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ORIGINAL REPORT

Trajectory of Performance Status and Symptom Scores for Patients With Cancer During the Last Six Months of Life

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ABSTRACT

Purpose
Ontario's cancer system is unique because it has implemented two standardized assessment tools population-wide to improve care: the Edmonton Symptom Assessment System (ESAS) measures severity of nine symptoms (scale 0 to 10; 10 indicates the worst) and the Palliative Performance Scale (PPS) measures performance status (scale 0 to 100; 0 indicates death). This article describes the trajectory of ESAS and PPS scores 6 months before death.

Patients and Methods
Observational cohort study of cancer decedents between 2007 and 2009. Decedents required ≥1 ESAS or PPS assessment in the 6 months before death for inclusion. Outcomes were the decedents' average ESAS and PPS scores per week before death.

Results
Ten thousand seven hundred fifty-two (ESAS) and 7,882 (PPS) decedents were included. The mean age was 65 years, half were female, and approximately 75% of assessments occurred in cancer clinics. Average PPS score declined slowly over the 6 months before death, starting at approximately 70 and ending at 40, declining more rapidly in the last month. For ESAS symptoms, average pain, nausea, anxiety, and depression scores remained relatively stable over the 6 months. Conversely, shortness of breath, drowsiness, well-being, lack of appetite, and tiredness increased in severity over time, particularly in the month before death. More than one third of the cohort reported moderate to severe scores (ie, 4 to 10) for most symptoms in the last month of life.

Conclusion
In this large outpatient cancer population, trajectories of mean ESAS scores followed two patterns: increasing versus generally flat. The latter was perhaps due to available treatment (eg, prescriptions) for those symptoms. Future research should prioritize addressing symptoms that worsen over time.

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INTRODUCTION

Optimal cancer care requires managing symptom needs across the disease trajectory, but particularly at the end of life when symptoms often worsen. For many patients with cancer at the end of lives, however, symptom needs go unmet.[1-3] In order to improve end-of-life symptom management, providers need systematic and standardized means to identify symptom issues. Moreover, measuring functional decline can help determine when to enhance palliative care support and focus care on symptom issues and quality of life in an appropriate and timely manner.

Two tools were developed for measuring symptom problems and functional decline in palliative cancer populations: the Edmonton Symptom Assessment System (ESAS)[4] and the Palliative Performance Scale (PPS).[5] The ESAS is a patient-reported, validated, and reliable tool[6-8] to measure symptom severity and is widely used in palliative cancer populations. The PPS, a modification of the Karnofsky performance scale,[9] is a provider-reported, validated tool for assessing the performance status of a patient in a palliative population.[10-14] Previous studies of ESAS[15-20] and PPS[11,21-24] were limited by a focus on palliative inpatient populations, cross-sectional analysis of scores, and small sample sizes. There is a dearth of information on longitudinal symptom and performance scores before death, which would aid in understanding the changing burden of symptoms at the end of life. Moreover, to be relevant to oncologists practicing in a typical cancer clinic, research is needed on large samples of outpatient cancer populations and not limited to only those identified as at

end of life or admitted to an inpatient hospice facility. In the United States, only 38.5% of deaths occurred under the care of a hospice program; of those only 38.3% were patients with cancer.[25]

Since 2007, all cancer centers in Ontario, Canada, including some homecare providers, have systematically collected ESAS and PPS scores in outpatients with cancer.[26] The resulting database contains a province-wide outpatient cancer cohort with an unparalleled number of observations containing symptom and functional status scores. This study's main objective is to describe the trajectory of ESAS and PPS scores in the 6 months before death. Based on previous research on PPS[11-14,20-23] and end-of-life symptoms,[15-20] we hypothesized that the average PPS score for the population would decline to the end-of-life stage (ie, 30 to 0) in the final few weeks of life and that all nine ESAS symptoms would substantially increase in severity in the final few weeks of life.

PATIENTS AND METHODS

Study Population

This longitudinal observational study examined a cohort of patients with cancer across the province of Ontario, Canada, during the study period of January 1, 2007, to March 31, 2009. Ontario is Canada's most populous province, with more than 13 million residents, and an ethnically diverse population.[27] The study was approved by the ethics committee of the Sunnybrook Health Sciences Centre and followed data confidentiality and privacy guidelines of the Institute for Clinical Evaluative Sciences.

Linking multiple administrative health care databases, we began with an initial cohort of adult patients who had a confirmed cancer diagnosis in the provincial cancer registry, a valid provincial health insurance number, and at least one ESAS or PPS assessment during the study period. We then included those patients who had a date of death within the study timeframe and had at least one ESAS or PPS assessment in the last 26 weeks before death.

To compare patients equally across time, we aligned patients' dates of death as time zero and then counted backward 26 weeks (approximately 6 months) from death or up to the date of cancer diagnosis, if shorter. For example, 1 week before death included all ESAS or PPS assessments days 1 to 7 before death, and so on. Week 0 included assessments on the same date as death only.

Patients with ESAS or PPS assessments were mostly from ambulatory cancer care and some home settings, from all regions of the province, of any cancer diagnoses, and of any adult age. Scores were reported by the patient (ESAS) or provider (PPS) during visits to the cancer center or the home. Assessments occurred on an opportunistic basis; the aim was to have assessments completed at every cancer clinic or home visit. However, in reality, estimates show that patients and providers complete assessments at half their clinic visits on average.[28]

Outcomes

The main outcome was the average assessment score (ESAS and PPS) per week closer to death. The ESAS is a patient-reported, validated, and reliable tool[6-8] to measure symptom severity and is widely used in palliative cancer populations. The nine symptoms assessed on a scale of 0 to 10 are (0 = none; 10 = worst possible): anxiety, lack of appetite, depression, drowsiness, nausea, pain, shortness of breath, tiredness, and well-being. Previous research has categorized the severity of ESAS scores as none (0), mild (1 to 3), moderate (4 to 6), and severe (7 to 10), and scores ≥ 4 were clinically significant.[26,29,30] Therefore, a priori, we chose to analyze the odds ratio of reporting a moderate to severe score (0 to 3 $v \geq 4$) for each symptom respectively, controlling for other covariates. We also report the proportion of patients reporting symptom scores ≥ 4 at each week to death.

The PPS ranges from 0 to 100 (100 = best), in 10-point increments: based on a patient's level of ambulation, activity level, evidence of disease, ability to do self-care, intake, and level of consciousness. Patients with scores in the range of 100 to 70 are considered stable, 60 to 40 are considered transitional, and 30 to 0 are considered end of life.[12]

Data Sources and Covariates

The ESAS and PPS assessment dates and scores were captured in the Symptom Management Reporting Database. Date of death, age at first assessment, sex, health insurance validity, and neighborhood income quintile (based

Table 1. Patient Characteristics of ESAS and PPS Cohort at Baseline

Characteristic	ESAS (n = 10,752) No.	ESAS (n = 10,752) %	PPS (n = 7,882) No.	PPS (n = 7,882) %
Age, years				
18-29	48	0.45	38	0.48
30-39	159	1.48	134	1.70
40-49	681	6.33	522	6.62
50-59	1,875	17.44	1,406	17.84
60-69	2,964	27.57	2,122	26.92
70-79	3,219	29.94	2,326	29.51
80-89	1,664	15.48	1,213	15.39
90-100	142	1.32	121	1.54
Sex				
Female	5,046	46.93	3,738	47.42
Male	5,706	53.07	4,144	52.58
Primary cancer type				
Lung	3,970	36.92	2,611	33.13
GI	2,531	23.54	2,045	25.95
Genitourinary	1,141	10.61	843	10.70
Breast	881	8.19	716	9.08
Gynecologic	662	6.16	442	5.61
Hematology	509	4.73	410	5.20
Head and neck	341	3.17	255	3.24
CNS	189	1.76	159	2.02
Skin	190	1.77	151	1.92
Other	139	1.29	108	1.37
Primary unknown	127	1.18	93	1.18
Sarcoma	72	0.67	49	0.62
Charlson score				
1+	2,259	21.01	1,678	21.29
0	8,493	78.99	6,204	78.71
Income quintile				
1	2,093	19.52	1,531	19.49
2	2,294	21.39	1,631	20.76
3	2,139	19.95	1,591	20.25
4	2,153	20.08	1,559	19.84
5	2,045	19.07	1,544	19.65
No. of assessments in the last 6 months				
1	3,873	36.02	3,062	38.85
2	1,901	17.68	1,341	17.01
3	1,153	10.72	787	9.98
4	802	7.46	605	7.68
5	570	5.30	369	4.68
6	388	3.61	262	3.32
7	323	3.00	227	2.88
8	221	2.06	163	2.07
9	171	1.59	120	1.52
10+	1,350	12.56	946	12.00
Assessment location				
Cancer center clinic	8,848	82.29	5,744	72.87
Home	1,904	17.71	2,138	27.13

Abbreviations: ESAS, Edmonton Symptom Assessment System; PPS, Palliative Performance Scale.

on postal code linkage)[31] were determined using the Registered Persons Database.[32] Cancer type and diagnosis date was captured using the Ontario Cancer Registry, a population-based cancer registry[33] that captures an estimated 64% of Ontario's patients with cancer (B. Li, personal communication, August 2010). Comorbidity was calculated for the 12 months before first assessment using the Deyo-modification of the Charlson score[34] based on diagnoses coded in the Canadian Institute for Health Information's Discharge Abstract Database.[35] Finally, the number of cancer center visits were determined using the National Ambulatory Care Reporting System, which contains all visits made by patients with a valid provincial health insurance card number. Data

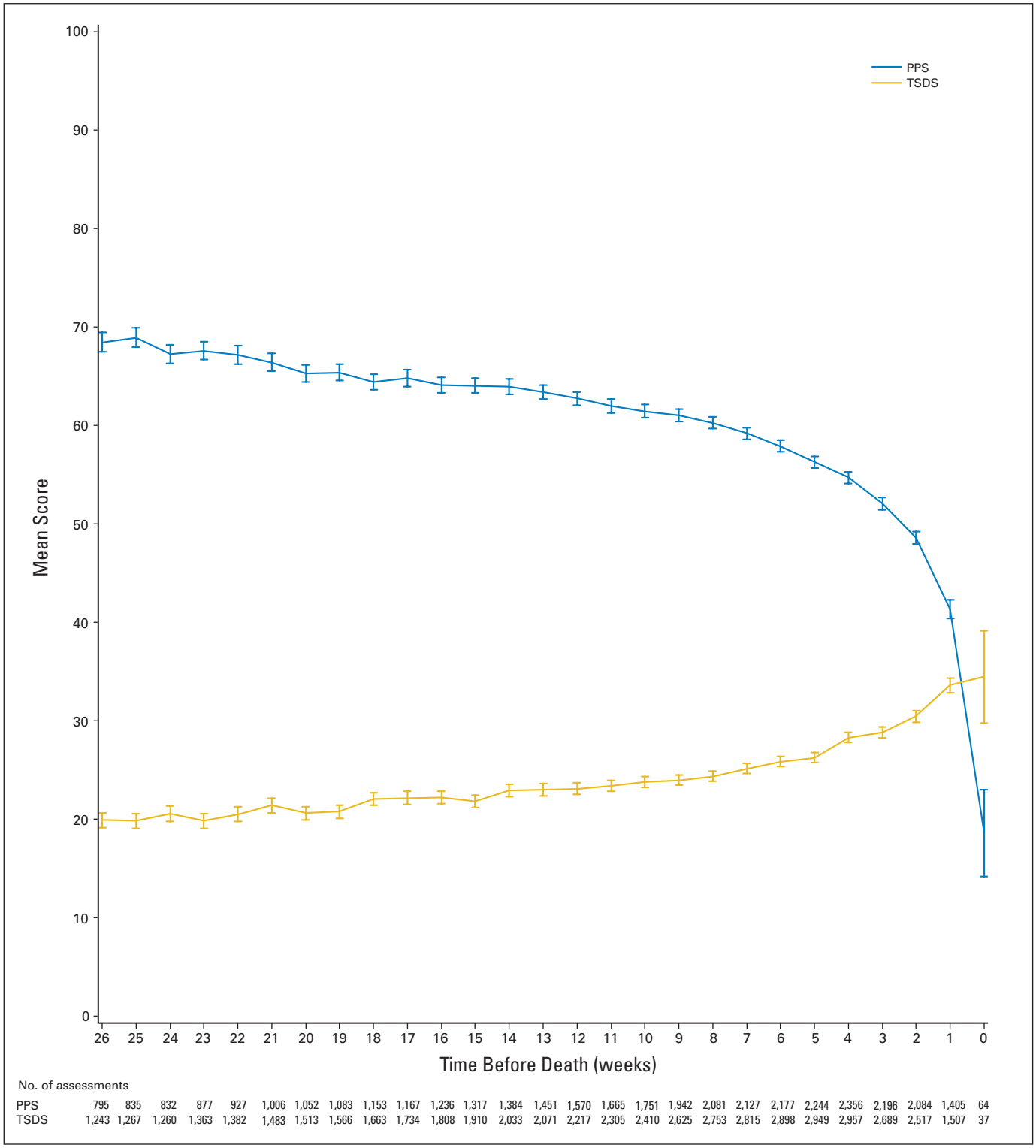

Fig 1. Mean Edmonton Symptom Assessment System (total symptom distress score [TSDS]) and Palliative Performance Scale (PPS) score. (*) Values below data points represent the total number of complete assessments available at a given week. Bars represent 95% CIs for the respective mean scores.

linkage was completed using an encrypted health insurance number unique to each patient.

Statistical Analysis

The mean PPS and ESAS scores and characteristics of their respective distributions were calculated in weeks before death. This study reports the scores for each symptom as well as a total symptom distress score (TSDS)—the sum of all scores except well-being.[36] A series of univariate and multivariate logistic regression models were performed using SAS version 9.2 (Stata Corp, College Station, TX). We modeled the odds ratio of having versus not having a moderate to severe symptom score (≥ 4), including time (in weeks), age at first assessment, sex, income quintile, Charlson score ($0 \nu \geq 1$), and cancer type as covariates. Covariates were categorical except time (continuous). The four most common cancer types in our cohort were considered in the model (ie, lung, gastrointestinal, genitourinary, and breast); all other cancer types were grouped as other. Multivariate models controlled for correlations between repeated measures on individuals using generalized estimating equations.[37] A piecewise regression model[38] was used to examine the change in the intercept and slope of the log odds for each symptom in the last month before death based on results of initial descriptive analyses; the change in intercept at week 4 before death is not described in further detail as it was shown to be statistically insignificant for most symptoms and not clinically significant. Wald and likelihood ratio tests were used to test the significance of the regression coefficient for the change in slope. No statistical adjustment was made for multiple testing.

RESULTS

During the study period, 45,118 unique patients were identified, of whom 12,196 (ESAS) and 8,927 (PPS) died. Of those, the eligibility criteria identified a cohort of 10,752 patients who had at least one ESAS assessment (total of 56,759 assessments) and 7,882 patients who had at least one PPS assessment (total of 38,777 assessments) in the 6 months before death. This represents an estimated one fifth of all cancer deaths in Ontario during the study period, based on Canada statistics data.[39,40] Seven thousand five hundred eight patients were in both cohorts; 94% of PPS assessments (n = 36,425) were done on the same day as an ESAS assessment. Approximately 20% of our cohort had their cancer diagnosis and death occur within a 6-month period. More than 80% of ESAS and 70% of PPS assessments were completed in ambulatory cancer clinics (ν the home). For both cohorts, the mean age was 65, nearly three fourths were older than 59, half were female, and approximately 20% had comorbidities beyond metastatic cancer (Charlson score ≥ 1; Table 1). In the last 6 months of life, patients had an average of 5.3 ESAS assessments (standard deviation [SD], 9.7) and 4.9 PPS assessments (SD, 8.7), and an average of 9.9 (SD, 9.1) and 10.0 (SD, 9.1) cancer center visits, respectively. Each week before death has a large sample size of assessments except week 0 (day of death), which is reported but not considered in the analyses due to the small sample size.

The trajectory of average PPS performance score started at 68.4 (SD, 14.4) at 26 weeks before death, decreased slightly over time, and reached 54.7 (SD, 14.2) at 4 weeks before death (Fig 1). In the last month of life, the average PPS score decreased more rapidly, reaching 41.3 (SD, 18.0) at 1 week before death. The trajectory of average TSDS

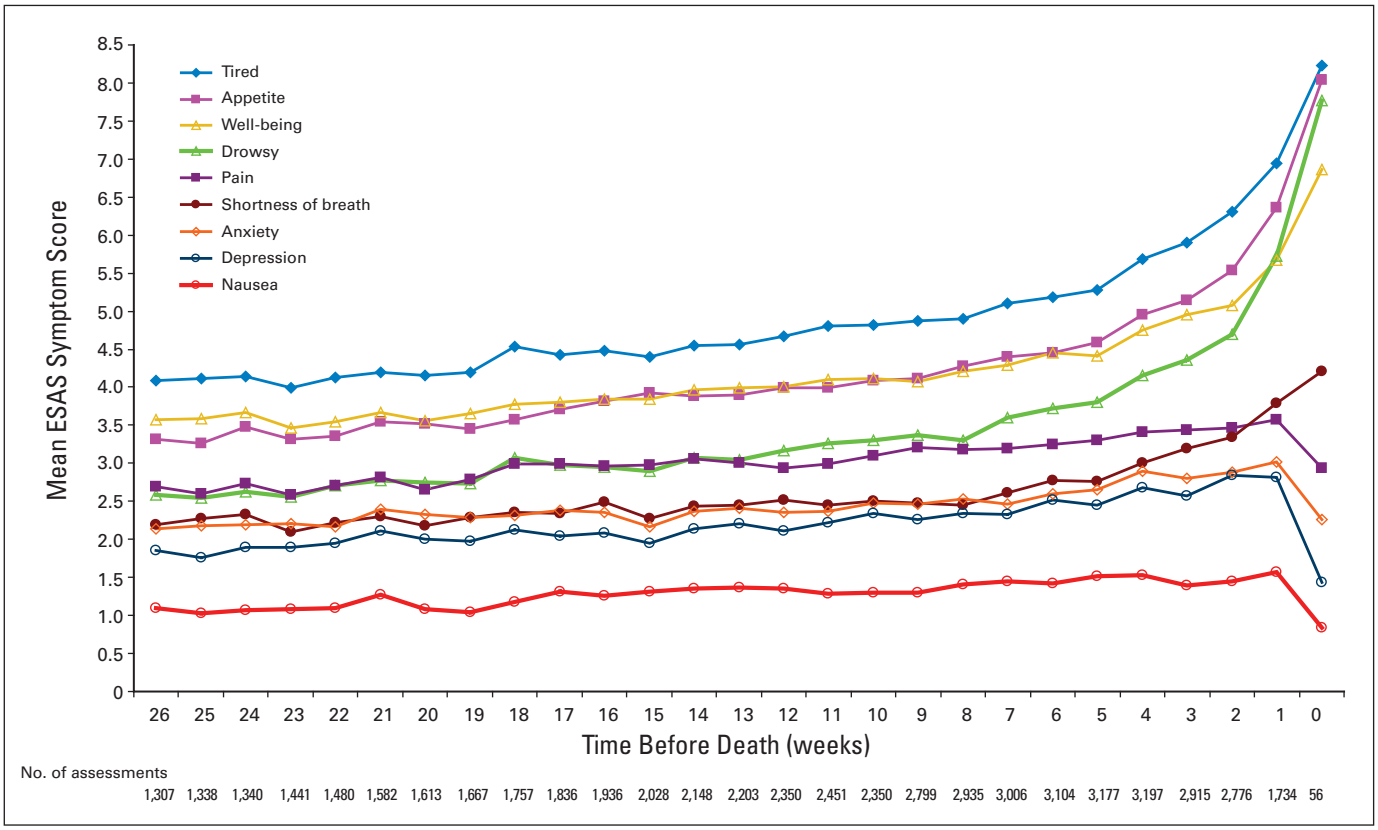

Fig 2. Mean Edmonton Symptom Assessment System (ESAS) symptom scores over time. Number of assessments is maximum number available among all nine symptoms. Missing ESAS values for a given symptom were not included when calculating the mean.

started at 19.9 (SD, 13.4) at 26 weeks before death, increased slightly over time, and reached 28.3 (SD, 14.1) at 4 weeks before death. In the last month of life, the average TSDS increased more rapidly, reaching 33.6 (SD, 14.5) at 1 week before death.

Mean symptom score trajectories followed two general patterns: symptom scores that remained generally flat across time and those that increased over time, particularly in the last month of life (Fig 2). Overall, the flatter scores increased no more than 1 point on the ESAS scale over time and included nausea, depression, anxiety, and pain; these mean scores ranged from 1.1 (nausea) to 2.7 (pain) at 26 weeks before death and ranged from 1.6 (nausea) to 3.6 (pain) at 1 week before death. Conversely, the scores that generally increased over the last 6 months of life included shortness of breath, drowsiness, well-being, lack of appetite, and tiredness; these scores ranged from 2.2 (shortness of breath) to 4.1 (tiredness) at 26 weeks before death and ranged from 3.8 (shortness of breath) to 6.9 (tiredness) at 1 week before death.

The overall proportion of the cohort reporting symptom scores of ≥ 4 (moderate to severe) at any given week increased closer to death (Fig 3). Moreover, more than one third of the cohort reported moderate to severe scores for all symptoms except nausea in the last month of life. For four of the symptoms (ie, drowsiness, tiredness, well-being, lack of appetite), more than two thirds of the cohort reported moderate to severe scores. For PPS scores, only 1% to 2% of the cohort had a score of 0 to 30 (ie, end-of-life stage) for the period of 26 to 8 weeks before death. This proportion of the cohort reporting 0 to 30 PPS scores increased to 8%, 17%, and 37% at 4, 2, and 1 weeks before death, respectively.

Table 2 shows the results of the multivariate analysis used to evaluate the odds ratio of reporting a score ≥ 4 (moderate to severe) for each respective ESAS symptom, controlling for other covariates. Each week closer to death before the last month of life significantly increases a patient's odds of having a moderate-severe symptom score by 2% to 4% (95% CI, 1.02 to 1.04). During the last month of life, each week closer to death increased these odds ratios, ranging from 9% (95% CI, 1.05 to 1.19) for depression to 41% (95% CI, 1.32 to 1.50) for drowsiness. Age did not consistently affect the odds of reporting a moderate to severe score across all symptoms. Generally, however, patients younger than 60 years had higher odds of reporting moderate to severe nausea or pain, whereas patients older than 69 years had lower odds. Females had significantly higher odds of reporting moderate to severe symptom scores across all symptoms, except shortness of breath (lower odds) and pain and depression (not significant). Having comorbidities significantly increased one's odds of having moderate to severe anxiety (1.09; 95% CI, 1.00 to 1.18), depression (1.10; 95% CI, 1.01 to 1.20), drowsiness (1.11; 95% CI, 1.02 to 1.20), and tiredness (1.21; 95% CI, 1.10 to 1.33). No distinct patterns emerged when comparing the odds ratios by cancer type, except that compared to lung cancer, patients with nonlung cancer had approximately 50% lower odds of reporting moderate to severe shortness of breath.

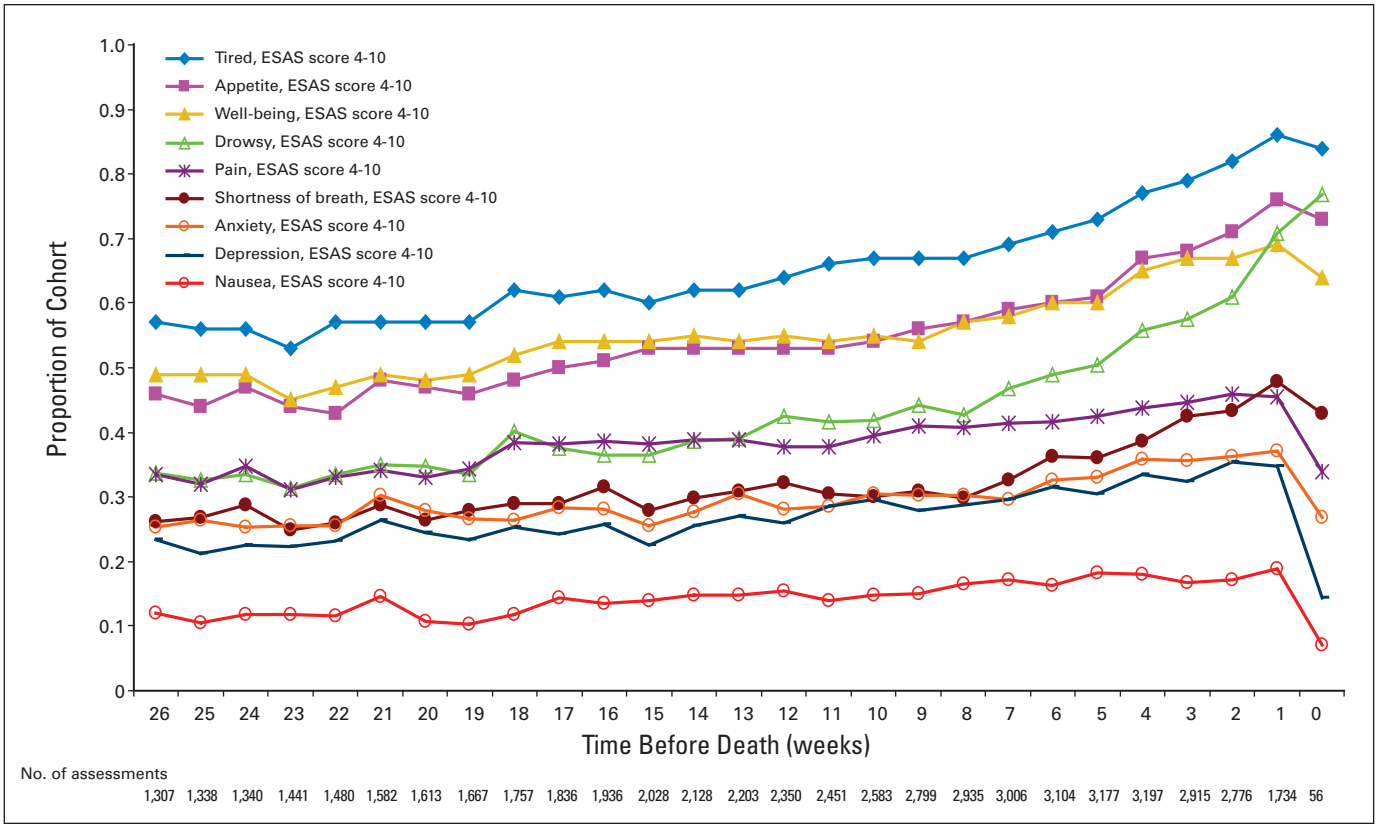

Fig 3. Proportion of cohort reporting severe to moderate Edmonton Symptom Assessment System (ESAS) scores (ie, 4 to 10) over time. Number of assessments is the maximum number available among all nine symptoms. Missing ESAS values for a given symptom were not included when calculating the proportion.

Table 2. OR of Having an ESAS Symptom Score ≥ 4 Controlling for Other Covariates, Using GEE Logistic Regression

Covariate	Anxiety		Appetite		Depression		Drowsy		Nausea		Pain		Shortness of Breath		Tired		Well-Being	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
No.*	17,138		31,669		15,894		25,008		8,505		22,342		18,527		37,833		31,874	
%*	30.91		56.85		28.67		44.95		15.19		39.90		33.37		67.48		58.90	
Time: each week closer to death																		
Before the last 4 weeks of life (weeks −26 to −5)	1.02	1.02 to 1.03	1.03	1.02 to 1.04	1.03	1.02 to 1.03	1.04	1.03 to 1.05	1.02	1.02 to 1.03	1.02	1.02 to 1.03	1.03	1.02 to 1.03	1.04	1.03 to 1.04	1.03	1.02 to 1.03
In the last 4 weeks of life (piece-wise regression; weeks −4 to 0)	1.09	1.03 to 1.16	**1.22†**	**1.14 to 1.30**	**1.09†**	**1.05 to 1.19**	**1.41†**	**1.32 to 1.50**	1.06	0.98 to 1.14	1.03	0.97 to 1.09	**1.12†**	**1.06 to 1.19**	**1.36†**	**1.26 to 1.48**	**1.13†**	**1.05 to 1.21**
Age, years																		
18-29	0.88	0.52 to 1.47	**0.39**	**0.25 to 0.62**	0.91	0.52 to 1.58	0.78	0.48 to 1.26	0.95	0.51 to 1.76	0.90	0.56 to 1.43	0.74	0.43 to 1.25	0.83	0.51 to 1.35	0.84	0.51 to 1.38
30-39	**0.74**	**0.56 to 0.99**	0.88	0.68 to 1.13	**0.73**	**0.53 to 0.99**	1.11	0.85 to 1.46	**1.55**	**1.17 to 2.06**	1.26	0.97 to 1.63	**0.74**	**0.55 to 0.98**	1.07	0.8 to 1.42	0.88	0.67 to 1.15
40-49	0.97	0.84 to 1.12	0.96	0.83 to 1.1	1.02	0.88 to 1.18	1.09	0.95 to 1.25	**1.19**	**1.02 to 1.39**	**1.29**	**1.13 to 1.47**	0.91	0.78 to 1.06	0.99	0.85 to 1.16	0.99	0.86 to 1.14
50-59	1.08	0.98 to 1.19	0.96	0.88 to 1.05	**1.12**	**1.01 to 1.24**	1.08	0.99 to 1.19	**1.18**	**1.05 to 1.31**	**1.19**	**1.09 to 1.31**	1.01	0.91 to 1.12	1.05	0.95 to 1.17	1.01	0.92 to 1.12
60-69 (reference)	1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00	
70-79	1.02	0.94 to 1.11	0.97	0.89 to 1.05	1.03	0.95 to 1.13	**1.09**	**1 to 1.19**	**0.95**	**0.86 to 1.05**	**0.90**	**0.83 to 0.97**	1.07	0.98 to 1.17	1.08	0.98 to 1.18	0.99	0.91 to 1.08
80-89	0.93	0.83 to 1.04	1.07	0.97 to 1.19	0.96	0.86 to 1.08	1.04	0.94 to 1.15	**0.72**	**0.64 to 0.82**	**0.74**	**0.67 to 0.82**	0.99	0.89 to 1.11	1.11	0.98 to 1.26	0.97	0.87 to 1.09
90-100	**0.68**	**0.49 to 0.96**	1.03	0.78 to 1.35	0.78	0.55 to 1.1	1.17	0.86 to 1.58	**0.48**	**0.31 to 0.75**	**0.67**	**0.5 to 0.91**	0.89	0.63 to 1.25	1.47	1 to 2.15	0.90	0.66 to 1.24
Sex																		
Male (reference)	1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00	
Female	**1.23**	**1.15 to 1.32**	**1.15**	**1.08 to 1.23**	1.05	0.98 to 1.13	**1.09**	**1.02 to 1.17**	**1.38**	**1.27 to 1.49**	1.07	1 to 1.14	**0.86**	**0.8 to 0.92**	**1.22**	**1.12 to 1.32**	**1.11**	**1.04 to 1.2**
Income quintile																		
1	1.03	0.93 to 1.15	0.99	0.9 to 1.09	1.09	0.98 to 1.22	0.96	0.87 to 1.06	0.95	0.84 to 1.07	1.08	0.98 to 1.2	0.96	0.86 to 1.07	0.95	0.84 to 1.06	**0.84**	**0.76 to 0.94**
2	1.04	0.94 to 1.15	0.96	0.87 to 1.06	1.10	0.99 to 1.23	0.92	0.84 to 1.02	0.95	0.85 to 1.07	1.02	0.93 to 1.13	0.98	0.88 to 1.09	0.97	0.87 to 1.09	**0.88**	**0.79 to 0.98**
3	1.11	1 to 1.23	1.05	0.95 to 1.16	1.08	0.97 to 1.21	1.03	0.93 to 1.14	**1.15**	**1.02 to 1.29**	1.05	0.95 to 1.16	1.08	0.97 to 1.2	0.98	0.87 to 1.11	0.93	0.83 to 1.03
4	1.04	0.94 to 1.16	0.99	0.9 to 1.09	1.04	0.93 to 1.16	0.97	0.87 to 1.07	0.96	0.85 to 1.09	0.95	0.86 to 1.05	0.96	0.86 to 1.07	0.93	0.83 to 1.05	0.89	0.8 to 0.99
5 (reference)	1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00	
Charlson score																		
0 (reference)	1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00	
1+	**1.09**	**1 to 1.18**	1.02	0.94 to 1.1	**1.1**	**1.01 to 1.2**	**1.11**	**1.02 to 1.2**	0.97	0.88 to 1.07	1.02	0.95 to 1.1	1.03	0.95 to 1.13	**1.21**	**1.1 to 1.33**	1.04	0.95 to 1.13
Cancer type																		
Lung (reference)	1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00		1.00	
GI	**0.88**	**0.8 to 0.96**	**1.21**	**1.12 to 1.32**	1.04	0.95 to 1.14	1.02	0.94 to 1.11	**1.28**	**1.16 to 1.41**	1.03	0.95 to 1.11	**0.36**	**0.33 to 0.39**	0.95	0.87 to 1.05	0.97	0.89 to 1.06
Genitourinary	0.93	0.83 to 1.05	1.04	0.93 to 1.16	1.12	0.99 to 1.27	**1.12**	**1 to 1.26**	**1.27**	**1.11 to 1.45**	**1.41**	**1.26 to 1.57**	**0.41**	**0.36 to 0.47**	**1.14**	**1 to 1.3**	1.08	0.96 to 1.22
Breast	**0.84**	**0.73 to 0.96**	**0.88**	**0.78 to 1**	1.00	0.86 to 1.15	**0.87**	**0.76 to 0.99**	0.87	0.75 to 1.01	1.10	0.97 to 1.24	**0.52**	**0.45 to 0.6**	0.94	0.82 to 1.09	**0.87**	**0.76 to 0.99**
Other	0.93	0.85 to 1.02	0.99	0.91 to 1.08	1.04	0.94 to 1.14	1.07	0.98 to 1.17	0.94	0.85 to 1.05	**1.12**	**1.02 to 1.22**	**0.42**	**0.38 to 0.46**	1.05	0.95 to 1.17	0.98	0.89 to 1.07

NOTE. Bold indicates significant value $P < .05$.
Abbreviation: OR, odds ratio; ESAS, Edmonton Symptom Assessment System; GEE, generalized estimating equation.
*The missing data are not counted.
†The regression coefficient for the change in slope was significant.

DISCUSSION

This study examines the trajectories of average ESAS and PPS scores in the last 6 months of life in a province-wide, exclusively outpatient, cancer cohort of all cancer types. The results include nearly 57,000 ESAS and 39,000 PPS assessments, making this the largest longitudinal study to examine the symptom and performance status trajectories before death to our knowledge.

Contrary to our initial hypothesis, the average symptom trajectories show that not all symptom scores substantially increase in severity in the final weeks before death. The symptoms that have generally flat average scores in the last 6 months of life, namely pain, nausea, anxiety, and depression, also have available treatment interventions to manage them, such as prescription medications. Moreover, standardized symptom assessment itself may contribute to the flatter trajectories, facilitating early identification and treatment of symptom problems, and prevention of worsening symptoms, though these relationships require further investigation. Conversely the other symptoms—lack of appetite, tiredness, drowsiness, well-being, and shortness of breath—may be more difficult to treat even after being identified.

Comparing our results to other research on symptom prevalence at the end of life, including a large systematic review,[41] is difficult because those studies prospectively identified patients as at the end of life, whereas this study retrospectively examines ambulatory patients with cancer without consideration to end-of-life classification. Thus, our study includes patients who may not have appeared as imminently dying. As well, tools used to identify symptoms differ. Despite these differences, it is noteworthy that the systematic review[41] reported a pooled symptom prevalence of 45% for pain, 30% for anxiety, and 17% for nausea in the last 2 weeks of life, which is similar to the proportions reported by our cohort. These results suggest that patients with cancer have high symptom burden as they approach death regardless of end-of-life identification. Further research is needed to determine how to use the prevalence of and changes in symptom scores to predict time to death in an outpatient cancer population.

The distribution of PPS scores in our study is vastly different than in other studies that strictly focus on a dying inpatient population. A meta-analysis[14] and a large cohort study[12] of patients served in hospice or palliative care units have 49% and 45% of their cohort with PPS scores of 30 to 0 at initial admission, respectively, whereas our cohort only has 8% with the same scores at 4 weeks before death. Although

our inclusion criteria differ from the other studies, our results are important since an ambulatory cohort represents what most oncologists encounter in clinical practice; even though some patients may have appeared healthier than others at the same time point before death, all patients in our cohort died within 6 months.

In this outpatient, ambulatory population, the average scores across the last 6 months of life decline within the transition stage (ie, 70 to 40), thus disproving our hypothesis that PPS scores would decline to below 30 (ie, end-of-life stage) in the final weeks of life, as indicated by previous research in palliative inpatient and hospice populations.[11-14,20-23] Our results show that for ambulatory patients with cancer, if providers wait until PPS scores are in the end-of-life stage before initiating palliative care services, most patients would not receive palliative care until days before death. Our results also suggest that perhaps initiating palliative care during the transition stage for ambulatory patients would allow for earlier integration of supportive services, which can reduce symptom burden and may increase survival.[42] However, further research is required to determine survival times based on specific PPS scores using appropriate study designs (eg, survival analysis), which this descriptive study does not address.

This study is also limited by the opportunistic nature of data collection. Some providers or patients did not complete the tools at every visit. Patients with worse symptoms may be more likely to complete an assessment, thus overestimating the average symptom burden. In contrast, since our study cohort consists primarily of ambulatory patients (ie, those healthy enough to come to clinic), our results likely underestimate the true symptom burden among all patients with cancer approaching death. Nonetheless, the sample size is unparalleled with ample responses at each week. As well, our results may not be generalizable to all patients with cancer, only those receiving care from cancer centers. We were also unable to identify when patients were identified by providers as end of life, if at all. However, this study illuminates the symptom burden and performance status in the last 6 months of life in a broad cancer population that is representative of what most oncologists encounter in daily clinical practice. Finally, the prevalence of symptom burden may be worse in other cancer populations that have not implemented a population-wide, standardized assessment system, especially if standardized assessment helps to mitigate the worsening of symptoms.

The standardized assessment of symptom severity and performance status in Ontario's cancer system provides the unique opportunity to describe the trajectory of ESAS and PPS scores in a large outpatient cancer population. Average performance status declines closer to death, but not to as low a level as typically seen in studies of palliative populations. Mean symptom score trajectories followed two patterns: increasing versus generally flat over time. The availability of treatment options (eg, prescription drugs) may partially explain the flatter trajectories of certain symptoms (eg, pain), whereas other symptoms without clear treatment interventions had increasing trajectories; however, since drug treatment data was not available, a causal relationship requires further investigation. Future research should prioritize addressing symptoms that worsen over time. The high proportion of moderate to severe symptoms scores in the final weeks of life represents opportunities for improved patient care at end of life.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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