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ORIGINAL ARTICLE

# Distress levels in patients with oropharyngeal vs. non-oropharyngeal squamous cell carcinomas of the head and neck over 1 year after diagnosis: a retrospective cohort study

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**Abstract**

*Background* Human papillomavirus (HPV)-related cancers have been associated with different demographic profiles and disease characteristics than HPV-unrelated cancers in head and neck patients, but distress and other symptoms have not been compared. The aim of this study was to assess whether distress levels, fatigue, pain, anxiety, depression, and common psychological and practical problems differ between head and neck cancer patients with HPV-related vs. HPV-unrelated carcinomas (using oropharyngeal carcinoma (OPC) and non-OPC cancers as surrogates for HPV status).

*Methods* Distress, depression, anxiety, fatigue, pain, and common problems were examined in 56 OPC and 90 non-OPC patients at 4 timepoints during the first year following diagnosis. Two-level hierarchical linear modeling was used to examine effects.

*Results* The HPV-related OPC group was more likely to be younger ($p = 0.05$), Caucasian ($p = 0.001$), non-smokers ($p = 0.01$), earn more ($p = 0.04$), and present with more advanced stage ($p < 0.0001$). At baseline, OPC patients reported only higher pain scores ($p = 0.01$) than non-OPC patients. Total problems decreased more in the OPC group ($p = 0.08$) than the non-OPC group from baseline to 12-month follow-up. In both groups, scores on distress, depression, psychosocial problems, and practical problems decreased similarly over time.

*Conclusions* Despite a difference in the clinico-demographic characteristics of HPV-related vs. HPV-unrelated patients, only baseline pain levels and total problems over time differed between the two groups.

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**Keywords** Head and neck cancer · Distress · Oropharyngeal · Human papillomavirus · Psychosocial oncology · Health-related quality of life

## Background

Distress in cancer patients is a prevalent and significant problem, with incidence rates of distress in North America estimated at 35 to 45% at all phases of the illness [1–3]. Head and neck cancer (HNC) patients have among the highest levels of distress of all cancer patients [3], but distress experienced by HNC patients is frequently overlooked by oncologists [4]. Distress, though related to quality of life (QOL), represents a distinct entity, which has increasingly been adopted as the "6th vital sign" in cancer care [4]. The NCCN defines distress as a multifactorial unpleasant emotional experience that "extends along a continuum, ranging from common normal feelings of vulnerability, sadness and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis" [5]. Distress is typically measured using short screening tools such as the Distress Thermometer and Problem Checklist [5], and then followed-up with more in-depth assessment of specific identified issues. In contrast, QOL measures are typically longer and assess a broader spectrum of domains, including specific physical, social, cognitive, spiritual, emotional, and role functioning. The implementation of a program to routinely screen for distress in this patient population has proven feasible [6] and can help inform what supportive measures are most needed to help patients through treatment and recovery.

Recently, numerous studies have shown a rising incidence of head and neck cancers related to human papillomavirus (HPV) in contrast to HNC related to traditional risk factors of alcohol and tobacco use [7–11]. Patients with HPV related HNC are characterized by a very different socio-demographic profile than HNC cancers related to smoking and/or alcohol [12]. To date, little has been written about distress levels in this emerging population. The interventions and support needed by HPV-related HNC patients may vary quite significantly from those of patients with traditional tobacco and/or alcohol-related HNC. Our study sought to explore whether distress levels, fatigue, pain, anxiety, depression, and common psychological and practical problems differ between patients with HPV-related and HPV-unrelated HNC by comparing distress between oropharyngeal carcinoma (OPC) and non-OPC patients as a surrogate for these two distinctive groups. Secondary objectives were to investigate the effects of disease stage on the same parameters. Patients were assessed around the time of diagnosis, and again 3, 6, and 12 months later.

## Methods

The Alberta Cancer Research Ethics Committee approved this study. A database was created using information gathered from two existing datasets: one containing measures of distress and one containing clinico-pathological information. Distress data were collected from HNC patients prospectively in two protocols in which new patients of all cancer types were screened for distress during their first visit to the Tom Baker Cancer Centre (TBCC), and again 3, 6, and 12 months later [13, 14]. Specific tools used in the distress screening were distress, fatigue, and pain thermometers [15–17], the Canadian Problem Checklist [18], and the Psychosocial Screen for Cancer (PSSCAN Part C) [19]. Socio-demographic data, including age, gender, marital status, education, ethnic/cultural background, income, and first language, were collected during the distress screening. Clinico-pathological data were collected as part of a separate retrospective chart review of HNC patients treated at the TBCC between 2003 and 2010 inclusive. The following variables were extracted: pathology, date of diagnosis, alcohol consumption, tobacco consumption, Karnofsky Performance Score (KPS), stage, and treatment modalities (surgery, radiation, chemotherapy).

Databases were combined to include all patients with newly diagnosed, non-metastatic squamous cell carcinoma of the head and neck (SCCHN) with available screening for distress data. Patients were excluded if they had non-head and neck primaries, non-squamous cell head and neck cancers, metastatic disease, or were treated with palliative intent. Patients whose clinico-pathologic data was missing were also excluded. Patients were stratified into those with OPC and those with non-OPC as surrogates for HPV-related and HPV-unrelated cancers, respectively; OPC included squamous cell primaries of the tonsils, base of tongue, and soft palate. For the purpose of this study, primaries of the oral cavity and nasopharynx were included in the non-OPC group.

## Statistical analysis

From the combined dataset, we compared the two groups (OPC and non-OPC) on each baseline characteristic using Wilcoxon Rank-Sum, chi-square, and Fisher exact tests. We then compared the changes on the five distress-related outcomes (distress (DT), fatigue, pain, anxiety, and depression), total practical problems, total psychosocial problems, and total problems between the OPC and non-OPC groups (centered +0.5/−0.5) from baseline to 12-month follow-up. In order to differentiate the effects of OPC vs. non-OPC diagnosis from those of disease severity on distress outcomes (because the two were correlated), we then examined the changes in these eight outcomes by adjusting for two stage groups (centered

−0.5/+0.5): earlier stage (stage = I/II) and advanced stage (stage = III/IV) over time. We also looked at the effects of treatment on outcomes (i.e., surgery ± chemoradiation), since treatment types were also related to diagnosis and disease stage. However, treatment and stage were highly related so we chose to focus on stage only for the secondary analysis. The treatment effects are not presented. Two-level hierarchical linear models (HLM) were used to examine group effect at baseline, time effect, and group-by-time effect, as well as stage effect at baseline, time effect, and stage-by-time effect, respectively. We used the MIXED procedure in SAS (SAS Institute, Cary, NC) to fit the two-level HLM with random intercept models. All missing data were assumed as missing at random. The natural logarithm transformation was used on pain, anxiety, and depression to reach the normal distribution. We summed the practical problems and the psychosocial problems separately. In order to correct their skewed distributions, we truncated scores as equal to 5 if they were above (or equal to) 5. All statistical analyses were completed using SAS 9.3 version. For all tests, $\alpha$ was fixed at 0.05, two-tailed.

## Results

Baseline distress data was available for 208 HNC patients. After combining the clinico-pathological data, 62 patients (29.8%) were excluded: 24 had non-HNC primaries; 17 had non-squamous cell carcinomas; 6 were treated with palliative intent; 6 received no treatment; 5 had recurrent disease; and 4 had no available clinico-pathologic data. A total of 56 patients with OPC and 90 patients with non-OPC cancers were included in the analyses.

Distress data at 12-month follow-up were available for 35 (62.5%) OPC patients and 55 (61.1%) non-OPC patients. Lack of data during 3-, 6-, and 12-month follow-up was due to patients who were deceased, as well as those who could not be contacted or who were excused due to ill health, refused further contact, or were missed at 3-month (or 6-month) follow-up but re-joined the study at 6- or 12-month follow-up. However, all 146 patients with baseline data were included in the HLM analyses (Fig. 1).

### Demographics and clinico-pathological characteristics

At baseline, the OPC patients were significantly more likely to be Caucasian ($p = 0.001$), and to have a household income above $50,000/year ($p = 0.04$). The non-OPC patients were more likely to be older at diagnosis ($p = 0.05$). No significant differences were found in gender, marital status, English as a first language, or education. The two groups also had similar Karnofsky Performance Status (KPS) scores at baseline ($p = 0.61$). There was no significant difference in the alcohol consumption between two groups ($p = 0.75$); however, the non-OPC patients smoked more than the OPC patients ($p = 0.01$).

The OPC patients presented with statistically and significantly more advanced stage disease (III/IV stage, $p < 0.0001$). Treatment also differed significantly between the two groups with the majority of OPC patients receiving combined chemotherapy and radiation compared to the non-OPC group who were more evenly split between surgery only and combined CT/RT (Table 1).

### Distress-related measures for HPV-related vs. HPV-unrelated groups

*Baseline*

At the baseline assessment time, during the first visit to the TBCC, pain levels were significantly higher in the OPC than non-OPC patients ($p = 0.01$), but there were no group differences on any of the other distress-related measures.

*Rate of change from baseline to 12-month follow-up*

From baseline to 12-month follow-up, all distress-related measures decreased significantly for both groups, and no significant group-by-time effects were found. However, pain and fatigue increased at 3-month follow-up for both groups, and then decreased successively at 6- and 12-month follow-up (Table 2; Fig. 2a, c). We also found that there was a statistical trend suggesting that total problems in the OPC group decreased ($p = 0.08$, $b = -0.06$, and CI [−0.11; −0.01]) more than the non-OPC group.

### Distress-related measures for stage levels

Of the 146 patients analyzed, 49 were diagnosed with earlier stage (I/II), and 44 (89.8%) of these were non-OPC patients. Ninety were diagnosed with advanced stage (III/IV), and nearly half (53.3%) of these were OPC patients. There were seven patients whose cancer stage remained unknown. At 12-month follow-up, the assessments were completed for 28 (57.1%) patients with earlier stage and 58 (64.4%) patients with advanced stage.

In the non-OPC group, of those with earlier stage, 24 (61.5%) had only surgery, 12 (30.8%) received radiation (RT) ± chemotherapy (CT), and 7.7% of them received surgery combined with CT/RT treatments. In the same group, of those with advanced stage, 3 (7.3%) received only surgery, 26 (63.4%) received CT/RT, and 12 (29.3%) received surgery combined CT/RT treatments.

In the OPC group, of the majority who had advanced stage, 37 (88.1%) received CT/RT treatments, and 5 (11.9%) received surgery combined with CT/RT treatments. No one received only surgery. Of the few early-

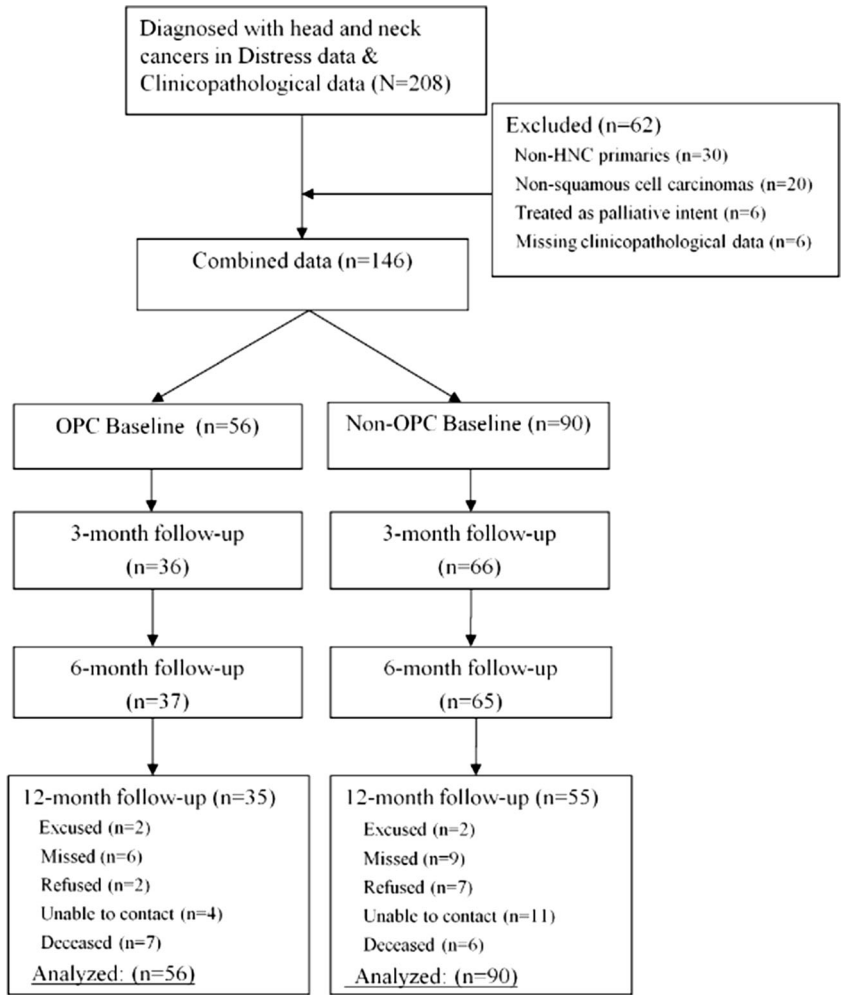


**Fig. 1** Study flowchart

stage patients in this group, two (50%) of them received only surgery, rwo (50%) other patients received CT/RT, and no one received combined treatments.

*Baseline*

At baseline, patients with advanced stage disease reported significantly higher pain ($p = 0.0002$) than the patients with earlier stage. There was a trend for slightly higher fatigue in advanced stage patients than in earlier stage patients ($p = 0.06$, $b = 0.88$, and CI [−0.003; 1.76]). No differences were found in DT, anxiety, depression, total practice problems, total psychosocial problems, and total problems between stage groups at baseline (Fig. 2b, d).

*Rate of change from baseline to 12-month follow-up*

For both stage groups, the slopes of the eight distress-related measures decreased significantly from baseline to 12-month follow-up. However, fatigue increased in the advanced stage group from baseline to 3-month follow-up and then decreased successively at 6-month and 12-month follow-up (Table 2). No stage by time interaction effects were found on any of the distress-related outcomes.

## Discussion

This exploratory study is the first to compare distress data between patients with oropharyngeal and non-oropharyngeal squamous cell carcinomas of the head and neck as surrogate markers for HPV-positive vs. negative cancers, and follow trajectories of distress and other symptoms over a full year. The main difference observed between patients with OPC vs. non-OPC was higher levels of pain at baseline in the OPC (HPV-related) patients, which was statistically significant. This difference might reflect differences in stage and treatment modality since a significantly greater proportion of the OPC patients presented with more advanced disease, and were more likely to receive combined chemoradiation as therapy. Indeed, in this sample, when analyzed by disease stage, results showed that those with more advanced disease stages had higher pain and

**Table 1** Summaries of the patient characteristics by OPC and non-OPC groups

| Characteristics | OPC ($n$ = 56) $n$ (%) | Non-OPC ($n$ = 90) $n$ (%) | $P$ |
|---|---|---|---|
| Age of diagnosis | | | 0.05 |
| Median (range) (years) | 58.4 (36.0–78.7) | 62.2 (22.0–91.5) | |
| Gender | | | 0.10 |
| Male | 46 (82.1) | 63 (70.0) | |
| Female | 10 (17.9) | 27 (30.0) | |
| Marital status | | | 0.22 |
| Married/living common law | 42 (75.0) | 58 (64.4) | |
| Single | 13 (23.2) | 29 (32.2) | |
| Unknown | 1 (1.8) | 3 (3.3) | |
| Ethnicity | | | <0.0001 |
| Caucasian | 49 (87.5) | 61(67.8) | |
| Other ethnic | 1 (1.8) | 17 (18.9) | |
| Unknown | 6 (10.7) | 12 (13.3) | |
| Income | | | 0.04 |
| <$50,000 | 18 (32.1) | 40 (44.4) | |
| $50,000 and above | 30 (53.6) | 31 (34.4) | |
| Unknown | 8 (14.3) | 19 (21.1) | |
| English as 1st language | | | 0.37 |
| Yes | 52 (92.9) | 78 (86.7) | |
| No | 3 (5.4) | 9 (10.0) | |
| Unknown | 1 (1.8) | 3 (3.3) | |
| Education | | | 0.26 |
| High school or lower | 23 (41.1) | 45 (50.0) | |
| College or higher | 31 (55.4) | 41 (45.6) | |
| Unknown | 2 (3.6) | 4 (4.4) | |
| Tobacco consumption (current or previous) | | | 0.01 |
| Median (range) (parks/year) | 12.0 (0.0–175.0) | 25.0 (0.0–98.0) | |
| Alcohol consumption | | | 0.75 |
| None or <7 drinks/week | 30 (53.6) | 48 (53.3) | |
| ≥7 drinks/week | 21 (37.5) | 27 (30.0) | |
| Unknown | 5 (8.9) | 15 (16.7) | |
| KPS | | | 0.61 |
| ≤80 | 7 (12.5) | 7 (7.8) | |
| >80 | 47 (83.9) | 63 (70.0) | |
| Unknown | 2 (3.6) | 20 (22.2) | |
| Stage | | | <0.0001 |
| I/II | 5 (8.9) | 44 (48.9) | |
| III/IV | 48 (85.7) | 42 (46.7) | |
| Unknown | 3 (5.4) | 4 (4.4) | |
| Treatment | | | <0.0001 |
| Surgery only | 3 (5.4) | 30 (33.3) | |
| CT and/or RT | 41 (73.2) | 38 (42.2) | |
| Surgery combined CT/RT | 5 (8.9) | 16 (17.8) | |
| No treatment | 7 (12.5) | 6 (6.7) | |

Wilcoxon rank-sum, chi-square, or Fisher exact test

*KPS* Karnofsky Performance Status, *CT* chemotherapy, *RT* radiation therapy

**Table 2** Distress-related measures at baseline and during follow-up by OPC vs. non-OPC groups and stage

| Distress-related measures | Baseline | | 3-month | | 6-month | | 12-month | | Baseline | | 3-month | | 6-month | | 12-month | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OPC | Non-OPC | OPC | Non-OPC | OPC | Non-OPC | OPC | Non-OPC | Stage | | Stage | | Stage | | Stage | |
| | | | | | | | | | I/II | III/IV | I/II | III/IV | I/II | III/IV | I/II | III/IV |
| Distress (DT) | | | | | | | | | | | | | | | | |
| *n* | 54 | 89 | 36 | 66 | 37 | 65 | 35 | 55 | 48 | 88 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 4.9 | 4.7 | 3.4 | 2.8 | 2.8 | 2.6 | 2.3 | 2.8 | 4.8 | 5.0 | 2.2 | 3.6 | 2.2 | 3.0 | 2.5 | 2.6 |
| SD | 2.9 | 2.8 | 2.4 | 3.0 | 2.8 | 2.5 | 2.7 | 2.9 | 3.0 | 2.8 | 2.8 | 2.6 | 2.2 | 2.7 | 2.9 | 2.8 |
| Pain | | | | | | | | | | | | | | | | |
| *n* | 49 | 76 | 36 | 66 | 37 | 65 | 35 | 55 | 41 | 80 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 3.6 | 2.4 | 3.8 | 2.5 | 2.2 | 1.7 | 2.3 | 1.4 | 2.1 | 3.2 | 2.2 | 3.4 | 1.1 | 2.2 | 1.3 | 2.0 |
| SD | 3.4 | 2.9 | 2.7 | 3.1 | 2.8 | 2.6 | 2.9 | 2.1 | 3.0 | 3.1 | 3.0 | 2.9 | 2.3 | 2.6 | 2.2 | 2.5 |
| Fatigue | | | | | | | | | | | | | | | | |
| *n* | 54 | 88 | 36 | 66 | 37 | 65 | 35 | 55 | 47 | 88 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 3.7 | 3.6 | 5.2 | 4.0 | 3.7 | 3.1 | 3.1 | 2.6 | 3.5 | 3.8 | 3.1 | 5.4 | 2.5 | 3.8 | 2.1 | 3.1 |
| SD | 3.1 | 2.9 | 2.8 | 3.2 | 2.6 | 2.8 | 2.9 | 2.7 | 3.1 | 2.9 | 3.2 | 2.5 | 2.8 | 2.6 | 2.8 | 2.7 |
| Anxiety | | | | | | | | | | | | | | | | |
| *n* | 56 | 88 | 36 | 66 | 37 | 65 | 35 | 55 | 49 | 88 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 9.4 | 10.0 | 7.4 | 6.9 | 7.0 | 6.5 | 6.3 | 6.5 | 10.1 | 9.7 | 6.3 | 7.5 | 6.2 | 6.8 | 6.8 | 6.2 |
| SD | 4.6 | 4.5 | 3.2 | 3.0 | 2.8 | 2.4 | 2.4 | 2.9 | 4.6 | 4.5 | 2.3 | 3.2 | 2.0 | 2.5 | 3.1 | 2.1 |
| Depression | | | | | | | | | | | | | | | | |
| *n* | 56 | 88 | 36 | 66 | 37 | 65 | 35 | 55 | 49 | 88 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 6.9 | 7.0 | 6.3 | 5.8 | 6.0 | 5.8 | 6.1 | 6.0 | 7.2 | 6.9 | 5.5 | 6.2 | 5.6 | 5.9 | 6.1 | 5.8 |
| SD | 3.2 | 3.5 | 2.7 | 2.5 | 2.4 | 2.7 | 2.1 | 3.1 | 3.7 | 3.2 | 2.1 | 2.6 | 2.4 | 2.2 | 3.0 | 2.1 |
| Total practical problems | | | | | | | | | | | | | | | | |
| *n* | 56 | 90 | 36 | 66 | 37 | 65 | 35 | 55 | 49 | 90 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 1.3 | 1.2 | 0.6 | 0.4 | 0.4 | 0.5 | 0.3 | 0.5 | 1.4 | 1.1 | 0.3 | 0.6 | 0.2 | 0.5 | 0.5 | 0.4 |
| SD | 1.4 | 1.5 | 1.0 | 0.7 | 0.8 | 0.9 | 1.0 | 0.8 | 1.7 | 1.3 | 0.6 | 0.9 | 0.5 | 1.0 | 1.1 | 0.8 |
| Total psychosocial problems | | | | | | | | | | | | | | | | |
| *n* | 56 | 90 | 36 | 66 | 37 | 65 | 35 | 55 | 49 | 90 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 2.5 | 2.4 | 1.6 | 1.6 | 1.5 | 1.1 | 1.1 | 1.2 | 2.4 | 2.5 | 1.3 | 1.9 | 1.0 | 1.4 | 1.1 | 1.2 |
| SD | 2.1 | 2.3 | 1.6 | 1.7 | 1.7 | 1.2 | 1.8 | 1.3 | 2.4 | 2.2 | 1.5 | 1.8 | 1.3 | 1.4 | 1.2 | 1.6 |
| Total problems | | | | | | | | | | | | | | | | |
| *n* | 56 | 90 | 36 | 66 | 37 | 65 | 35 | 55 | 49 | 90 | 41 | 56 | 34 | 64 | 28 | 58 |
| Mean | 3.8 | 3.6 | 2.2 | 2.0 | 1.9 | 1.6 | 1.4 | 1.7 | 3.8 | 3.6 | 1.6 | 2.5 | 1.2 | 2.0 | 1.6 | 1.6 |
| SD | 3.0 | 3.1 | 2.2 | 2.1 | 2.1 | 1.7 | 2.4 | 1.9 | 3.4 | 3.0 | 1.7 | 2.4 | 1.6 | 1.9 | 1.8 | 2.2 |

fatigue both at baseline and over follow-up. This cannot simply be attributed to OPC status, however, as the later stage group consisted of about half OPC and half non-OPC patients.

Interestingly, pain and fatigue were significantly increased over baseline at 3 months, particularly in the HPV-related OPC group, while all other measures of distress decreased linearly from baseline to follow up. Although the literature supports decreases in distress levels over time, most found the highest levels of distress to be present at the end of treatment. In one study of HNC patients, quality of life was found to be lowest at 3-month post diagnosis then gradually increased over the next 9 months [20]. Another study found the highest level of depression to be at 3-week post treatment with radiation for HNC while anxiety decreased after treatment but was higher at 18 months follow-up [21]. Landis et al. found that there was a sustained risk of depression throughout 1-year follow-up, perhaps due to long-term or delayed effects of diagnosis or treatment [22]. Sherman et al. suggested that the immediate aftermath of treatment may be a particularly demanding period [23]. Regardless of whether symptoms of distress are highest at diagnosis, through

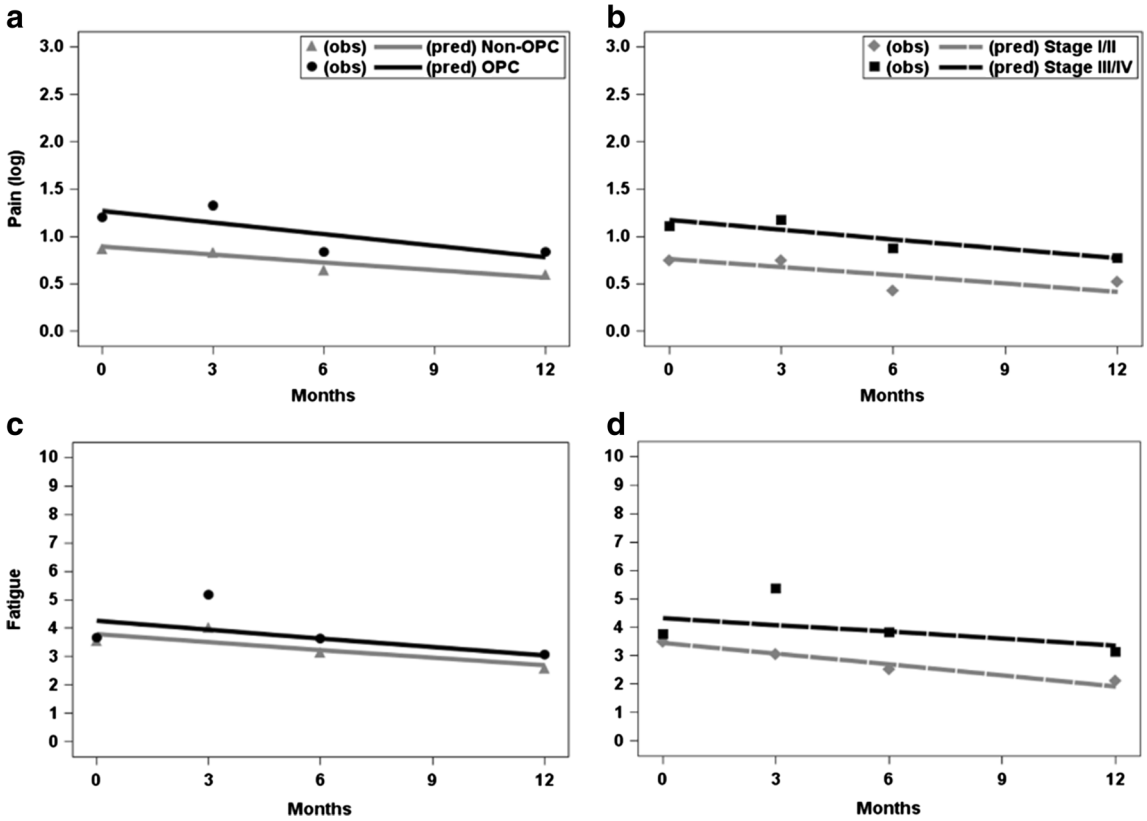


**Fig. 2** **a** Observed means (*circle vs. triangle*) and predicted trends (*black vs. grey solid lines*) over 12 months for pain (logarithm) between OPC and non-OPC. **b** Observed means (*diamond vs. square*) and predicted trends (*grey vs. black break lines*) over 12 months for pain (logarithm) between stages I/II and stages III/IV. **c** Observed means (*circle vs. triangle*) and predicted trends (*black vs. grey solid lines*) over 12 months for fatigue between OPC and non-OPC. **d** Observed means (*diamond vs. square*) and predicted trends (*grey vs. black break lines*) over 12 months for fatigue between stages I/II and stages IV

treatment or in the post-treatment period, screening and interventions should be appropriately carried out and made available.

HPV-related HNC patients are characterized by a very different socio-demographic profile than HNC cancers related to smoking and/or alcohol [12]. Differences in patient demographics may have an impact on distress: younger age and higher tumor-related and treatment-related physical symptoms (such as altered appearance and inability to talk or eat) are predictive of higher anxiety scores [21]. Similarly, Graeff et al. found that baseline depression, stage, treatment, and KPS were major factors predicting post-treatment quality of life [24]. In keeping with the literature, in our cohort, the HPV-related OPC patients were more likely to be Caucasian, younger, non-smokers, and have a higher household income. Despite these differences, aside from reported levels of pain and fatigue, the OPC vs. non-OPC patients did not differ in other measures of distress, although most absolute scores in the OPC group were worse than the non-OPC cohort.

The relatively small sample size in this study limits our ability to adjust for confounding variables that may obscure real differences. For instance, adjusting for differences in time between treatment and assessment could influence results. At our institution, the usual concurrent chemoradiation regimen is a 6.5-week course of daily radiation and up to 3 cycles of cisplatin chemotherapy. Therefore, at 3 months, OPC patients may have just completed treatment, while non-OPC patients may have had time to recover from their primarily surgical treatment. We initially investigated treatment effects on outcomes as well as looking at stage effects, but the two were highly correlated so we focused on stage effects as potentially more important. However, these covariations point out the importance of attempting to disentangle OPC status from disease severity and treatment effects. Another limitation of our study is that a number ($n = 82$) of participants did not provide data for all timepoints. It is conceivable that the participants who did not provided data were unable to do so due to increasing disability or disease progression; hence, our interpretation of improvements over time on distress and symptoms may apply only to those who recovery from cancer treatments.

We compared OPC vs. non-OPC patients as surrogates for HPV-related vs. non-HPV related SCCHN because, in the time frame the data collection occurred, tumor testing for HPV was not routinely done. Recognizing that not every

OPC is associated with HPV and some non-OPC tumors can be associated with the virus [25], the similarities seen between the OPC and non-OPC groups may in part be due to misclassification, an inherent limitation in this retrospective study. However, existing literature suggests that HPV-positive HNCs are predominantly oropharyngeal carcinomas (OPCs), while non-oropharyngeal carcinomas (non-OPCs) are much less commonly related to HPV [22]. Given the steadily rising prevalence of OPC [26], understanding any differences in the needs of this growing patient population is important regardless of the underlying etiology.

## Conclusion

In conclusion, this is the first report that stratifies HNC by OPC and non-OPC suggesting that there are differences in levels of pain and fatigue among HNC patients with OPC tumors. Patients with more advanced stages of disease fared worse than those with earlier stage cancers, which could confound the effects of OPC status and underlines the importance of taking into account both diagnosis and treatment. Recognizing that our exploratory study is limited by its small sample size, we believe a larger, prospective study focusing on pain, fatigue, and anxiety among HNC patients, stratified by HPV-status, is needed and may provide clarification on these differences in order to help guide supportive interventions for this growing patient population.

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**Authors' contributions** MS collected the clinical data, assimilated the existing databases, and participated in drafting the manuscript. LC was involved in the design and coordination of the study, data analysis and interpretation, and as well as helped to draft the manuscript. HL participated in the design of the study and manuscript preparation. LZ performed the statistical analyses and interpretation, and drafted the methods and results section of the manuscript. BB spearheaded the collection of the distress data, reviewed, and edited the manuscript. AW participated in collection of the distress data, reviewed and edited the manuscript. SG participated in the collection the distress data, and edited the manuscript. DH conceived of the study, participated in its design and coordination and helped to draft and edit the manuscript.

All authors read and approved the final manuscript.

**Compliance with ethical standards** The Alberta Cancer Research Ethics Committee approved this study.

**Competing interests** The authors declare that they have no competing interests.

**Author's information** LEC holds the Enbridge Research Chair in Psychosocial Oncology, cofunded by the Canadian Cancer Society and Alberta Cancer Foundation, and along with BDB has been responsible for developing and testing methods of implementing screening for distress as the "6th vital sign" in cancer care worldwide. The data in this paper was extracted from clinical trials which evaluated the efficacy of routine online screening for distress on subsequent psychosocial and physical outcomes.

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