outpatients in palliative care, whereas sleeping difficulties was not.^{22–24}

In the current study, the prevalence of definite anxiety (11%) and definite depression (10%) reported on HADS (score ≥ 11), were lower compared with

Table 2 Prevalence and severity of symptoms and problems reported by 201 patients using the WISP instrument at baseline

Symptoms/problems categories	Symptoms/problems reported on WISP							
	Prevalence		Severity					
			A little		Quite a bit		Very much	
	N	%	N	%	N	%	N	%
Pain*	12	6	3	25	3	25	6	50
Cough	11	5.5	5	45.5	4	36.4	2	18.2
Bloating	7	3.5	2	28.6	2	28.6	3	42.9
Diarrhoea	5	2.5	2	40	0	0	3	60
Hearing problems	4	2	1	25	1	25	2	50
Shakiness	4	2	2	50	2	50	0	0
Itching	4	2	0	0	1	25	3	75
Impaired emotional function*	4	2	1	25	2	50	1	25
Impaired physical function*	3	1.5	0	0	2	66.7	1	33.3
Incontinence†	3	1.5	1	33.3	1	33.3	1	33.3
Oedema	3	1.5	2	66.7	0	0	1	33.3
Weight loss	3	1.5	0	0	1	33.3	2	66.7
Hiccup	2	1	0	0	1	50	1	50
Sore mouth	2	1	2	100	0	0	0	0
Vision problems	2	1	1	50	1	50	0	0
Burning sensation	2	1	0	0	1	50	1	50
Skin problems	2	1	1	50	1	50	0	0
Sweats	2	1	0	0	0	0	2	100
Sleeping difficulties*	1	0.5	0	0	0	0	1	100
Nausea*	1	0.5	0	0	1	100	0	0
Vomiting	1	0.5	0	0	1	100	0	0
Hypersalivation	1	0.5	1	100	0	0	0	0
Bleeding	1	0.5	0	0	0	0	1	100

*Symptoms and problems already covered by the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care, for example, pain reported in a specific location was classified as 'pain'.

†Including urinary, faecal and unspecified incontinence.

WISP, Write In three Symptoms/Problems.

what was found in earlier studies with outpatients with advanced cancer, where the prevalence of definite anxiety ranged from 15% to 35%, and the prevalence of definite depression ranged from 11% to 24%.^{25–27} Chilean patients in palliative care may report lower prevalence of definite depression and anxiety because they were recently diagnosed with advanced cancer, and perhaps they were not fully aware of their prognosis and complications, especially if they were new patients who have been detected end-stage cancer and never received any prior antineoplastic treatment (about 52% of our study population). According to the Chilean Ministry of Health, patients must be admitted to palliative care and receive treatment no later than five working days from their diagnosis of advanced cancer.¹¹

Concerning the WISP instrument, patients reported 18 additional S/Ps not covered by the EORTC QLQ-C15-PAL at baseline. Most of these S/Ps were also voluntarily reported on an open-ended question in the only two studies we have identified using this approach in similar populations.^{28 29} The most prevalent additional

S/Ps reported in our study were cough (reported by 5.5% of the participants), bloating (3.5%) and diarrhoea (2.5%); our prevalences were similar to those reported by 200 patients using an open-ended question in the study by Homsí *et al*²⁹ and slightly higher compared with the prevalence of cough (1.6%), diarrhoea (1.4%) and bloating (0.4%) reported in a previous study using WISP in 5447 patients admitted to specialist palliative care in Denmark.¹⁶ In line with the symptom severity reported on WISP in Denmark,¹⁶ 70% of the additional S/Ps reported on WISP in our study were moderate to severe, confirming that patients voluntarily report symptoms when they are perceived as severe.^{29 30} This stresses the relevance of supplementing brief, standardised instruments such as EORTC QLQ-C15-PAL with WISP for an exhaustive symptom assessment.

In the present study, the levels of symptoms found for fatigue, pain and sleeping difficulties were lower compared with what was found in previous European studies using the EORTC QLQ-C15-PAL or the EORTC QLQ-C30 questionnaires at the start of

Table 3 Symptoms, problems and overall quality of life at baseline in relation to sociodemographic and clinical characteristics from 201 patients

	EORTC QLQ-C15-PAL						HADS					
	PF mean (SD)	EF mean (SD)	FA mean (SD)	NV mean (SD)	PA mean (SD)	DY mean (SD)	SL mean (SD)	AP mean (SD)	CO mean (SD)	QOL mean (SD)	ANX mean (SD)	DEP mean (SD)
All	70 (30)	70 (30)	41 (31)	12 (26)	39 (33)	9 (20)	32 (35)	26 (36)	23 (31)	68 (24)	4.9 (3.9)	4.5 (3.9)
Sex												
Men	73 (29)	71 (31)	36 (31)*	10 (25)	37 (32)	7 (17)	30 (35)	23 (34)	21 (29)	69 (23)	4.6 (3.9)	4.3 (3.6)
Women	68 (31)	68 (30)	46 (31)	14 (28)	42 (34)	12 (23)	34 (35)	29 (37)	24 (34)	68 (25)	5.3 (3.9)	4.7 (4.2)
Age												
<65 years	69 (30)	69 (32)	43 (31)	14 (26)*	41 (32)	13 (22)*	38 (34)*	26 (36)	27 (34)	65 (25)	5 (3.8)	4.6 (4.1)
≥65 years	72 (30)	70 (29)	40 (31)	11 (27)	38 (34)	7 (18)	27 (35)	26 (36)	19 (29)	71 (23)	4.9 (4)	4.4 (3.8)
Civil status												
Single	65 (30)*	73 (29)	41 (30)	11 (25)	44 (34)	11 (22)	32 (36)	26 (36)	24 (33)	69 (22)	4.7 (3.7)	4.3 (3.8)
Married/cohabiting	75 (29)	67 (32)	41 (33)	13 (28)	36 (31)	8 (19)	32 (35)	25 (36)	22 (30)	68 (25)	5.1 (4.1)	4.6 (4)
Residence												
Private residence	73 (29)*	69 (32)	41 (32)	12 (26)	38 (34)	8 (20)	33 (36)	27 (36)	22 (31)	68 (25)	5.1 (4.2)	4.5 (4)
Others' residence	64 (30)	70 (26)	40 (28)	13 (27)	41 (30)	12 (19)	29 (32)	22 (35)	25 (31)	69 (20)	4.4 (2.8)	4.3 (3.7)
Cohabitation status												
Living alone	74 (29)	63 (42)	40 (33)	6 (8)	32 (40)	9 (22)	30 (43)	27 (33)	9 (22)	71 (21)	4.7 (4.5)	3.7 (2.7)
Living with partner	77 (28)	65 (32)	45 (33)	16 (31)	33 (30)	8 (20)	35 (38)	30 (34)	20 (29)	67 (26)	5.4 (4.4)	4.3 (3.6)
Living alone with children	67 (29)	78 (26)	37 (27)	8 (23)	44 (34)	7 (17)	26 (34)	27 (38)	27 (33)	68 (20)	4.7 (3.7)	4.3 (3.7)
Living with others	66 (29)	70 (29)	37 (32)	15 (30)	41 (32)	13 (24)	33 (35)	20 (34)	25 (35)	71 (24)	4.5 (3.3)	4 (3.7)
Living with partner and children	71 (32)	67 (31)	43 (32)	11 (24)	41 (34)	9 (18)	32 (33)	26 (38)	22 (31)	68 (25)	5 (4)	5.3 (4.6)
Children												
No children	72 (30)	74 (32)	30 (24)†	8 (18)†	37 (31)	12 (19)	30 (36)	18 (32)	20 (28)	73 (19)	4 (3)	3.9 (3.2)
Children, at least one younger than 18 years	61 (34)	66 (34)	60 (33)	25 (37)	50 (35)	14 (24)	43 (40)	38 (43)	33 (35)	61 (28)	6.3 (5.4)	4.8 (4.7)
Children, all at least 18 years old	72 (29)	69 (30)	39 (31)	11 (25)	38 (33)	8 (20)	30 (34)	25 (35)	21 (30)	69 (24)	4.8 (3.7)	4.5 (3.9)
Education												
Primary education	73 (29)	66 (30)	40 (30)	13 (28)	39 (32)	10 (23)	36 (37)	27 (38)	19 (32)	71 (24)	5.4 (4)	4.7 (4)
Secondary education	67 (30)	74 (29)	40 (31)	12 (26)	43 (31)	8 (16)	30 (33)	26 (34)	24 (28)	68 (23)	4.6 (3.8)	4.3 (3.7)
Higher education	74 (30)	70 (33)	43 (35)	10 (22)	33 (37)	13 (20)	25 (33)	22 (35)	30 (36)	61 (25)	4.3 (3.8)	4.4 (4.1)
Diagnosis												
Stomach	75 (28)	73 (30)	41 (28)	14 (33)	38 (34)	9 (26)	35 (38)	31 (34)	35 (36)	59 (27)	4.4 (3.6)	4.6 (3.7)
Colorectal	75 (25)	70 (30)	36 (30)	12 (28)	29 (26)	7 (17)	26 (28)	19 (35)	29 (35)	65 (25)	5.1 (3.6)	4 (3.7)
Breast	67 (34)	69 (35)	50 (34)	9 (18)	15 (41)	16 (25)	32 (34)	30 (39)	19 (31)	66 (27)	5 (3.9)	4.2 (3.9)
Lung	66 (34)	74 (30)	29 (28)	8 (24)	33 (30)	11 (16)	15 (29)	20 (36)	17 (24)	74 (29)	5.2 (4.2)	5.2 (4.6)
Prostate	73 (31)	65 (31)	30 (36)	6 (13)	32 (36)	2 (8)	26 (41)	28 (43)	15 (29)	74 (21)	5.3 (3.8)	4.1 (3.1)
Gallbladder	82 (22)	68 (36)	43 (33)	11 (30)	32 (31)	12 (22)	33 (30)	42 (45)	18 (23)	77 (17)	3.6 (3.1)	2.6 (2.5)
Other cancer	68 (31)	70 (29)	44 (31)	15 (28)	43 (32)	10 (20)	37 (36)	23 (33)	22 (31)	69 (21)	5 (4.2)	4.8 (4.3)

Continued

Table 3 Continued

	EORTC QLQ-C15-PAL						HADS					
	PF mean (SD)	EF mean (SD)	FA mean (SD)	NV mean (SD)	PA mean (SD)	DY mean (SD)	SL mean (SD)	AP mean (SD)	CO mean (SD)	QOL mean (SD)	ANX mean (SD)	DEP mean (SD)
Any prior antineoplastic treatment												
Yes	73 (29)	71 (32)	39 (30)	12 (26)	39 (33)	9 (18)	32 (34)	22 (36)*	20 (30)	69 (23)	4.8 (4)	3.8 (3.2)
No	68 (30)	68 (29)	42 (33)	13 (27)	40 (32)	10 (22)	31 (36)	29 (36)	25 (33)	68 (25)	5 (3.8)	5.1 (4.4)
Current antineoplastic treatment												
Yes	53 (25)*	53 (23)*	55 (30)	20 (29)*	43 (26)	22 (33)	39 (28)	36 (33)	39 (37)	57 (22)	7.2 (2.8)*	8 (3.1)*
No	71 (30)	71 (31)	40 (31)	12 (26)	39 (33)	9 (19)	31 (35)	25 (36)	22 (31)	69 (24)	4.8 (3.9)	4.3 (3.9)
Hospital												
Sotero del Rio	74 (29)	73 (28)	37 (31)	11 (25)	37 (32)	11 (21)	27 (32)	21 (32)	21 (29)	68 (24)	4.1 (3)	4 (4)
San Juan de Dios	69 (29)	71 (29)	42 (30)	42 (30)	15 (30)	7 (21)	34 (39)	30 (41)	21 (32)	70 (22)	5.4 (4.3)	4.9 (3.8)
Salvador	66 (32)	60 (37)	49 (33)	49 (33)	13 (26)	10 (15)	41 (38)	34 (39)	27 (35)	64 (23)	5.9 (4.4)	4.4 (3.6)
Felix Bulnes Cerda	64 (27)	66 (28)	41 (33)	41 (33)	11 (24)	8 (21)	37 (34)	22 (33)	30 (34)	72 (29)	5.9 (4.9)	5.8 (4.2)

*Mann-Whitney U test.

†Kruskal-Wallis test $p < 0.05$.

ANX, anxiety; AP, appetite loss; CO, constipation; DEP, depression; DY, dyspnoea; EF, emotional functioning; EORTC QLQ-C15-PAL, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care; FA, fatigue; HADS, Hospital Anxiety and Depression Scale; NV, nausea/vomiting; PA, pain; PF, physical functioning; QOL, quality of life; SL, sleeping difficulties.

palliative care,^{3-5 20 27 31} but similar to one Canadian study.² Some explanations of the better S/P mean scores in this study may be that patients had a better physical function than reported in previous studies,^{3-5 20 27 31} where outpatients had a good performance status (KPS range 50–100; median 90). This may reflect that some of the sickest patients were not included in this study, perhaps because they were not referred to palliative care, for example, only 62 (16%) of the 394 patients admitted to the four palliative care services had a lower KPS (< 50). Another explanation could be that Chilean patients are on average referred earlier to palliative care compared with patients in other countries.

During the first month of palliative care, we observed significant improvement in emotional functioning, pain, sleeping difficulties, constipation and anxiety. This is encouraging as it shows that, despite being in an advanced stage of their disease, and thus expected to get worse, the symptomatology of these Chilean patients improved following the initiation of palliative care. In agreement with our results, several studies from other parts of the world have found that pain, sleeping difficulties, emotional functioning and constipation improved significantly after 2–4 weeks of palliative care.³⁻⁶ In addition, two previous studies, one conducted in Italy using ESAS (The Edmonton Symptom Assessment Scale)³² and the other in Denmark using HADS,⁴ showed a significant reduction of anxiety after the first week of palliative care.

In this study, a negative change in nausea/vomiting and QOL scores was seen for patients living in others' residence compared with those who lived in their private residence. Perhaps this reflects that these patients received less help, for example, from their closest family, since some of them at the time of the study lived in nursing homes. While patients overall improved in emotional functioning during the first month of palliative care, patients living alone with children deteriorated. This may indicate that single parents are a particularly vulnerable group whose concerns, for example, about the future of their children, may increase even if they are admitted to palliative care. Furthermore, the worst baseline scores in anxiety, depression and physical functioning were observed in patients receiving current antineoplastic treatment compared with those not in treatment, which may explain why these patients had a positive change in these S/Ps, since it has been shown that symptoms with the highest baseline scores are more likely to have the greatest improvement.^{32 33}

Relatively few studies have investigated how patient characteristics were associated with changes in S/P scores following the initiation of palliative care, and found that female gender and older age were associated with symptom improvement,⁷⁻⁹ which differs from our results where sex and age were not significantly associated with change in the level of S/Ps.

Table 4 Change in symptoms, problems and overall quality of life from baseline to follow-up in relation to sociodemographic and clinical characteristics from 177 patients who completed the study

	N	Δ EORTC QLQ-C15-PAL *										Δ HADS		
		PF	EF	FA	NV	PA	DY	SL	AP	CO	QOL	ANX	DEP	
All	177	2	8+	-4	-1	-11+	-3	-9+	-5	-8+	-1	-2+	0	
Sex														
Men	92	2	11	-3	2	-10	0	-9	-2	-6	-3	-1	0	
Women	85	2	8	-6	-5	-12	-5	-9	-8	-9	0	-1	0	
Age														
<65 years	75	5	10	-5	1	-12	-4	-16	-3	-11	0	-2	0	
≥65 years	102	0	8	-4	-2	-10	-2	-3	-5	-5	-2	-2	0	
Civil status														
Single	75	4	3	-2	1	-15	-6	-5	-4	-8	-2	0	0	
Married/cohabiting	102	1	13	-6	-2	-8	0	-12	-5	-8	1	-2	-1	
Residence														
Private residence	130	0	11	-6	-3	-9	-2	-10	-7	-7	1	-1	0	
Others' residence	47	6	4	-2	4	-15	-5	-6	4	-10	-8	-1	0	
Cohabitation status														
Living alone	10	10	19	-5	1	2	-7	0	6	3	0	-1	0	
Living with partner	39	5	18	-15	-2	-10	-2	-23	-11	-10	0	-1	0	
Living alone with children	34	-3	-9	5	6	-15	-2	-1	-7	-7	-2	0	0	
Living with others	40	5	11	-4	-8	-15	-5	-10	-1	-16	-6	-2	0	
Living with partner and children	54	-2	9	-3	0	-9	0	-5	-2	-3	2	-1	-1	
Children														
No children	18	7	6	-2	-1	-13	-9	-8	0	-9	-4	-1	1	
Children, at least one younger than 18 years	19	3	9	-15	-7	-15	-2	-12	0	-16	-2	-3	-1	
Children, all at least 18	140	1	9	-3	0	-10	-2	-9	-6	-6	-1	-2	0	
Education														
Primary education	83	0	12	-5	-6	-12	-5	-17	-7	-4	0	-2	0	
Secondary education	65	5	4	-4	5	-19	1	-1	-4	-9	-3	-1	0	
Higher education	29	1	11	-5	2	-8	-4	-3	0	-14	4	-1	0	
Diagnosis														
Stomach	20	-5	8	5	10	-6	-2	-14	10	-15	7	0	0	
Colorectal	22	8	18	-6	1	-8	-2	-11	5	-19	6	-2	-1	
Breast	16	2	21	-20	-2	-33	2	-19	-11	0	7	-2	-1	
Lung	19	15	9	0	1	-11	-5	0	-4	6	-3	-1	-1	
Prostate	18	7	13	2	0	-15	0	-11	-20	0	-2	-2	-1	
Gallbladder	10	-9	16	-17	-7	-3	-13	-10	-37	-13	-5	0	0	

Continued

Table 4 Continued

	N	Δ EORTC QLQ-C15-PAL *										Δ HADS		
		PF	EF	FA	NV	PA	DY	SL	AP	CO	QOL	ANX	DEP	
Other cancer	72	-1	1	-4	-4	-7	-4	-5	-1	-8	-6	-1	1	
Any prior antineoplastic treatment														
Yes	90	4	7	-8	-2	-10	-2	-10	-4	-4	-2	-1	-1	
No	87	0	11	-2	1	-13	-3	-8	-5	-11	1	-2	-1	
Current antineoplastic treatment														
Yes	11	19	23	-12	-3	-10	-15	-27	-15	-18	-1	-4	-3	
No	166	1	7	-5	0	-10	-2	-8	-4	-7	-1	-2	0	
Hospital														
Sotero del Rio	85	2	5	-3	2	-11	-4	-6	3	-6	-1	-1	-1	
San Juan de Dios	44	-2	4	-2	-1	-13	-2	-5	-6	-4	4	-3	0	
Salvador	30	6	25	-17	-7	-10	-2	-19	-14	-17	-2	-3	-1	
Felix Bulnes Cerda	18	6	5	3	-1	-3	-3	-13	-15	-9	-10	-1	-1	
Δ=score at follow-up - score at baseline.														
* A positive Δ difference in the two functioning scales and overall QOL reflects improvement and a negative Δ difference reflects relief in symptom scales.														
+Wilcoxon signed-rank p<0.05.														
ANX, anxiety; AP, appetite loss; CO, constipation; DY, dyspnoea; EF, emotional functioning; EORTC QLQ-C15-PAL, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care; FA, fatigue; HADS, Hospital Anxiety and Depression Scale; NV, nausea/vomiting; PA, pain; PF, physical functioning; QOL, quality of life; SL, sleeping difficulties														

Δ=score at follow-up - score at baseline.

* A positive Δ difference in the two functioning scales and overall QOL reflects improvement and a negative Δ difference reflects relief in symptom scales.

†Wilcoxon signed-rank $p<0.05$.

Core 15 Palliative Care; FA, fatigue; HADS, Hospital Anxiety and Depression Scale; NV, nausea/vomiting; PA, pain; PF, physical functioning; QOL, quality of life; SL, sleeping difficulties.

Table 5 Significant associations between patient characteristics and changes in symptom/problem scores from baseline to follow-up obtained from multiple linear regression analyses with backwards stepwise selection

	N	EORTC QLQ-C15-PAL				HADS			
		Δ PF* (CI 95%)	Δ EF* (CI 95%)	Δ NV† (CI 95%)	Δ AP† (CI 95%)	Δ QOL* (CI 95%)	Δ ANX† (CI 95%)	Δ DEPT (CI 95%)	
Intercept		0.8	9	-1.2	4.5	1.5	-1.3	0.2	
Residence									
Others' residence	47			13.7 (3.2 to 24.3)		-9.7 (-18.7 to -0.7)			
Private residence	130			0 (ref. group)		0 (ref. group)			
Cohabitation status									
Living alone	10		10.2 (-12.7 to 33.1)	-1.3 (-19.3 to 16.7)					
Living with partner	39		9 (-5 to 23)	-1.8 (-12.8 to 9.3)					
Living alone with children	34		-17.8 (-32.3 to -3.2)	3.4 (-8.1 to 14.9)					
Living with others	40		2.3 (-11.6 to 16.2)	-16 (-28.3 to -3.7)					
Living with partner and children	54		0 (ref. group)	0 (ref. group)					
Diagnosis									
Stomach	20				10.9 (-6.6 to 28.4)				
Colorectal	22				5.5 (-11.5 to 22.4)				
Breast	16				-9.6 (-27.5 to 8.3)				
Lung	19				-3.2 (-22.4 to 16)				
Prostate	18				-19.4 (-37.8 to -1.1)				
Gallbladder	10				-35.7 (-59.2 to -12.2)				
Other cancer	72				0 (ref. group)				
Current antineoplastic treatment									
Yes	11	18.6 (0.1 to 37.1)					-2.7 (-5.1 to -0.3)	-2.9 (-5.4 to -0.4)	
No	166	0 (ref. group)					0 (ref. group)	0 (ref. group)	

Only the seven scales for which subgroup differences were found are shown.
Δ=score at follow-up - score at baseline.
Age, sex, civil status, children, education, prior antineoplastic treatment and hospital were not significantly associated with any of the outcomes and therefore not shown. No patient characteristics were significantly associated with pain, fatigue, dyspnoea, sleeping difficulties and constipation, and thus these outcomes are not shown.
* A positive value reflects improvement in the two functioning scales and overall QOL from baseline to follow-up compared with the reference group.
† A negative value reflects symptom relief in the symptom scales from baseline to follow-up compared with the reference group. Significant association between patient characteristics and outcomes p<0.05.
ANX, anxiety; AP, appetite loss; CI, confidence intervals; DEP, depression; EF, emotional functioning; EORTC QLQ-C15-PAL, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 15 Palliative Care; HADS, Hospital Anxiety and Depression Scale; NV, nausea/vomiting; PF, physical functioning; QOL, quality of life; ref., reference.

Strengths of this study include that it is the first to investigate S/Ps and QOL at the start of palliative care and over time among patients receiving palliative care in Chile, thus providing new knowledge of their symptomatology. Furthermore, patients' symptomatology was systematically measured by PRO questionnaires such as the EORTC QLQ-C15-PAL and HADS, which are instruments widely used in palliative care³⁴ and also validated in the Chilean population,^{35 36} and that we combined these instruments with the WISP.

A limitation of the study was the small sample size, restricting the possibility to perform comparisons of the symptomatology between hospitals. Due to the large number of analyses performed on the association between different variables and symptomatology, some of the significant associations found in this study may have occurred by chance. Additionally, it was not possible to include patients from other types of services than outpatients, because most of the palliative care services did not have an inpatient unit and palliative home care was provided by other services/teams.

In future research, it would be relevant to include more patients and palliative care services to get a broader overview of the current symptomatology of patients receiving palliative care in Chile. It would also be relevant to compare the symptomatology of patients receiving or not antineoplastic treatment and to study patients with other life-threatening diagnoses than cancer.

CONCLUSIONS

In this longitudinal study conducted in four Chilean palliative care services, patients reported moderate-to-severe levels of S/Ps at admittance to palliative care. The high performance status observed raises the important question of whether the most severely ill patients were less likely to be referred to palliative care. This should be further investigated. Emotional functioning, pain, sleeping difficulties, constipation and anxiety improved significantly during the first month of palliative care. Several sociodemographic and clinical variables were associated with changes in S/P scores. This information on patients' symptomatology may guide clinicians to more effective interventions that can improve the quality of life of patients receiving palliative care.

Acknowledgements We are very grateful to all the patients who participated in this study and willingly filled in the questionnaires. We would like to thank Dr María Angélica Becerra, Dr Daniel Leiva, Dr Rodrigo Fernández and Dr Magaly Sacta for their support to conducting this study in their palliative care services. The invaluable collaboration in the data collection of the psychologists Pedro Rojas and Scarlett Cisternas is highly appreciated.

Contributors All authors made substantial contributions to the design, analysis of data, critical revision and approved the publication, participating sufficiently to take responsibility for the content of this article.

Funding This study was supported by 'Becas-Chile Scholarship' from the Advanced Human Capital Program of the National Commission for Scientific and Technological Research-CONICYT. The scholarship was used for salary to the first author of this paper (LR-C).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Study approval was obtained from two Chilean local ethics committees: Comité de Ética Científico Adultos Servicio de Salud Metropolitano Oriente ID-CECSSMO27122016, Comité Ético Científico Servicio de Salud Metropolitano Sur Oriente ID-CECSSMSO17082017 (names in Spanish). Written informed consent for participation was obtained from all patients involved in this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The data utilised in this study are available through the first author at the Palliative Care Research Unit, Department of Geriatrics and Palliative Medicine, Bispebjerg Hospital, University of Copenhagen. Restrictions apply to the availability of these data.

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REFERENCES

- 1 Kaasa S, Loge JH. Quality of life in palliative care: principles and practice. *Palliat Med* 2003;17:11–20.
- 2 Bedard G, Zeng L, Zhang L, *et al.* Minimal important differences in the EORTC QLQ-C15-PAL to determine meaningful change in palliative advanced cancer patients. *Asia Pac J Clin Oncol* 2016;12:e38–46.
- 3 Arraras JL, de la Vega FA, Asin G, *et al.* The EORTC QLQ-C15-PAL questionnaire: validation study for Spanish bone metastases patients. *Qual Life Res* 2014;23:849–55.
- 4 Strömberg AS, Sjogren P, Goldschmidt D, *et al.* A longitudinal study of palliative care: patient-evaluated outcome and impact of attrition. *Cancer* 2005;103:1747–55.
- 5 Kyriaki M, Eleni T, Efi P, *et al.* The EORTC core quality of life questionnaire (QLQ-C30, version 3.0) in terminally ill cancer patients under palliative care: validity and reliability in a Hellenic sample. *Int J Cancer* 2001;94:135–9.
- 6 Lam K, Chow E, Zhang L, *et al.* Determinants of quality of life in advanced cancer patients with bone metastases undergoing palliative radiation treatment. *Support Care Cancer* 2013;21:3021–30.
- 7 Zimmermann C, Burman D, Follwell M, *et al.* Predictors of symptom severity and response in patients with metastatic cancer. *Am J Hosp Palliat Care* 2010;27:175–81.
- 8 Yennurajalingam S, Urbauer DL, Casper KLB, *et al.* Impact of a palliative care consultation team on cancer-related symptoms in advanced cancer patients referred to an outpatient supportive care clinic. *J Pain Symptom Manage* 2011;41:49–56.
- 9 Tai S-Y, Lee C-Y, Wu C-Y, *et al.* Symptom severity of patients with advanced cancer in palliative care unit: longitudinal assessments of symptoms improvement. *BMC Palliat Care* 2016;15:32.
- 10 Ministerio de Salud, Chile. *Redes de atención GES Y no GES 2019: División de Gestión de la red Asistencial, Subsecretaría de Redes Asistenciales*, 2019: 1–180.
- 11 Ministerio de Salud, Chile. *Guía clínica AUGÉ "Alivio del Dolor por cáncer avanzado y Cuidados Paliativos". Series Guías Clínicas MINSAL*, 2011: Subsecretaría de Salud Pública,

- División de Prevención y Control de Enfermedades, Secretaría Técnica AUGÉ*, 2011: 4–66.
- 12 Jimenez de la Jara J, Bastias G, Ferreccio C, *et al*. A snapshot of cancer in Chile: analytical frameworks for developing a cancer policy. *Biol Res* 2015;48:10.
 - 13 Ministerio de Salud, Chile. *Informe técnico 2013-2014: Programa Nacional Alivio del Dolor Y Cuidados Paliativos: Subsecretaría de Salud Pública, División de Prevención Y control de Enfermedades, Departamento de Manejo integral de Cáncer Y Otros Tumores*, 2014: 3–47.
 - 14 Yates JW, Chalmer B, McKegney FP. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer* 1980;45:2220–4.
 - 15 Groenvold M, Petersen MA, Aaronson NK, *et al*. The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. *Eur J Cancer* 2006;42:55–64.
 - 16 Rojas-Concha L, Hansen MB, Petersen MA, *et al*. Which symptoms and problems do advanced cancer patients admitted to specialized palliative care report in addition to those included in the EORTC QLQ-C15-PAL? A register-based national study. *Support Care Cancer* 2020;28:1725–35.
 - 17 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361–70.
 - 18 Groenvold M, Petersen MA. *Addendum to the EORTC QLQ-C30 scoring manual: scoring of the EORTC QLQ-C15-PAL*, 2006.
 - 19 Johnsen AT, Petersen MA, Pedersen L, *et al*. Symptoms and problems in a nationally representative sample of advanced cancer patients. *Palliat Med* 2009;23:491–501.
 - 20 Hansen MB, Ross L, Petersen MA, *et al*. Age, cancer site and gender associations with symptoms and problems in specialised palliative care: a large, nationwide, register-based study. *BMJ Support Palliat Care* 2022;12:e201–10.
 - 21 Fonseca C M, Schlack V C, Mera M E, *et al*. Evaluación de la calidad de vida en pacientes Con cáncer terminal. *Rev Chil Cir* 2013;65:321–8.
 - 22 Ventafridda V, De Conno F, Ripamonti C, *et al*. Quality-Of-Life assessment during a palliative care programme. *Ann Oncol* 1990;1:415–20.
 - 23 Potter J, Hami F, Bryan T, *et al*. Symptoms in 400 patients referred to palliative care services: prevalence and patterns. *Palliat Med* 2003;17:310–4.
 - 24 Kang JH, Kwon JH, Hui D, *et al*. Changes in symptom intensity among cancer patients receiving outpatient palliative care. *J Pain Symptom Manage* 2013;46:652–60.
 - 25 Hopwood P, Howell A, Maguire P. Screening for psychiatric morbidity in patients with advanced breast cancer: validation of two self-report questionnaires. *Br J Cancer* 1991;64:353–6.
 - 26 Akechi T, Okuyama T, Sugawara Y, *et al*. Screening for depression in terminally ill cancer patients in Japan. *J Pain Symptom Manage* 2006;31:5–12.
 - 27 Strömberg AS, Goldschmidt D, Groenvold M, *et al*. Self-Assessment in cancer patients referred to palliative care: a study of feasibility and symptom epidemiology. *Cancer* 2002;94:512–20.
 - 28 Alsirafy SA, Abd El-Aal HH, Farag DE, *et al*. High symptom burden among patients with newly diagnosed incurable cancer in a developing country. *J Pain Symptom Manage* 2016;51:e1–5.
 - 29 Homsi J, Walsh D, Rivera N, *et al*. Symptom evaluation in palliative medicine: patient report vs systematic assessment. *Support Care Cancer* 2006;14:444–53.
 - 30 Alsirafy SA, Al-Alimi KA, Thabet SM, *et al*. Voluntary reporting to assess symptom burden among Yemeni cancer patients: common symptoms are frequently missed. *J Community Support Oncol* 2016;14:117–21.
 - 31 Leppert W, Majkiewicz M. Validation of the Polish version of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 15 - Palliative Care in patients with advanced cancer. *Palliat Med* 2013;27:470–7.
 - 32 Modonesi C, Scarpi E, Maltoni M, *et al*. Impact of palliative care unit admission on symptom control evaluated by the Edmonton symptom assessment system. *J Pain Symptom Manage* 2005;30:367–73.
 - 33 Lund Rasmussen C, Johnsen AT, Petersen MA, *et al*. Change in health-related quality of life over 1 month in cancer patients with high initial levels of symptoms and problems. *Qual Life Res* 2016;25:2669–74.
 - 34 Stiel S, Pastrana T, Balzer C, *et al*. Outcome assessment instruments in palliative and hospice care—a review of the literature. *Support Care Cancer* 2012;20:2879–93.
 - 35 Rojas-Concha L, Hansen MB, Petersen MA. Content validation of the EORTC QLQ-C15-PAL with advanced cancer patients and health care professionals from palliative care services in Chile. *BMC Palliat Care* 2020;19:1–10.
 - 36 Villoria E, Lara L. Assessment of the hospital anxiety and depression scale for cancer patients. *Rev Med Chil* 2018;146:300–7.