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Symptom burden among head and neck cancer patients in the first year after diagnosis: Association with primary treatment modality

Catherine O. Allen-Ayodabo[a,b], Antoine Eskander[a,b,c,d,i], Laura E. Davis[a], Haoyu Zhao[b], Alyson L. Mahar[e], Irene Karam[f], Simron Singh[a,b,g,i,j], Vaibhav Gupta[h,i], Lev D. Bubis[h], Lesley Moody[i,j], Lisa Barbera[b,f,k], Natalie G. Coburn[a,b,c,h,i,j,*]

[a] Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Canada
[b] Institute for Clinical Evaluative Sciences (IC/ES), Canada
[c] Odette Cancer Centre, Surgical Oncology, Sunnybrook Health Sciences Centre, Canada
[d] Department of Otolaryngology – Head & Neck Surgery, Sunnybrook Health Sciences Centre, Canada
[e] Department of Community Health Sciences, University of Manitoba, Canada
[f] Department of Radiation Oncology, University of Toronto, Canada
[g] Odette Cancer Centre, Medical Oncology, Sunnybrook Health Sciences Centre, Canada
[h] Division of General Surgery, Department of Surgery, University of Toronto, Canada
[i] Institute of Health Policy, Management and Evaluation, University of Toronto, Canada
[j] Cancer Care Ontario, Toronto, Canada
[k] Division of Radiation Oncology, Department of Oncology, Tom Baker Cancer Centre, University of Calgary, Canada

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ABSTRACT

Purpose: Head and neck cancer (HNC) and its treatment affects quality of life, with significant symptom burden. The main objectives of this study were to examine symptom trajectories of HNC patients by treatment and to identify factors associated with high ESAS scores.

Methods and materials: We conducted a retrospective cohort study in patients diagnosed with HNC in Ontario, Canada from 2007 to 2015 using linked health administrative databases. The primary outcome was a monthly patient self-reported moderate-to-severe (≥ 4) symptom score in the year following diagnosis. Multivariable Modified Poisson regression analyses with robust variance were used to investigate factors associated with moderate-to-severe scores.

Results: Of 13,827 HNC patients identified, 4793 had ≥ 1 ESAS assessment within 12 months of cancer diagnosis. Overall, 60% (n = 2708) and 65% (n = 2903) of patients reported moderate-to-severe pain and poor appetite, respectively. The proportion of patients reporting a score ≥ 4 increased significantly during treatment and was most pronounced for those who received chemoradiation (CRT). On multivariable analysis, patients who were female (Relative Risk (RR) 1.15, 95% CI 1.08–1.23, received CRT, had a higher comorbidity burden (RR 1.31, 1.23–1.39), and had a diagnosis of oropharyngeal (1.10, 1.02–1.19), or oral cavity cancer (1.31, 1.19–1.45), were at an increased risk of reporting severe pain scores ($p < 0.01$ for all).

Conclusion: The majority of HNC patients report high pain scores, with symptom burden highest during the treatment phase, and especially for patients who received radiation or chemoradiation. This large study highlights the need for proactive symptom management during the HNC patients' cancer journey.

Introduction

Head and neck cancer (HNC) accounts for an estimated 5% to 10% of all cancers in Europe and North America and is one of the most common cancers in Asia and South East Asia [1]. Treatment involves surgery, radiotherapy, and chemoradiation, either independently, or in combination. While often curative, these multi-modality treatments adversely impact short and long-term quality of life (QOL) and patient wellbeing, with high rates of toxicity [2,3]. For example, one study recorded acute toxicity for severe dysphagia (Grade 3) among 87% of the patients using National Cancer Institute Common Terminology Criteria for Adverse Events weekly during Intensity-Modulated

* Corresponding author at: Sunnybrook Health Sciences Centre, 2075 Bayview Ave., Room T2 011, Toronto, ON M4N 3M5, Canada.
E-mail address: natalie.coburn@sunnybrook.ca (N.G. Coburn).

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Radiation Therapy (IMRT) [4]. Moderate pain, fatigue and mucositis (Grade 2) were other short-term toxicities noted [4]. Importantly, uncontrolled symptoms may lead to unscheduled treatment interruptions or alteration of treatment plans, resulting in poorer oncologic response [5]. There is evidence that even a one day interruption of radiation treatment for HNC can result in a decrease in the local control rate [5], highlighting the importance for early recognition and management of symptoms during treatment.

The province of Ontario, Canada has one of the most regionalized HNC treatment programs in the world [6,7]. Patients are insured under a government-run healthcare system and are managed at one of seven Regional Cancer Centers (RCCs). As part of a provincial symptom screening program, established in 2007 by Cancer Care Ontario (CCO), patients complete a symptom assessment using the Edmonton Symptom Assessment Scale (ESAS) during clinic visits in RCCs [8] to allow real-time review of patient-reported symptoms by the provider. ESAS scores provided at patient encounters are collected centrally by CCO, creating the largest compilation of Patient Reported Outcomes (PRO) for cancer patients globally. It is valuable to leverage patient-reported ESAS scores to define the timing, extent and factors associated with high symptom burden during and after cancer therapies.

Our previous review of symptom scores in the year following cancer diagnosis demonstrated that oropharyngeal cancer patients had the highest symptom scores of all patients with cancer [9]. This concerning finding highlights the potential for better supportive care to decrease symptom morbidity during this period. This present study aimed to understand the drivers of high burden for HNC patients and our main objectives were to (1) examine symptom severity and trajectories in the 12 months following diagnosis by primary tumour location and (2) identify factors associated with high ESAS scores for HNC patients.

Methods and materials

Study design and population

We conducted a retrospective descriptive cohort study to assess ESAS scores in patients diagnosed with a squamous cell carcinoma of the oral cavity, oropharynx, and larynx/hypopharynx, captured in the Ontario Cancer Registry from January 2007 to December 2015. As the ESAS program was phased in, from 2007 to 2010, data collection improved from 2010 to 2015. The registry captures 96% of incident cancer diagnoses in the province [10,11]. Patients included in the study were aged 18 years and older, had a valid Ontario Health Insurance Plan number, and completed at least one ESAS assessment within the 12 months following diagnosis.

We excluded patients who had more than one cancer diagnosis before or during the study period, were missing information on treatment location, had an invalid or missing identification number in the databases, and who received radiotherapy before diagnosis. We also excluded patients who died within one year of diagnosis, had no death date or no follow up within the last 6 months of the study period to ensure comparable follow-up for all patients and so that symptoms would not be attributable to the events around the time of death. Patients who were unable to receive traditional chemotherapy and instead received target therapy with Cetuximab within 180 days of diagnosis were excluded because this is infrequently used in Ontario and its unique toxicity profile could potentially obscure the primary treatments effects.

Data sources

We linked CCO's Symptom Management Reporting Database, which contains all ESAS assessments, to administrative datasets for patients covered under the public health system using unique encoded patient identifiers. Administrative data sources included the Ontario Cancer Registry (OCR), a computerized database of information on incidence of and mortality from cancer for all persons residing in Ontario; Same Day Surgery (SDS) database, which records patient-level data for same day surgery or procedure stay; Discharge Abstract Database (DAD), containing information for all hospitalizations; National Ambulatory Care Reporting System (NACRS), a database of patient visits to hospital and community-based ambulatory care settings including visits to the emergency department; Ontario Health Insurance Plan (OHIP) Claims Database, with information on all healthcare provider claims covered by OHIP; Registered Person Database (RPDB), providing demographic information (date of birth, sex, and date of death, if applicable); Ontario Marginalization Index (ONMARG), which quantifies the degree of marginalization across Ontario in 4 major dimensions including material deprivation, residential instability, dependency, and ethnic concentration; Immigration, Refugees and Citizenship Canada (IRCC) Permanent Resident Database includes immigration application records for people who are landed immigrants in Ontario; Local Health Integration Network (LHIN) datasets contain information about hospital referral regions in Ontario; Institution Information System refers to datasets containing information about Ontario Health care institutions funded by the Ministry of Health and Long Term Care (MOHLTC); Cancer Activity Level Reporting (ALR) contains patient-level activity focused on radiation and systemic therapy services and outpatient oncology clinic visits; New Drug Funding Program database (NDFP) includes information about the chemotherapy drugs that are publicly funded under the Ontario Public Drug Programs.

The study protocol was approved by the Research Ethics Board of Sunnybrook Health Sciences Center. Institute of Clinical Evaluative sciences' privacy and confidentiality policies were maintained.

Outcomes

ESAS has been validated and widely used as a screening tool (Appendix Fig. 4) to elicit patients' own assessment of the severity of nine common cancer-associated symptoms: pain, tiredness, nausea, anxiety, depression, lack of appetite, drowsiness, shortness of breath, and poor wellbeing [12–16]. Symptom severity is assessed on a scale from 0 (absent) to 10 (most severe), which were categorized as no symptoms (0), mild (1–3), moderate (4–6), or severe (7–10) according to a previously-validated conversion scale [17,18]. In this study, we further categorized these scores into moderate-to-severe (≥ 4), and severe (≥ 7) scores per month from diagnosis to ESAS score measurement [18]. Months were defined in 30-day blocks from the index date of patient diagnosis in the OCR record, if a patient reported more than one ESAS assessment in one month, the highest score was used.

Covariates

Age was categorized as < 50, 50–59, 60–69, 70–79, and 80 years and older. Urban or rural residence was determined based on the Rurality Index of Ontario (RIO) 2008 score [19]. Communities are scored 0 (most urban) to 100 (most rural) based on the density of the population, total population and the time needed get to a health center [19]. These categories were major urban (0–9), non-major urban (10–44), and rural (45 or greater) [20,21]. We defined socioeconomic status based on the material deprivation dimension of an asymmetrically standardized index, ONMARG, which contains information on educational attainment, single-parent families, unemployment, government transfer payments, proportion of individuals with low income, and proportion of homes needing major repair into a single index that can be transformed into categorical (quintile) variables [22]. Comorbidity score was categorized into 5 groups: 0–3, 4–5, 6–7, 8–9, and 10+, defined by the sum of Aggregated Diagnosis Groups (ADG) at the time of diagnosis and calculated using the Johns Hopkins ACG® system, and data from the RPDB, OHIP, DAD, and NACRS [23]. The RCC where patients with ESAS were registered for treatment was designated as the treatment center. Immigration status was categorized into two groups:

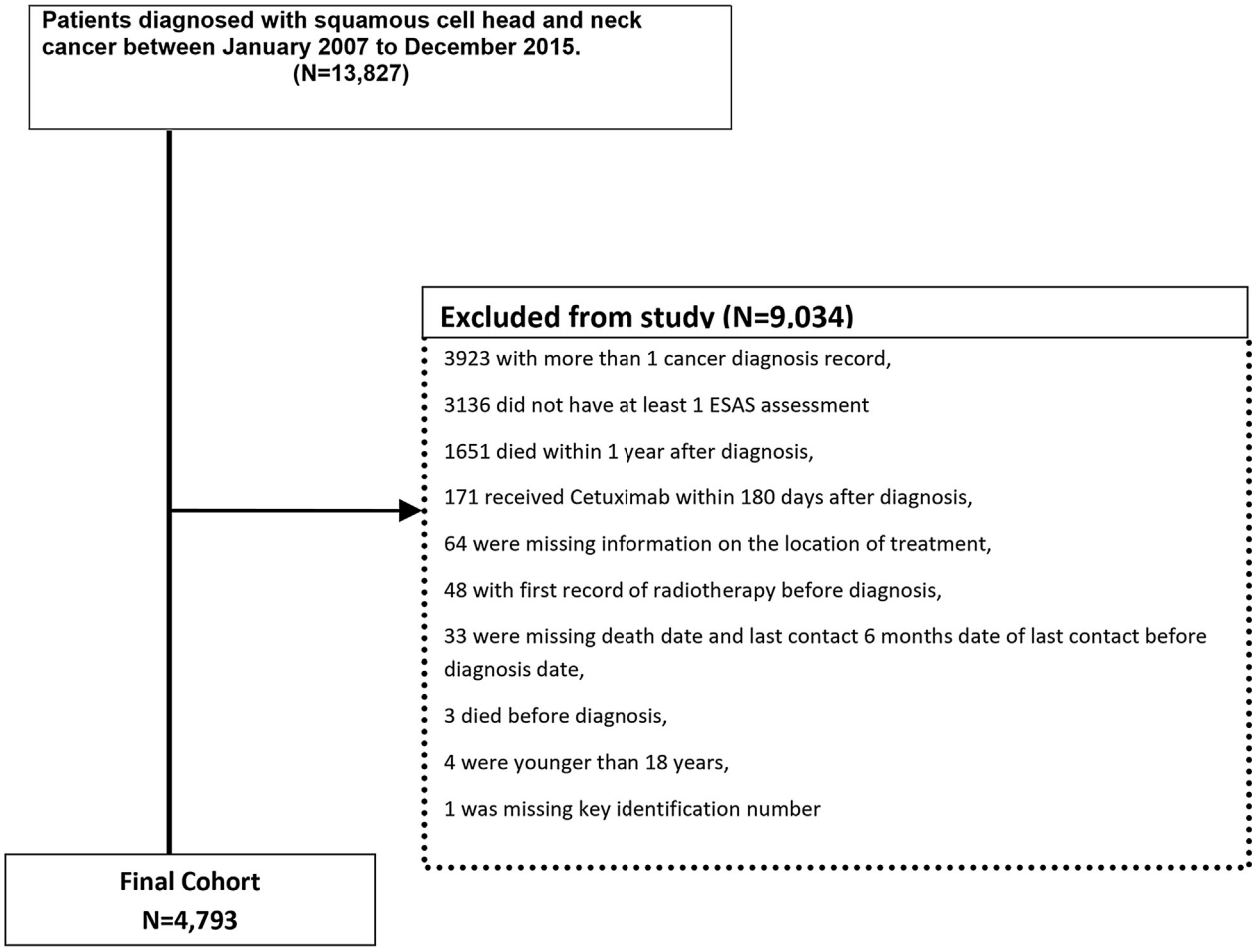

Fig. 1. Cohort creation.

Immigrant for those who have a record in the IRCC database, and non-immigrant for those who have no record.

Treatment received was standard in our cohort which depends on the cancer subsite and stage. In Ontario, most larynx/hypopharynx cancer patients are treated with an organ preservation approach (radiation/chemoradiotherapy) except for very small, superficial T1a tumors which are confined to a single vocal cord and the very large T4a tumors invading into key structures – thyroid cartilage or cricoid cartilage that are treated with primary surgery [6]. Oropharyngeal cancer patients received radiation/chemoradiation with the exception of a few rare patients in more recent years that have been enrolled in trials comparing transoral robotic surgery to a primary radiotherapy approach [24]. There were only 66 patients recruited into this trial in all of Canada, which would not have significantly impacted our study given the very small number [24]. Oral cavity cancer patients in Ontario almost always undergo surgery and receive primary radiotherapy with adjuvant treatment tailored towards high risk features on final pathology [25]. There are of course a small cohort of patients that are not surgical candidates and are therefore managed with palliative radiotherapy or comfort measures only [25]. Intensity-Modulated Radiation Therapy was standard in Ontario as of 2002/2003 depending on the treatment center to doses of 70 Gy for primary radiotherapy in 35 fractions (usually 2 Gy per fraction), and 60–66 Gy for adjuvant treatment in 30–33 fractions. Other dosing schedules were not well captured in the administrative data. Only Cisplatin was included for chemotherapy in our cohort.

Five distinct treatment groups were defined based upon treatments received within the first year following diagnosis: (1) surgery, (2) radiotherapy, (3) concurrent chemoradiotherapy (CRT), (4) surgery followed by radiotherapy, and (5) surgery followed by CRT. Receipt of chemotherapy was defined as one or more chemotherapy record in the OHIP, NDFP or the ALR database within 12 months of diagnosis. Receipt of radiotherapy was defined as one or more ALR radiotherapy record within 12 months of diagnosis (Appendix Table 2). Cancer subsite was stratified into a three-level variable (larynx/hypopharynx, oropharynx and oral cavity) using ICD-O-3 topography codes (Appendix Table 1). Months from diagnosis is the month of ESAS assessment from diagnosis and it was created by adjusting for repeated measurement. Year of diagnosis is the year that a diagnosis of head and neck cancer was captured in the Ontario Cancer Registry.

Statistical analysis

Demographic and clinical characteristics at baseline were presented with proportions. We compared patients reporting at least one ESAS assessment in the 12 months following diagnosis to patients who did not in order to determine generalizability. Chi-squares tests were used to test for differences. Patients reporting moderate-to-severe and severe scores in the 12-months after diagnosis were represented graphically. Symptom trajectories were illustrated by plotting the proportion of patients with moderate-to-severe scores each month from diagnosis. Symptom trajectories were further stratified by treatment received. (Appendix Table 4).

Multivariable Modified Poisson regression models with robust variance were used to investigate factors associated with reporting at least one moderate-to-severe and severe symptom score for pain and poor appetite in the year following diagnosis. We selected high pain score as it is potentially amenable to treatment; lack of appetite was selected as

it was the most commonly reported symptom. Generalized estimating equations with exchangeable correlation structures were used to account for clustering of repeated measurements at the patient level [26]. Covariates were identified *a priori* as sex, age at diagnosis, comorbidity, immigration status, treatment modality, treatment center, months from diagnosis, year of diagnosis, deprivation quintile, rurality, and cancer subsite. All identified risk factors were included in the model and the results were considered significant if p-value ≤ 0.05. The analyses were performed using SAS Enterprise Guide, version 7.1(SAS Institute, Cary, NC).

Results

A total of 13,827 patients were diagnosed with a squamous cell HNC from January 2007 to December 2015. 4793 patients had at least one ESAS assessment within 12 months of diagnosis and met the study inclusion criteria (Fig. 1). Demographic and clinical characteristics differed to some extent for patients with and without an ESAS assessment in the year following diagnosis (Appendix Table 5). Patients who completed ESAS assessment were more likely to be younger, males, have oropharyngeal cancer, receive CRT or radiation therapy and be treated at a designated regional cancer center.

A median of five ESAS assessments (IQR 2–9) were recorded for each patient in the first year after diagnosis. Patient demographics are presented in Table 1. The average age at diagnosis was 61.6 (SD 11.3) years and most patients were male (77%). The majority were non-immigrants (93%). Cancer of the oropharynx comprised almost 40% of cases (n = 1884). The data collection improved from 2010 to 2015, and 85% of HNC patients reported an ESAS score in the latter years of the study. Treatment received within the first year following diagnosis were CRT alone (29%), radiation alone (27%), surgery alone (16%), surgery with radiation (11%), surgery with CRT (10%), or no treatment (7%). Overall, 75.5% received radiotherapy, with or without chemotherapy.

Proportion of patients reporting at least one score ≥ 4 in the 12 months after diagnosis were most common for moderate-to-severe fatigue (69%), poor well-being (68%), lack of appetite (65%), pain (60%), and anxiety (51%) (Fig. 2). After stratifying by treatment, CRT compared to best supportive care was associated with a considerably higher symptom burden in the 12 months after diagnosis (which was similarly high among patients receiving radiation therapy alone. (Appendix Table 4).

Symptom trajectories were highest at 8–16 weeks after diagnosis, with the exception of anxiety, which peaked in the first two months following diagnosis (Figs. 3–5 and supplemental Figs. 1–3). Moderate-to-severe depression and shortness of breath, remained consistent across the 12 months from diagnosis (Appendix Fig. 1). After stratifying by treatment received, symptom trajectories followed a similar pattern among patients who received chemoradiation or radiation alone (Figs. 4 and 5).

On multivariable analysis, patient demographics and treatment were risk factors for reporting moderate-to-severe pain and lack of appetite (Table 2). Female patients had higher risk of reporting elevated scores for pain (RR 1.15, 95%CI 1.08–1.23) and poor appetite (RR 1.16, 95%CI 1.10–1.23). Patients older than 60 years had significantly lower risk of reporting elevated scores for pain when compared to those younger than 60 years. Patients with higher comorbidity burden had an increased risk of an elevated pain score (RR 1.31, 95%CI 1.23–1.39) and poor appetite (RR 1.21, 95%CI 1.14–1.28). Lowest SES was significantly associated with the risk of reporting high scores for pain and poor appetite. All treatment modalities were less likely to report moderate-to-severe scores compared to those receiving CRT, indicating that CRT had the highest risk of reporting elevated symptoms. For example, patients receiving surgery alone had a 50% decreased risk of reporting lack of appetite compared to patients receiving CRT (RR 0.49, 95%CI 0.43–0.57.) Patients with oral cavity cancer had the highest risk of moderate-to-severe scores for pain, (RR 1.31, 1.19–1.45) whereas oropharyngeal cancer patients had the highest risk for poor appetite (RR1.37, 1.28–1.47). Rurality of residence, immigration status, year of diagnosis, and treatment centre were not significantly associated with reporting moderate-to-severe ESAS scores.

Table 1
Characteristics of HNC patients who reported at least one ESAS score in the initial 12 months following diagnosis (N = 4793).

Baseline Characteristics	N = 4793 (%)
Sex	
F	1087 (22.7%)
M	3706 (77.3%)
Age categories	
< 50	604 (12.6%)
50–59	1564 (32.6%)
60–69	1543 (32.2%)
70–79	726 (15.1%)
> =80	356 (7.4%)
Rurality	
Missing	46 (1.0%)
Major urban	2991 (62.4%)
Non-major urban	1393 (29.1%)
Rural	363 (7.6%)
Deprivation Quintile	
.	63 (1.3%)
1	886 (18.5%)
2	902 (18.8%)
3	929 (19.4%)
4	973 (20.3%)
5	1040 (21.7%)
Comorbidities	
0 – 3	902 (18.8%)
4–5	1024 (21.4%)
6–7	1006 (21.0%)
8–9	839 (17.5%)
10 +	1022 (21.3%)
Immigration Status	
Non-immigrant	4472 (93.3%)
Immigrant	321 (6.7%)
Treatment modalities	
Best Supportive care	354 (7.4%)
Surgery	744 (15.5%)
Radiation	1277 (26.6%)
Surgery plus Radiation	503 (10.5%)
Chemoradiation	1381 (28.8%)
Surgery plus Chemoradiation	460 (9.6%)
Other	74 (1.5%)
Cancer subsite	
Larynx/Hypopharynx	1336 (27.9%)
Oropharynx	1884 (39.3%)
Oral cavity	1573 (32.8%)
Diagnosis year	
2007	115 (2.4%)
2008	198 (4.1%)
2009	369 (7.7%)
2010	399 (8.3%)
2011	582 (12.1%)
2012	677 (14.1%)
2013	775 (16.2%)
2014	784 (16.4%)
2015	894 (18.7%)
Had contact with an RCC	4474 (93.3%)

Discussion

This study examines patient-reported symptoms for a large sample of HNC patients during the 12 months following diagnosis, establishing symptom trajectories and factors associated with moderate-to-severe symptom burden. Tiredness, poor well-being, pain, and lack of appetite are the most common symptoms and they are particularly heightened during the treatment phase (8–16 weeks from diagnosis). We observed that 60–70% of HNC patients regardless of their treatment status reported moderate-to-severe scores for these symptoms. However, the

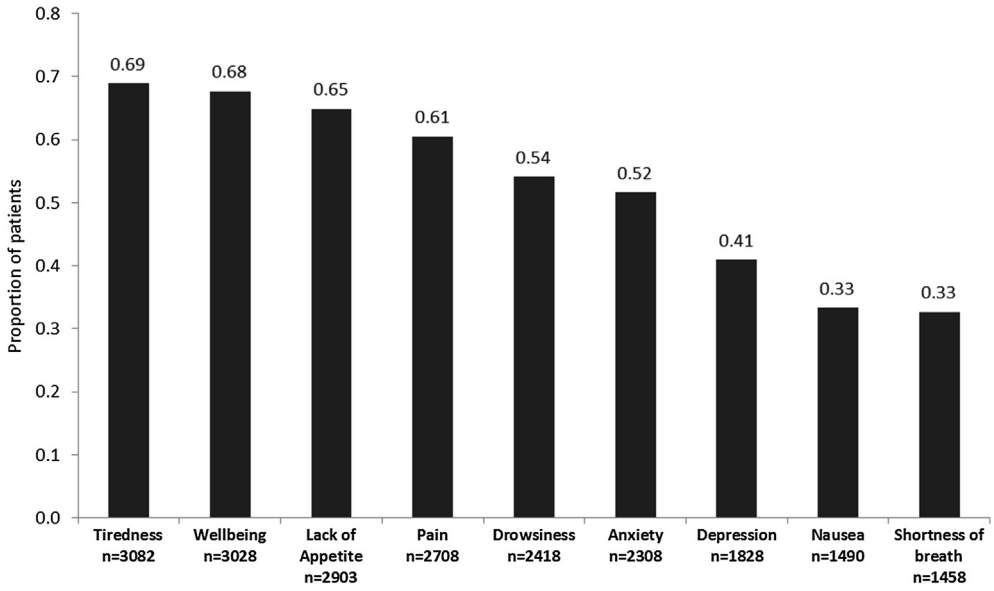

Fig. 2. Proportion of patients reporting at least one moderate-to-severe symptom score in the 12 months following diagnosis (n = 4474).

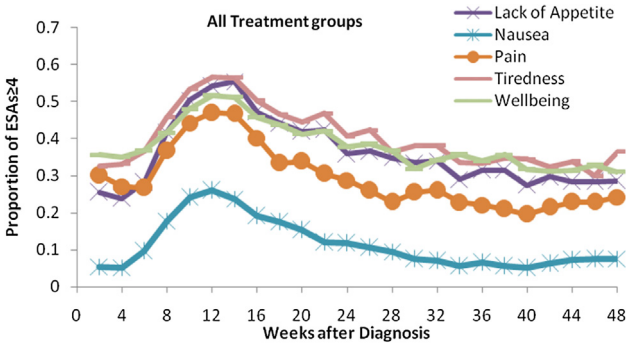

Fig. 3. Trajectories of moderate-to-severe symptoms for all HNC patients by week of assessment.

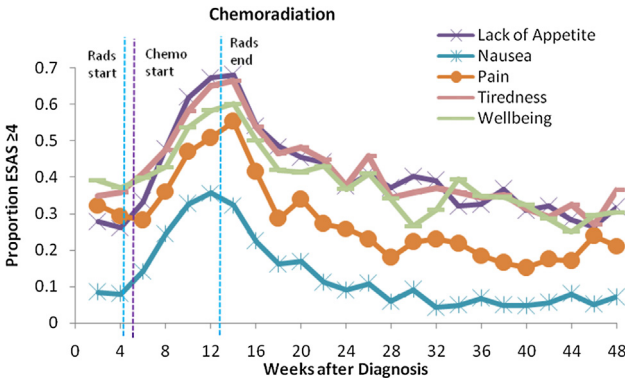

Fig. 4. Trajectories of moderate-to-severe symptoms for HNC patients who received Chemoradiation by week of assessment.

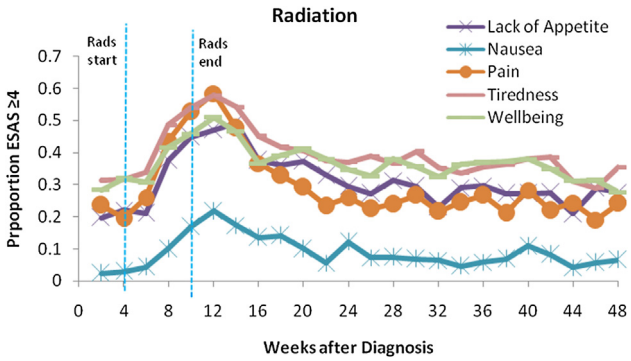

Fig. 5. Trajectories of moderate-to-severe symptoms for HNC patients who received Radiation alone by week of assessment.

highest symptom burden was noted among those receiving radiation or CRT, either as primary or adjuvant treatment. Patients receiving CRT had higher symptom scores than surgery + CRT and this probably relates to the fact that those in the trimodality group (surgery + CRT) received a lower dose of radiation as it was in the adjuvant setting, although, the exact dose and volume of radiotherapy is not currently available in our datasets. Patient characteristics including young age, female sex, high comorbidity, and low socioeconomic status were significantly associated with moderate-to-severe symptoms, which are also supported by the literature [9,23,26–28]. Younger patients (< 60 years) may have higher risk of reporting high symptoms scores due to their functional requirement for daily activities, type of treatment received, and more aggressive disease behavior [29,30]. While females were less likely than males to complete symptom screening, they had a higher risk for reporting higher symptoms [31].

Importantly, our study found that symptom burden peaked sharply during treatment. Failure to intervene upon patient symptoms likely contributes to adverse health care outcomes which are associated with poor patient experience, and significant health care costs [32]. Prior research demonstrates a very high rate (28–55%) of peri-treatment events (emergency department visits and unplanned hospitalizations) in HNC patients during the 90 days after initiation of treatment [32]. These peri-treatment events may result in the interruption of treatment which has been shown to cause poorer oncologic outcomes [5].

Symptom trajectories demonstrate a very consistent and predictable pattern of elevated symptom scores which is ideally actionable for future quality improvement interventions. The proportion of patients reporting moderate -to-severe pain improved towards the end of the study period as shown in Figs. 2–4. We are not aware of any specific changes to pain management protocols in Ontario during this time period that could have accounted for improvement performing analysis to explore the potential reasons for this improvement could be explored in future studies. ESAS in HNC patients can be used as a flag for severe symptoms and initiate the use of recommended initiatives, such as short timing for follow up through regularly scheduled clinic visits or self-

Table 2
Multivariable Modified Poisson Regression with Generalized Estimating Equations for relative risk of Score ≥ 4 (Moderate-to-Severe) by ESAS Symptom).

Covariate	Lack of appetite Adjusted RR (95% CI)*		Pain Adjusted RR (95% CI)*	
Sex				
Male (reference)	–			–
Female	**1.16 (1.10–1.23)**		**1.15**	**(1.08–1.23)**
Age categories (years)				
< =60 (reference)		–		–
61–70	0.98	(0.93–1.04)	**0.85**	**(0.80–0.91)**
71–80	1.01	(0.92–1.10)	**0.77**	**(0.69–0.84)**
81 +	**1.19**	**(1.05–1.34)**	0.88	(0.77–1.02)
Rurality Index				
0-9 (reference)		–		–
10–30	0.97	(0.91–1.03)	0.97	(0.90–1.04)
31–50	0.97	(0.89–1.04)	1.03	(0.94–1.13)
51–70	0.96	(0.84–1.09)	0.86	(0.74–1.01)
71 + and unknown	1.10	(0.93–1.29)	1.13	(0.95–1.34)
Deprivation quintile				
5 (reference)		–		–
1 least marginalized	**0.90**	**(0.84–0.97)**	**0.81**	**(0.74–0.89)**
2	0.94	(0.87–1.02)	**0.89**	**(0.82–0.97)**
3	1.01	(0.94–1.08)	**0.91**	**(0.84–0.99)**
4	0.97	(0.90–1.04)	0.95	(0.87–1.03)
ACG comorbidity scores				
0-9 (reference)		–		–
10 +	**1.21**	**(1.14–1.28)**	**1.31**	**(1.23–1.39)**
RCC where ESAS was taken				
G (reference)		–		–
A	**0.88**	**(0.78–1.00)**	1.02	(0.89–1.18)
B	0.91	(0.81–1.02)	1.09	(0.96–1.24)
C	**1.10**	**(1.00–1.20)**	1.09	(0.98–1.22)
D	1.02	(0.93–1.11)	1.02	(0.91–1.14)
E	1.04	(0.96–1.13)	**1.25**	**(1.14–1.37)**
F	0.99	(0.88–1.11)	1.07	(0.93–1.22)
D	1.02	(0.93–1.11)	1.02	(0.91–1.14)
E	1.04	(0.96–1.13)	**1.25**	**(1.14–1.37)**
Immigration status				
Non-immigrants		**–**		**–**
Immigrants	0.92	(0.83–1.02)	1.09	(1.09–1.21)
Treatment modality				
Chemoradiation (reference)		–		–
Best Supportive care	**0.59**	**(0.51–0.69)**	**0.72**	**(0.60–0.85)**
Surgery	**0.49**	**(0.43–0.57)**	**0.61**	**(0.53–0.70)**
Radiation	**0.79**	**(0.73–0.85)**	0.98	(0.90–1.06)
Surgery + Radiation	**0.84**	**(0.77–0.93)**	0.94	(0.84–1.05)
Surgery + Chemoradiation	**0.93**	**(0.86–0.99)**	**0.91**	**(0.83–1.00)**
Cancer subsite				
Larynx/Hypopharynx (reference)		–		–
Oropharynx	**1.37**	**(1.28–1.47)**	**1.10**	**(1.02–1.19)**
Oral cavity	**1.29**	**(1.18–1.42)**	**1.31**	**(1.19–1.45)**
Diagnosis year				
2015 (reference)		–		–
2007	**1.63**	**(1.41–1.90)**	**1.25**	**(1.02–1.54)**
2008	**1.29**	**(1.11–1.49)**	1.11	(0.93–1.32)
2009	**1.22**	**(1.10–1.35)**	0.92	(0.81–1.04)
2010	**1.33**	**(1.21–1.47)**	1.05	(0.94–1.18)
2011	**1.37**	**(1.26–1.50)**	1.09	(0.99–1.20)
2012	**1.19**	**(1.10–1.30)**	1.01	(0.92–1.11
2013	1.04	(0.96–1.14)	0.96	(0.87–1.05)
2014	1.01	(0.93–1.10)	**0.89**	**(0.81–0.97)**
Months from diagnosis				
1 month (reference)		–		–
2 months	**1.54**	**(1.42–1.67)**	**1.25**	**(1.16–1.35)**
3 months	**2.13**	**(1.97–2.31)**	**1.71**	**(1.58–1.84)**
4 months	**1.98**	**(1.83–2.16)**	**1.54**	**(1.42–1.66)**
5 months	**1.65**	**(1.51–1.80)**	**1.13**	**(1.04–1.24)**
6 months	**1.48**	**(1.35–1.62)**	0.94	(0.85–1.04)
7 months	**1.34**	**(1.22–1.47)**	**0.79**	**(0.71–0.87)**
8 months	**1.27**	**(1.15–1.41)**	**0.79**	**(0.71–0.89)**
9 months	**1.14**	**(1.02–1.27)**	**0.68**	**(0.60–0.77)**
10 months	1.11	(0.99–1.24)	**0.65**	**(0.58–0.74)**
11 months	1.06	(0.95–1.19)	**0.68**	**(0.59–0.77)**
12 months	1.09	(0.98–1.22)	**0.76**	**(0.68–0.85)**

Bolded values are statistically significant (P < 0.05).
* RR, relative risk; 95% CI, 95% Confidence Interval.

management strategies to help patients cope with their symptoms prior to presentation in the emergency department [33]. Moreover, symptoms like fatigue, drowsiness, and lack of appetite, without conventional therapies, could be tackled by connecting patients to helpful support systems. Patient counselling has been shown improve fatigue, an effect which lasted up to four weeks [34].

This study advances knowledge on symptom trajectories of the patients receiving the current standard of care and may be interpreted as a call to action. These results will be shared with stakeholders at Cancer Care Ontario that will investigate what can be implemented at the systems level to improve the patient experience and symptom burden during treatment. This study also lays the groundwork for other population-based study intending to use this specific dataset. The results of this study must be interpreted in the context of its design. The timing of ESAS assessments is opportunistic, being completed when a patient presents for clinical care at an RCC. As symptoms may worsen immediately following provision of treatment, the symptom scores reported may actually under-report the true burden of symptoms. At the time of our study, it was not possible to capture patient symptoms in the emergency department, hospital, or hospice care, perhaps missing patients with the highest symptom burden. Survey completion rate was low in the earlier years of the study. However, in the latter years (2010–2015), completion rates were high (85%) and patients completed a median of five symptom assessments in the year following diagnosis. This, together with our large sample size increases our confidence in the generalizability of our results. Finally, the treatment group was assigned by actual provision of care. The analysis is performed based upon an assumption that patients received the treatment that was planned by their care team. It is possible that some patients were planned for multi-modal therapy, but due to intolerance, had to discontinue the treatment plan. The administrative data used in this study is limited in both the availability and accuracy of data points such as radiotherapy dose and number of chemo cycles, however, given the very regionalized and standardized program in Ontario, we feel that treatment dose (and receipt of chemotherapy) is strongly linked to tumor subsite and would therefore not significantly change our results or conclusions. ESAS has been proven to be reliable and valid, it is however a generalized screening tool, and cancer-specific PROs may be necessary to assess the impact of therapy on site-specific outcomes, such as dysphagia for HNC patients. Careful selection of these PROs can have a significant impact on population level assessment of treatment morbidity. This is particularly important now as many trials are diligently working to study de-escalated treatment [35].

Conclusions

In conclusion, this study highlights the application of PROs for monitoring symptoms in HNC patients' journey. Symptoms are highest during the treatment phase (8–16 weeks from diagnosis), especially for patients who received radiation and CRT. Validating the impact of screening with PROs on decreasing peri-treatment events, namely emergency department visits and unplanned hospitalizations, will establish further value in a cohort of patients that could benefit from quality improvement interventions.

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Declaration of Competing Interest

Natalie Coburn received salary support from Cancer Care Ontario as the Clinical Lead of Patient Reported Outcomes and Symptom Management.

Lisa Barbera received honoraria from the Genentech Company. The other authors declare no competing interests.

Parts of this study have been presented at the 72nd annual meeting of the Canadian Society of Otolaryngology-Head and Neck Surgery, in Quebec City, Canada, June 17–19, 2018.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.oraloncology.2019.09.026.

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